Integration of the Duke Activity Status Index into Preoperative Risk Evaluation: A Multicentre Prospective Cohort Study

Duminda N. Wijeysundera MD PhD [1,2,3,4,5], W. Scott Beattie MD PhD [3,5], Graham S. Hillis MB ChB PhD [6], Tom E.F. Abbott MA PhD [7,8], Mark A. Shulman MBBS MPH [9], Gareth L. Ackland PhD [7,8], C. David Mazer MD [1,2,3], Paul S. Myles MBBS MPH DSc [9], Rupert M. Pearse MBBS MD[8], Brian H. Cuthbertson MB ChB MD [3,4,10] on behalf of the METS Study Investigators

Affiliations

[1] Department of Anesthesia, St. Michael's Hospital, Toronto, Ontario, Canada

[2] Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, Ontario, Canada

[3] Department of Anesthesiology and Pain Medicine, University of Toronto, Toronto, Ontario, Canada

[4] Institute of Health Policy Management and Evaluation, University of Toronto, Ontario, Canada

[5] Department of Anesthesia and Pain Management, University Health Network, Toronto, Ontario, Canada

[6] Department of Cardiology, Royal Perth Hospital and University of Western Australia, Western Australia, Australia

[7] The William Harvey Research Institute, Queen Mary University of London, London, UK

[8] Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

[9] Department of Anaesthesiology and Perioperative Medicine, Alfred Hospital and Monash University, Melbourne, Victoria, Australia

[10] Department of Critical Care Medicine, Sunnybrook Health Sciences Centre

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Correspondence

Duminda N. Wijeysundera, MD PhD FRCPC FAHA

Department of Anesthesia, St. Michael's Hospital

30 Bond Street, Toronto, Ontario, Canada M5B 1W8

Tel: 416-864-5825

Email: d.wijeysundera@utoronto.ca

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SUMMARY

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 years) at elevated cardiac risk who had inpatient noncardiac surgery. The primary outcome was 30-day death or myocardial injury. Secondary outcomes were 30-day death or myocardial infarction, in-hospital moderate-or-severe complications, and one-year 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 one-point increase above 34; 95% CI, 0.96 to 0.99) and one-year death or new disability (odds ratio 0.96 per one-point increase above 34; CI, 0.92 to 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 one-point decrease below 34; CI, 1.00 to 1.09), and moderate-or-severe complications (odds ratio 1.03 per one-point decrease below 34; CI, 1.01 to 1.05).

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

Key Words: preoperative evaluation; functional capacity; Duke Activity Status Index; postoperative complications; surgery

INTRODUCTION

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') following a standard preoperative interview. While 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 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 identification of patients at 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 (Supplemental Table 1) was developed in a sample of English-speaking adults undergoing exercise testing in the United States,[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 disagreement as to how best to convert DASI scores to estimated metabolic equivalents.[10,11] It is also unclear as to what specific thresholds in DASI scores define 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] While 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 complications and moderate-and-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 elevated risk of postoperative morbidity.

MATERIALS AND METHODS

Design

This report adhered to the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) 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 United Kingdom. All 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 previously reported.[5,17] This present analysis included all eligible participants who underwent surgery, regardless of whether they underwent preoperative cardiopulmonary exercise testing. Thus, 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 years or older, scheduled for elective inpatient noncardiac surgery under general and/or regional anaesthesia, and deemed to have one or more risk factors for cardiac complications or coronary artery disease (Supplemental Table 2). Of the 1741 individuals who consented to participate in the METS study, 1546 were included in this nested cohort analysis (Figure 1). Participants completed the DASI questionnaire on the date of recruitment and underwent blood sampling to measure serum N-terminal pro-B-type natriuretic peptide (NT pro-BNP) concentrations at any point between recruitment and surgery. The blood samples were stored at -70°C to -80°C in each study site, and then analysed at the Aberdeen Royal Infirmary (Aberdeen, UK) using the Siemens Vista™ immunoassay analyser (Siemens

Healthcare Diagnostics Ltd, Frimley, UK). Participants, healthcare providers, and outcome adjudicators were blinded to DASI scores and NT pro-BNP results. Additionally, anaesthesiologists in the preoperative evaluation clinic or operating theatre subjectively rated participants' functional capacity based on their usual preoperative history. Subjectively assessed functional capacity was categorised as 'poor' (<4 metabolic equivalents), 'moderate' (4 to 10 metabolic equivalents), or 'good' (>10 metabolic equivalents). After surgery, participants underwent daily electrocardiograms and blood sampling to measure troponin concentrations, until the third postoperative day or hospital discharge (whichever came first). Participants were also followed daily while 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 (Supplemental Table 3).[18–20] After hospital discharge, 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-or-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 while remaining blinded to DASI and NT pro-BNP results.[23] The endpoint of moderate-or-severe complications included fatal events.

Statistical Analyses

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 chi-square or Fisher exact test, while 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, the covariates 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 threshold.[12] In the model predicting moderate-or-severe complications, the covariates were age, sex, and high-risk surgery, which was defined as intra-peritoneal, intra-thoracic, or supra-inguinal vascular procedures.[7] To account for non-linear relationships between continuous predictor variables (i.e., DASI, 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 (ORs) with 95% confidence intervals (CIs). Model discrimination was characterised by the c-index, while 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. Additionally, several sensitivity analyses were performed to evaluate the robustness of our primary analysis. Firstly, the analyses were repeated after multiple imputation to account for missing baseline data (i.e., DASI score, creatinine concentration, 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 current guideline-recommended assessment algorithms)[1,12] were included as additional covariates 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 covariate 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 substudy was determined by the sample size calculation for the METS study, which has been previously described.[5,17]

Subset Analysis on New Postoperative Disability

To understand whether DASI scores also predicted functional recovery at one-year following surgery, we conducted a subset analysis of METS study participants in whom self-reported disability status was prospectively measured using the validated 12-item World Health

Organisation Disability Assessment Schedule (WHODAS) 2.0 instrument.[25,26] As part of a pre-specified substudy on the prognostic performance of the six-minute walk test, the WHODAS questionnaire was administered before surgery and subsequently at one year post-surgery.[27] The questionnaire consists of 12 items, each of which is scored from zero to four. The sum of all item responses is the WHODAS Disability Score, which ranges from zero to 40 and can be expressed as a 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 one year after surgery, where new disability was defined as postoperative WHODAS Disability Score that exceeded 25% and represented at 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 one year after surgery. The covariates 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 into the METS study at 25 hospitals in Canada, Australia, New Zealand, and the United Kingdom. From this overall sample, 1546 participants were included in this substudy, of whom 1540 (99.7%) completed 30-day follow-up. The characteristics of the substudy cohort are presented in Table 1. Their median age was 65 years (IQR 57 to 62), 41% (n=629) were female, 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 above the high-risk threshold of 300 ng/L.[12] While only seven participants completely missed their DASI questionnaires, 64 individuals had one or more missing responses to individual items in the questionnaire (Supplemental Table 1). The item with the highest frequency of missing responses (n=45) was the question, "*Can you have sexual relations?*". Among the 1475 participants (95%) who responded to all questionnaire items, the median DASI score was 42.7 (interquartile range 28.7 to 53.0).

Postoperative Outcomes

By 30 days after surgery, 187 (12.1%) 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-or-severe complications. The specific types of complications associated with postoperative myocardial injury are presented in Supplemental Table 4.

Prediction of 30-Day Postoperative Death or Myocardial Injury

In unadjusted comparisons, participants who did versus did not experience 30-day death or myocardial injury differed with respect to age, cardiovascular comorbidities (i.e., coronary artery disease, cerebrovascular disease, hypertension, atrial fibrillation), renal function, RCRI score, NT pro-BNP concentrations, 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 (Supplemental Figure 1). Based on visual inspection of this plot, there was maximum at a score of about 34. Approximately 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

Restricted cubic spline analyses showed a non-linear unadjusted association between DASI scores and 30-day death or myocardial infarction (Supplemental Figure 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-or-Severe Complications

In unadjusted comparisons, participants who did versus did not experience moderate-or-severe complications differed with respect to sex, cardiovascular comorbidities (i.e., cerebrovascular disease, atrial fibrillation), NT pro-BNP concentration, surgery, but not DASI score (Supplemental Table 5). Restricted cubic spline analyses demonstrated a non-linear adjusted

association between the DASI score and postoperative complications (Supplemental Figure 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-or-severe complications (Supplemental Table 6).

Sensitivity Analyses

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

Subset Analysis on New Postoperative Disability

About 35% (n=546) of patients in the primary analysis cohort completed preoperative WHODAS questionnaires, of whom 17% (n=95) had preoperative moderate-severe-or-complete disability and 95% (n=517) completed one-year follow-up (Supplemental Figure 4). The subset cohort (Supplemental 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 versus 25% in the primary cohort). By one-year after surgery, 14 individuals (2.6%) had died, 46 (8.4%) had new disability, and 60 (11.6%) had either died or developed new disability.

In unadjusted comparisons, participants who did versus did not experience new disability or death within one year after surgery differed with respect to some cardiovascular comorbidities (i.e., heart failure, atrial fibrillation), smoking status, and possibly preoperative disability status (Supplemental Table 9). Restricted cubic spline analyses suggested a non-linear adjusted association between the DASI score and new disability or death within one year after surgery (Supplemental Figure 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 one year after surgery (Supplemental Table 10).

Post-Hoc Comparison of DASI Thresholds Versus Subjective Assessment

Since 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. While 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 (Supplemental Table 11).

DISCUSSION

In this nested cohort analysis of the METS study, a preoperative DASI score threshold of 34 points improved 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, patients with self-reported functional capacity better than a DASI score of 34 had a lower risk of 30-day myocardial injury and one-year new disability, while 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-or-severe complications. This threshold retained prognostic importance for identifying patients at elevated cardiac risk even after accounting for preoperative 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 one in five individuals with concerning DASI scores were subjectively assessed as having poor functional capacity by their responsible anaesthesiologists. Overall, the results help inform clinicians seeking practical approaches to better incorporate evaluation of functional capacity into usual preoperative risk assessment.

Notably, when considering outcomes ascertained during the same short-term postoperative time-frame (i.e., ≤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 myocardial infarction and moderate-or-severe complications.[29,30] While DASI scores *below* 34 demarcated a high-risk plateau for experiencing myocardial injury, scores *above* 34 demarcated a low-risk plateau for experiencing

myocardial infarction and moderate-or-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. Additionally, while 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 worse than 34 are associated with greater risks of myocardial injury, myocardial infarction and moderate-or-severe complications, while scores better than 34 are associated with lower risks of these same events.

While it is tempting to interpret the clinical relevance of a DASI score by converting it to estimated metabolic equivalents, 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 confirms this uncertainty: a DASI score of 34 corresponded to a peak oxygen consumption of 17 to 18 mL/kg/min (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 since peak oxygen consumption was correlated with DASI scores but not postoperative cardiac complications in the METS study.[5]

An increasing body of literature has demonstrated that preoperative BNP or NT pro-BNP concentrations improve the accuracy of preoperative cardiac risk assessment, even when used in combination with clinical risk factors.[13,32] While our analysis confirms these prior findings, it highlights that natriuretic peptides do not substitute for 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 coefficient -0.21, $P<0.001$), suggesting that they measure related but different prognostically important constructs.[5]

Our study has several important limitations that should be considered. *First*, while the METS study was relatively large multicentre prospective cohort study, it was likely biased towards excluding very high-risk patients, largely due to 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*, while 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 the 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 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 overall response rates are improved while 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 prehabilitation (i.e., multimodal preoperative exercise training and nutritional supplementation), intensive perioperative hemodynamic management to minimise hypotension, and enhanced postoperative monitoring. *Finally*, this present study was a *post-hoc* – albeit methodologically robust – secondary analysis of 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, natriuretic peptides).[5,17] Thus, further studies are needed to confirm the findings of our present 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-or-severe complications and one-year new disability or death after major inpatient noncardiac surgery. In general, patients with DASI scores lower than 34 points experienced elevated risks of these complications, even after accounting for their 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.

AUTHOR CONTRIBUTIONS

All authors contributed to the contributed to the conception and design of the study. All authors contributed to the acquisition, analysis and interpretation of the data. DNW wrote the first draft of the manuscript. All authors revised the manuscript critically for important intellectual content. All authors read and approved the final version of the manuscript.

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DECLARATION OF INTERESTS

Prof Hillis has undertaken consultancy work for Johnson and Johnson and GlaxoSmithKline, as well as received honoraria from Novartis. Dr Ackland has undertaken consultancy work for GlaxoSmithKline. Prof Pearse has received research grants and/or honoraria from Edwards Lifesciences, Intersurgical, BBraun and GlaxoSmithkline.

FIGURE LEGENDS

Figure 1: Participant screening, recruitment and follow-up in primary nested cohort analysis of METS study cohort

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Table 1: Characteristics of study sample

	Overall Cohort (N = 1546)	Missing Data (n)
Demographics		
Age, years		
Median (IQR)	65 (57 – 72)	
Mean (SD)	64 (10)	
Female sex	629 (41%)	
Preoperative Characteristics		
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 to 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‡		58
eGFR ≥60 mL/min/1·73 m^2	1311 (88%)	
eGFR 30 to 59 mL/min/1·73 m^2	144 (9%)	
eGFR <30 mL/min/1·73 m^2 or dialysis	33 (2%)	
Preoperative natriuretic peptide concentration		61
NT pro-BNP <100 ng/L	826 (56%)	
NT pro-BNP 100 ng/L to <300 ng/L	470 (32%)	
NT pro-BNP ng/L ≥300 ng/L	189 (13%)	
Revised Cardiac Risk Index§		58
Class I	557 (37%)	
Class 2	677 (46%)	

Class 3	204 (14%)
Class 4	50 (3%)
Operative Characteristics	
Procedure type – no. (%)	
Vascular	29 (2%)
Intra-thoracic	35 (2%)
Intra-peritoneal or retro-peritoneal	489 (32%)
Urologic or gynaecologic	457 (30%)
Head-and-neck	109 (7%)
Orthopaedic	388 (25%)
Other	39 (3%)

Abbreviations: eGFR, estimated glomerular filtration rate

* Current smoker or quit within previous one year
† Prior diagnosis of asthma, reactive airways 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, versus requirement for insulin). All missing Revised Cardiac Risk Index scores were related to missing preoperative creatinine concentration data.

Table 2: Bivariate comparisons between patients who did versus did not suffer 30-day postoperative death or myocardial injury

	Alive at 30 Days Without Myocardial Injury (n=1359)	30-Day Death or Myocardial Injury (n = 187)	P-Value
Demographics			
Age – years, mean (SD)	63 (10)	70 (10)	<0.001
Female sex – no. (%)	554 (41%)	75 (40%)	0.86
Preoperative Characteristics			
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‡			
eGFR ≥60 mL/min/1·73 m^2	1165 (89%)	146 (80%)	0.002
eGFR 30 to 59 mL/min/1·73 m^2	114 (8%)	30 (16%)	
eGFR <30 mL/min/1·73 m^2 or dialysis	27 (2%)	6 (3%)	
Preoperative natriuretic peptide concentration			
NT pro-BNP <100 ng/L	763 (59%)	63 (35%)	<0.001
NT pro-BNP 100 ng/L to <300 ng/L	403 (31%)	67 (37%)	
NT pro-BNP ng/L ≥300 ng/L	138 (11%)	51 (28%)	
Revised Cardiac Risk Index§			
Class I	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 – no. (%)			
Vascular	20 (2%)	9 (5%)	<0.001
Intra-thoracic	28 (2%)	7 (4%)	

Intra-peritoneal or retro-peritoneal	435 (32%)	54 (29%)
Urologic or gynaecologic	415 (31%)	42 (22%)
Head-and-neck	102 (8%)	7 (4%)
Orthopaedic	320 (24%)	68 (37%)
Other	39 (3%)	0 (0%)

Abbreviations: eGFR, estimated glomerular filtration rate

* Current smoker or quit within previous one year
† Prior diagnosis of asthma, reactive airways 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). All missing Revised Cardiac Risk Index scores were related to missing preoperative creatinine concentration data.

Table 3: Adjusted association of DASI score and other clinical risk factors with 30-day postoperative death or myocardial injury*

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 to 0.99)	0.002
Thresholds extrapolated from transformed variable		
≤34 points	1.97 (1.28 to 3.04)	
35 points	1.92 (1.26 to 2.90)	
40 points	1.67 (1.20 to 2.31)	
45 points	1.44 (1.14 to 1.83)	
50 points	1.26 (1.09 to 1.46)	
55 points	1.09 (1.03 to 1.16)	
58.2 points (maximum score)	Reference	
Revised Cardiac Risk Index†		
Class 1	Reference	0.07
Class 2	1.08 (0.74 to 1.59)	
Class 3	1.65 (1.02 to 2.68)	
Class 4	2.05 (0.97 to 4.35)	
Preoperative NT pro-BNP concentration		
<300 ng/L	Reference	
≥300 ng/L	2.43 (1.60 to 3.69)	<0.001

* 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, versus requirement for insulin). All missing Revised Cardiac Risk Index scores were related to missing preoperative creatinine concentration data.

Table 4: Adjusted association of DASI score and other clinical risk factors with 30-day postoperative death or myocardial infarction*

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 to 1.09)	0.04
Thresholds extrapolated from transformed variable		
5 points	3.63 (1.05 to 12.61)	
10 points	2.90 (1.04 to 8.15)	
15 points	2.32 (1.03 to 5.26)	
20 points	1.86 (1.02 to 3.40)	
25 points	1.49 (1.01 to 2.20)	
30 points	1.19 (1.01 to 1.42)	
≥34 points	Reference	
Revised Cardiac Risk Index†		
Class 1 or 2	Reference	
Class 3 or 4	2.22 (0.93 to 4.35)	0.07
Preoperative NT pro-BNP concentration		
<300 ng/L	Reference	
≥300 ng/L	1.55 (0.58 to 4.19)	0.38

* 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, versus requirement for insulin). All missing Revised Cardiac Risk Index scores were related to missing preoperative creatinine concentration data.