The Duke Activity Status Index in Patients with Chronic Kidney Disease: A Reliability Study

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Summary

Background and objectives Exercise capacity is impaired at a younger age in CKD patients than in the general population. This study examined the reliability of the Duke Activity Status Index (DASI) questionnaire as a measure of exercise capacity in medically stable adults with stage 3–4 CKD (estimated GFR [eGFR], 15–59 ml/min per 1.73 m²).

Design, setting, participants, & measurements Peak oxygen uptake (VO₂peak), estimated from DASI responses and cardiopulmonary exercise test measurements, was obtained at baseline and 6 months in a derivation sample (n=23) and once in a validation sample (n=20). Bland–Altman analysis and linear mixed models were used to estimate bias, concordance correlation coefficients, and intraclass correlation coefficients as the proportion of the variance due to participant (intertest reliability) and method (test–retest reliability).

Results The two samples were homogeneous with respect to age (mean 60±14 years), eGFR (35.5±15 ml/min per 1.73 m²), male sex (53%), and diabetes (56%). Mean measured VO₂peak was 16.5±4 ml/kg per min. The DASI questionnaire overestimated VO₂peak by 4.3 ml/kg per min. Intertest reliability was 53% when eGFR was ≥35 ml/min per 1.73 m² (median) and 60% when eGFR was <35 ml/min per 1.73 m² (P<0.01). Test–retest reliability was 81% when eGFR was <35 ml/min per 1.73 m² and 71% when eGFR was ≥35 ml/min per 1.73 m² (P<0.01).

Conclusions The DASI questionnaire may be a reliable measure of exercise capacity in CKD patients, especially when eGFR is <35 ml/min per 1.73 m². Larger prospective studies are needed to determine its prognostic value.

Introduction

The prevalence of CKD is increasing worldwide and is considered a public health priority in the United States (1). Patients with CKD have impaired exercise capacity (EC), commonly resulting in physical disability, reduced quality of life, and increased health care resource utilization (2). EC is defined as the maximal ability to perform aerobic work (VO₂peak), and is the fundamental physiologic determinant of the ability to perform common daily activities safely and independently (3–5).

Loss of functional independence occurs when VO₂peak falls <15 ml/kg per min in women and 18 ml/kg per min in men, occurring typically by age 80–85 years in healthy individuals (6,7). Patients with stage 3–4 CKD (estimated GFR [eGFR], 15–59 ml/min per 1.73 m²) reach these thresholds 20 years earlier, contributing to the low rate of independent functioning seen in this patient population (8,9).

Reduced EC is associated with increased cardiovascular mortality in the general population (10) and in patients with CKD (11). Progressive deterioration of EC parallels eGFR decline (12) and may herald increased cardiovascular risk at any stage of CKD (13–15). At the initiation of dialysis, mortality rates increase when VO₂peak is below a critical level of 17.5 ml/kg per min (16). However, exercise rehabilitation can trigger cardioprotective mechanisms (17–20), increase EC, and improve health-related quality of life (8).

Appropriate assessment of EC is essential for patient risk stratification and the implementation and evaluation of exercise rehabilitation programs. Direct measurement of VO₂peak by the cardiopulmonary exercise test (CPET; reference standard test) is complex, costly, and physically demanding for patients, limiting its routine application in clinical practice (21). Simple questionnaires may be preferred for screening and classification purposes in medically stable ambulatory patients (22).

The Duke Activity Status Index (DASI) is a self-administered questionnaire designed to assess physical function and predict EC within an office setting (23), and has been validated in patients with chronic cardiac and respiratory conditions (24–26). Although the DASI questionnaire has been used in renal disease populations (12,27,28), reliability and validity studies are lacking in CKD patients. The aim of this study was to assess the reliability and validity of the DASI questionnaire as a predictor of EC in patients with CKD.

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Materials and Methods

Study Design and Objectives

We conducted a cross-sectional analysis of the test–retest reliability and intertest reliability (validity) of the DASI questionnaire. Because the questionnaire was initially developed for use in cardiac disease, we sought to derive a correction factor for the conversion of the DASI raw score into VO₂peak for use in patients with CKD. Therefore, a derivation cohort who performed both the DASI questionnaire and CPET at two time points, 6 months apart to minimize recall bias, provided a correction factor and test–retest reliability data. A validation cohort was used to verify the performance of the corrected DASI questionnaire versus the reference standard method CPET.

Participants

Medically stable adults with stage 3–4 CKD were recruited over 6 months from two outpatient nephrology clinics (predialysis and post-transplant) in the Calgary area of the Alberta Health Services (29). Patients were eligible for the study if their eGFR was ≥15 and <60 ml/min per 1.73 m², according to Modification of Diet in Renal Disease formula (30). Patients were excluded if any of the following criteria for medical instability had occurred within the month before enrollment: acute cardiorespiratory disease, including acute coronary syndrome, congestive heart failure, or pneumonia; uncontrolled diabetes, with plasma glucose >20 mmol/L or <4 mmol/L on at least two occasions; uncontrolled hypertension with systolic BP > 180 mmHg or diastolic BP >110 mmHg on at least two occasions; persistent hyperkalemia, with K+ >5.5 mmol/L; or musculoskeletal abnormalities exacerbated by or precluding exercise. Individuals who met the inclusion criteria were invited to attend an information session before confirming their intent to participate. The University of Calgary Conjoint Health Research Ethics Board approved the study protocol and each participant gave written informed consent.

Outcome

The outcome of interest was the concordance (absolute agreement) between the VO₂peak directly measured and its estimate obtained using the DASI questionnaire. Measures of agreement included both intertest reliability (between-method agreement/validity) and test–retest reliability (within-method agreement).

CPET and Direct-Measured VO₂peak

A symptom-limited CPET was performed on a cycle ergometer (Ergoline 800; SensorMedics, Yorba Linda, CA) using a workload increment of 5–20 W/min to yield an 8- to 12-minute test (3). VO₂peak was determined from direct gas analysis using a breath-by-breath system (Vmax; SensorMedics), which was calibrated before every test according to the manufacturer’s recommendations. BP and a 12-lead electrocardiogram were monitored during testing, and ratings of shortness of breath and leg discomfort were recorded every 2 minutes using the Borg 6–20 rating of perceived exertion scale (31). Participants were asked to maintain a pedaling speed of 50–70 rpm and were encouraged to give maximal effort. Standard indications for test termination were followed (3). All tests were performed in the morning, with medications taken as prescribed. The CPET technician was blinded to the DASI score. Results of the CPET were not disclosed to the study participants.

DASI-Estimated VO₂peak

The DASI questionnaire (23) consists of 12 items pertaining to the patient’s perceived ability to perform daily activities (Supplemental Materials) and takes fewer than 10 minutes to complete. Weighted averages for each question are based on the known energy requirement of the activity (in metabolic equivalent units). Responses are summed to give a raw DASI score (from 0 to 58.2) used to estimate VO₂peak in milliliters per kilogram per minute. The DASI questionnaire was mailed to study participants 1 week before their scheduled CPET, with instructions to complete the questionnaire 2 days before the CPET and bring it to their testing session. No teaching or familiarization with the questionnaire was required. The DASI score was not disclosed to the study participants.

Independent Variables

Data on clinical characteristics, CKD causes, documented diagnosis of diabetes or cardiovascular disease (i.e., cerebrovascular, peripheral or coronary artery disease, and heart failure), and history of hypertension were obtained from the CKD database (29), and were defined based on the diagnosis-related group classification and International Classification of Diseases, Ninth Revision. Laboratory data were extracted from the same database.

Statistical Analyses

Power and Sample Size. From data on variance components from previous studies (8), we estimated that a sample of 20 participants, each receiving two measurements, was necessary to demonstrate a significant difference (two-sided P value of 0.05) of 5 units in the response variable by measurement method (within-cluster covariate) with power >85% (32).

Descriptive Analyses. Data are expressed as mean ± SD or as frequencies, as appropriate. Correlation was studied estimating the interclass Pearson coefficient (precision; relative agreement) and the Lin concordance correlation coefficient (CCC; absolute agreement) between measured and estimated VO₂peak values (validity). Unadjusted and stratified differences (bias) and 95% limits of agreement were estimated using the Bland–Altman method (i.e., overall and by presence and absence of comorbidities, sex, and categories of age and eGFR).

Regression Models. Linear mixed models were used to estimate the adjusted intraclass correlation coefficient (ICC; adjusted measure of absolute agreement). These models were built on the patient identifier treated as a random factor (random intercept models) and the measurement method as a fixed predictor to estimate the “method effect” (bias). The above-listed independent variables were used to control for confounding, to test interaction effects and other random effects, and to allow heteroscedastic residuals. Model comparison was performed by using likelihood ratio tests and checking the information criteria. Measures of reliability (ICCs) were estimated under the assumption of equal or unequal reliability (homo- or heteroscedasticity
of the random effects). Residual analyses were performed to check model validity. Analyses were performed using Stata 11.2 SE software (StataCorp, College Station, TX).

Results
Patient Characteristics
The study profile is shown in Figure 1. Eighty consecutive patients were approached and 60 patients attended the information sessions. Forty-three patients (predialysis CKD, n=26; transplant, n=17) agreed to participate. Participants who were eligible but did not consent (n=20) were similar to study participants in terms of age, sex, eGFR, and comorbidities. The first consecutive 23 enrolled patients completed both the DASI questionnaire and CPET at baseline and at 6 months for test–retest reliability analysis (derivation sample). The subsequent 20 patients completed the CPET and DASI questionnaire once (validation sample). Patient characteristics are shown in Table 1. The derivation and validation samples were similar in terms of demographic, clinical, and laboratory characteristics. Direct-measured and DASI-estimated \( \text{VO}_2\text{peak} \) values were similar in the two patient groups. Transplant patients were younger (55±10 years versus 60±14 years) and had higher eGFR (45.4±10 ml/min per 1.73 m\(^2\) versus 35.5±15 ml/min per 1.73 m\(^2\)). Both direct-measured and DASI-estimated \( \text{VO}_2\text{peak} \) values had good linear correlation with eGFR, with Pearson correlation coefficients of 0.42 (\( P<0.01 \)) and 0.34 (\( P=0.02 \)), respectively.

Analyses of Agreement
The results of unadjusted agreement analyses (concordance) are summarized in Table 2. DASI-estimated \( \text{VO}_2\text{peak} \) tended to overestimate direct-measured \( \text{VO}_2\text{peak} \) (average bias of 4.3 ml/kg per min; 95% limits of agreement, −5.3 to 14) with a CCC of 0.41 (95% CI, 0.24–0.60). Bias estimates were similar across categories of patient characteristics including levels of kidney function and diabetes. In adjusted analyses (mixed model including diabetes as fixed factor, subject/method as random factors, and eGFR to explain residual heteroscedasticity; not shown), the bias due to method (fixed effect) was 2.1 ml/kg per min (95% CI, 1.5–3 ml/kg per min).

A correction factor was derived from concordance analysis, on the basis of the major axis changes compared with the line of perfect agreement (Figure 2, top panels). When the correction factor was applied (corrected DASI-estimated \( \text{VO}_2\text{peak} \) = DASI-estimated \( \text{VO}_2\text{peak} \) × 0.638 + 3.056), the between-method agreement improved to a CCC of 0.62 (95% CI, 0.43–0.80). When the correction factor was applied in the validation cohort, a similar improvement in the CCC was observed (Table 2), although all estimates were less precise in this smaller sample (one measurement per participant) (Figure 2, bottom panels). All remaining

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Figure 1. Study profile. Flow diagram of patient identification, enrollment, and distribution in the derivation and validation samples.
calculations were performed applying the correction factor to the DASI-estimated \( \dot{V}O_2\text{peak} \).

**Variance Components**

Table 3 summarizes the results of regression analyses. Adjusted analyses show that on average the study participants had direct-measured \( \dot{V}O_2\text{peak} \) values of 17 ml/kg per min (95% CI, 16–19 ml/kg per min). The only variable with a significant fixed effect was diabetes (\( \dot{V}O_2\text{peak} \) values 3 ml/kg per min lower; 95% CI, 2.56 to 20.7). None of the other clinical characteristics or laboratory variables had significant fixed or random effects. However, residual variance was smaller in participants with eGFR, 35 ml/min per 1.73 m² (median) than in those with eGFR $\leq$ 35 ml/min per 1.73 m² (P, 0.01). It can be seen that the full model (model 2), relaxing the assumption of equal method reliability did not significantly improve the fit compared with the reduced model (model 1), indicating that test–retest reliability was similar.

Figure 3 shows the ICCs calculated from these regression models. The ICC estimates the between- and within-method reliability as the proportion of the total variance in the data due to patient and measurement methods. The ICC due to patient, intertest reliability, or validity of the DASI questionnaire was estimated at 53% in participants with eGFR between 35 and 59 ml/min per 1.73 m² and at 60% in those with eGFR between 15 and 34 ml/min per 1.73 m². Finally, despite tests being performed 6 months apart, the test–retest (intratest) reliability was similar across methods, again with better performance of both in participants with eGFR between 15 and 34 ml/min per 1.73 m² (81%) than in those with greater eGFR (71%).

**Discussion**

We conducted a reliability study of the DASI questionnaire (23) as a predictor of EC in CKD patients. The main findings of our study are as follows. First, DASI-estimated \( \dot{V}O_2\text{peak} \) values have a relatively high degree of agreement (53%–60%) with those measured with the reference standard CPET (validity). Second, both the DASI questionnaire and CPET are equally and highly reliable in...

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**Table 1. Baseline patient characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Derivation Sample (n=23)</th>
<th>Validation Sample (n=20)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>60 (±14)</td>
<td>59 (±13)</td>
<td>0.69</td>
</tr>
<tr>
<td>Female</td>
<td>11 (47)</td>
<td>8 (40)</td>
<td>0.60</td>
</tr>
<tr>
<td>Renal transplant</td>
<td>10 (43)</td>
<td>7 (35)</td>
<td>0.57</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>13 (56)</td>
<td>9 (45)</td>
<td>0.45</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>18 (78)</td>
<td>19 (95)</td>
<td>0.19</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td>7 (30)</td>
<td>4 (20)</td>
<td>0.45</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>30.2 (±6.5)</td>
<td>32.9 (±7.5)</td>
<td>0.21</td>
</tr>
<tr>
<td>Estimated GFR (ml/min per 1.73 m²)</td>
<td>35.5 (±15.0)</td>
<td>36.8 (±10.8)</td>
<td>0.74</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>126.0 (±14.9)</td>
<td>127.5 (±16.7)</td>
<td>0.68</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>37.3 (±3.1)</td>
<td>38.4 (±3.1)</td>
<td>0.26</td>
</tr>
<tr>
<td>Direct-measured ( \dot{V}O_2\text{peak} ) (ml/kg per min)</td>
<td>16.2 (±3.9)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16.6 (±6.5)</td>
<td>0.84</td>
</tr>
<tr>
<td>DASI-estimated ( \dot{V}O_2\text{peak} ) (ml/kg per min)</td>
<td>20.2 (±6.2)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>19.7 (±8.9)</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Estimate reported as mean (±SD) or n (%) as appropriate. DASI, Duke Activity Status Index.

<sup>a</sup>Direct-measured \( \dot{V}O_2\text{peak} \) at 6 months: 16.1 (±4.2).

<sup>b</sup>DASI-estimated \( \dot{V}O_2\text{peak} \) at 6 months: 20.8 (±6.5).

**Table 2. Bland–Altman analysis**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Lin CCC (95% Confidence Interval)</th>
<th>Slope</th>
<th>Intercept</th>
<th>Bias (95% Limits of Agreement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derivation (uncorrected)</td>
<td>0.41 (0.24, 0.59)</td>
<td>0.63</td>
<td>3.05</td>
<td>4.37 (−5.32, 14.06)</td>
</tr>
<tr>
<td>Derivation (corrected)</td>
<td>0.62 (0.43, 0.80)</td>
<td>1.00</td>
<td>−0.01</td>
<td>−0.01 (−6.87, 6.87)</td>
</tr>
<tr>
<td>Validation (uncorrected)</td>
<td>0.67 (0.45, 0.91)</td>
<td>0.73</td>
<td>1.99</td>
<td>3.16 (−7.92, 14.25)</td>
</tr>
<tr>
<td>Validation (corrected)</td>
<td>0.75 (0.55, 0.95)</td>
<td>1.15</td>
<td>−1.54</td>
<td>−0.92 (−9.18, 7.35)</td>
</tr>
</tbody>
</table>

Bland–Altman (agreement), analysis of direct-measured \( \dot{V}O_2\text{peak} \) (milliliters per kilograms per minute) and Duke Activity Status Index–estimated \( \dot{V}O_2\text{peak} \) before and after correction using derivation sample data (46 measurements from 23 participants) and validation sample data (20 measurements from 20 participants). The Lin concordance correlation coefficient (CCC) is a measure of agreement (intraclass correlation coefficient). Slope and intercept summarize the change in the major axis versus the line of perfect agreement (slope expected to be 1 and intercept 0); difference refers to the average (95% limits of agreement) or mean difference (Bland–Altman).
CKD patients, with a test–retest reliability between 71% and 81%. Third, estimates of reliability vary by levels of kidney function, both being higher in participants with eGFR < 35 ml/min per 1.73 m². Our study has important implications for clinical practice and future research of EC in CKD.

Although formal reliability studies are lacking, the DASI questionnaire has been used in kidney research (2,28). One
study indicates that DASI scores are lower in CKD patients than in participants with normal kidney function, and scores decrease as kidney function declines (12). The mean VO2peak in both the derivation and validation cohorts of this study was similar to previous studies (8,9). To our knowledge, this is the first study to examine the relationship between VO2peak values predicted from the DASI questionnaire and those measured with CPET. We found that in CKD patients DASI-estimated VO2peak tends to overestimate measured VO2peak by approximately 4.3 ml/kg per min (2.1 ml/kg per min in adjusted models). In our study, this translated into a coefficient of agreement of approximately 40%, which could be significantly improved to 60% by applying a correction factor. There are several reasons that may explain this amount of bias. First, although it is possible that the intermethod agreement has been overestimated in this small cohort, it is important to note that the agreement was even higher in the validation cohort (75%). In addition, the bias was smaller after adjusting for diabetes; it is possible that other unmeasured comorbid factors may contribute to the residual bias. Second, the equation to derive VO2peak from the DASI score was developed in cardiac patients and may not apply to the CKD population. The correlation between calculated and measured VO2peak was 0.58 in the original study (23) but was lower in other patient populations (26,33). Although our correction factor partly addressed this issue, the questionnaire items and their relative weights may be further modified in the presence of CKD. Third, and more importantly, the questionnaire tool may need to be revised because the weighting of each question may not reflect the same level of physical exertion as it did when the DASI questionnaire was first implemented, partly due to development of technology to assist household activities.

The second important finding of our study is the high test–retest reliability of the DASI questionnaire in CKD, similar to that of CPET. A test–retest CPET reliability of 98% has been reported in patients with ESRD when measures are taken 1 week apart (34). The lower reliability in our data (72%–82% depending on the severity of CKD) may be partly explained by the longer interval between the tests (6 months), during which true changes in physical capacity may have occurred. However, independent of the underlying mechanisms leading to these changes in the true VO2peak, both methods in our study were affected in the same way and resulted in being similarly reliable.

The third important finding of our study is the varying degree of reliability observed by level of kidney function. The agreement between direct-measured and DASI-estimated VO2peak was significantly greater when eGFR was 15–34 ml/min per 1.73 m^2 (median). Patients with a lower eGFR may be a more homogeneous group in terms of EC than patients with more preserved eGFR. It is possible that in individuals with more severe CKD and lower EC (12), DASI scores tend to more closely reflect the relationship between perceived physical capacity and true VO2peak. Therefore, further research to determine the utility of the DASI questionnaire in patients with CKD should focus on participants with stage 4–5 CKD (eGFR <30 ml/min per 1.73 m^2).

This study has several limitations. First, lack of randomization of the order of testing may have introduced systematic bias in the estimate of the intermethod agreement. However, the DASI questionnaire was always completed first to avoid the possibility that the cycle ergometer experience could influence the subjective responses to the questionnaire. Second, we maintained the scheduled follow-up appointments, resulting in a 6-month interval between repeated measures. Although it is likely
that questionnaire response recall bias was eliminated, this long interval may have biased downward the estimates of reliability. Third, we powered the study to detect a bias of 5 mL/kg per min in the VO2peak between methods in clinically stable patients with CKD, but could not include follow-up data in the study design. All comparisons were made in this clinically stable and relatively healthy CKD population under the assumption that exercise testing is the reference standard of EC. However, data from a more heterogeneous patient population, including clinically unstable patients and long-term patient outcomes, are necessary to establish the utility of the DASI questionnaire in CKD.

In summary, our data show that the DASI questionnaire can be reliably used as a measure of EC in clinically stable patients with CKD. The DASI questionnaire has a relatively high agreement with VO2peak measured with CPET, especially if a correction factor is applied to the raw data. The high intrarater reliability of the DASI questionnaire indicates its potential for use in clinical practice, especially in participants with stage 4–5 CKD. Larger prospective studies are needed to determine the prognostic value of this questionnaire and to assist the design of intervention studies to improve the EC of the growing CKD population.

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Disclosures

None.

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