CHEST

Construct Validity and Minimal Important Difference of 6-Minute Walk Distance in Survivors of Acute Respiratory Failure

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OBJECTIVE: The 6-min walk distance (6MWD), a widely used test of functional capacity, has limited evidence of construct validity among patients surviving acute respiratory failure (ARF) and ARDS. The objective of this study was to examine construct validity and responsiveness and estimate minimal important difference (MID) for the 6MWD in patients surviving ARF/ARDS.

METHODS: For this secondary data analysis of four international studies of adult patients surviving ARF/ARDS (N = 641), convergent and discriminant validity, known group validity, predictive validity, and responsiveness were assessed. MID was examined using anchor- and distribution-based approaches. Analyses were performed within studies and at various time points after hospital discharge to examine generalizability of findings.

RESULTS: The 6MWD demonstrated good convergent and discriminant validity, with moderate to strong correlations with physical health measures ($|r| = 0.36$-0.76) and weaker correlations with mental health measures ($|r| = 0.03$-0.45). Known-groups validity was demonstrated by differences in 6MWD between groups with differing muscle strength and pulmonary function (all $P < .01$). Patients reporting improved function walked farther, supporting responsiveness. 6MWD also predicted multiple outcomes, including future mortality, hospitalization, and health-related quality of life. The 6MWD MID, a small but consistent patient-perceivable effect, was 20 to 30 m. Findings were similar for 6MWD % predicted, with an MID of 3% to 5%.

CONCLUSIONS: In patients surviving ARF/ARDS, the 6MWD is a valid and responsive measure of functional capacity. The MID will facilitate planning and interpretation of future group comparison studies in this population. CHEST 2015; 147(5):1316-1326

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ABBREVIATIONS: 6MWD = 6-min walk distance; ALTOS = ARDSNet Long Term Outcomes Study; ARF = acute respiratory failure; ED-5D = Euro-QOL; HRQL = health-related quality of life; ICAP = Improving Care of Acute Lung Injury Patients; MID = minimal important difference; PF = physical functioning; SF-36 = Medical Outcomes Survey 36-Item Short Form

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Patients who survive acute respiratory failure (ARF) and ARDS frequently experience important and long-lasting physical impairments.[1,2] The 6-min walk distance (6MWD) is a widely used measure of functional capacity in studies of patients surviving ARF/ARDS.[1] Robust literature on the validity of the 6MWD exists for geriatric, cardiac, neurologic, and COPD populations,[3-9] but a comprehensive validation of the 6MWD has not been done among patients surviving ARF/ARDS. These patients differ from chronically ill populations due to acute onset of physical impairments and younger age; therefore, determining the validity, responsiveness, and minimal important difference (MID), defined as the smallest difference perceivable by patients, for the 6MWD is important for planning and interpretation of future research studies.[10] The present study used data from four international longitudinal studies to examine the construct validity of the 6MWD in patients surviving ARF/ARDS.

Materials and Methods

Study Design

Secondary analyses were performed using data from two US-based studies (ARDSNet Long Term Outcomes Study [ALTOS] and Improving Care of Acute Lung Injury Patients [ICAP])[11,12] and two Australian-based studies.[13,14] Patients from these studies with at least one 6MWD assessment in the 12 months after critical illness were included. The ALTOS included patients surviving ARDS from 12 hospitals across five study sites, with 6- and 12-month follow-up occurring between 2008 and 2012.[11] ALTOS subjects were recruited based on participation in at least one of three co-enrolling National Heart, Lung, and Blood Institute ARDS Network randomized trials evaluating aerosolized albuterol vs placebo (Albuterol to Treat Acute Lung Injury [ALTA] trial),[15] early vs delayed enteral feeding (Early vs Delayed Enteral Feeding to Treat People With Acute Lung Injury or Acute Respiratory Distress Syndrome [EDEN] trial),[16] and omega-3 fatty acid and antioxidant supplement vs placebo (Omega-3 Fatty Acid/Antioxidant Supplementation for Treating People With Acute Lung Injury or Acute Respiratory Distress Syndrome [OMEGA] trial).[17] The ICAP study was a prospective cohort study in patients surviving ARDS recruited from four academic teaching hospitals in Baltimore, Maryland, with 3-, 6-, and 12-month follow-up occurring between 2005 and 2009.[12] The Denehy et al[13] study was a blinded randomized trial of intensive rehabilitation across ICU, hospital, and community settings vs usual physiotherapy care in patients with ARF in a single hospital in Melbourne, Victoria, Australia. Patient assessments at hospital discharge and 3-, 6-, and 12-month follow-up between 2008 and 2010 were included in this analysis. The Elliott et al[14] study was a blinded randomized trial of an 8-week home-based rehabilitation program conducted in patients with ARF recruited from 12 hospitals across three study sites in Australia. Patient evaluations conducted at 1, 8, and 26 weeks after hospital discharge (coded as hospital discharge, 3 and 6 month, for this analysis) between 2005 and 2009 were included in this analysis. In all studies, the randomized interventions did not have an effect on physical outcomes, so patients in both arms of each trial were pooled for this analysis.[11,13,14,18,19]

All studies obtained informed consent from participants and were approved by relevant institutional review boards (Johns Hopkins School of Medicine IRB-X #NA_00041630 [ICAP] and IRB-5 #NA_00013113 [ALTOS]; Austin Health Human Research Ethics Committee #H2006/02424 [Denehy]; and University of Technology at Sydney Human Research Ethics Committee #2004000062 [Elliott]). Consistent with the 2012 Berlin consensus meeting,[20] we use the term "ARDS" rather than "acute lung injury" throughout this article.

Study Measures

The primary study measure 6MWD was based on American Thoracic Society guidelines[21] in all studies with modest variations, including using a single 6MWD at each follow-up in the studies (as done in prior ARF/ARDS research[2]) and using the longest available distance (based on American Thoracic Society guidelines[21]) during home visits. The 6MWD was presented in meters and as % predicted (calculated using US[22] and Australian[23] normative values) for all studies except Elliott et al[14] in which % predicted values were not available.

Well-established performance-based and patient-reported measures reflecting important aspects of physical functioning (PF) were used to assess convergent and known-groups validity of the 6MWD. These include the 4-m timed walk speed (in meters per second),[24-26] manual muscle testing using the Medical Research Council sum score[27,28] (range, 0-60, with <48 indicating ICU-acquired weakness[29]), and spirometry[30] (reported as FEV_1 % predicted based on normative values[31]). Patient-reported measures included the Medical Outcomes Survey 36-Item Short Form (SF-36)[32] PF domain, the Functional Performance Inventory[33] overall score, and the Euro-QOL (EQ-5D)[34] mobility subscale. These measures often are used in studies of physical outcomes in patients surviving ARF/ARDS.[35-39]

Well-established patient-reported mental health measures were used to assess discriminant validity, including the SF-36 mental health domain, anxiety subscales of the Hospital Anxiety and Depression Scale[40] and EQ-5D, and the overall posttraumatic stress disorder symptom score of the Impact of Event Scale–Revised.[41] Prior reports of the correlation between physical and mental health measures have been weak (typically, $r<0.3$).[42-44]

Hospitalization, mortality, alive-at-home status (whether patients were living at home), return to normal activity (return to work, school, homemaking, or volunteering as was occurring prior to hospitalization), and health-related quality of life (HRQL) up to 12 months postdischarge were used to test predictive validity. Data were obtained through patient or proxy report, although medical records were also used in Denehy et al.[13] Hospitalizations occurring within 3 and 6 months can be self-reported with 98% and 96% accuracy, respectively.[45] Mortality data were not available in Elliott et al.[14]

The normed version of the SF-36 PF domain score, available in all studies, was used to assess responsiveness. Patient rating of global change in PF, administered at 6 and 12 months in the Denehy et al[13] trial, was also used in responsiveness analyses. This measure asked patients to rate improvement in their ability to perform daily PF activities using a visual analog scale with 0 indicating no improvement and 10 indicating maximum improvement.

Statistical Analysis

Construct Validity: Pearson correlations were used to examine convergent and discriminant validity. To establish convergent validity, we

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