HHS Public Access

Author manuscript

Thorax. Author manuscript; available in PMC 2019 December 03.

Published in final edited form as:

Thorax. 2017 October ; 72(10): 884–892. doi:10.1136/thoraxjnl-2016-209400.

Are physical measures related to patient-centered outcomes in ARDS survivors?

Kitty S. Chan, PhD[1], **Lisa Aronson Friedman, ScM**[2,3], **Victor D. Dinglas, MPH**[2,3], **Catherine L. Hough, MD, MSc**[4], **Carl Shanholtz, MD**[5], **E. Wesley Ely, MD, MPH**[6,7], **Peter E. Morris, MD**[8], **Pedro A. Mendez-Tellez, MD**[2,9], **James C. Jackson, PsyD**[6], **Ramona O. Hopkins, PhD**[10,11,12], **Dale M. Needham, FCPA, MD, PhD**[2,3,13]

[1]Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

[2]Outcomes After Critical Illness and Surgery (OACIS) Group,

[3]Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

[4]Division of Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle, WA, USA

[5]Division of Pulmonary and Critical Care Medicine, University of Maryland, Baltimore, MD, USA

[6]Division of Allergy, Pulmonary, and Critical Care Medicine, Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN, USA

[7]Geriatric Research, Education and Clinical Center Service, Department of Veterans Affairs Medical Center, Tennessee Valley Healthcare System, Nashville, TN, USA

[8]Division of Pulmonary, Critical Care & Sleep Medicine, University of Kentucky, Lexington, KY, USA

[9]Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

[10]Department of Medicine, Pulmonary and Critical Care Division, Intermountain Medical Center, Murray, Utah, USA

[11]Center for Humanizing Critical Care, Intermountain Health Care, Murray, Utah, USA

Corresponding Author: Kitty S. Chan, Ph.D., Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, 624 North Broadway Room #633, Baltimore, MD 21205-1901 (Telephone: 410-614-4043; kchan10@jhu.edu).

Author Contributions: KSC and DMN contributed to study conception and design. VDD, CLH, CS, PEM, PAM-T, JCJ, ROH and DMN contributed data for the study. LAF conducted analyses and all authors contributed to analysis and interpretation. KSC drafted the manuscript and all other authors critically revised it for important intellectual content. All authors approved the submitted manuscript. KSC and DMN are responsible for the overall content and affirm that the manuscript is an accurate account of the reported study and that no important aspects of the study have been omitted.

Conflicts of Interest and Source of Funding: The authors have no conflicts of interest to declare. This research was supported by the NHLBI (R24 HL111895, R01HL091760, R01HL091760–02S1, R01HL096504, R01HL88045 and P050HL73994), the Johns Hopkins Institute for Clinical and Translational Research (ICTR) (UL1 TR 000424–06), and the ALTA and EDEN/OMEGA trials (contracts for sites participating in this study: HSN268200536170C, HHSN268200536171C, HHSN268200536173C, HHSN268200536174C, HSN268200536175C, and HHSN268200536179C).

[12]Psychology Department and Neuroscience Center, Brigham Young University, Provo, Utah, USA

[13]Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Abstract

Objective: To inform selection of physical measures for studies of ARDS survivors within 12 months of ARDS

Methods: Secondary analysis of data from 6-month survivors participating in a U.S. multicenter prospective study (ARDSNet Long-Term Outcome Study [ALTOS], N=134) or a multi-site prospective study in Baltimore, MD (Improving Care of Acute Lung Injury Patients [ICAP], N=99). Physical measures, assessed at 6-month follow-up, were categorized according to the World Health Organization's International Classification of Disability and Health: body functions and structures, activity, and participation. Patient-centered outcomes were evaluated at 6 and 12-months: survival, hospitalization, alive at home status, and health-related quality of life. Pearson correlation, linear and logistic regression models were used to quantify associations of physical measures with patient-centered outcomes.

Main Results: No 6-month body functions and structures measure demonstrated consistent association with 6- or 12-month outcomes in multivariable regression. The 6-minute walk test, an activity measure, was associated with 6-month SF-36 physical component scores (PCS, beta range: 0.99 to 1.52, $p<0.05$). Participation measures (Functional Performance Inventory, FPI; Instrumental Activities of Daily Living, IADLs) were associated with SF-36 PCS (beta range: FPI, 1.51 to 1.52; IADL, −1.88 to −1.32; all $p<0.05$) and Euro-QoL-5D utility score (beta range: FPI, 2.00 to 3.67; IADL, −2.89 to −2.50; all $p<0.01$) at 6- and 12-months.

Conclusions: Participation measures better reflect patient quality-of-life than measures of body functions and structures within 12 months of ARDS among 6-month survivors, and are recommended for inclusion as a core measure in future studies.

Keywords

patient outcome assessment; exercise tests; muscle strength; functional status; anthropometry

INTRODUCTION

Survivors of acute respiratory distress syndrome (ARDS) frequently experience long-lasting physical impairments.[1] Clinical research in this patient population have used a wide range of performance-based and patient-reported physical measures, from evaluations of muscle mass and strength to the performance of activities of daily living (ADL).[2] This heterogeneity contributes to problems with interpreting and synthesizing evidence across studies.[3] Bringing greater consistency to outcomes measurement is an important methodological challenge for critical care research.[3–5]

Physical measures, particularly performance-based measures, such as manual muscle testing (MMT) and the 6 minute walk test, have demonstrated reliability and validity in ARDS and

other groups of intensive care unit (ICU) survivors.[6,7] In addition, in-patient measures of muscle strength was associated with mortality by 90 days[8] and 1-year[9] in critically ill patients. This literature is an important start for identifying core outcome measures. However, there is limited empirical research with head-to-head comparisons of physical measures to help researchers determine the optimal measures for evaluating post-discharge outcomes of ARDS survivors.

The current analysis will directly compare performance-based and patient-reported physical measures used in two different studies of ARDS survivors, based on independent associations with a range of patient-centered outcomes (i.e., survival, hospitalization, and alive at home status, and HRQL), assessed concurrently and in the subsequent six months. Our goal is to help inform the selection of a minimum set of physical measures for future clinical research studies in the field. Among 6-month survivors of ARDS, we examined the associations of physical measures assessed at 6-month follow-up with 6- and 12-month patient-centered outcomes. Physical measures are categorized according to the World Health Organization's International Classification of Functioning, Disability and Health (ICF) framework to help evaluate how useful measures from different categories within the ICF framework are for inferring a range of patient-centered outcomes.

METHODS

Study Design and Data Sources

Secondary analyses were performed using data from two studies, the ARDSNet Long-Term Outcome Study (ALTOS) and the Improving Care of Acute Lung Injury Patients (ICAP) study.[10,11] ALTOS included ARDS survivors from 12 hospitals across five study sites in the U.S.[10] ALTOS subjects were recruited based on participation in at least one of three co-enrolling randomized trials, conducted by the National Heart, Lung, and Blood Institute (NHLBI) ARDS Network, evaluating aerosolized albuterol versus placebo (ALTA trial)[12], early versus delayed enteral feeding (EDEN trial)[13], and omega-3 fatty acid and antioxidant supplement versus placebo (OMEGA trial)[14]. ICAP was a prospective cohort study that included ARDS survivors from 13 ICUs in 4 academic teaching hospitals in Baltimore, MD.[11] Patients who survive to 6-months and have 6 and 12 month follow-up are included in this analysis. Participants missing data on any 6 month physical measure were excluded from analysis. Analyses of 12-month patient-centered outcomes, excluding survival, are conducted among 12-month survivors.

Measures

Our analysis focused on physical measures and patient-centered outcomes that were available in the ALTOS and ICAP studies, and recommended or used in prior studies of physical outcomes in ARF/ARDS survivors.[1,2,15]

Patient-Centered Outcomes.—A range of patient-centered outcomes were available and selected for inclusion in this analysis. These outcomes included death and any hospitalization between 6 and 12 month follow-up, as well as alive at home status (whether patients were alive and living at home or not, among those who resided at home at baseline)

and health-related quality of life (HRQL) at 6 and 12 month follow-up. Data on survival (12-month), hospitalization, and alive at home status were obtained via patient or proxy report, as well as search of publicly available data sources (including the Social Security death index[16]) for the mortality outcome. Patient-reported HRQL was evaluated using the Medical Outcomes Study Short-Form 36 survey version 2 (SF-36)[17] physical component score (PCS) and the EQ-5D-3L[18,19] utility score.

Physical Measures.—Physical measures, including performance-based and patient-reported assessments, were evaluated at 6-month follow-up and categorized as body functions and structures, activity, and participation according to the ICF framework[20]. *Body Functions and Structures* were measured by a range of clinical assessments performed in both studies. Pulmonary function was assessed using spirometry[21] and reported as percent predicted forced expiratory volume in 1 second (FEV1) using normative values[22]. In the study protocol for ICAP, spirometry was not performed at 6-month if already assessed at 3-month follow-up. Therefore, 3-month FEV1 values were used for ICAP subjects missing 6-month values. Overall muscle strength was assessed by manual muscle testing (MMT) and scored according to Medical Research Council (MRC) criteria[23,24] (range, 0 to 60, with <48 indicating "ICU-acquired weakness,"[25]) and by percentage of predicted value for hand grip strength[26]. Maximal inspiratory pressure (MIP), a measure of respiratory muscle strength[27,28], and upper arm anthropometric assessment of percent muscle[29,30], which was calculated based on the mean of three triceps skinfold and three mid-arm circumference measurements, were also evaluated. *Activity* was represented by the 4-meter gait speed (ALTOS only) and the six-minute walk test (6MWT, both studies). The 4-meter gait speed was performed and scored according to published standards.[31] The 6WMT, as a percentage of the predicted value, was performed based on the American Thoracic Society (ATS) guidelines[32] with modest variation, including performing a single 6MWT at each follow-up (as done in prior ARDS research[1]) and using the longest available distance (based on ATS guidelines[32]) during home visits. *Participation* was represented by patient reports of Activities of Daily Living (ADLs)[33] and Instrumental Activities of Daily Living (IADL)[34] in the ICAP study, and the Functional Performance Inventory (FPI)[35] overall score in ALTOS.

Statistical Analysis

Identical statistical analyses were performed for ALTOS and ICAP. For the bivariable analyses, data from the two studies were also combined to maximize sample size and statistical power.

Bivariable Analyses.—Associations between 6-month physical measures with 6- and 12-month patient-centered outcomes were quantified using Pearson correlation coefficients for continuous outcomes (i.e., SF-36 PCS, EQ-5D utility score) and unadjusted logistic regression analysis for binary outcomes (i.e. survival to 12-months and alive at home status).

Multivariable Analyses.—We used multivariable regression models to test the independent associations of 6-month physical measures with each 6- and 12-month patient-centered outcome. Linear regression models were used for SF-36 PCS and EQ-5D utility scores, and logistic regression models were used for survival, hospitalization, and alive at

home status. These associations were examined separately for ICAP and ALTOS. All models included % predicted FEV1, % muscle area, MIP, MMT, hand grip, and 6MWT. In ICAP models, ADLs and IADLs were also included while 4-meter gait speed and FPI were added to ALTOS models. As a sensitivity analysis, we included baseline age, gender, race, body-mass index, Charlson Comorbidity Index and Functional Comorbidity Index in these models to examine the robustness of the associations observed (data available upon request). Variance Inflation Factors (VIF) were computed for each multivariable regression model to assess for multicollinearity.[36] Loess graphs were inspected to confirm that linear models are appropriate for modeling the relationship between each physical assessment and patient-centered outcome. SAS® 9.4 was used for all analyses.

We also calculated standardized estimates for regression models to facilitate comparison of the strength of association across 6-month physical measures. Estimates for physical measures are standardized to the scale of the outcome in each model. These data are provided in an online supplement (Appendix Tables A1–A4).

RESULTS

Patient characteristics were similar between ALTOS and ICAP 6-month survivors (Table 1), although ICAP had a higher proportion of Black participants and longer lengths of stay and a higher proportion of ALTOS patients had pneumonia. At 6 months, survivors from both studies had similar muscle strength, with ALTOS survivors having modestly higher FEV1 percent predicted, lower arm muscle area, and higher 6MWT percent predicted.

Survivors from both studies had comparable alive at home status and HRQL scores at both follow-ups, and relatively few deaths occurring between 6 and 12 months. A modestly larger proportion of ALTOS 6-month survivors did not have a hospital readmission between 6 and 12 months.

Unadjusted Associations with *Concurrent* 6-Month Patient-Centered Outcomes

Body functions and structures measures were not associated with being alive at home at 6 months in either study (Table 2). However, these measures were positively correlated with 6-month HRQL outcomes (Pearson $r \leq 0.38$), with MMT and grip strength demonstrating consistent association with SF-36 PCS in both ICAP and ALTOS. Activity measures 6MWT and 4-m gait speed were consistently associated with HRQL outcomes in both studies (Pearson $r \geq 0.34$, all $p<0.01$). Participation measures, IADL in ICAP and FPI in ALTOS, were significantly correlated with both HRQL outcomes (Pearson r range: −0.46 to −0.38 for IADL; 0.59 to 0.63 for FPI, all $p<0.01$).

Unadjusted Associations with *Future* 12-Month Patient-Centered Outcomes

Among 12-month survivors, manual muscle test assessed at 6 month was significantly associated with SF-36 PCS at 12 months, but few other 6-month body functions and structures measures were consistently associated with 12 month outcomes across the two studies (Table 3). Activity measures 6MWT and 4-m gait speed and participation measures IADL and FPI were consistently and positively associated with both HRQL outcomes in the following 6 months (all $p< 0.01$). Significant correlation with survival status, hospitalization

and being alive at home in the subsequent 6 months were also observed with 6MWT, 4-m gait speed and IADL, but these associations were not consistently observed in both studies.

Independent Associations with *Concurrent* 6-Month Patient-Centered Outcomes

No body functions and structures measures at 6 months demonstrated independent associations with 6-month outcomes in both studies (Table 4). The lack of consistent association of muscle strength measures (MMT, MIP, and handgrip) with the SF-36 PCS, a physically oriented HRQL outcome, was particularly noteworthy. In contrast, the 6MWT was associated with the SF-36 PCS in both studies. Participation measures, IADL in ICAP and FPI in ALTOS, were associated with both HRQL outcomes. Multicollinearity was not observed across the ICF measures, including for the ADL and IADL measures, indicating distinct independent associations with the patient-centered outcomes for these two participation measures. With few exceptions, models including baseline variables produced comparable results.

Independent Associations with *Future* 12-Month Patient-Centered Outcomes

None of the 6-month physical measures demonstrated significant independent association with survival or hospitalization status in the next six months (Table 5). FEV1 was associated with being alive at home at 12-months, although the direction of the association differed in ICAP and ALTOS. Patient-reported participation measures, IADL in ICAP and FPI in ALTOS, were associated with both 12-month HRQL outcomes. Grip strength and 6MWT were also significantly associated with HRQL, but these associations were observed in only one of the two studies. Sensitivity analyses based on models with patient demographic and clinical variables were generally comparable.

DISCUSSION

Using two multi-site, longitudinal clinical studies of ARDS survivors, our study provides empirical data among 6-month survivors on the associations of physical measures with a range of patient-centered outcomes (i.e., survival, hospitalization, alive at home, and HRQL), which will be informative for current efforts to determine core outcome sets[4,5] for this population.

Few measures of body functions and structures (e.g., muscle area and 3 different measures of muscle strength) were independently associated with 6- and 12-month outcomes. Furthermore, these associations were not consistently observed across the two studies. However, patient-reported participation measures, IADL and FPI, demonstrated independent associations with both HRQL outcomes at 6 and 12 months. Performance based 6MWT was independently associated with the 6-month physically oriented SF-36 PCS outcome in both studies, but was only associated with the broader EQ-5D outcome in ICAP at 6-month. Significant independent associations of participation measures with future survival, hospitalization, and alive at home status were observed, although these associations were not consistently observed in both studies.

These results suggest that participation measures may be more useful than measures of body functions and structures (e.g., muscle strength) for inferring concurrent 6-month and future

12 month patient health-related quality of life. Specifically, for researchers interested in these patient-centered outcomes, our findings provide validity evidence supporting the use of the IADL or FPI patient-reported measures in future follow-up studies of ARDS survivors. The performance-based 6MWT may be useful for researchers more focused on the physical aspects of patient functioning and quality of life of ARDS survivors. The lack of significant independent associations for ADLs likely reflects that few patients experience impairments in these basic activities by 6-month follow-up. This low variation in ADLs across patients would limit the measure's associations with 6- and 12-month patient-centered outcomes during the post-hospitalization recovery period.

Our findings may be helpful in future studies when limited time and resources warrant selection of a reduced battery of physical measures. It is important to note that while some measures, such as MIP or grip strength, were not independently associated with the patient-centered outcomes evaluated in our study, these measures can still provide valuable information on specific aspects of health targeted by the test, or possibly on patient-centered outcomes not examined in our study. The physical measures we recommended based on our empirical findings are intended to support current efforts to identify a minimum set of outcome measures that all studies in this field would use (i.e. a "core outcome set").[5] For studies that aim to elucidate mechanism of action of a treatment, the inclusion of relevant physical and other mechanistic measures, as well as patient-centered outcomes, may be beneficial in understanding how the intervention exerts its effect.

Whether a measure is informative of an outcome of interest is an important criterion during measure selection. However, other criteria, including feasibility[37], are important to consider. Notably, performance-based activity measures have greater resource needs than self-reported participation measures. For instance, although our findings suggest that 6MWT and IADLs are both informative of patient HRQL, the 6MWT requires an in-person visit, basic equipment, appropriate physical surroundings, and substantial time (at least 21 minutes for a single test given the required pre-test rest break[38], to perform the test). In contrast, the self-reported IADLs can be administered in 2–3 minutes via a survey or telephone interview.[39] For researchers interested in the patient-centered outcomes examined in our study, IADLs may be more suitable particularly when in-person visits are not feasible, as in some national multi-center studies.

The general lack of association between measures of body functions and structures with the patient-centered outcomes evaluated in our study is an important finding. In prior studies, muscle weakness during hospitalization has been associated with out-patient mortality.[8,9] However, our analyses were focused on selecting post-discharge physical measures, evaluated at 6-month follow-up, rather than in-hospital measures. This difference in findings at these time points suggest that the value of physical measures for inferring patient-centered outcomes may change over the course of a patients' recovery.[1,11] In addition, the patient-centered outcomes examined in our study are influenced by numerous health and environmental factors, particularly in the post-discharge period, which individual anatomic or physiological tests are unlikely to adequately reflect.

Our study also highlights challenges of using physical measures to infer some patient-centered outcomes in the post-hospitalization period. Few of the physical measures at 6 months demonstrated significant independent associations with survival, hospitalization or alive at home status. The lack of association with survival may be due, in part, to relatively few deaths observed after 6-month follow-up in both studies. For the alive at home outcome, many non-physical issues including those described as “environmental factors” in the ICF framework,[20] such as the availability of caregivers and home-based environmental adaptations (e.g., installation of a ramp instead of stairs to enter the home setting), can influence this outcome.

This study has important strengths, including empirically evaluating the independent association of a wide range of physical measures with multiple patient-centered outcomes at 6- and 12-months. Many measures, especially those for body functions and structures, were available in two independent studies, allowing for comparison of findings across different samples of ARDS survivors. However, our study has several limitations. First, some activity and participation measures were included only in one study; hence, we could not evaluate generalizability of findings for these specific measures in both studies. Second, this study focused on 6-month survivors and the association of 6-month physical measures with 6 and 12 month patient-centered outcomes in ARDS survivors in the U.S.; hence, the findings may not generalize to other patient populations, other time points in ARDS survivors’ recovery, or other patient-centered outcomes. Future research is needed to confirm our findings in other samples of survivors of critical illness, including non-U.S. samples for international generalizability. Third, while we conducted sensitivity analysis of our findings by including baseline demographic and clinical variables in our multivariable analyses, we did not have the data to examine other potentially important variables such as pre-ICU functional status and health-related quality of life. Fourth, we used complete case analysis in our study, which could have introduced bias for our study estimates as patients with complete data may be healthier in general. Finally, our study modeled the physical measures as continuous variables. Although the appropriateness of this modelling of the physical measures was confirmed for purposes of regression modelling, it was beyond the scope of this analysis to attempt to determine how to optimally model each physical measure with each patient-centered outcomes examined in this study.

CONCLUSION

Bringing greater consistency to outcomes measurement is an important methodological challenge for critical care research.[3–5] For clinical researchers selecting physical measures for studies of ARDS survivors over their first 12 months of recovery, participation measures such as instrumental activities of daily living, will more closely reflect patient HRQL, than measures of body functions and structures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

The authors thank Dr. Elizabeth Colantuoni for guidance on the statistical methods used in this study.

REFERENCES

1. Herridge MS, Tansey CM, Matté A, et al. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med. 2011;364:1293–1304. doi:10.1056/NEJMoa1011802. [PubMed: 21470008]
2. Turnbull AE, Rabiee A, Davis WE, et al. Outcome Measurement in ICU Survivorship Research from 1970–2013: A Scoping Review of 425 Publications. Crit Care Med.
3. Blackwood B, Clarke M, McAuley DF, McGuigan PJ, Marshall JC, Rose L. How outcomes are defined in clinical trials of mechanically ventilated adults and children. Am J Respir Crit Care Med. 2014;189(8):886–893. doi:10.1164/rccm.201309-1645PP. [PubMed: 24512505]
4. Needham DM. Understanding and improving clinical trial outcome measures in acute respiratory failure. Am J Respir Crit Care Med. 2014;189(8):875–877. doi:10.1164/rccm.201402-0362ED. [PubMed: 24735026]
5. Blackwood B, Marshall J, Rose L. Progress on core outcome sets for critical care research. Curr Opin Crit Care. 2015;21(5):439–444. doi:10.1097/MCC.0000000000000232. [PubMed: 26263299]
6. Parry SM, Granger CL, Berney S, et al. Assessment of impairment and activity limitations in the critically ill: a systematic review of measurement instruments and their clinimetric properties. Intensive Care Med. 2015. doi:10.1007/s00134-015-3672-x.
7. Chan KS, Pfoh ER, Denehy L, et al. Construct Validity and Minimal Important Difference of 6-Minute Walk Distance in Survivors of Acute Respiratory Failure. CHEST J. 2015;(5). doi:10.1378/chest.14-1808.
8. The TEAM Study Investigators. Early mobilization and recovery in mechanically ventilated patients in the ICU: a bi-national, multi-centre, prospective cohort study. Crit Care. 2015;19(1):81. doi:10.1186/s13054-015-0765-4. [PubMed: 25715872]
9. Hermans G, Van Mechelen H, Clerckx B, et al. Acute Outcomes and 1-Year Mortality of Intensive Care Unit-acquired Weakness. A Cohort Study and Propensity-matched Analysis. Am J Respir Crit Care Med. 2014;190(4):410–420. doi:10.1164/rccm.201312-2257OC. [PubMed: 24825371]
10. Needham DM, Wozniak AW, Hough CL, et al. Risk Factors for Physical Impairment after Acute Lung Injury in a National, Multi-Center Study. Am J Respir Crit Care Med. 2014:1–33. doi:10.1164/rccm.201401-0158OC.
11. Fan E, Dowdy DW, Colantuoni E, et al. Physical complications in acute lung injury survivors: a two-year longitudinal prospective study. Crit Care Med. 2014;42(4):849–859. doi:10.1097/CCM.0000000000000040. [PubMed: 24247473]
12. Matthay M a, Brower RG, Carson S, et al. Randomized, placebo-controlled clinical trial of an aerosolized β_2-agonist for treatment of acute lung injury. Am J Respir Crit Care Med. 2011;184:561–568. doi:10.1164/rccm.201012-2090OC. [PubMed: 21562125]
13. Rice TW, Wheeler AP, Thompson BT, et al. Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury: The EDEN Randomized Trial. JAMA J Am Med Assoc. 2012;307:795–803. doi:10.1001/jama.2012.137.
14. Rice TW, Wheeler AP, Thompson BT, deBoisblanc BP, Steingrub J, Rock P. Enteral omega-3 fatty acid, gamma-linolenic acid, and antioxidant supplementation in acute lung injury. JAMA. 2011;306:1574–1581. doi:10.1001/jama.2011.1435. [PubMed: 21976613]
15. Angus DC, Carlet J. Surviving intensive care: a report from the 2002 Brussels Roundtable. Intensive Care Med. 2003;29(3):368–377. doi:10.1007/s00134-002-1624-8. [PubMed: 12536269]
16. Social Security Death Index. http://ssdi.rootsweb.ancestry.com/cgi-bin/ssdi.cgi. Accessed January 13. 2011.
17. Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 Health Survey Manual and Interpretation Guide.; 1993 http://books.google.com/books/about/SF_36_health_survey.html?id=WJsgAAAAMAAJ.

18. Williams A EuroQol - A new facility for the measurement of health-related quality of life. Health Policy (New York). 1990;16(3):199–208.
19. Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Med Care. 2005;43(3):203–220. doi: 10.1097/00005650-200503000-00003. [PubMed: 15725977]
20. World Health Organization. International Classification of Functioning, Disability and Health. Geneva: World Health Organization; 2001.
21. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):319–338. doi:10.1183/09031936.05.00034805. [PubMed: 16055882]
22. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population.
23. Fan E, Ciesla ND, Truong AD, Bhoopathi V, Zeger SL, Needham DM. Inter-rater reliability of manual muscle strength testing in ICU survivors and simulated patients. Intensive Care Med. 2010;36:1038–1043. doi:10.1007/s00134-010-1796-6. [PubMed: 20213068]
24. Medical Research Council. Aids to the Investigation of the Peripheral Nervous System. London: Her Majesty's Stationary Office; 1976.
25. De Jonghe B, Sharshar T, Lefaucheur J-P, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA. 2002;288:2859–2867. doi:10.1001/jama.288.22.2859. [PubMed: 12472328]
26. Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: normative data for adults. Arch Phys Med Rehabil. 1985;66(2):69–74. doi: 10.1177/1758998313479874. [PubMed: 3970660]
27. ATS/ERS. Statement on Respiratory Muscle Testing. Am J Respir Crit Care Med. 2002;166(4): 518–624. doi:10.1164/rccm.166.4.518. [PubMed: 12186831]
28. Harik-Khan RI, Wise R a., Fozard JL. Determinants of maximal inspiratory pressure: The Baltimore longitudinal study of aging. Am J Respir Crit Care Med. 1998;158(5 I):1459–1464. doi: 10.1164/ajrccm.158.5.9712006. [PubMed: 9817693]
29. Frisancho AR. Anthropometric Standards for the Assessment of Growth and Nutritional Status. Ann Arbor, MI: University of Michigan Press; 1990.
30. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey: Anthropometry Procedures Manual.; 2009.
31. Kon SSC, Canavan JL, Nolan CM, et al. The 4-metre gait speed in COPD: Responsiveness and minimal clinically important difference. Eur Respir J. 2014;43(5):1298–1305. doi: 10.1183/09031936.00088113. [PubMed: 24177002]
32. American Thoracic Society Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166:111–117. [PubMed: 12091180]
33. Katz S, Ford AB, Moskowitz RW, Jackson B a, Jaffe MW. Studies of illness in the aged. J Am Med Assoc. 1963;185(12):914–919. doi:10.1001/jama.1963.03060120024016.
34. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969;9(3):179–186. doi:10.1093/geront/9.3_Part_1.179. [PubMed: 5349366]
35. Leidy NK. Psychometric properties of the functional performance inventory in patients with chronic obstructive pulmonary disease. Nurs Res. 1999;48:20–28. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=10029398. [PubMed: 10029398]
36. Belsley DA, Kuh E, Welsch RE. Regression Diagnostics: Identifying Influential Data and Sources of Collinearity. New York: Wiley; 1980.
37. Reuben D, Magasi S, McCreath HE, et al. Motor Assessment using the NIH Toolbox. Neurology. 2013;80(11 Suppl 3):S65–S75. [PubMed: 23479547]
38. Holland a. E, Spruit M a., Troosters T, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J. 2014;44(6):1428–1446. doi:10.1183/09031936.00150314. [PubMed: 25359355]

39. Improving Long-Term Outcomes Research for Acute Respiratory Failure. http://www.improvelto.com/instruments/. Accessed December 14, 2015.

KEY QUESTIONS

What is the key question?

Which physical measures are informative of current and future patient-centered outcomes in survivors during their first year of recovery after acute respiratory distress syndrome?

What is the bottom line?

No measure of body functions and structures (e.g., muscle strength) were associated with 12-month quality of life. Participation measures (e.g., instrumental activities of daily living) are associated with quality of life and are recommended for future studies focused on evaluating and improving these outcomes in ARDS survivors.

Why read on?

This study provides detailed empirical analyses to directly compare a wide range of physical status measures based on their associations with important patient-centered outcomes, including survival to 12 months, hospitalization, being alive at home and health-related quality of life to help identify a core set of physical status measures for future studies of ARDS survivors.

140 character conclusion for Twitter feed.

IADLs, not body functions & structures measures, are related to ARDS survivors' quality of life and should be included in future studies.

Table 1.

ARDS Survivor Characteristics by Study[1]

Baseline Variables	**ICAP (N=99)**	**ALTOS (N=134)**
Demographic and Clinical Characteristics		
Age, years mean (sd)	48.2 (14.0)	48.9 (14.6)
Male, n (%)	55 (55.6)	68 (50.7)
BMI kg/m^2 mean (sd)	28.3 (6.8)	31.0 (7.8)
Race n (%)		
White	58 (59.2)	121 (90.3)
Black	39 (39.8)	9 (6.7)
Other	1 (1.0)	4 (3.0)
Primary lung injury n (%)		
Pneumonia	48 (50.0)	85 (66.9)
Sepsis	18 (18.8)	20 (15.7)
Aspiration	11 (11.5)	11 (8.7)
Trauma	5 (5.2)	6 (4.7)
Transfusions	5 (5.2)	5 (3.9)
Other	9 (9.4)	0 (0)
Charlson Comorbidity Index, mean (sd)	2.0 (2.2)	1.1 (1.7)
Functional Comorbidity Index, mean (sd)	1.5 (1.4)	1.8 (1.3)
APACHE II score, mean (sd)[2]	23.8 (8.2)	25.4 (7.8)
Ventilation duration, days mean (sd)	12.7 (12.5)	11.3 (10.1)
ICU length of stay, days mean (sd)	17.8 (17.3)	15.1 (11.9)
Hospital length of stay, days mean (sd)	29.4 (22.8)	22.2 (16.3)
6 Month Physical Measures[3]		
Body Structure and Function Measures		
FEV1, mean % predicted (sd)	71.5 (18.9)	78.8 (18.6)
Arm muscle area, mean % (sd)	52.3 (12.3)	44.7 (18.1)
MIP, mean % predicted (sd)	83.8 (35.2)	91.1 (31.0)
MMT, mean % maximum MRC score (sd)	91.1 (8.7)	92.5 (7.3)
Handgrip strength, mean % predicted (sd)	77.7 (24.5)	78.5 (25.2)
Activity Measures		
6MWT, mean % predicted (sd)	58.5 (20.1)	67.2 (19.7)
4-m gait speed, mean (sd) in m/ sec (ALTOS only)	--	1.0 (0.3)
Participation Measures		
Number of ADL dependencies, mean (sd) (range 0–6, ICAP only)	0.2 (0.8)	--
Number of IADL dependencies, mean (sd) (range 0–8, ICAP only)	1.8 (2.1)	--
FPI-Total score, mean (sd) (range: 0–2, ALTOS only)	--	2.0 (0.6)

Baseline Variables	ICAP (N=99)	ALTOS (N=134)
6 Month Patient-Centered Outcomes[3]		
Alive and living at home, n (%)	92 (96.8)	125 (94.0)
SF-36 PCS score, mean (sd)	39.7 (11.3)	38.5 (11.6)
EQ-5D Utility score, mean (sd)	0.8 (0.2)	0.7 (0.2)
12 Month Patient-Centered Outcomes[3]		
Alive to 12 months, n (%)	95 (96.0)	129 (96.3)
No hospitalization, n (%) between 6 and 12 months	59 (72.8)	98 (78.4)
Alive and living at home, n (%)	88 (93.6)	120 (90.2)
SF-36 PCS score, mean (sd)	41.4 (10.5)	41.4 (12.8)
EQ-5D Utility score, mean (sd)	0.8 (0.2)	0.7 (0.2)

Abbreviations: sd: standard deviation; BMI: Body mass index; kg/m^2: kilogram per meter squared; APACHE: Acute Physiology and Chronic Health Evaluation; ICU: intensive care unit; FEV1: forced expiratory volume in 1 second; MIP: maximal inspiratory pressure; MMT: manual muscle testing; MRC: Medical Research Council; 6MWT: six minute walk test; 4-m: 4-meter; m/sec: meter per second; ADL: activities of daily living; IADL: instrumental activities of daily living; FPI: Functional Performance Inventory; SF-36 PCS: Medical Outcomes Short-Form 36 Physical Component Score; EQ-5D: Euro-QOL.

[1]Only ARDS patients who survive to 6 month follow-up are included in this study.

[2]Estimated APACHE II score based on conversion from APACHE III to APACHE II (Reference: Schneider et al., *J Crit Care* 2013;28:885–888).

[3]Based on non-missing values; Missing values—6-month physical measures (none for any variable in both studies); 6-month outcome (alive at home, N=4, 4% for ICAP, N=1, 0.7% for ALTOS; SF-36 PCS, N=0 for ICAP and ALTOS; EQ-5D, N=0 for ICAP, N=1, 0.7% for ALTOS); 12-month outcomes (alive to 12 months, N=0 for ICAP and ALTOS; No hospitalization, N=18, 18.2% for ICAP, N=9, 6.7% for ALTOS; alive at home, N=5, 5.0% for ICAP, N=1, 0.7% for ALTOS; SF-36 PCS, N=9, 9.1% for ICAP, N=10, 7.5% for ALTOS; EQ-5D, N=8, 8.1% for ICAP, N=9, 6.7% for ALTOS).

Table 2.

Bivariable Associations of 6 Month Physical Measures with 6 Month Patient-Centered Outcomes

	Alive at Home[a]	Health-Related Quality of Life	
6 Month Physical Measures	**Odds Ratio (95% CI)**	**SF-36 PCS Pearson *r* (95% CI)**	**EQ-5D Utility Pearson *r* (95% CI)**
Body Structure and Function Measures			
FEV1, each 10% predicted			
Combined Sample	1.03 (0.75,1.41)	0.19 (0.06,0.31) **	0.08 (−0.05,0.21)
ICAP	1.30 (0.74,2.29)	0.10 (−0.10,0.29)	−0.01 (−0.21,0.19)
ALTOS	0.98 (0.66,1.44)	0.27 (0.11,0.42) **	0.18 (0.01,0.34) *
Arm muscle area, each 10%			
Combined Sample	1.11 (0.79,1.55)	0.16 (0.04,0.29) *	0.18 (0.05,0.30) **
ICAP	1.57 (0.66,3.76)	0.27 (0.08,0.44) **	0.14 (−0.06,0.32)
ALTOS	1.00 (0.67,1.48)	0.10 (−0.07,0.27)	0.16 (−0.01,0.32)
MIP, each 10% predicted			
Combined Sample	1.04 (0.86,1.25)	0.20 (0.08,0.32) **	0.15 (0.02,0.27) *
ICAP	1.11 (0.77,1.60)	0.12 (−0.08,0.31)	0.08 (−0.12,0.27)
ALTOS	1.02 (0.81,1.29)	0.28 (0.12,0.43) **	0.23 (0.06,0.38) **
MMT, each 10% of maximum MRC score			
Combined Sample	1.42 (0.73,2.77)	0.32 (0.20,0.43) **	0.25 (0.12,0.36) *
ICAP	2.02 (0.72,5.68)	0.28 (0.09,0.45) **	0.17 (−0.03,0.35)
ALTOS	1.20 (0.48,3.01)	0.38 (0.22,0.51) **	0.33 (0.17,0.48) **
Grip strength, each 10% predicted			
Combined Sample	1.05 (0.82,1.35)	0.19 (0.06,0.31) **	0.11 (−0.02,0.24)
ICAP	1.21 (0.71,2.05)	0.21 (0.02,0.39) *	0.10 (−0.10,0.29)
ALTOS	1.01 (0.76,1.34)	0.17 (0.00,0.33) *	0.12 (−0.05,0.29)
Activity Measures			
6MWT, each 10% predicted			
Combined Sample	1.44 (1.08,1.92) *	0.43 (0.32,0.53) **	0.34 (0.22,0.45) **
ICAP	2.00 (1.12,3.58) *	0.43 (0.25,0.58) **	0.37 (0.19,0.53) **
ALTOS	1.36 (0.94,1.95)	0.48 (0.33,0.60) **	0.38 (0.22,0.52) **
4-m gait speed, each 0.11 m/sec (ALTOS only)	1.11 (0.83,1.48)	0.46 (0.32,0.59) **	0.44 (0.29,0.56) **
Participation Measures			
Number of ADL dependencies (ICAP only)	0.56 (0.30,1.04)	−0.06 (−0.26,0.14)	−0.10 (−0.29,0.10)
Number of IADL dependencies (ICAP only)	0.66 (0.40,1.08)	−0.46 (−0.60,−0.29) **	−0.38 (−0.54,−0.20) **
FPI-Total, per 0.20 unit[≠] (ALTOS only)	1.19 (0.95,1.50)	0.59 (0.46,0.69) **	0.63 (0.52,0.72) **

Abbreviations: FEV1: forced expiratory volume in 1 second; MIP: maximal inspiratory pressure; MMT: manual muscle testing; MRC: Medical Research Council; 6MWT: six minute walk test; 4-m: 4-meter; m/sec: meter per second; ADL: activities of daily living; IADL: instrumental activities of daily living; FPI: Functional Performance Inventory; SF-36 PCS: Medical Outcomes Short-Form 36 Physical Component Score; EQ-5D: Euro-QOL.

*p<0.05;

**p<0.01;

Combined Sample n=233; ICAP n=99; ALTOS n=134

[a]Alive at home outcome for 6m (Yes=1, No=0; Combined: 1, n=217, 95%, 0, n=11, 5%; ICAP: 1, n=92, 97%, 0, n=3, 3%; ALTOS: 1, n=125, 94%; 0, n=8, 6%);

[†]0.11 m/sec is an estimated MCID for the 4-m gait speed test based on prior study among COPD patients (Reference: Kon et al. *Eur Respir J.* 2014;43(5):1298–1305);

[‡]0.20 is an estimated MCID for the Functional Performance Inventory;

Table 3.

Bivariable Associations of 6 Month Physical Measures with 12 Month Patient-Centered Outcomes

6 Month Physical Measures	Alive between 6 and 12m[a]	No Hospitalization between 6 and 12m[b]	Alive at Home at 12m[c]	SF-36 PCS 12m	EQ-5D Utility 12m
	OR (95% CI)	OR (95% CI)	OR (95% CI)	Pearson r (95% CI)	Pearson r (95% CI)
Body Structure and Function Measures					
FEV1, each 10% predicted					
Combined Sample	1.11 (0.79,1.55)	1.08 (0.92,1.28)	1.00 (0.78,1.28)	0.18 (0.05,0.31) **	0.02 (−0.11,0.15)
ICAP	1.78 (1.05,3.04) *	0.84 (0.63,1.12)	1.72 (1.10,2.71) *	0.12 (−0.09,0.32)	−0.09 (−0.29,0.12)
ALTOS	0.68 (0.39,1.20)	1.27 (1.01,1.59) *	0.75 (0.53,1.06)	0.22 (0.04,0.38) *	0.11 (−0.07,0.28)
Arm muscle area, each 10%					
Combined Sample	1.04 (0.70,1.54)	0.93 (0.76,1.14)	1.12 (0.86,1.45)	0.08 (−0.05,0.22)	0.09 (−0.05,0.22)
ICAP	0.64 (0.25,1.60)	0.87 (0.59,1.30)	0.53 (0.24,1.20)	0.24 (0.03,0.42) *	0.17 (−0.04,0.36)
ALTOS	1.20 (0.79,1.82)	0.98 (0.77,1.24)	1.22 (0.93,1.60)	0.03 (−0.15,0.20)	0.03 (−0.15,0.20)
MIP, each 10% predicted					
Combined Sample	1.21 (0.96,1.51)	1.04 (0.94,1.14)	1.09 (0.94,1.26)	0.15 (0.02,0.28) *	0.03 (−0.10,0.17)
ICAP	1.31 (0.89,1.93)	1.03 (0.90,1.18)	1.12 (0.86,1.45)	0.01 (−0.19,0.22)	−0.18 (−0.37,0.03)
ALTOS	1.15 (0.85,1.54)	1.04 (0.90,1.19)	1.09 (0.91,1.32)	0.25 (0.07,0.41) **	0.20 (0.02,0.36) *
MMT, each 10% of maximum MRC score					
Combined Sample	0.97 (0.41,2.28)	1.21 (0.81,1.82)	1.44 (0.86,2.43)	0.32 (0.19,0.43) **	0.23 (0.10,0.36) **
ICAP	1.33 (0.48,3.70)	1.04 (0.57,1.90)	1.23 (0.51,2.95)	0.34 (0.14,0.51) **	0.03 (−0.18,0.23)
ALTOS	0.59 (0.13,2.67)	1.39 (0.80,2.40)	1.69 (0.85,3.36)	0.31 (0.14,0.46) **	0.41 (0.25,0.54) **
Grip strength, each 10% predicted					
Combined Sample	0.90 (0.70,1.16)	1.08 (0.95,1.24)	0.98 (0.82,1.19)	0.08 (−0.05,0.21)	0.05 (−0.09,0.18)
ICAP	0.97 (0.65,1.44)	1.17 (0.94,1.46)	0.97 (0.69,1.35)	0.08 (−0.13,0.28)	−0.10 (−0.30,0.11)
ALTOS	0.86 (0.62,1.19)	1.03 (0.87,1.22)	0.99 (0.79,1.24)	0.09 (−0.09,0.26)	0.13 (−0.05,0.30)
Activity Measures					
6MWT, each 10% predicted					
Combined Sample	1.16 (0.84,1.59)	1.27 (1.08,1.50) **	1.13 (0.90,1.41)	0.42 (0.30,0.53) **	0.23 (0.10,0.35) **
ICAP	1.21 (0.76,1.91)	1.20 (0.94,1.54)	1.14 (0.77,1.67)	0.43 (0.24,0.58) **	0.22 (0.02,0.41) *

6 Month Physical Measures	Alive between 6 and 12m[a]	No Hospitalization between 6 and 12m[b]	Alive at Home at 12m[c]	SF-36 PCS 12m	EQ-5D Utility 12m
	OR (95% CI)	OR (95% CI)	OR (95% CI)	Pearson r (95% CI)	Pearson r (95% CI)
ALTOS	1.12 (0.71,1.75)	1.32 (1.05,1.67)*	1.17 (0.88,1.56)	0.44 (0.28,0.57)**	0.28 (0.11,0.44)**
4-m gait speed, each 0.11 m/sec (ALTOS only)	0.91 (0.71,1.17)	1.29 (1.06,1.58)*	1.01 (0.82,1.24)	0.42 (0.27,0.56)**	0.34 (0.17,0.48)**
Participation Measures					
Number of ADL dependencies (ICAP only)	0.67 (0.35,1.29)	0.90 (0.52,1.53)	0.76 (0.39,1.45)	0.01 (−0.19,0.22)	0.00 (−0.21,0.20)
Number of IADL dependencies (ICAP only)	0.55 (0.34,0.91)*	1.13 (0.87,1.47)	0.69 (0.49,0.98)*	−0.38 (−0.54,−0.18)**	−0.29 (−0.47,−0.09)**
FPI-Total, per 0.20 unit‡ (ALTOS only)	0.96 (0.71,1.30)	1.14 (0.99,1.32)	1.16 (0.96,1.39)	0.50 (0.36,0.62)**	0.42 (0.26,0.55)**

Abbreviations: FEV1: forced expiratory volume in 1 second; MIP: maximal inspiratory pressure; MMT: manual muscle testing; MRC: Medical Research Council; 6MWT: six minute walk test; 4-m: 4-meter; m/sec: meter per second; ADL: activities of daily living; IADL: instrumental activities of daily living; FPI: Functional Performance Inventory; SF-36 PCS: Medical Outcomes Short-Form 36 Physical Component Score; EQ-5D: Euro-QOL.

*p<0.05;

**p<0.01;

OR = Odds Ratio;

[a]Alive between 6 and 12m (Yes=1, No=0, Combined: 1, n=224, 96%; 0, n=9, 4%; ICAP: 1, n=95, 96%; 0, n=4, 4%; ALTOS:1, n=129, 96%; 0, n=5, 4%);

[b]No Hospitalization between 6 and 12m (Yes=1, No=0, Combined: 1, n=157, 76%; 0, n=49, 24%; ICAP: 1, n=59, 73%; 0, n=22, 27%; ALTOS: 1, n=98, 78%; 0, n=27, 22%);

[c]Alive at home outcome for 12m (Yes=1, No=0; Combined: 1, n=208, 92%, 0, n=19, 8%; ICAP: 1, n=88, 94%, 0, n=6, 6%; ALTOS: 1, n=120, 90%; 0, n=13, 10%);

†0.11 m/sec is an estimated MCID for the 4-m gait speed test based on prior study among COPD patients (Reference: Kon et al. *Eur Respir J.* 2014;43(5):129881305);

‡0.20 is an estimated MCID for the Functional Performance Inventory

Table 4.

Multivariable Associations of 6 Month Physical Measures with 6 Month Patient-Centered Outcomes

	Alive at home[a] At 6 month Odds Ratio (95% CI)		SF-36 PCS At 6 month Beta (95% CI)		EQ-5D Utility At 6 month Beta (95% CI)	
6 Month Physical Measures	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**
	N=95	**N=133**	**N=99**	**N=134**	**N=99**	**N=133**
Body Structure & Function						
FEV1, each 10% predicted	1.46 (0.53,4.02)	0.88 (0.55,1.39)	0.00 (−1.12,1.12)	0.76 (−0.14,1.65)	−1.09 (−2.98,0.79)	0.60 (−1.07,2.27)
% muscle area, each 10%	1.91 (0.58,6.24)	0.94 (0.61,1.45)	2.21 (0.57,3.85) **	−0.39 (−1.32,0.54)	1.80 (−0.97,4.56)	−0.31 (−2.04,1.42)
MIP, each 10% predicted	0.90 (0.54,1.50)	0.99 (0.76,1.30)	0.19 (−0.45,0.83)	0.31 (−0.25,0.87)	0.37 (−0.70,1.44)	0.45 (−0.59,1.49)
MMT, each 10% max MRC score	1.12 (0.18,7.06)	0.89 (0.27,2.91)	0.56 (−1.94,3.06)	2.19 (−0.36,4.73)	−0.57 (−4.78,3.65)	1.57 (−3.23,6.36)
Grip strength, each 10% predicted	0.76 (0.39,1.49)	0.97 (0.67,1.40)	−0.32 (−1.24,0.59)	−0.34 (−1.02,0.34)	−0.94 (−2.48,0.60)	−0.67 (−1.94,0.60)
Activity						
6 min walk, each 10% predicted	1.86 (0.80,4.32)	1.32 (0.83,2.09)	1.52 (0.37,2.66) *	0.99 (0.03,1.94) *	2.77 (0.84,4.70) **	0.59 (−1.20,2.37)
4 meter walk speed (per 0.11 m/s)	--	0.94 (0.69,1.29)	--	0.55 (−0.13,1.23)	--	1.17 (−0.09,2.44)
Participation						
No. ADL dependencies (ICAP only)	0.49 (0.12,1.99)	--	0.63 (−1.86,3.12)	--	−0.14 (−4.34,4.05)	--
No. IADL dependencies (ICAP only)	0.91 (0.46,1.80)	--	−1.88 (−2.94,−0.82) **	--	−2.50 (−4.28,−0.72) **	--
FPI-Total, per 0.20 unit‡ (ALTOS only)		1.17 (0.87,1.56)		1.52 (0.89,2.15) **		3.67 (2.50,4.84) **
Model Fit; Variance Explained	**AUC=0.88**	**AUC=0.75**	**R^2=0.29**	**R^2=0.43**	**R^2=0.17**	**R^2=0.41**

Abbreviations: FEV1: forced expiratory volume in 1 second; MIP: maximal inspiratory pressure; MMT: manual muscle testing; MRC: Medical Research Council; 6MWT: six minute walk test; 4-m: 4-meter; m/sec: meter per second; ADL: activities of daily living; IADL: instrumental activities of daily living; FPI: Functional Performance Inventory; SF-36 PCS: Medical Outcomes Short-Form 36 Physical Component Score; EQ-5D: Euro-QOL.

*p≤0.05;

**p≤ 0.01;

[a]Alive at home outcome for 6m (Yes=1, No=0; ICAP: 1, n=92, 97%, 0, n=3, 3%; ALTOS: 1, n=125, 94%; 0, n=8, 6%);

†0.11 m/sec is an estimated MCID for the 4-m gait speed test based on prior study among COPD patients (Reference: Kon et al. *Eur Respir J.* 2014;43(5):1298–1305);

"–" = Measure not available in dataset;

‡0.20 is an estimated MCID for the Functional Performance Inventory. There was no evidence of multi-collinearity (Variance inflation factor ≤ 1.59 for independent variables estimated within each models).

Table 5.

Multivariable Association of 6 Month Physical Measures with 12 Month Patient-Centered Outcomes

	Alive between 6 and 12 month[a] Odds Ratio (95% CI)		No Hospitalization between 6 and 12 month[b] Odds Ratio (95% CI)		Alive at home 12 month[c] Odds Ratio (95% CI)		SF-36 PCS 12 month Beta (95% CI)		EQ-5D Utility 12 month Beta (95% CI)	
6 Month Physical Measures	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**
	N=99	**N=134**	**N=81**	**N=125**	**N=94**	**N=133**	**N=90**	**N=124**	**N=91**	**N=125**
Body Structure & Function										
FEV1, each 10% predicted	2.47 (0.90,6.81)	0.50 (0.23,1.08)	0.76 (0.54,1.05)	1.26 (0.97,1.63)	2.25 (1.10,4.59) *	0.63 (0.41,0.97) *	0.39 (−0.71,1.49)	0.60 (−0.49,1.70)	−0.69 (−2.81,1.42)	0.17 (−1.90,2.24)
% muscle area, each 10%	0.64 (0.11,3.85)	1.25 (0.75,2.09)	0.77 (0.50,1.20)	0.92 (0.69,1.22)	0.41 (0.12,1.42)	1.07 (0.77,1.48)	1.56 (−0.01,3.14)	−0.99 (−2.14,0.15)	2.36 (−0.67,5.39)	−1.84 (−4.01,0.33)
MIP, each 10% predicted	1.21 (0.58,2.51)	1.35 (0.92,1.98)	1.01 (0.85,1.20)	0.93 (0.79,1.09)	0.85 (0.57,1.29)	1.19 (0.95,1.49)	−0.14 (−0.75,0.47)	0.35 (−0.34,1.04)	−0.52 (−1.69,0.66)	0.75 (−0.56,2.05)
MMT, each 10% max MRC score	0.56 (0.11,2.89)	0.48 (0.06,3.56)	0.96 (0.44,2.10)	1.06 (0.51,2.24)	1.01 (0.29,3.50)	1.54 (0.61,3.87)	2.25 (−0.19,4.70)	2.25 (−0.87,5.36)	−1.41 (−6.07,3.25)	9.03 (3.13,14.93) **
Grip strength, each 10% predicted	0.96 (0.51,1.83)	0.93 (0.61,1.43)	1.36 (0.98,1.88)	0.93 (0.76,1.15)	1.04 (0.65,1.68)	0.94 (0.70,1.26)	−0.96 (−1.88,−0.03)	−0.79 (−1.63,0.05)	−2.05 (−3.84,−0.27)	−0.97 (−2.56,0.62)
Activity										
6 min walk, each 10% predicted	0.56 (0.22,1.46)	1.31 (0.71,2.39)	1.36 (0.98,1.87)	1.11 (0.81,1.51)	0.69 (0.35,1.36)	1.21 (0.85,1.71)	1.73 (0.64,2.83) **	1.13 (−0.06,2.33)	2.31 (0.20,4.42) *	0.51 (−1.73,2.75)
4 meter walk speed (per 0.11 m/s)	--	0.78 (0.54,1.13)	--	1.22 (0.94,1.58)	--	0.81 (0.64,1.03)	--	0.70 (−0.12,1.52)	--	0.79 (−0.77,2.35)
Participation										
No. ADL dependencies (ICAP only)	0.62 (0.15,2.54)	--	0.89 (0.50,1.57)	--	0.83 (0.25,2.74)	--	1.05 (−1.35,3.44)	--	0.65 (−3.96,5.25)	--
No. IADL dependencies (ICAP only)	0.41 (0.19,0.91) *	--	1.50 (1.02,2.20) *	--	0.54 (0.31,0.96) *	--	−1.32 (−2.40,−0.24) *	--	−2.89 (−4.96,−0.81) **	--
FPI-Total, per 0.20 unit (ALTOS only)	--	1.05 (0.71,1.55)	--	1.04 (0.86,1.25)	--	1.17 (0.90,1.53)	--	1.51 (0.72,2.29) **	--	2.00 (0.52,3.49) **

	Alive between 6 and 12 month[a] Odds Ratio (95% CI)		No Hospitalization between 6 and 12 month[b] Odds Ratio (95% CI)		Alive at home 12 month[c] Odds Ratio (95% CI)		SF-36 PCS 12 month Beta (95% CI)		EQ-5D Utility 12 month Beta (95% CI)	
6 Month Physical Measures	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**	**ICAP**	**ALTOS**
	N=99	**N=134**	**N=81**	**N=125**	**N=94**	**N=133**	**N=90**	**N=124**	**N=91**	**N=125**
Model Fit; Variance Explained	**AUC=0.95**	**AUC=0.83**	**AUC=0.74**	**AUC=0.71**	**AUC=0.91**	**AUC=0.78**	**R^2=0.27**	**R^2=0.34**	**R^2=0.15**	**R^2=0.23**

Abbreviations: FEV1: forced expiratory volume in 1 second; MIP: maximal inspiratory pressure; MMT: manual muscle testing; MRC: Medical Research Council; 6MWT: six minute walk test; 4-m: 4-meter; m/sec: meter per second; ADL: activities of daily living; IADL: instrumental activities of daily living; FPI: Functional Performance Inventory; SF-36 PCS: Medical Outcomes Short-Form 36 Physical Component Score; EQ-5D: Euro-QOL.

[a] Alive between 6 and 12M (Yes=1, 0=No, ICAP: 1, n=95, 96%; 0, n=4, 4%; ALTOS:1, n=129, 96%; 0, n=5, 4%);

[b] No Hospitalization between 6 and 12M (Yes=1, 0=No, ICAP: 1, n=59, 73%; 0, n=22, 27%; ALTOS: 1, n=98, 78%; 0, n=27, 22%);

[c] Alive at home outcome for 12m (Yes=1, 0=No; ICAP: 1, n=88, 94%, 0, n=6, 6%; ALTOS: 1, n=120, 90%; 0, n=13, 10%);

[d] FEV1 at 6M for ICAP has missing values imputed using 3M values; No imputation of FEV1 values were performed for ALTOS.

[e] Model fit is based on pseudo R^2 for alive at home and R^2 for SF-36 PCS and EQ5D Utility.

* p≤0.05;

** p≤ 0.01;

"–" = Measure not available in dataset;.

† 0.11 m/sec is an estimated MCID for the 4-m gait speed test based on prior study among COPD patients (Reference: Kon et al. *Eur Respir J.* 2014;43(5):129881305);

‡ 0.20 is an estimated MCID for the Functional Performance Inventory. There was no evidence of multi-collinearity (Variance inflation factor ≤ 1.59 for independent variables estimated within each models)