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Association of ultrasound-derived quadriceps muscle size with muscle strength and exercise capacity in adults with chronic obstructive pulmonary disease: a systematic review and meta-analysis protocol

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2026100116

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 October 2026 and was last updated on 27 October 2026.

INTRODUCTION

Review question / Objective Among adults with chronic obstructive pulmonary disease (COPD), how strongly is ultrasound-derived quadriceps muscle size associated with quadriceps or knee-extensor muscle strength, and how strongly is it associated with exercise capacity? Muscle size will include ultrasound-measured rectus femoris/quadriceps cross-sectional area and muscle thickness. The primary objective is to quantify the pooled bivariate association with local muscle strength; the secondary objective is to quantify the association with exercise capacity, mainly six-minute walk distance or incremental shuttle walk distance. We will examine the consistency of associations across measurement approaches without inferring predictive performance or causality from cross-sectional correlations.

Rationale Peripheral muscle dysfunction is clinically relevant in COPD, yet objective tests of

quadriceps strength and exercise capacity may be burdensome in some settings. Quadriceps ultrasonography provides a portable measure of local muscle size, but muscle size is not interchangeable with muscle force or whole-body exercise performance. Previous systematic reviews have described applications of musculoskeletal ultrasonography in COPD, while individual studies have reported markedly different associations between muscle size and functional measurements. A quantitative synthesis focusing on anatomically defined ultrasound size measures and directly corresponding functional domains may clarify the magnitude, heterogeneity, and clinical boundaries of these associations. The review is intended to inform interpretation of ultrasound findings in COPD assessment, not to establish diagnostic thresholds or the effectiveness of a rehabilitation intervention.

Condition being studied Chronic obstructive pulmonary disease is characterized by persistent respiratory symptoms and airflow limitation,

frequently accompanied by systemic manifestations such as muscle wasting and lower-limb weakness. Quadriceps dysfunction can contribute to restricted mobility, exercise intolerance, and disability. Ultrasonography can quantify local quadriceps muscle cross-sectional area and thickness at the bedside or in outpatient rehabilitation, but the extent to which these structural measures correspond to measured strength and exercise performance remains uncertain.

METHODS

Search strategy We will search MEDLINE via PubMed, Embase, Web of Science Core Collection, and the Cochrane Library (CENTRAL and Cochrane Reviews), using database-specific combinations of controlled vocabulary and free-text terms for (1) COPD, (2) quadriceps/rectus femoris or related thigh muscles, and (3) ultrasonography or muscle size/area/thickness. The planned PubMed strategy is: ("Pulmonary Disease, Chronic Obstructive"[MeSH] OR COPD[tiab] OR "chronic obstructive pulmonary disease"[tiab]) AND ("Quadriceps Muscle"[MeSH] OR quadriceps[tiab] OR "rectus femoris"[tiab] OR "vastus lateralis"[tiab] OR "vastus intermedius"[tiab] OR "thigh muscle"[tiab]) AND ("Ultrasonography"[MeSH] OR ultrasound*[tiab] OR ultrasonograph*[tiab] OR sonograph*[tiab] OR "muscle thickness"[tiab] OR "cross-sectional area"[tiab]). We will apply no outcome, year, or language restrictions. Reference lists and citation networks of relevant studies and previous reviews will be checked, and searches will be updated before final synthesis. Exact executed search strings, search dates, and hit counts will be preserved in the review record. Chinese sources (CNKI and Wanfang) will be searched as an additional source where accessible.

Participant or population Adults aged 18 years or older with a clinician-established diagnosis of COPD, regardless of sex or disease severity. Stable COPD is the preferred setting for the primary synthesis; studies during exacerbation will be identified and considered separately. Where studies include healthy or other disease controls, only separately extractable COPD data will contribute to the pooled associations.

Intervention Not applicable as a treatment intervention. The exposure of interest is ultrasound-derived quadriceps muscle size, defined as rectus femoris/quadriceps cross-sectional area and/or muscle thickness, measured

at a cross-sectional or pretreatment baseline assessment.

Comparator No between-group comparator is required. The analysis evaluates within-COPD bivariate correlations between ultrasound muscle size and functional outcomes. Non-COPD comparison groups, where present, will not enter these correlation meta-analyses.

Study designs to be included Analytical cross-sectional studies; observational cohort studies with eligible cross-sectional measurements; and baseline observations from intervention studies. Eligible studies must measure ultrasound-derived quadriceps size and relevant function within a separable adult COPD sample.

Eligibility criteria Eligible reports must provide original adult COPD data with ultrasound-measured quadriceps/rectus femoris cross-sectional area or thickness and quadriceps/knee-extensor strength or exercise capacity measured at a compatible time point. Studies reporting an extractable bivariate correlation (Pearson r or Spearman ρ), or a statistic convertible under verified assumptions, will enter quantitative synthesis. Reports measuring the relevant variables without a usable correlation will be retained for narrative evaluation and authors may be contacted. Duplicate or overlapping cohorts will be reconciled by recruitment setting, dates, and sample characteristics. Exclusions include animal studies, reviews, case reports, conference-only abstracts, protocols without results, studies without separable COPD data, and studies evaluating only elastography, echo intensity, or ultrasound indices unrelated to muscle size. Adjusted regression coefficients, odds ratios, or ROC areas will not be treated as correlations.

Information sources Electronic databases: PubMed/MEDLINE, Embase, Web of Science Core Collection, and the Cochrane Library (CENTRAL and Cochrane Reviews). Additional sources: reference lists of included articles and previous systematic reviews; forward citation tracking; relevant trial registries as a source of linked publications; and, where accessible, CNKI and Wanfang. Investigators will be contacted when an eligible study lacks an extractable correlation or has inconsistent numerical results. Conference abstracts will be used for citation tracking but not pooled as stand-alone evidence.

Main outcome(s) The primary outcome is the bivariate association between ultrasound-derived quadriceps muscle size and quadriceps or knee-

extensor muscle strength at a cross-sectional or pretreatment baseline time point. Preferred strength measures are maximal voluntary isometric quadriceps contraction or knee-extension force; isokinetic knee-extension peak torque will be used if no isometric measure is reported. The effect measure is the correlation coefficient r , transformed to Fisher's z for meta-analysis and back-transformed for presentation. Handgrip strength is not an eligible substitute for local quadriceps strength in the primary analysis.

Additional outcome(s) The secondary outcome is the bivariate association between ultrasound-derived quadriceps muscle size and exercise capacity, prioritizing six-minute walk distance (6MWD) and, where unavailable, incremental shuttle walk test distance (ISWT), using baseline or cross-sectional measurements. Five-repetition sit-to-stand and other performance tests, if reported, will be summarized separately and not pooled with field-walking tests. Longitudinal correlations between changes in muscle size and changes in function will be described separately from baseline associations.

Data management All retrieved records will be retained with source database, search date, identifier, and deduplication history. DOI, PMID, normalized titles, authors, and years will be used to reconcile records. Two review authors will verify eligibility and extract data into a structured worksheet including actual analyzable COPD sample size, ultrasound location and method, strength or capacity measure, correlation type, coefficient, time point, and cohort provenance. Disagreements will be resolved by discussion or a third reviewer. Conflicting abstract, table, and figure values will be logged and checked against the original article or authors. All exclusion decisions and analysis datasets will be archived.

Quality assessment / Risk of bias analysis Two reviewers will independently appraise observational association data using the Joanna Briggs Institute (JBI) critical appraisal checklist for analytical cross-sectional studies, or the corresponding JBI tool for cohort designs. Baseline observational data reported within trials will be appraised for the association question rather than assumed to have low risk of bias from trial randomization. The assessment will consider population selection, COPD definition, standardized ultrasound measurement, reliable functional outcomes, confounding and statistical analysis, missing data, and selective reporting of correlations. Disagreements will be resolved by

consensus or adjudication; results will inform sensitivity analyses and interpretation.

Strategy of data synthesis Pearson correlation coefficients will be transformed using Fisher's $z = \text{atanh}(r)$, with sampling variance $1/(n-3)$, where n is the actual analyzable COPD sample. Associations with local muscle strength and exercise capacity will be synthesized separately. A random-effects inverse-variance model with restricted maximum likelihood (REML) estimation of between-study variance will be used; confidence intervals will use a Hartung-Knapp approach, with conservative adjustment if needed in sparse analyses. Pooled estimates will be back-transformed to r with 95% confidence intervals. Heterogeneity will be summarized using Q , I^2 , and τ^2 , with prediction intervals where informative. One prespecified effect per independent cohort per outcome domain will be used in primary analyses. The ultrasound hierarchy is rectus femoris cross-sectional area, then rectus femoris thickness, then other quadriceps component thickness; the functional hierarchy is isometric knee-extensor strength before isokinetic peak torque, and 6MWD before ISWT. Separately reported Spearman coefficients and strictly derivable r values will be examined in sensitivity analyses. A narrative synthesis will be provided where pooling is inappropriate. Funnel-plot asymmetry or Egger testing will only be considered for an outcome with at least ten independent studies.

Subgroup analysis If the evidence base is sufficiently populated, exploratory subgroup analyses will compare cross-sectional area versus muscle thickness, isometric versus isokinetic strength measurements, and 6MWD versus ISWT. Study setting (stable versus exacerbated COPD) and ultrasound acquisition protocols may be explored only when enough independent cohorts are available. The interpretation will emphasize uncertainty; different pooled coefficients will not be described as statistically different without an appropriate between-subgroup or joint-model test. Multiple estimates from the same participants will not be treated as independent observations.

Sensitivity analysis Planned sensitivity analyses include leave-one-study-out analyses; restriction to directly reported Pearson r ; exclusion of coefficients reconstructed from simple-regression standardized beta or R-squared; exclusion of Spearman rho; restriction to rectus femoris cross-sectional area; and exclusion of studies with unclear COPD subgroup sizes, high appraisal concerns, or potential overlapping recruitment. Alternative reasonable choices of ultrasound

measures and strength tests within the same cohort will be examined without double-counting. Where discrepancies exist between abstracts, tables, and figures, source-priority decisions and alternative values will be recorded and tested. Analyses will be reported regardless of statistical significance.

Language restriction No language restrictions.

Country(ies) involved China.

Other relevant information Prospective registration and protocol transparency: no database searches, full-text screening, correlation extraction, or pooled calculations have been undertaken before this registration. The primary outcome and the rule for selecting one correlation per cohort will be specified before formal searching and extraction. Final eligibility, numerical verification, quality assessment, and synthesis will begin after registration; any subsequent deviations will be documented with dates and reasons. Qiuhan Wu and Weihao Ke are designated as equal first contributors. Weihao Ke is the registration correspondent; Zhenyu Wang and Fang Liu are designated as co-corresponding authors. This review addresses the association between ultrasound muscle size and function, not the causal effect of blood-flow-restriction training.

Keywords chronic obstructive pulmonary disease; quadriceps; rectus femoris; ultrasonography; muscle strength; exercise capacity; meta-analysis.

Dissemination plans Results will be prepared for submission to a peer-reviewed respiratory, rehabilitation, or ultrasound journal and may be presented at relevant clinical or research meetings. The final manuscript will report the prospective registration timing and all substantive protocol amendments.

Contributions of each author

Author 1 - Qiuhan Wu - Conceptualization; review coordination; study selection; interpretation of findings; drafting and revision of the manuscript.

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