Does upper extremity exercise improve dyspnea in patients with COPD? A meta-analysis

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Received 22 May 2012; accepted 1 August 2012
Available online 16 August 2012

Summary
Background: Although unsupported upper extremity exercise (UUEE) is recommended in the guidelines for pulmonary rehabilitation (PR), it is controversial whether UUEE improves dyspnea in patients with COPD. The present study conducted a meta-analysis of randomized controlled trials to clarify whether UUEE could improve dyspnea in COPD patients.

Methods: A computerized search through PubMed and Embase (up to Mar 2012) was performed to obtain sample studies. Methodological quality was assessed using the PEDro scale. Weighted mean differences (WMDs), and 95% confidence intervals (CIs) were calculated and heterogeneity was assessed with the I² test. The overall effect sizes were compared with the minimum clinically important difference (MCID).

Results: 240 patients from 7 studies were included in this meta-analysis. The mean PEDro score was 7.0 (SD = 1.7). The results indicated UUEE relieved dyspnea and arm fatigue during activities of daily living (ADL) (WMD = −0.58, −0.55 scores; 95% CI = −1.13 to −0.02, −1.08 to −0.01), however, the overall treatment effects were lower than the MCID of 1 unit for the Borg scale. There was no statistical significance for dyspnea and arm fatigue during intervention (WMD = −0.34, 0.24 scores; 95% CI = −0.78 to 0.09, −0.33 to 0.81).

Abbreviations: COPD, chronic obstructive pulmonary disease; ADL, activities of daily living; PR, pulmonary rehabilitation; LEE, lower-extremity exercise; UUEE, unsupported upper extremity exercise; RCTs, randomized controlled trials; PEDro, Physiotherapy Evidence Database; MCID, minimum clinically important difference; WMD, weighted mean difference; CI, confidence interval; HRQL, health-related quality of life; ITT, intention-to-treat analysis; SUEE, supported upper extremity exercise; CRDQ, chronic respiratory disease questionnaire.

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http://dx.doi.org/10.1016/j.rmed.2012.08.002
Introduction

Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality worldwide and results in an economic and social burden. As the disease advances, some patients develop systemic manifestations, exercise intolerance, and peripheral muscle dysfunction. Dyspnea (e.g. breathlessness) is one of the most important and debilitating symptoms in patients with COPD. Progressive dyspnea causes fatigue and reduces health-related quality of life (HRQL). To minimize dyspnea and arm fatigue, people with COPD often reduce the use of their arms during activities of daily living (ADL) such as cooking, brushing teeth or driving. Pulmonary rehabilitation (PR) programs improve exercise capacity and reduce both fatigue and dyspnea in patients with COPD. However, such programs primarily focus on lower-extremity exercise (LEE) training. The latest evidence-based clinical practice guidelines and statements on PR recommend that unsupported upper limb training also should be included in a comprehensive PR program. Nevertheless, the role and effectiveness of unsupported upper extremity exercise (UUEE) has not been well established.

PR aims to improve quality of life for patients with COPD by improving functional capacity and reducing dyspnea. Nowadays, there are published randomized controlled trials (RCTs) regarding the effect of UUEE on dyspnea. However, it is controversial whether UUEE improve dyspnea in patients with COPD. Some published reviews believed that UUEE could improve arm exercise capacity, but its effect on dyspnea and arm fatigue remained unclear. So the present study undertook a meta-analysis of RCTs to clarify whether UUEE can improve dyspnea in patients with COPD. The findings of this meta-analysis maybe offer quantifiable proof of UUEE relieving dyspnea and guide clinical practice pertaining to UUEE in individuals with COPD.

Method

Data sources and searches

A computerized search was performed through PubMed and Embase databases (up to Mar 2012) for original research articles published in English, Italian and Spanish, using the following keywords: (COPD OR chronic obstructive pulmonary disease OR chronic obstructive lung disease OR chronic obstructive airflow disease OR emphysema OR chronic airflow limitation OR chronic airway obstruction) AND (arm OR upper extremity OR upper limb) AND (exercise therapy OR exercise OR rehabilitation OR respiratory rehabilitation OR pulmonary rehabilitation OR physical exercise OR physiotherapy OR physical therapy OR training OR exercise capacity OR exercise test OR exercise endurance).

Conclusions: UUEE can relieve dyspnea and arm fatigue in patients with COPD during ADL and should be included in the PR program, however, there is currently a lack of clinical evidence to support UUEE relieving dyspnea and arm fatigue. Further study is urgent to investigate these effects of UUEE.

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Data extraction and quality assessment

To assess eligibility, data and trial quality information from the papers selected for inclusion in the meta-analysis were extracted independently by two investigators (WX Zhang and J Sun). A third investigator (JH Yan) was consulted in case of disagreement to improve accuracy. The analytical data missing from the primary reports were requested from their authors. Methodological quality of the trials was assessed using the PEDro scale. Two investigators rated each study independently and assigned a maximum score out of 10. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Data analysis

All data were combined using STATA version 11.0 (Stata Corporation, College Station, Texas, USA). For continuous outcomes (e.g. dyspnea and arm fatigue score), a mean
difference was calculated using weighted mean difference (WMD) in this study. Homogeneity among studies was tested. Heterogeneity across studies was tested by using the $I^2$ statistic, which was a quantitative measure of inconsistency across studies. Studies with an $I^2$ statistic of 25%–50% were considered to have low heterogeneity, those with an $I^2$ statistic of 50%–75% were considered to have moderate heterogeneity, and those with an $I^2$ statistic of >75% were considered to have a high degree of heterogeneity. The effect sizes were weighted by the inverse of the population variance and combined with a fixed-effect model when there was low heterogeneity ($I^2 < 50\%$). Otherwise a random-effect model was used to perform statistical analysis. Subgroup analysis with rejecting the large-heterogeneity trial to provide biased results, was indicated when significant heterogeneity was found among the primary findings of the trials. An assessment of publication bias was desirable but not feasible with the limited number of studies in this study. Whenever possible, the overall treatment effect was compared with its minimum clinically important difference (MCID). The MCID for Borg scores was set at 1 score.

Results

Bibliographic search results

A total of 316 potential studies were retrieved from the computer searches. Following screening of study titles and abstracts, 229 articles were considered to be unrelated to the aims of the study. 87 potentially relevant studies identified for full-text analysis, 80 studies were excluded. Reasons for exclusion are presented in Fig. 1. Finally, 7 RCTs were selected for this meta-analysis, and only 1 RCT was published in non-English.

Characteristics of the included trials

Table 1, included 7 trials, shows important demographic and clinical characteristics of the patients in each trial. Most patients were elderly and had moderate to severe COPD. These studies were published between 1988 and 2012. The sample size of the RCT ranged from 22 to 50 (total 240). However, gender and age of distribution between treatment and control groups was not stated in only one trial, other 6 trials including 136 males and 76 females. Overall, duration of UEE program lasted 3–8 weeks and exercise time lasted 20–40 min, however, only 3 studies mentioned exercise time. In addition, most of the RCTs took the increased resistance arm training except only one RCT taking the incremental upper limb endurance training mode. All of the selected trials included detailed characteristics of the UEE Programs in Table 1 and the outcome data of each included trial are described in Table 2.

Studies which investigated the upper extremity exercise were subdivided into supported upper extremity exercise (SUEE) or unsupported upper extremity exercise (UUEE) according to whether the weight of the arm was supported or unsupported. In this study, the major upper extremity exercise model of the incorporation of RCTs was UUEE except one trial combining SUEE and UUEE. Hence, UEE meant or represented UUEE in this meta-analysis.
<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Patients No. (M/F); grade</th>
<th>Study group (n)</th>
<th>Intervention (i.e. UAE; UEET; ATP) group</th>
<th>Design/Measurement mode</th>
<th>Assessing dyspnea</th>
<th>Duration (weeks)/Exercise time</th>
<th>Frequency (days/week)</th>
<th>Control group Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ries et al., 1988</td>
<td>28 (NA); moderate to severe</td>
<td>UAE-GR (8) UAE-PNF (9) Control (11)</td>
<td>UAE: Arm ergometry; GR: 5 low resistance high repetition exercises; PNF: 3 progressive resistance training with free weights/UULET; the simulated ADL test</td>
<td>Borg-m</td>
<td>8/NA</td>
<td>Every other day for one week; then once daily</td>
<td>Walking training</td>
<td></td>
</tr>
<tr>
<td>Sivori et al., 1998</td>
<td>28 (23/5); severe</td>
<td>UEET (14) LEET (14)</td>
<td>UUEET/the endurance test</td>
<td>Borg</td>
<td>8/20 min</td>
<td>3</td>
<td>Lower limb training</td>
<td></td>
</tr>
<tr>
<td>Holland et al., 2004</td>
<td>38 (24/14); severe to very severe</td>
<td>UAE (22) Control (16)</td>
<td>Incremental unsupported upper limb endurance training/UULET</td>
<td>Borg-m</td>
<td>6/NA</td>
<td>7</td>
<td>Lower limb endurance training.</td>
<td></td>
</tr>
<tr>
<td>Marrara et al., 2008</td>
<td>22 (12/10); severe</td>
<td>UE (8) LL (8) Control (6)</td>
<td>UUEET (elbow flexion; elbow extension; primitive diagonal; functional diagonal; inclined supine)/standard daily physical activities test</td>
<td>Borg-m</td>
<td>6/30 min</td>
<td>3</td>
<td>Control: bronchial hygiene therapy; LL aero: treadmill</td>
<td></td>
</tr>
<tr>
<td>Costi et al., 2009</td>
<td>50 (33/17); moderate to severe</td>
<td>UEET (25) Control (25)</td>
<td>UUEET: 15 sessions of resistance exercises using Dumbbells/6MRT; standard ADL field test</td>
<td>Borg-m</td>
<td>3/NA</td>
<td>7</td>
<td>Lower extremities and general exercises.</td>
<td></td>
</tr>
<tr>
<td>Janaudis-Ferreira et al., 2011</td>
<td>36 (21/15); severe</td>
<td>ATP (17) Control (19)</td>
<td>Unsupported ATP: 18 sessions of increased resistance arm training with freeweights/UULET; 6PBRT; identical work level; ADL</td>
<td>Borg</td>
<td>6/NA</td>
<td>3</td>
<td>Sham training consisted of upper limb flexibility and stretching exercises</td>
<td></td>
</tr>
<tr>
<td>McKeough et al., 2012</td>
<td>38 (23/15); moderate</td>
<td>Strength (9) Endurance (11) Combined (9) Control (9)</td>
<td>Arm endurance (supported and unsupported) and strength (unsupported) training/endurance arm crank test (identical work rate used); UULET</td>
<td>Borg-m</td>
<td>8/20 min</td>
<td>3</td>
<td>Standard leg endurance and strength training</td>
<td></td>
</tr>
</tbody>
</table>

M/F: Male/Female; NA: not applicable; UAE: unsupported arm exercise; GR: gravity resisted exercise; PNF: proprioceptive neuromuscular facilitation exercise; Borg-m: modified Borg dyspnea scale; LL: lower limbs; aero: aerobic/endurance training; Borg: Borg dyspnea scale; BFS: Breathlessness and Fatigue Scale; UUEET: unsupported upper extremity exercise training; LEET: lower extremity exercise training; 6MRT: 6-min ring test; ADL: activities of daily living; ATP: arm training program; UULET: unsupported upper limb exercise test; 6PBRT: 6-min pegboard and ring test.
Quality assessment of the included trials

Two investigators (WX Zhang and J Sun) agreed on every item of the PEDro scores. Individual scores attributed to each aspect of the PEDro scale, by both assessors, are summarized in Table 3. The mean PEDro score of the 7 trials was 7.0 (SD = 1.7).

Meta-analyses of outcome measures

In this meta-analysis, dyspnea and arm fatigue were assessed by the Borg (or modified Borg). In total, 7 RCTs were included in 4 separate meta-analyses (Figs. 2–5), with the effect size being interpreted descriptively using WMD.

Dyspnea during ADL and intervention

During ADL, three studies\textsuperscript{20,23,24} were combined in a fixed effects meta-analysis model because there was no evidence of between-study heterogeneity in treatment effect (p for heterogeneity = 0.875; $I^2 = 0.0\%$). The pooled meta-analysis result indicated that there was a statistical difference between the intervention group and the control group (WMD = −0.58; 95% CI = −1.13 to −0.02; p = 0.043) (Fig. 2). However, the overall treatment effect was lower

![Table 2](image)

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Patients No.</th>
<th>Dyspnea (scores)</th>
<th>Arm fatigues (scores)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ADL</td>
<td>Intervention</td>
</tr>
<tr>
<td>Ries et al, 1988\textsuperscript{20}</td>
<td>17 vs. 11</td>
<td>0.02 ± 0.43</td>
<td>−1.15 ± 1.75</td>
</tr>
<tr>
<td>Sivori et al, 1998\textsuperscript{21}</td>
<td>14 vs. 14</td>
<td>NR</td>
<td>−1.71 ± 1.66</td>
</tr>
<tr>
<td>Holland et al, 2004\textsuperscript{22}</td>
<td>22 vs. 16</td>
<td>NR</td>
<td>−0.29 ± 2.22</td>
</tr>
<tr>
<td>Marrara et al, 2008\textsuperscript{23}</td>
<td>8 vs. 6</td>
<td>−0.1 ± 1.04</td>
<td>0.4 ± 0.89</td>
</tr>
<tr>
<td>Costi et al, 2009\textsuperscript{24}</td>
<td>25 vs. 25</td>
<td>−1.24 ± 1.8</td>
<td>−0.34 ± 1</td>
</tr>
<tr>
<td>Janaudis-Ferreira et al, 2011\textsuperscript{25}</td>
<td>17 vs. 19</td>
<td>NR</td>
<td>−0.4 ± 2</td>
</tr>
<tr>
<td>McKeough et al, 2012\textsuperscript{26}</td>
<td>29 vs. 9</td>
<td>NR</td>
<td>0.31 ± 2.6</td>
</tr>
</tbody>
</table>

NR: not reported; ADL: activities of daily living.

![Table 3](image)

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Random allocation</th>
<th>Concealed location</th>
<th>Baseline similar</th>
<th>Blinding (subject)</th>
<th>Blinding (therapist)</th>
<th>Blinding (assessor)</th>
<th>Measures for &gt;85%</th>
<th>ITT Group comparison</th>
<th>Point measures</th>
<th>Total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ries et al, 1988\textsuperscript{20}</td>
<td>√</td>
<td>×</td>
<td>√</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>√</td>
<td>√</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Sivori et al, 1998\textsuperscript{21}</td>
<td>√</td>
<td>×</td>
<td>√</td>
<td>×</td>
<td>×</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Holland et al, 2004\textsuperscript{22}</td>
<td>√</td>
<td>×</td>
<td>√</td>
<td>×</td>
<td>×</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Marrara et al, 2008\textsuperscript{23}</td>
<td>√</td>
<td>×</td>
<td>√</td>
<td>×</td>
<td>×</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Costi et al, 2009\textsuperscript{24}</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>×</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Janaudis-Ferreira et al, 2011\textsuperscript{25}</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>×</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>McKeough et al, 2012\textsuperscript{26}</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>×</td>
<td>×</td>
<td>√</td>
<td>×</td>
<td>√</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD score

7.0 ± 1.7

Note: ITT = Intention-to-treat analysis; √ = PEDro criteria met; × = PEDro criteria not met.
than the MCID of the Borg scale compared with 1 score. There were 6 trials measuring pre- and post-intervention dyspnea change in this meta-analysis. These studies were combined in a fixed effect model since there was small heterogeneity of between-study in treatment effect (p for heterogeneity = 0.410; I² = 0.9%). The pooled result showed no statistical difference between the intervention group and the control group (WMD = 0.34; 95% CI = 0.78 to 0.09; p = 0.124) (Fig. 3).

Arm fatigue during ADL and intervention

Two trials were conducted a meta-analysis on arm fatigue during ADL using a fixed effects meta-analysis model without heterogeneity in treatment effect (p for heterogeneity = 0.355; I² = 0.0%). The result indicated that there was a statistical difference between the two groups (WMD = 0.55; 95% CI = 1.08 to 0.01; p = 0.046) (Fig. 4). However, the overall treatment effect was lower than the MCID of the Borg scale compared with 1 score. Four trials were conducted a meta-analysis on arm fatigue during intervention using a fixed effects meta-analysis model because of the minimal heterogeneity in treatment effect (p for heterogeneity = 0.252; I² = 26.6%). The pooled meta-analysis result indicated that there was no difference between the two groups (WMD = 0.24; 95% CI = −0.33 to 0.81; p = 0.407) (Fig. 5).

Discussion

Qualitative findings

The results of meta-analysis suggest that UUEE can relieve dyspnea and arm fatigue in patients with COPD during ADL and should be included in the PR program, however, there is currently a lack of clinical evidence to support UUEE relieving dyspnea and arm fatigue. So, whether can UUEE relieve dyspnea clinically in patients with COPD remains still unclear. Further larger-sample clinical trials are a priority needed to substantiate the current findings and investigate the long-term effects of UUEE.

Practice implications

Dyspnea is a primary symptom of COPD and an important outcome measure for PR. Numerous standardized measures have been developed to evaluate dyspnea and are being used increasingly in clinical trials. The MCID is not well-defined for these measures but is important in interpreting

Figure 2  A Forest plot of the meta-analysis of 3 studies comparing unsupported upper extremity exercise with control for change in dyspnea during activities of daily living. The weight (or influence) of the study is calculated by STATA version 11.0. Each block represents a study and the area of each block is proportional to the precision of the mean treatment effect in that study. The horizontal line represents each study's 95% confidence interval (CI) for the treatment effect. The centre of the diamond is the average treatment effect across studies, and the width of the diamond denotes its 95% CI.

Figure 3  A Forest plot of the meta-analysis of 6 studies comparing unsupported upper extremity exercise with control for change in dyspnea during intervention. See Fig. 2 legend for explanation of symbols used.
the clinical meaning of results of studies in this area. Any amount of change is greater than the MCID threshold is reckoned to be meaningful or important.

The results showed that there was a statistical difference between the intervention group and the control group on dyspnea and arm fatigue during ADL, that is to say the scores of the intervention group were significantly less than those in the control group. This finding is in keeping with positive improvements in dyspnea correlating with negative Borg scores, which suggest UUEE may reduce dyspnea and arm fatigue during ADL in patients with COPD. Multiple mechanisms are accounting for UUEE reducing dyspnea. UUEE improved auxiliary respiratory muscle endurance and muscle strength and increased thoracic muscles and expansion of the rib cage resulting in the diaphragm being in a better position to play a better role, and modulated dynamic hyperinflation. Moreover, the accessory muscles assisted with the postural support of the arm diminishing their participation in ventilation and the respiratory work to the diaphragm. However, dyspnea or fatigue changes in Borg ratings pre-and postintervention were lower than the MCID of 1 score, which shows that these changes are not clinically important difference. In addition, there was no statistical difference on dyspnea and arm fatigue during intervention between the two groups. Considering that the most appropriate way to evaluate whether or not the intervention impacted dyspnea and arm fatigue is to compare them at iso-work, 3 RCTs comparing outcome measures during ADL were believed at iso-work due to the standard ADL field test. However, only 2 RCTs compared outcome measures during intervention at identical work level. Hence, it must be extremely cautious about this finding, and the present study did not draw a conclusion that there was ineffective for UUEE improving dyspnea and arm fatigue during intervention in patients with COPD in clinics.

In addition, there is no consensus of opinion regarding the duration of the PR intervention. No clinical trials have focused on the impact of program duration on arm training outcomes. In the present study, although duration of UUEE program lasted only 3–8 weeks, the results indicated UUEE can improve dyspnea and arm fatigue during ADL, which suggests that short UUEE program duration of 8 weeks has the potential effects to reduce symptoms in patients with COPD. However, further research is required to investigate these.

Limitations

Some limitations of this study should be taken into account. Firstly, the present meta-analysis includes a small number of studies involving small numbers of participants (range 8–25 per intervention group). Overestimation of the treatment effect is more likely in smaller trials compared with larger samples. Secondly, these trials ranged from 3 to 8 weeks in length, with participants training from 3 days a week to daily. The possibility that the samples were heterogeneous coupled with the diverse UUEE protocols, may limit the reliability of the results. Finally, retrieval of conference proceedings, unpublished studies was not undertaken, which created the potential for publication bias.
Conclusions

Despite such limitations, the findings suggest that UUEE can improve dyspnea and arm fatigue during ADL in patients with COPD and should be included in the PR program. Further larger-sample RCTs with standardized training methodology are a priority needed to examine the effects of clinical outcome measures, and should pay more attention to determine the clinical significance and compare dyspnea and arm fatigue with iso-work. Additional studies need to focus on the best type of UEE because most studies are lacking of other types of training (e.g. endurance vs. resistance, supported vs. unsupported). Research on the field is worthwhile and should be continued.

Conflict of interest statement

The authors have no competing interests to declare. This work was performed at the State Key Laboratory of Respiratory Disease, First Affiliated Hospital, Guangzhou Medical College, Guangzhou, PR China.

Authors’ contributions

LPan and YZ Guo contributed to concepts and design of the study. Data were collected and analyzed by all the co-authors.

Acknowledgements

We thank the authors of the original articles who provided additional data and information about their work beyond that included in their published articles.

References


