The effect of exercise on outcomes for hospitalised older acute medical patients: an individual patient data meta-analysis

Introduction

SIR—In most acute hospital general medical wards, physiotherapy is a key component of the multidisciplinary model of care. However, few studies have investigated the effects of additional exercise for acutely hospitalised older adults. A recent systematic comprehensive review identified two randomised controlled trials (RCT) and one pseudo randomised controlled trial that have investigated the effects of additional exercise in this patient group [1, 2]. Results of meta-analysis for functional outcomes favoured the additional exercise group, but the effects were small and not statistically significant.

Many factors are likely to influence the response to additional exercise for older general medical patients who typically present with a diverse range of medical conditions, co-morbidities, prognoses, functional abilities, and community and family supports. Previous studies did not identify the patients most likely to respond to the intervention. This may be related to the meta-analysis methods in which pooling of group mean aggregate data may obscure the varying responses of individual patients to additional exercise.

The primary aims of this study were to investigate the effects of additional exercise for older medical patients on functional outcomes and healthcare utilisation, and to identify baseline characteristics of patients who are most and least likely to respond to intervention using an individual patient data (IPD) meta-analysis of previously conducted trials. Secondary aims were to identify floor and ceiling effects associated with functional outcome measures in a large sample and to investigate the sources of heterogeneity between trials.

Methods

This study adhered to the QUOROM statement [3] and methodological guidelines provided by the Cochrane Collaboration Working Group on IPD Meta-analysis [4].

Searching, study selection and quality assessment

Studies were identified from a systematic review that investigated the effects of exercise for acutely hospitalised older medical patients [1]. Of the nine trials identified in the review, six multidisciplinary intervention trials were excluded as they did not allow the unique effects attributable to exercise to be partitioned. Three trials were therefore suitable for IPD meta-analysis. The internal validity of the included trials was assessed using the PEDro scale [1, 2, 5].

Data management

Eligible patients were contacted and invited to collaborate in an IPD meta-analysis. All those contacted responded and IPD were obtained from two of the three eligible trials [6, 7]. Ethics approval was obtained from the relevant University and Hospital Human Research Ethics Committees.

Outcome measures

The primary outcome was Barthel Index (BI) scores at hospital discharge [8, 9]. Secondary outcomes included discharge destination, hospital length of stay (LOS), timed up and go (TUG) test score at hospital discharge [10] and adverse events (falls, intensive care unit admission, mortality and readmission within 28 days of hospital discharge). The functional ambulation classification (FAC) categorises patients according to their ability to ambulate over a 10-foot distance [11] and was employed for subgroup analysis.

Data analysis

Data analyses were performed using SPSS for Windows version 12.0 and STATA version 7.0. All randomised patient data were included and intention to treat analysis performed. The effect of the intervention on continuous and dichotomous outcomes was analysed using multiple linear and logistic regression modelling, respectively. Cox regression analysis was used to test the effects of the intervention on acute and network (acute plus rehabilitation) LOS. For further statistical methods, see Appendix 1 in Supplementary Data (http://www.ageing.oxfordjournals.org/).

Results

Study characteristics

Both the included trials investigated the effects of additional exercise for older medical patients compared to usual care, and were conducted in acute public hospitals in Melbourne, Australia. A physiotherapist prescribed an individually tailored exercise program (upper and lower limb strengthening exercises and walking programme) for each patient in the intervention group in both trials. The programme was administered twice each day for approximately 20–30 min by an allied health assistant. Usual care at both hospitals included daily medical assessments, 24 h nursing assistance and allied health services by referral. See Appendix 2 and 3 in Supplementary Data (http://www.ageing.oxfordjournals.org/) for patient admission characteristics and trial quality assessment.
Research letters

Outcomes

Barthel index

Significant interaction between admission BI category and treatment effect were identified (likelihood ratio test: \( \chi^2(3) = 10.72, P = 0.01 \)). The intervention significantly improved discharge BI scores for patients with admission BI scores of 21–60 points, but not for those with admission BI scores in the lowest and highest categories (Table 1).

Subgroup analysis

Patients who required assistance or supervision to ambulate (FAC = 2–4) at the time of hospital admission were the most responsive to the intervention (Table 2). There was an inconclusive effect of the intervention on discharge BI scores for patients who were unable to ambulate (FAC = 1) or were independently ambulant (FAC = 5–6) at hospital admission. Almost 50% of independently ambulant patients scored 95 or 100 on the BI at hospital admission.

Timed up and go

There was no evidence of any treatment effect on discharge TUG scores (coefficient \(-0.85 (-3.39 to 1.70), P = 0.51\)). For patients unable to perform the TUG at hospital admission (34%), Fisher’s exact test indicated no effect of the intervention on the proportion of these patients who could perform the TUG at hospital discharge (\( P = 1.0 \)).

Hospital outcomes

The intervention had no effect on the proportion of patients discharged home compared to those not discharged home (OR 1.23 (0.75–2.01), \( P = 0.42 \)) or those discharged to inpatient rehabilitation compared to those not discharged to inpatient rehabilitation (OR 0.67 (0.39–1.16), \( P = 0.15 \)).

Table 1. Multiple linear regression model of discharge Barthel Index scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coef</th>
<th>Std error</th>
<th>P-value</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission BI category(^a):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (BI 21–60)</td>
<td>22.31</td>
<td>4.75</td>
<td>0.00</td>
<td>12.95 31.68</td>
</tr>
<tr>
<td>3 (BI 61–90)</td>
<td>51.55</td>
<td>4.88</td>
<td>0.00</td>
<td>41.95 61.16</td>
</tr>
<tr>
<td>4 (BI 91–100)</td>
<td>60.58</td>
<td>5.42</td>
<td>0.00</td>
<td>49.92 71.24</td>
</tr>
<tr>
<td>Intervention(^b) (interaction term):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (BI 0–20)</td>
<td>−6.49</td>
<td>6.64</td>
<td>0.33</td>
<td>−19.56 6.58</td>
</tr>
<tr>
<td>2 (BI 21–60)</td>
<td>16.10</td>
<td>7.08</td>
<td>0.03</td>
<td>2.17 30.03</td>
</tr>
<tr>
<td>3 (BI 61–90)</td>
<td>6.41</td>
<td>7.22</td>
<td>0.38</td>
<td>−7.80 20.63</td>
</tr>
<tr>
<td>4 (BI 91–100)</td>
<td>6.94</td>
<td>7.88</td>
<td>0.39</td>
<td>−8.57 22.45</td>
</tr>
<tr>
<td>Age(^c)</td>
<td>−0.29</td>
<td>0.11</td>
<td>0.01</td>
<td>−0.52 −0.07</td>
</tr>
<tr>
<td>Hospital</td>
<td>3.70</td>
<td>1.78</td>
<td>0.04</td>
<td>0.19 7.21</td>
</tr>
<tr>
<td>Constant</td>
<td>33.07</td>
<td>4.64</td>
<td>0.00</td>
<td>23.94 42.20</td>
</tr>
</tbody>
</table>

Hospital: Jones et al.\(^7\) = 0, de Morton et al.\(^6\) = 1. Group: Control = 0, Intervention = 1.
\(^a\) Admission Barthel Index 1 (0–20) is the reference category.
\(^b\) Treatment effect for patients in each admission Barthel Index category.
\(^c\) Age is centred at 80 years.

Table 2. Multiple linear regression models of discharge BI scores for subgroups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coef</th>
<th>Std error</th>
<th>P-value</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAC = 1 ((n = 50))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>2.86</td>
<td>5.73</td>
<td>0.62</td>
<td>−8.66 14.39</td>
</tr>
<tr>
<td>Admission Barthel</td>
<td>0.87</td>
<td>0.18</td>
<td>0.00</td>
<td>0.50 1.24</td>
</tr>
<tr>
<td>Hospital</td>
<td>5.05</td>
<td>5.60</td>
<td>0.37</td>
<td>−6.21 16.32</td>
</tr>
<tr>
<td>Constant</td>
<td>16.75</td>
<td>7.76</td>
<td>0.04</td>
<td>1.13 32.37</td>
</tr>
<tr>
<td>FAC = 2–4 ((n = 162))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>5.39</td>
<td>2.03</td>
<td>0.01</td>
<td>1.38 9.40</td>
</tr>
<tr>
<td>Admission Barthel</td>
<td>0.79</td>
<td>0.06</td>
<td>0.00</td>
<td>0.67 0.91</td>
</tr>
<tr>
<td>Age</td>
<td>−0.32</td>
<td>0.14</td>
<td>0.03</td>
<td>−0.61 −0.04</td>
</tr>
<tr>
<td>Hospital</td>
<td>0.88</td>
<td>2.06</td>
<td>0.67</td>
<td>−3.19 4.95</td>
</tr>
<tr>
<td>Constant</td>
<td>48.47</td>
<td>13.09</td>
<td>0.00</td>
<td>22.62 74.31</td>
</tr>
<tr>
<td>FAC = 5–6 ((n = 81))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>−1.74</td>
<td>1.50</td>
<td>0.25</td>
<td>−4.71 1.24</td>
</tr>
<tr>
<td>Admission Barthel</td>
<td>0.49</td>
<td>0.07</td>
<td>0.00</td>
<td>0.35 0.63</td>
</tr>
<tr>
<td>Hospital</td>
<td>2.14</td>
<td>1.92</td>
<td>0.27</td>
<td>−1.69 5.98</td>
</tr>
<tr>
<td>Constant</td>
<td>48.68</td>
<td>6.59</td>
<td>0.00</td>
<td>35.56 61.79</td>
</tr>
</tbody>
</table>

Hospital: Jones et al.\(^7\) = 0, de Morton et al.\(^6\) = 1. Group: Control = 0, Intervention = 1.
The odds of discharge to home were significantly higher (OR 2.05 (1.25–3.36, P = 0.00)) and the odds of discharge to an inpatient rehabilitation hospital significantly lower (OR 0.31 (0.18–0.53), P = 0.00) for patients in the de Morton et al. [6] trial compared to those in the Jones et al. [7] trial.

There was no evidence that the intervention influenced acute hospital LOS (HR 1.09 (0.89–1.33), P = 0.40). The probability of patient discharge at any given time was significantly higher for patients in the trial reported by de Morton et al. [6] compared to those in the Jones et al. [7] trial (log rank test, χ²(1) = 4.42, P = 0.04). The median acute LOS was 7.0 (IQR 4.0–10.0) and 6.0 days (IQR 4.0–10.0) in the control and intervention groups, respectively. There was weak evidence to show that the intervention group patients had a higher chance of hospital network discharge at any given time compared to the control group (HR 1.16 (0.95–1.43), P = 0.14). Patients in the Jones et al. [7] trial generally had a longer network LOS compared to those in the de Morton et al. [6] trial (log rank test, χ²(1) = 7.50, P = 0.01).

There was no evidence of an effect of treatment on adverse events (see Appendix 4 in Supplementary Data, http://www.ageing.oxfordjournals.org/).

### Discussion

This study indicates that older persons who are admitted to acute care medical settings and who required supervision or assistance to ambulate at admission are the most responsive to additional exercise during hospitalisation. It makes intuitive clinical sense that this patient subgroup, who require the assistance of a healthcare professional to remain physically active during hospitalisation, were found to be the most responsive. For this subgroup, additional exercise intervention resulted in discharge BI scores that were 5.4 points higher than the scores for those in the control group. This is likely to be an important average difference. For example, a change of 5 points in BI score occurs when one additional ADL activity on the BI is performed ‘independently’ compared to ‘with assistance’. An effect of the same size would occur if a person who was previously ‘unable to do’ an activity became capable of doing the same activity ‘with assistance’. This difference was apparent despite potential underestimation of the effect size because of a ceiling effect in the BI and a generic ‘mobility and strengthening’ programme for all patients.

Independently ambulant patients are less physically constrained by the hospital environment. However, the BI ceiling effect confounded the ability to accurately measure change in functional ability for patients who were independently ambulant at hospital admission. There is a requirement for an outcome measure that can sensitively measure changes in functional ability across the broad range of abilities that typically exist for acute general medical patients in order to draw valid conclusions regarding the responsiveness (or lack of it) of this patient subgroup to an additional exercise intervention. Analysis of discharge TUG scores that only included patients with higher levels of physical ability indicate that the intervention did not significantly influence their walking speed/balance over short distances.

On average, non-ambulant patients at hospital admission improved by 18.4 BI points in the control group and 24.9 points in the intervention group between hospital admission and discharge. For patients in this subgroup who were pre-morbidly non-ambulant, it was unlikely that an additional exercise intervention during a typically short acute hospital stay would have significantly improved functional outcome. A larger sample is required to further investigate the effects of additional exercise in this patient subgroup.

Healthcare utilisation outcomes were not significantly influenced by the intervention but significant statistical heterogeneity was detected between hospital trials. The complexity and diversity of factors that influence the discharge destination and hospital LOS of older acute medical patients are likely to result in these outcomes being relatively insensitive measures of exercise intervention effectiveness. Patients in the Jones et al. [7] trial were, on average, three years older, had a mean BI score of 57 and a median FAC score of 3 compared to 67 and 4, respectively, in the trial by de Morton et al. [6]. Differences in patient function may reflect the differences in patient case mix between hospitals. Case mix difference, in association with differences in hospital admission and discharge policy and procedures, may explain the differences in health care utilisation outcomes between trials. In addition, differences in the quality of the trial method, particularly the adequacy of randomisation allocation concealment and blinding procedures, may have been an additional source of heterogeneity between trials.

The findings in this study have clinical significance for patient assessment, planning and physiotherapy services for older medical patients in acute care. Identifying the patient subgroup most likely to benefit from an intervention may facilitate effective targeting of healthcare services. In this study, additional exercise significantly improved discharge BI scores for patients who required assistance or supervision to ambulate at the time of acute hospital admission. However, limitations associated with the BI confounded the ability to investigate the effect of the intervention for patients capable of higher functions. Further research is needed to develop a functional outcome measure that can sensitively measure changes in function across the broad range of abilities that typically exist in an older acute medical population and to review the exercise programmes that are most effective during acute hospitalisation. This study also highlights the advantages of IPD meta-analysis over analysis of group mean meta-analysis results, as there is a potential for important information to be obscured by analysis of group mean data.

### Key points

- Few studies have previously investigated the effects of additional exercise for older medical patients in the acute hospital setting.
Research letters

- Response of individual patients to additional exercise was highly variable across older medical patients.
- Additional exercise significantly improved discharge function scores for patients who required assistance or supervision to ambulate at the time of acute hospital admission.
- The Barthel Index has a ceiling effect for measuring the functional ability of older medical patients in the acute hospital setting.
- Identifying the patient subgroup most likely to benefit from an intervention facilitates the effective targeting of healthcare services.

Centre where work was done
Monash University, Department of Physiotherapy, School of Primary Health Care, Faculty of Medicine, Nursing and Health Sciences.

Conflicts of interest
All authors declare that they have no conflict of interest and therefore have nothing to declare.

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References


c-reactive protein levels predict the incidence of delirium and recovery from it

Introduction

SIR—Delirium (acute confusional state, a sudden onset, fluctuating state of cognitive decre ment and disordered consciousness) is a very common condition that complicates the hospital treatment of many older people, particularly in the specialties of medicine, orthopaedics, and general and cardiovascular surgery. It is greatly distressing, life-shortening, and associated with longer hospital stays and residual cognitive impairment [1]. No laboratory test exists to assist in the diagnosis of delirium and thus its diagnosis depended only on clinical observations [2] and is often missed even in specialist centres [3]. The most consistent known risk factor is pre-existing dementia, suggesting that delirium is actually a part of the syndrome of dementia itself [4]. Its mechanism is unknown and, although anticholinergic activity has been given precedence as a basis for specific therapeutics for many years, no randomised controlled trials of cholinergic enhancement have been published. A possible neuroinflammatory basis for delirium is also emerging and low levels of insulin-like growth factor I (IGF-I) have recently been found as a risk factor for incident delirium [5].