

# Severity assessment criteria recommended by the British Thoracic Society (BTS) for community-acquired pneumonia (CAP) and older patients. Should SOAR (systolic blood pressure, oxygenation, age and respiratory rate) criteria be used in older people? A compilation study of two prospective cohorts

PHYO K. MYINT<sup>1,2,3</sup>, AJAY V. KAMATH<sup>4</sup>, SARAH L. VOWLER<sup>5</sup>, DAVID N. MAISEY<sup>1</sup>, BRIAN D. W. HARRISON<sup>2,4</sup>

<sup>1</sup>Department of Medicine for the Elderly, Norfolk and Norwich University Hospital, Colney Lane, Norwich NR4 7UY, UK

<sup>2</sup>School of Medicine, Health Policy and Practice, University of East Anglia, Norwich NR4 7TJ, UK

<sup>3</sup>Clinical Gerontology Unit, Department of Public Health and Primary Care, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK

<sup>4</sup>Department of Respiratory Medicine, Norfolk and Norwich University Hospital, Colney Lane, Norwich NR4 7UY, UK

<sup>5</sup>Centre for Applied Medical Statistics, Department of Public Health and Primary Care, University of Cambridge, Forvie Site, Robinson Way, Cambridge CB2 2SR, UK

Address correspondence to: P. K. Myint, Clinical Gerontology Unit, Level 2 F&G Block, Box-251, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK. Tel: (+44) 1223 217292; Fax: (+44) 1223 336928 Email: Pkyawmyint@aol.com

## Abstract

**Objectives:** to assess the usefulness of the British Thoracic Society guidelines for severity assessment of community-acquired pneumonia (CAP) in predicting mortality and to explore alternative criteria which could be more useful in older patients.

**Design:** compilation study of two prospective observational cohorts.

**Setting and participants:** a university hospital in Norfolk, UK with a catchment population of 568,000. Subjects were 195 patients (median age = 77 years) who were included in two prospective studies of CAP.

**Main outcome measure:** all-cause mortality occurring within the 6 week follow-up.

**Results:** sensitivity, specificity, positive and negative predictive values for study outcome using CURB and CURB-65 were assessed in 189 patients, and CRB-65 in 192 patients out of a total of 195 patients. Our results were comparable with the original study by Lim *et al.* Although CURB-65 and CRB-65 included age criteria, in effect they did not materially improve the specificity in predicting high-risk patients in both studies. We found that oxygenation measured by ventilation perfusion mismatch ( $\text{PaO}_2:\text{FiO}_2$ ) was the best predictor of outcome in this slightly older cohort [odds ratio (OR) = 0.99 (0.98–0.99),  $P = 0.0001$ ]. We derived a new set of criteria; SOAR (systolic blood pressure, oxygenation, age and respiratory rate) based on our findings. Their sensitivity, specificity, positive and negative predictive values were 81.0% (58.1–94.6), 59.3% (49.6–68.4), 27.0% (16.6–39.7) and 94.4% (86.2–98.4), respectively, confirming their comparability with existing criteria.

**Conclusions:** our study confirms the usefulness of currently recommended severity rules for CAP in this older cohort. SOAR criteria may be useful as alternative criteria for a better identification of severe CAP in advanced age where both raised urea level above 7 mmol/l and confusion are common.

**Keywords:** BTS guidelines, community-acquired pneumonia (CAP), mortality, older people, elderly

## Introduction

Community-acquired pneumonia (CAP) is the most common reason for acute admission to hospital in the UK (50,000–83,000/annum) [1, 2]. The hospital mortality in patients whose pneumonia leads to cardiac arrest is up to 100% [3, 4]. Therefore, rapid identification and appropriate management of severe CAP is crucial [5, 6].

The British Thoracic Society (BTS) regularly updates its guidelines for CAP [7–9]. The most recent recommendation in its assessment was the CURB criteria {severe pneumonia = presence of  $\geq 2$  of [new confusion, urea  $> 7$  mmol/l, respiratory rate (RR)  $\geq 30$ /min and blood pressure (systolic blood pressure (systolic BP)  $< 90$  or diastolic blood pressure (diastolic BP)  $\leq 60$  mmHg]} and CURB-65 (addition of age  $\geq 65$  years, high risk being a score  $\geq 3$ ) described by Lim *et al.* [10]. These authors also suggested CRB-65 where the urea criterion was removed ( $\geq 2$  criteria = severe) [10].

Whilst the Pneumonia Severity Index (PSI) recommended by the American Thoracic Society (ATS) [11] is widely used in North America, it is difficult to apply in day-to-day practice as it involves measuring multiple parameters. On the other hand, both CURB and CURB-65 include confusion and raised urea ( $> 7$  mmol/l) in their severity criteria, which may be less useful in the elderly as both conditions are common in acutely unwell older people [12, 13].

In this study, we assessed the accuracies of CURB, CURB-65 and CRB-65 using combined data from two previously conducted prospective cohort studies of CAP. The current study had a higher proportion of older patients than previous studies as our second cohort included patients aged  $\geq 65$  years only. We attempted to identify the most and least useful clinical indicators of severity of CAP for predicting death in this series. As the ratio of arterial oxygen concentration to the concentration of oxygen in the inspired air ( $\text{PaO}_2:\text{FiO}_2$ ) is a well-recognised indicator of ventilation perfusion mismatch and since it is an important component of the modified ATS criteria [14, 15], we also assessed the relationship of this parameter to mortality from CAP. Based on the findings, we derived a new rule, which comprises systolic BP, oxygenation, age and RR (SOAR) and assessed its usefulness.

## Methods

We used combined data from two previously performed prospective observational studies of CAP in hospitalised patients in a UK centre serving a population of 568,000. Detailed methodologies of both studies have been reported previously [16, 17]. Briefly, the combination of clinical features of pneumonia and new chest X-ray shadow (segmental or lobar) were used as the entry criteria, and the second cohort only included patients  $\geq 65$  years.

In the current study, three separate analyses were performed, one analysis for each purpose: (1) to assess the validity of currently recommended criteria; (2) to identify the most and the least significant variables in the current

rules in predicting death from CAP in this older cohort; and (3) to examine the value of ventilation perfusion mismatch using  $\text{PaO}_2:\text{FiO}_2$  for predicting mortality.

In the first analysis, we examined the accuracies of CURB, CURB-65 and CRB-65 rules in predicting death as described by Lim and colleagues [10]. Any patients with missing values for a criterion were excluded if it was not possible to tell from their remaining scores on which side of the cut point they fell.

In the second analysis, we identified the most and the least significant variables in CURB-65 in predicting death from CAP as it includes all the variables recommended in all three existing criteria. The first step was univariate logistic regression analysis for mortality outcome using the CURB-65 criteria (as continuous variables except confusion). Any predictor variable with  $P < 0.10$  was included in the second step, which involved backward stepwise multiple logistic regression with mortality as the outcome.

In the third analysis, we included all subjects who also had data on arterial blood gases (ABG) on admission and the concentration of oxygen they were receiving at the time of taking the ABG sample. Arterial oxygen concentration in mmHg [ $\text{PaO}_2$  in (kPa)  $\times 7.5006$  mmHg] and the ratio of  $\text{PaO}_2$  and  $\text{FiO}_2$  ( $\text{PaO}_2:\text{FiO}_2$ ,  $\text{PaO}_2$  in mmHg divided by  $\text{FiO}_2$  in decimal point) were added in the same two-step approach as in the second analysis.

From these analyses, as advancing age (A), high RR (R), low systolic BP (S) and poor oxygenation ( $\text{PaO}_2:\text{FiO}_2$ ) (O) were found to be significantly associated with death from CAP, we derived a new index (SOAR) using these criteria and assessed its usefulness in the fourth analysis ( $n = 134$ ). To examine the effect size, we performed multiple regression analyses for quartile categories of systolic BP, oxygenation, age and RR, which appeared to be the most significant predictors of mortality in multivariate analysis as continuous variables. In each analysis, quartile categorical data of the criterion of interest were entered simultaneously with other variables (as continuous) measures. We then defined severe pneumonia as the presence of  $\geq 2$  criteria out of four. A score of 1 was given for presence of each of the following (dichotomised variables): systolic BP  $< 90$  mmHg,  $\text{PaO}_2:\text{FiO}_2 < 250$ , age  $\geq 65$  years and RR  $\geq 30$ /min.

Statistical analyses were performed using SPSS for Windows versions 11.5, 12.0 and 13.0 (SPSS Inc., Chicago, IL). Sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV), odds ratios (OR) and their 95% confidence intervals (CIs) are reported as appropriate.

## Results

### Accuracies of the criteria (CURB, CURB-65 and CRB-65)

There were a total of 195 patients included in this analysis, of whom 28 died. Their ages ranged from 17 to 96 years

(median = 75). There were 111 males (56.9%). Excluding those with missing values left 189 patients (27 deaths) for validation of CURB and CURB-65, and 192 patients for CRB-65. Their sensitivities, specificities, PPV and NPV, and corresponding 95% (Clopper–Pearson) CIs for all three criteria in predicting death from CAP are presented in comparison with results from the study by Lim *et al.* [10] in Table 1.

**Value of individual variables in predicting death from CAP (Table 2)**

The 189 patients who had complete data on CURB-65 criteria were included in the second analysis. Univariate analysis showed that all the variables analysed were significantly associated with mortality from CAP. As a continuous variable, higher RR (OR =1.08; 95% CI = 1.02–1.14; *P* = 0.005) was the most significant variable and it remained significant

**Table 1.** Comparison of sensitivity, specificity, positive and negative predictive values for death in severe CAP for CURB, CURB-65 and CRB-65 rules in the current study with the validation study by Lim *et al.* [10]

Rule Score	Current study % (95% CI)	Lim <i>et al.</i> % (95% CI)
Median age-years ( <i>n</i> )	77 (195)	64.1 (1,068)
Centre	Single centre (two cohorts)	Three centres
Follow-up	42 days	30 days
CURB ≥2	<i>n</i> = 189	<i>n</i> = 214
Sensitivity	81.5 (61.9, 93.7)	75.0 (68.0–80.0)
Specificity	61.1 (53.2–68.7)	70.1(67.0–79.0)
PPV	25.9 (17.0–36.5)	20.5
NPV	95.2 (89.1–98.4)	96.5
CURB-65 ≥3	<i>n</i> = 189	<i>n</i> = 214
Sensitivity	81.5 (61.9–93.7)	75.0
Specificity	64.2 (56.3–71.6)	74.7
PPV	27.5 (18.1–38.6)	23.4
NPV	95.4 (89.6, 98.5)	96.7
CRB-65 ≥2	<i>n</i> = 192	<i>n</i> = 214
Sensitivity	85.2 (66.3–95.8)	80.0
Specificity	57.0 (49.0–64.6)	61.3
PPV	24.5 (16.2–34.4)	17.6
NPV	95.9 (89.9–98.9)	96.7

in multivariate analysis (OR 1.11; 95% CI = 1.04–1.19; *P* = 0.003). Age (1.09; 1.03–1.15; *P* = 0.003), confusion (2.95; 1.07–8.12; *P* = 0.04) and diastolic BP (0.96; 0.92–0.99; *P* = 0.008; reference = lower diastolic BP) were also significant, but urea (1.06; 1.00–1.12; *P* = 0.06) was only of borderline significance in the multivariate analysis; but this model was of poor fit so should not be used for prediction.

**Ventilation perfusion mismatch (PaO<sub>2</sub>:FiO<sub>2</sub>) in predicting mortality outcome (Table 2)**

One hundred and thirty patients (20 deaths) were eligible to be included in this analysis. Univariate analysis showed significant associations for mortality with age, confusion, BP and urea criteria. However, higher RR (1.06; 1.00–1.12; *P* = 0.07) achieved only borderline significance, and lower PaO<sub>2</sub> (0.98; 0.96–1.01; *P* = 0.19) showed no evidence of an association in the univariate analysis. Univariately, an increase in PaO<sub>2</sub>:FiO<sub>2</sub> by 1 unit was most significantly associated with a reduction in mortality (0.99; 0.98–0.99; *P* = 0.0001) followed by BP [systolic (0.97; 0.95–0.99) and diastolic (0.94; 0.91–0.98); *P* = 0.004 for both, reference = lower BP].

Multivariate analysis showed that higher PaO<sub>2</sub>:FiO<sub>2</sub> by 1 unit was the variable most significantly associated with a reduction in mortality (0.99; 0.98–0.99; *P* = 0.001). Both advancing age by 1 year (1.08; 1.02–1.14; *P* = 0.02) and systolic BP by 1 mmHg (0.97; 0.95–0.99; *P* = 0.01, reference = lower BP) remained significant in predicting death in multivariate analysis. However, confusion (binary) and urea (continuous) no longer showed evidence of an association with mortality.

**Subgroup analysis on usefulness of SOAR criteria**

A total of 134 patients were included in this analysis. Consistent with the multivariate analyses using a 1 unit increase, using quartile cut-off points also showed higher likelihood of death for those who are in the bottom quartiles of systolic BP (OR 9.91; 1.62–60.77) and oxygenation (3.55; 0.80–15.76), and lower likelihood of death for those in the bottom quartile of age (0.04; 0.003–0.47) and RR (0.16; 0.03–0.98) compared with top quartiles in this cohort. The multivariate

**Table 2.** Sample characteristics: median (range)/number (%) in those who died and those who were alive for the second and third analyses

Variable	Analysis 2 ( <i>n</i> = 189)		Analysis 3 ( <i>n</i> = 130)	
	Alive ( <i>n</i> = 162)	Dead ( <i>n</i> = 27)	Alive ( <i>n</i> = 110)	Dead ( <i>n</i> = 20)
Age (years)	74 (17–96)	83 (55–95)	72.5 (17.0–96.0)	81 (55–93)
Male	89 (54.9%)	17 (63%)	68 (61.8%)	13 (65%)
Confusion	33 (20.4%)	13 (48.1%)	19 (17.3%)	9 (45%)
Urea (mmol/l)	7.7 (1.0–58.5)	14.5 (6.3–52.9)	7.8 (1.0–58.5)	14.7 (6.3–52.9)
RR (rate/min)	24.0 (12.0–60.0)	28.0 (16.0–44.0)	24.0 (12.0–60.0)	29.0 (16.0–40.0)
Systolic BP (mmHg)	131.5 (74.0–216.0)	109.0 (80.0–180.0)	134.0 (74.0–216.0)	109.5 (80.0–172.0)
Diastolic BP (mmHg)	74.0 (40.0–135.0)	65.0 (37.0–100.0)	75.0 (40.0–135.0)	63.0 (40.0–90.0)
FiO <sub>2</sub> (%)	–	–	21.0 (21.0–100.0)	26.0 (21.0–100.0)
PaO <sub>2</sub> (mmHg)	–	–	63.0 (29.2–288.0)	58.7 (36.7–105.0)
PaO <sub>2</sub> :FiO <sub>2</sub>	–	–	265.7 (74.9–462.5)	179.2 (44.7–341.1)

Median (range) values were presented unless otherwise specified.

models, however, were of poor fit and therefore should not be used for prediction.

The number of patients who satisfied the SOAR criteria using dichotomised values were 18 (13.4%), 53 (39.6%), 37 (27.6%), 23 (17.2%) and three (2.2%) for score values of 0, 1, 2, 3 and 4, respectively. There were 21 deaths out of 134 patients. No deaths occurred when the score was 0 (0% mortality), and there were four deaths in those who scored 1 (7.5%), seven deaths each for score 2 (19%) and 3 (30%), and all three patients who scored 4 died (100%). The corresponding data for CURB-65 (score 0–5) were 0, 2.6, 8.2, 21.1, 35 and 100%, and for CRB-65 (score 0–4) were 0, 5.6, 18.8, 33.3 and 75% respectively, confirming the comparability of the new criteria with the BTS criteria.

The sensitivity, specificity, PPV and NPV values for predicting deaths within 6 weeks for each score for SOAR are presented in Table 3. Taking a cut-point of  $\geq 2$ , sensitivity = 81.0% (95% CI 58.1–94.6), specificity = 59.3% (49.6–68.4), PPV = 27.0% (16.6–39.7) and NPV = 94.4% (86.2–98.4) were observed in this slightly older cohort for severe pneumonia in predicting death from CAP identified by this rule.

## Discussion

Our study confirms the usefulness of the CURB, CURB-65 and CRB-65 in predicting mortality from CAP in this slightly older cohort compared with previous studies. The PPV values are low for all three rules in both the reported study and that of Lim *et al.* [10], which may be related to the prevalence of severe CAP in the populations studied. However, the NPV values are high, providing a useful, though not very discriminative, guide for mortality outcome.

As advancing age has been consistently shown to be associated with higher mortality from CAP in all studies to date, including age to assess CAP would seem to be appropriate. However, adding an age cut-off of 65 years or using it to replace the urea criterion does nothing to improve the sensitivity, specificity, PPV or NPV for patients admitted to hospital. Furthermore, in the elderly, urea  $>7$  mmol/l may be of borderline significance due to multiple confounding factors. The CRB-65 is marginally more sensitive but less specific compared with CURB and CURB-65. Its PPV and NPV, however, are comparable with those of CURB and CURB-65. Confusion is also common in acutely unwell older people and its inclusion might therefore be expected to lower the specificity in all three recommended criteria.

Since the original BTS study [18] emphasised the most important predictors for mortality, we addressed this in our study by a two-step approach. Increasing urea level lost its

significance in the third analysis. This suggests that it may not be a good measure in predicting severity of CAP, especially in older people (median age = 77 years in this study). Alternatively it could result from too small a sample size. Previous studies which found urea  $>7$  mmol/l to be an independent predictor of mortality included larger numbers of younger patients [18, 19]. The urea level may be confounded by multiple factors such as dehydration, hypertension and diabetes, the prevalence of which are high in an older population [20]. This could be examined by setting a higher cut-off point for urea in the elderly in future.

Higher RR was the most significant continuous variable in the second analysis, but it lost its significance in the third analysis probably due to the smaller sample size. The third analysis looked at associations with mortality in CAP after adding two more variables to existing criteria. The rationale was that the patients with more severe pneumonia would be more hypoxic (lower PaO<sub>2</sub>) and the PaO<sub>2</sub>:FiO<sub>2</sub> will be a good guide to the degree of ventilation perfusion mismatch reflecting severity of pneumonia. Both low PaO<sub>2</sub> ( $<60$  mmHg) and low PaO<sub>2</sub>:FiO<sub>2</sub> ( $<250$ ) are components of ATS guidelines indicating severity [11, 14, 15]. However, PaO<sub>2</sub> and FiO<sub>2</sub> were not recorded in all the patients in our cohorts, which limited our sample size to 130 patients.

Neill *et al.* [21] also looked at adding PaO<sub>2</sub>  $<7.3$  kPa (dichotomised) to the severity rule in CAP and found that the sensitivity was reduced but the specificity improved. In their study, the ‘presence of a positive rule’, i.e. satisfying  $\geq 2$  criteria of the modified BTS rule and a PaO<sub>2</sub>  $<7.3$  kPa, had a specificity of 95%. Our study showed no evidence of an association between lower PaO<sub>2</sub> (continuous) and mortality. We also found that the PaO<sub>2</sub>:FiO<sub>2</sub> variable was most significantly associated with CAP mortality. This contradicts the findings from a retrospective study with a similar number of patients [2].

These inconsistent results from different studies may be due to the varying nature (retrospective versus prospective) and methodological issues. The latter is apparent when we re-analysed the data using quartile cut-off points. Nevertheless, ventilation perfusion mismatch measured by PaO<sub>2</sub>:FiO<sub>2</sub> will be influenced by co-existing cardio-respiratory conditions such as chronic obstructive airways diseases or left ventricular failure. This could make it more useful as a reliable indicator of acute hypoxic insult with the advantage of taking into account pre-existing conditions. Using it as a criterion instead of urea or confusion in severity assessment of CAP in older people could be potentially useful.

To assess this, we derived a new rule, SOAR (systolic blood pressure, oxygenation, age and respiratory rate), based on our results and found that the new criteria are comparable

**Table 3.** Sensitivity, specificity, positive and negative predictive values and corresponding 95% confidence interval for new criteria SOAR (systolic blood pressure, oxygenation, age and respiratory rate) in 134 patients in predicting mortality

Score	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
$\geq 0$	100.0 (83.9–100.0)	0.0 (0.0–3.2)	15.7 (10.0–23.0)	NA
$\geq 1$	100.0 (83.9–100.0)	15.9 (9.7–24.0)	18.1 (11.6–26.3)	100.0 (81.5–100.0)
$\geq 2$	<b>81.0 (58.1–94.6)</b>	<b>59.3 (49.6–68.4)</b>	<b>27.0 (16.6–39.7)</b>	<b>94.4 (86.2–98.4)</b>
$\geq 3$	47.6 (25.7–70.2)	85.8 (78.0, 91.7)	38.5 (20.2–59.4)	89.8 (82.5–94.8)
$\geq 4$	14.3 (3.0–36.3)	100.0 (96.8–100.0)	100.0 (29.2–100.0)	86.3 (79.2–91.6)

with existing criteria. The main potential advantage of SOAR in older people is the exclusion of the urea and confusion criteria from the severity index. However, disappointingly, it did not improve identification of death from CAP within 6 weeks compared with the currently recommended rules in the BTS guidelines [9]. This may be explained by some of the limitations of the current study. We combined two historical cohorts, and changes, e.g. management of CAP, may have altered mortality over that time period. Furthermore, missing data have reduced the number of cases available for inclusion in SOAR criteria, and this could affect the findings.

Our results confirm the generalisability of the currently recommended BTS criteria in assessing CAP severity. Ventilation perfusion mismatch measured by PaO<sub>2</sub>:FiO<sub>2</sub> is potentially valuable. However, there are practical limitations. Blood gases are not essential in patients with CAP whose arterial oxygen saturation measured by pulse oximetry is >93% [22]. Furthermore, inspired oxygen is not always recorded as well as the PaO<sub>2</sub>. Nevertheless, larger studies involving older patients are needed to test the validity of these criteria. Also studies using a higher cut-point for urea and/or age in the elderly population may provide a better rule for older people.

In summary, current BTS guidelines for severity assessment of CAP are appropriate and applicable for older people in general. In this study, we assessed a new rule (SOAR), which is as sensitive and specific as current BTS-recommended rules. Due to the high prevalence of raised urea and confusion in acutely unwell older people, it is possible to develop a better CAP severity rule in this age group. It is debateable whether we should look for a better rule for older people or be happy with 'one size for all' current BTS criteria.

### Key points

- Raised urea >7 mmol/l, confusion and low diastolic BP included in current BTS guidelines for severity assessment of CAP are common in unwell older patients.
- Oxygenation measured by ventilation perfusion mismatch (PaO<sub>2</sub>:FiO<sub>2</sub>) was found to be the most significant predictor of death within 6 weeks in this series, which included a higher number of older people compared with previous studies on CAP.
- Using systolic BP (<90 mmHg), oxygenation (PaO<sub>2</sub>:FiO<sub>2</sub> <250), age (≥65 years) and respiratory rate (≥30/min) (SOAR) criteria derived in this cohort appeared to be as useful as CURB, CURB-65 and CRB-65, and it may be potentially useful in situation where a pre-existing high urea level or background confusion is present.
- A better rule for severity assessment of CAP with better specificity for older population is required.

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# Cardiopulmonary responses to eccentric and concentric resistance exercise in older adults

ALBERTO F. VALLEJO, EDWARD T. SCHROEDER, LING ZHENG, NICOLE E. JENSKY, FRED R. SATTLER

University of Southern California, Biokinesiology, Los Angeles, CA, USA

Address correspondence to: A. F. Vallejo. Email: [avallejo@usc.edu](mailto:avallejo@usc.edu)

## Abstract

**Background:** in older ambulatory persons, exercise strategies that are expected to generate beneficial muscle adaptations with low cardiopulmonary demands are needed.

**Objective:** we hypothesised that eccentric resistance exercise would be less demanding on the cardiovascular and pulmonary systems than bouts of concentric resistance exercise.

**Design:** the effects of eccentric and concentric resistance exercise were compared during leg squats at a submaximal intensity known to increase muscle mass.

**Subjects:** 19 older persons (15 women/four men, age  $65 \pm 4$  years) and 19 young reference controls (10 women/nine men; age  $25 \pm 2$  years) were enrolled.

**Methods:** participants completed eccentric-only and concentric-only exercise bouts 5–7 days apart.

**Results:** cardiovascular and pulmonary measures were collected from subjects during bouts consisting of three sequential sets of 10 repetitions at 65% of their voluntary concentric 1-repetition maximum force ( $68 \pm 16$  kg for older participants and  $94 \pm 36$  kg for young participants). Peak heart rate ( $119 \pm 10$  versus  $155 \pm 16$  b.p.m.), systolic blood pressure ( $129 \pm 18$  versus  $167 \pm 14$  mmHg), cardiac index ( $7.8 \pm 2.0$  versus  $9.2 \pm 1.5$  l/min/m<sup>2</sup>) and expired ventilation ( $20.5 \pm 5.7$  versus  $29.8 \pm 9.1$  l/min) were significantly lower during eccentric than during concentric bouts in the older subjects, respectively ( $P < 0.001$  for all comparisons). Similarly, peak heart rate, systolic blood pressure, cardiac index and expired ventilation were significantly lower during eccentric bouts in the young control subjects.

**Conclusions:** eccentric resistance exercise produced less cardiopulmonary demands and may be better suited for older persons with low exercise tolerance and at risk of adverse cardiopulmonary events.

**Keywords:** resistance exercise, cardiopulmonary demands, leg squats, elderly

## Introduction

Progressive resistance exercise is an effective means to increase skeletal muscle strength in older persons even into advanced age. Indeed, Fiatarone *et al.* showed that 3- to 4-fold increases in skeletal muscle strength could be achieved with resistance exercise in selected octogenarians and nonagenarians [1, 2]. Of importance, such improve-

ments translated to enhanced skeletal muscle power [3], which has been correlated with improved gait acceleration, stair climbing speed, improved get up and go times, and other functional measures (stair descent time, Berg balance test) in older persons [4, 5].

However, the metabolic demands and safety of this type of strenuous exercise for a broader population of community dwelling older persons with age-related cardiopulmonary