

# Association between statin medication use and improved outcomes during inpatient rehabilitation in older people

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## Abstract

**Background:** statin drugs may induce skeletal myopathy, but might also have the potential to improve rehabilitation outcomes by improving sarcopenia or by preventing intercurrent illness. We examined the association between statin use and functional outcomes in the rehabilitation of older people.

**Methods:** retrospective cohort study using routinely collected clinical data. Admissions to Royal Victoria Hospital, Dundee for inpatient rehabilitation over a 10-year period were identified. Data were available regarding demographics, statin therapy, antiplatelet therapy, admission and discharge Barthel scores, length of stay and comorbid disease. Multivariate analyses were performed to examine the difference between admission and discharge Barthel score in patients taking statins compared with those not taking statins.

**Results:** a total of 3,422 patients were included. Mean age was 81.4 years; 40% were male. Baseline Barthel scores were similar in the statin/non-statin groups, respectively (10.4/20 versus 10.3/20,  $P = 0.57$ ). Improvement in the Barthel score between admission and discharge was greater in the statin than non-statin group (3.59 versus 4.30 points,  $P < 0.001$ ) after adjustment for age, sex, baseline Barthel score and comorbid disease.

**Conclusion:** statin use was associated with improved Barthel scores on discharge from rehabilitation. This gain could contribute to improved outcomes as part of the rehabilitation package and requires further prospective investigation.

**Keywords:** *statins, rehabilitation, functional gains, elderly*

## Introduction

Statin (hydroxymethylglutaryl Co A reductase inhibitors) are commonly used to reduce serum cholesterol levels. They are highly effective at reducing the risk of cardiovascular events, in particular ischaemic heart disease and strokes, even in older people [1].

Although the risk of myalgic side effects observed in trials is very low, concern exists that such side effects are somewhat commoner in clinical practice [2], and such concerns may lead to clinicians discontinuing statin therapy. Such concerns are particularly important in rehabilitation settings, where removing potential barriers to successful rehabilitation is a key focus of medical input. Conversely, there is growing evidence linking cardiovascular disease

with disability in old age; up to half of the decline in physical function observed in older patients may be attributable to vascular disease [3]. Interventions to treat cardiovascular disease in older people may have beneficial effects on avoiding disability—not only via avoiding vascular events and their sequelae (e.g. stroke, heart failure), but by direct improvement of impaired skeletal muscle function seen in age-related sarcopenia [4], as has been shown with angiotensin-converting enzyme inhibitors [5].

In addition, statin use has been associated with improved outcomes in sepsis [6], particularly pneumonia [7]; conditions that frequently hamper the rehabilitative process. This may be due to anti-inflammatory actions of statins [8]; interestingly, proinflammatory cytokines have been implicated in the pathogenesis of sarcopenia,

providing another possible pathway by which statins might influence muscle function [9].

A recent systematic review of randomised trials of statin therapy was unable to ascertain whether statin therapy improved or worsened exercise capacity in younger patients [10]. Given the uncertainty around possible beneficial or deleterious effects of statin therapy on patients undergoing rehabilitation, we examined a large cohort of older rehabilitation patients to test whether statin use was associated with better or worse outcomes during the rehabilitation period.

**Methods**

We analysed data from a large, prospectively collected database containing details of all patients admitted to our Medicine for the Elderly rehabilitation unit between 1 January 1999 and 31 December 2008. The cohort has been described in detail previously [11]. Data were collected as part of routine clinical care and were analysed by the clinical team caring for the patients. Data on admission diagnoses, discharge medication, admission and discharge Barthel score, age, sex, place of admission and place of discharge were routinely collected. Patients were admitted for inpatient rehabilitation following stroke, fractured neck of femur or general medical and surgical illnesses. Patients underwent rehabilitation in a dedicated rehabilitation ward, with a full multidisciplinary team led by a geriatrician.

Data were utilised on age, sex, comorbid disease, statin therapy on discharge, antiplatelet therapy (as a proxy measure for vascular disease), admission and discharge 20-point Barthel scores [12], number of medications, length of stay and discharge destination. To ensure that the discharge prescription of statins reflected exposure to statins during the rehabilitation admission, prescription of statins on admission was checked in a sample of casenotes.

Data analysis was undertaken using SPSS version 17 (SPSS, Chicago, IL, USA). Patients who died during admission were excluded from the analysis, as were those without both admission and discharge Barthel scores. Baseline data were compared using Student’s *t*-test for normally distributed continuous variables, Mann–Whitney *U* test for non-normally distributed continuous variables, and Pearson’s Chi-squared test for categorical variables. Multivariate regression analysis was used to examine the association between statin use and improvement in the Barthel score between admission and discharge. Binary logistic regression analysis was used to examine associations with place of discharge. Length of stay was log-transformed before inclusion in regression analyses. Analyses were adjusted for age, sex, admission Barthel scores, total number of medications, antiplatelet use and comorbid disease.

**Results**

Of the 4,449 patients in the complete data set, 409 died during admission and were excluded. A total of 3,422 patients had Barthel scores on admission and discharge and were included in the analysis. Details are given in Table 1. Statin use at admission was checked in 128 sets of casenotes, and was consistent with discharge in 118/128 (92%) of cases.

After adjustment in multivariate analysis, statin use was associated with a greater improvement in the Barthel score during admission; 4.3 versus 3.7 points (difference: 0.6; 95% CI: 0.3–0.9, *P* < 0.001). Length of stay was not significantly different even after adjustment (1.0 days longer in the statin group; 95% CI –1.0 to 3.1 days, *P* = 0.33). The risk of discharge to a destination other than the patients own home was lower in those receiving statins (relative risk 0.65, 95% CI: 0.54–0.81, *P* < 0.001), but adjustment attenuated the relationship (adjusted relative risk 0.84; 95% CI: 0.651.09, *P* = 0.19). The association between statin use and improvement in the Barthel score was more evident for those admitted with a diagnosis of stroke (4.3 versus 3.5 points, difference 0.8; 95% CI: –0.2–1.8; *P* = 0.13) than with fracture as an admission diagnosis (3.6 versus 3.7 points, difference –0.1; 95% CI: –1.4 to 1.2, *P* = 0.87)

**Discussion**

Our results suggest that statin use is associated with greater improvement in function as measured by the Barthel score during inpatient rehabilitation in some older patients with a variety of medical and surgical conditions. These results do not support a deleterious effect on rehabilitation for the vast majority of those receiving such medications. Although statins are associated with multiple adverse side effects, including myalgia, myositis and occasionally rhabdomyolysis, a recent review concluded that was insufficient data to determine whether statins had a significant effect on muscle strength or endurance [10]. While a one-point improvement

**Table 1.** Characteristics of patients receiving and not receiving statins

	On statin ( <i>n</i> = 690)	Not on statin ( <i>n</i> = 2,732)	<i>P</i> -value
Mean age (years) (SD)	79 (7)	82 (8)	<0.001
Male sex (%)	322 (46.7)	1,044 (38.2)	<0.001
Mean admission Barthel score (SD)	10 (4)	10 (4)	0.57
Mean discharge Barthel score (SD)	15 (4)	14 (5)	<0.001
Median length of stay (days) (IQR)	36 (49)	36 (46)	0.65
Mean number of medications at discharge (SD)	9 (4)	7 (3)	<0.001

in the Barthel score is not in itself large enough to be of clinical significance, a combination of similar simple interventions, each with this degree of benefit, could potentially produce a clinically important augmentation of rehabilitation outcomes.

Patients receiving statins had similar functional ability on admission to rehabilitation as those not receiving statins. It is therefore unlikely that the observed association was solely due to those receiving statins being 'fitter' than those who did not receive statins, although an unmeasured component of function or comorbidity may contribute to the observed findings.

Our data were examined retrospectively and were not collected with this study aim in mind. The results should therefore be interpreted with caution; prospective studies examining statin prescription during admission (rather than at discharge as a proxy for use during admission) are needed, and more detailed data regarding the mechanism of action in this patient group needs to be collected to provide evidence of biological plausibility. Any beneficial effect of statins on function in rehabilitation could be due either to direct effects on skeletal muscle function, perhaps via an improvement in inflammation or vascular health, or could be due to a reduction in events (e.g. infections) that interrupt the rehabilitation process. Our study is unable to dissect out which of these mechanisms might be responsible for the observed association; prospective studies in rehabilitation cohorts, and ultimately, randomised controlled trials of statin therapy in rehabilitation will be required to examine these questions further.

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### Key points

- Statins commonly used in elderly population.
  - Statins are associated with greater functional gains in elderly patients in rehabilitation settings.
  - A prospective study is required.
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