# Changes in muscle mass during acute short-term hospitalization of elderly patients

*A mini-review*

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**Abstract**

*Introduction:* It has long been a presumption that hospitalization is associated with a loss of muscle mass in elderly patients. However, only a handful of studies have directly measured whether such a loss actually occurs. This mini-review highlights some of the most recent research related to changes in muscle mass during acute short-term hospitalization of elderly patients.

*Discussion:* Despite a high prevalence of physical inactivity during hospitalization, there is a lack of research measuring changes for habitual levels. The effect of inflammation on muscle mass in elderly patients is still uncertain. Nutritional supplementation beyond what is currently being prescribed in hospitals may have additional benefits on muscle mass. Dehydration prior to hospital admission may obscure true changes in muscle mass when using current state-of-the-art measures due to in-hospital rehydration.

*Concluding remarks:* The current literature does not support the notion of in-hospital loss of muscle mass in acutely admitted elderly patients; however, there is a need for more precise measures of muscle mass that are able to account for fluctuations in hydration status. Moreover, future studies assessing changes in muscle mass should also measure changes in physical activity levels, inflammation status and nutritional intake during acute hospitalization.

**Key words:** Disuse; Atrophy; Elderly; Inflammation; Hydration status; Protein intake



## 1. Introduction

There are several physiological changes related to increasing age in humans, one of which is the progressive loss of skeletal muscle mass [1]. This loss, which has been termed *sarcopenia*, is multifactorial in nature and its exact aetiology is yet to be established. A large body of research has been put into understanding this phenomenon, mostly focusing on factors such as physical inactivity, poor nutrition, inflammatory processes and endocrine changes. Interestingly, some researchers have suggested that repeated hospitalizations in elderly may accelerate sarcopenia [2]. It has long been a presumption that hospitalization is associated with a loss of muscle mass in elderly patients. However, only a handful of studies have directly measured whether such a loss actually occurs during acute hospitalization. A recent meta-analysis investigated changes in muscle mass in older patients during either elective or acute admission [3]. The electively admitted patients showed a decrease in muscle mass [standardized mean difference (95% confidence interval): -0.44 (-0.61, -0.27)], whereas the acutely admitted showed no change [-0.25 (-0.58, 0.09)]. Although only two studies were used in the analysis of acutely admitted patients, other studies that were not included show similar results [4,5]. Several factors may explain these findings. This mini-review highlights some of the most recent studies in the field of geriatrics with a focus on changes in muscle mass during acute short-term hospitalization of elderly patients. The main putative mechanisms explaining these findings are discussed and a hypothetical model illustrating changes in muscle mass is presented (Figure 1). Lastly, guidelines for future studies seeking to disentangle some of the causes that may contribute to hospital-associated loss of muscle mass are suggested.

**2. Physical inactivity**

Reduced levels of physical activity is thought to be the main cause of hospital-associated deconditioning and muscle atrophy [2]. This conjecture is based on studies that reduces muscle load by interventions such as bed rest [6], knee bracing [7], or reduced activity [8]; all of whom show significant muscle atrophy and strength deterioration in elderly. A 6.3% loss of leg muscle mass has been shown after ten days of bed rest in otherwise healthy elderly [6]. Similarly, reductions of 4.1% and 3.9% have been shown after seven [9] and five [10] days, respectively. In less extreme models, 14 days of either knee bracing [7] or reduced activity [8] has shown smaller, yet significant losses of muscle mass in elderly. Although hospitalized elderly patients may not necessarily be subjected to strict bed rest, previous studies have found very low levels of activity during short-term hospital stay [11,12]. Thus, it seems obvious that short-term hospitalization may result in a significant loss of muscle mass in elderly patients. However, despite a high prevalence of physical inactivity during hospitalization there is a lack of research measuring changes for habitual levels. Put in other words, activity may in fact be low during a hospital stay, but whether a reduction in activity has occurred is not clear. Old individuals with chronic illnesses might have habitual activity levels that fall far below those seen in healthy elderly [8]. It is nevertheless likely that both the physical and mental restraints experienced during illness are capable of confining physical activity to a minimum during hospitalization. Interestingly, a study of healthy elderly who were confined to ten days of bed rest found that physical activity was decreased following the intervention when compared to habitual levels [13]. Such repercussive effects of disuse may not only have short-term consequences, but could potentially cause long-term problems for already frail elderly. These findings are however yet to be validated in elderly patients.

### 3. Inflammation

Elderly patients hospitalized with an acute illness typically display signs of inflammation at time of admission [14]. The systemic level of C-reactive protein (CRP) is the most commonly used biomarker of inflammation [15]. In fact, not only does the admission level of CRP predict a prolonged length of hospital stay [16], but also earlier re-admission in elderly patients [17]. Furthermore, previous studies have found negative associations between CRP and muscle mass [18], lung function [19], and also the recovery of physical function and muscle strength in elderly patients [14,20]. Attenuated resistance training-induced hypertrophy has also been found in elderly patients with high degree of inflammation [5]. From this it would seem that muscle tissue, whether subjected to training or disuse, is negatively affected by high levels of systemic inflammation. The latter has however not yet been confirmed in elderly patients. High-level systemic inflammation is transient in nature and usually peaks within few days, thereby exerting potentially negative effects during the initial days of hospital stay. However, a recent study found that persistent inflammation during hospitalization seemed to counteract recovery of muscle strength [21], which suggests that the length of exposure to inflammation is of importance. Contrary, there was no muscle-preserving effect of treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) during two weeks of immobilization and six weeks of retraining in elderly with low-grade inflammation [22]. This could possibly be due to the already low levels of inflammation in these subjects (e.g. CRP ~1 $mg \cdot L^{-1}$), which were markedly lower than the typical levels found in elderly patients [5,14]. However, no changes in muscle mass could be detected in neither the control group nor the NSAID-treated group in a randomized controlled trial on hospitalized elderly patients [4]. Given the available literature, the effect of inflammation on muscle mass in elderly patients is still uncertain and large-scale trials are needed to establish whether a negative causal link actually exists in this cohort.

**4. Nutrition**

The term *anabolic resistance* has been used to describe the blunted protein synthetic response to dietary protein intake in elderly [23]. This has led some to suggest that the recommended dietary allowance for protein (0.8 g protein·kg·$d^{-1}$) should be increased for elderly [24]. Notably, it has been estimated that a mean protein intake of ~1.1 g protein·kg·$d^{-1}$ is necessary to reach a neutral nitrogen balance during short-term hospitalization of elderly [25]. Moreover, long-term (~ 24 d) patients with a high protein intake are more likely to increase physical function during hospitalization [20]. In a recent study, elderly patients were given in-hospital protein supplementation (~ 14 g·$d^{-1}$) in addition to 12 weeks of resistance training following discharge [26]. In fact, during the first 24-h of admission, protein intake was 0.74 g·$kg^{-1}$ and 1.56 g·$kg^{-1}$ in the intervention- and control group, respectively. Surprisingly, this did not result in any changes in muscle mass from admission to the three-month follow up assessment, despite significant difference in both total protein- and energy intake between intervention- and control group. However, any in-hospital loss of muscle mass may have been missed due to the re-assessments being made three-months after discharge. Yet, supplementation with 15 g of essential amino acids three times per day during ten days of bed rest resulted in a 6.3% loss of leg muscle mass in healthy elderly men [27], which questions whether nutritional interventions alone are adequate in preventing the negative effects of disuse on muscle mass in elderly. Nevertheless, it would seem as though nutritional intake is less than adequate for many elderly patients [25]. Most likely, undernourished patients may benefit from nutritional support, whereas does with sufficient protein intake may not. Further research is warranted to establish whether this has a clinically significant impact on muscle mass during short-term hospitalization.

## 5. Research methodology

It is vital to recognise that research methodology has a large impact on scientific findings. This fact is especially important with regard to the tools that are currently being used to measure changes in muscle mass. Those most commonly used include ultrasound, magnetic resonance imaging, computed tomography, dual energy x-ray absorptiometry (DEXA), and bioimpedance analysis [28]. These do however have a major limitation as they are all influenced by changes in hydration status. Given that elderly patients more often than not are dehydrated at hospital admission [29], true changes in muscle mass may be missed when using methods such as DEXA [30], which is a particularly worrisome default situation when patients are rehydrated during hospital stay. Theoretically, this means that in the patients where in-hospital atrophy actually occurs, true changes in muscle mass will be disguised as an unaltered or even an increase in muscle mass. In a recent study using DEXA, no changes in whole-body muscle mass were found during acute short-term (~7 d) hospitalization of elderly patients [5]. However, because changes in hydration status could not be accounted for, it is possible that a loss of muscle mass was missed. Clearly, more studies are needed where muscle mass is assessed in elderly patients using methods less affected by perturbations in hydration status than the current state-of-the-art.

In addition to the difficulty of acquiring valid measurements of muscle mass, assessments of physical activity also pertain some limitations. Studies typically use accelerometers attached to the lower limbs to differentiate between activities such as lying down, sitting and standing [11,12]. This method may however not be sensitive enough to detect step count in patients using walking aids and walking very slowly [31]. This is indeed a limitation, but it is arguable whether such a differentiation (i.e. between standing and walking) is of clinical importance at such low gait speeds and, importantly, if it has any effect on changes in muscle mass.

**6. Changes in muscle mass**

Do elderly patients lose muscle mass during acute short-term hospitalization? Based on the research mentioned previously it at least seems reasonable that some patients do; however, studies that have directly investigated in-hospital changes in muscle mass are extremely sparse. In fact, the small body of evidence actually suggests that there is no significant loss of whole-body muscle mass during short-term hospitalization [3–5]. Contrary, a significant loss of muscle mass was found in an observational cohort-study of elderly who were hospitalized for more than eight non-consecutive days within a year [32]. Although this finding cannot be used to conclude in-hospital atrophy, it does suggest an association between hospitalization and loss of muscle mass. Whether such a loss occurs prior to, during, or following hospital stay is therefore yet to be established. Based on the available literature Figure 1 illustrates a hypothetical model of the changes in muscle mass associated with short-term acute hospitalization of elderly patients together with the main putative mechanisms explaining these changes. Note that in this model muscle mass and physical activity have reached a new lower level after discharge compared to habitual levels, due not only to in-hospital changes, but also due to reductions during illness progression prior to hospital stay. However, when measurements are made following admission and prior to discharge, these changes may not be detected. Dehydration is also likely to occur during illness progression prior to hospitalization, whereupon rehydration follows through either intravenous or oral fluid-supplementation. It is therefore essential that future studies are able to account for, or to stabilize, hydration status before measuring baseline values of muscle mass so that true changes can be determined. The model also depicts the typical acute-phase systemic inflammatory response to illness or infection. Differences in the persistence of inflammation may however yield alternate results. Although the impact of nutrition on muscle mass is obvious, the current literature does not yet support that supplementation beyond what is currently being prescribed in hospitals have additional benefits on muscle mass.

## 7. Concluding remarks

Sarcopenia is a subtle phenomenon that is prevalent in the growing population of elderly. The suggestion that hospitalization might accelerate the loss of muscle mass with age [2] begs for research initiatives investigating changes in muscle mass during hospital stay in elderly patients. Clearly, more high-quality studies are needed that specifically targets this vulnerable population. Because in-hospital loss of muscle mass probably occurs in some elderly patients, there is a need for more precise measures of muscle mass that are able to account for fluctuations in hydration status. Regarding physical activity, accelerometer-based methods coupled with physiological measures such as heart rate and electrodermal activity may provide additional insight into the activity levels of hospitalized elderly.

## 8. Perspectives

Future studies assessing changes in muscle mass should also measure changes in physical activity levels, inflammation status and nutritional intake during acute hospitalization. Lastly, multifactorial intervention studies manipulating these factors should be conducted to elucidate their clinical significance; not only during hospital stay, but also following such episodes of acute illness.

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**Figure captions**

**Figure 1.** Hypothetical model of the main putative mechanisms explaining changes in muscle mass during short-term acute hospitalization of elderly patients.