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Mini Review

Hip Fracture Muscle Associations: Examining 70 Years of Evidence in Favor of More Targeted and Timely Muscle Oriented Prevention and Intervention Approaches

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Abstract

Background: Hip fracture injuries, surgery, preventive and rehabilitation efforts over the years have not yielded commensurate returns despite their laudable goals and great need.

Aim: This mini review aimed to examine support for the hypothesis that the routine evaluation and treatment of muscle as indicated both before and after a hip fracture injury occurs will yield more desirable outcomes than not.

Methods: A descriptive overview and analysis of all multiple available English language related papers housed in key data bases was undertaken in an effort to support this hypothesis.

Results: Although data stemming from longitudinal studies, as well as from randomized placebo controlled trials are limited, and highly diverse, cumulative findings appear to support a need for more careful routine evaluation of muscle attributes in high risk adults, followed by well-founded targeted long-term muscle related interventions to improve functioning and minimize falls risk, and hence the immense and innumerable challenges associated with sustaining one or more hip fractures among the elderly.

Conclusion: More carefully conceived preclinical as well as longitudinal studies of the possible negative influence of various aspects of muscle in the hip fracture disability cycle among larger more diverse samples are strongly indicated.

Keywords: *Aging; Falls; Hip Fracture; Muscles; Prevention; Sarcopenia; Surgery*

Introduction

Hip fractures, which have an enormous societal impact, remain devastating injuries among many older adults [1] that are anticipated to increase in numbers by 2050 as populations age [2-4], especially if novel approaches to examining and intervening to prevent this injury remain limited.

As outlined by Youm., *et al*. [5], although most fractures of the hip appear to result from a fall, in addition to the impact of direct loads on the hip that can induce a bone fracture, there is evidence that intrinsic factors, such as the influence of a sudden forceful or abnormally oriented contraction of the muscles surrounding the hip may be sufficient to produce a bone fracture, which is then followed rather than preceded by a fall. Thus, falls prevention efforts may fail if they do not specifically target and impact the nature of the possible underlying hip fracture muscular determinants.

As well, it can be expected that the presence of an age or any underlying medical condition associated with a possible progressive loss of muscle mass and strength, as well as associated decreases in the neural drive to the hip, knee or ankle muscles in particular, as well as anticipated muscle mass declines post-surgery due to immobility and pain, may set the stage for a persistent cycle of poor bone health and vulnerability towards incurring one or more bone fractures.

In addition, this aforementioned possible cycle of adverse events which can be expected to foster unwanted delays in recovery post hip fracture surgery can predictably heighten a situation for secondary falls and further bone fractures if the underlying factors influencing this state are overlooked or treated sub optimally. Malkov., *et al.* [6] further state that mid-thigh cross-sectional muscle area declines, decreases in muscle attenuation properties, and a greater degree of trochanteric soft tissue thickness can independently raise the risk for a hip fracture, and a worse than desired state post hip fracture surgery, especially in the presence of suboptimal nutrition [2].

Cummings., *et al*. [7] who argued that neither age-related osteoporosis nor the increasing incidence of falls with age sufficiently explains the exponential increase in the incidence of hip fracture with aging showed age declines in muscle mass and its possible impact on bone strength and protection should not be overlooked.

As per figure 1, we would argue that multiple age associated alterations in muscle function and structure may indeed pose undue burdens on increasing numbers of individuals as well as society if not assessed and treated in a timely way, including the generation of suboptimal bone health, physical activity limitations, falls, one or more hip fracture injuries and poor hip fracture recovery trajectories, increased mortality, and a high risk of institutionalization [8].

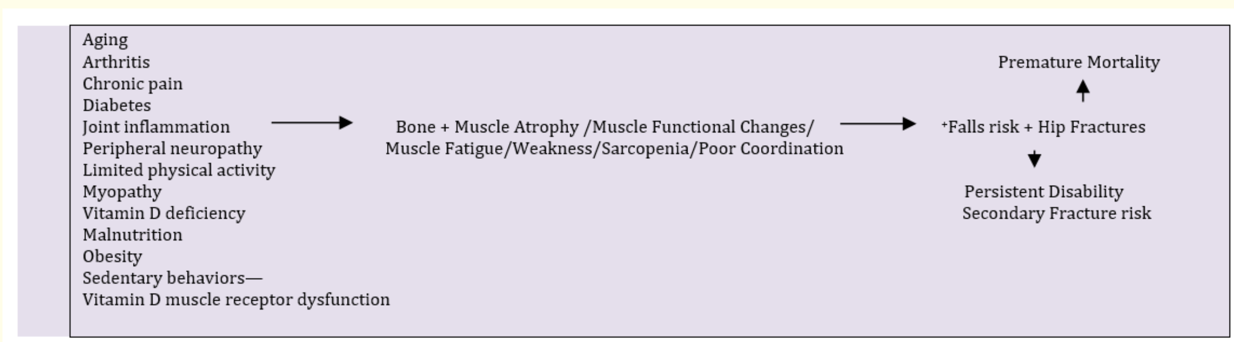

Figure 1: *Schematic representation of interaction of age related muscle mass determinants and muscle dysfunction as regards falls and hip fracture risk that can induce -muscle atrophy-neural changes -decreased aerobic capacity/strength-weight gain/increased muscle fat mass.*

Rationale

Current options to promote a high life quality and prevent hip fracture injuries, along with efforts currently applied to enhance the degree of functionality among older hip fracture surgical survivors remain limited and suboptimal at best, despite years of study.

However, aging, a state frequently accompanied by many health challenges, as well as by an intrinsic and progressive decline in muscle mass and strength, a condition known as sarcopenia that may not be inevitable, appears to expose the affected older adult to the increased risk of long term disability in the event muscles fail to protect the hip joint or exert abnormal forces on this joint that can lead to a hip fracture [9]. Research also suggests that this set of ideas is not just theoretical because sarcopenia, a condition that may be impacted by serum concentrations of the C-terminal fragment of agrin, a component of the neuromuscular junction involved in movement control is found to be elevated in older community-dwellers with sarcopenia and hip fractures [10]. It is possible this process, among others, which can possibly serve as a marker for muscle wasting, can further impair the ability of skeletal muscle to generate an adequate amount of force, carry out weight bearing activities efficiently, or impair the timing of protective reflexes and hence the ability to recover one's stable posture and to prevent a fall and fall-related injuries in the elderly [9].

Cummings., *et al*. [7] proposed that in order for a fall to cause a hip fracture: (a) the faller must be oriented in a way so as to impact the hip; (b) protective responses to combat injury must fail; (c) local soft tissues that can absorb energy may fail, and (d) the residual energy of the fall must exceed the strength of the hip joint bone mass. Since all of these events may be prevail in the context of aging, an exponential rise in the risk of hip fracture with advancing age is highly probable if this array of possible reversible situations is not addressed in a timely way. However, although this model suggests a combination of measurements of neuromuscular function and of bone strength may help to mitigate the risk of hip fractures and their often times dire consequences, is there any robust evidence to support such an effort? This seems imperative to examine if indeed it can answer some of the present unknowns that appear to remain unaffected by current surgical and pharmacologic approaches designed to prevent hip fracture disability because according to Calveri., *et al*. [2] among the factors that may markedly impact the clinical outcome of hip-fractured elderly, the age-related loss of muscle mass and function (sarcopenia) emerges as a most serious candidate, along with being associated with poor functional recovery outcomes following hip fracture surgery.

Aims

This mini review examines if there is indeed more need to explore a role for muscle in the pathogenesis and recovery of hip fracture injuries, a topic that has received attention, but where little objective progress has been made over time.

Methods

Available data located in PUBMED, were initially searched as this data base houses a majority of the most salient peer reviewed journals in the medical field. Other sites explored were Scopus, Web of Science, Science Direct, and Google Scholar. In all cases, clinical trials that did not focus on examining muscle in the context of definitive hip fracture injuries as incurred by the elderly, those that were implemented in laboratory settings or in animal models, those that were pilot or intervention studies, study proposals, and studies that examined artificial muscle building approaches, plus those articles discussing hip osteoarthritis rather than hip fractures were deemed ineligible for addressing the topic of specific current topic of interest. Since very similar publications exist, regardless of data base reviewed, no differentiation was currently made in terms of the nature of the muscle-associated conclusions reached in the available studies selected for review, and all muscle associated articles, regardless of research design were deemed acceptable if they discussed femoral neck or intertrochanteric fractures. In keeping with the exploratory nature of the paper, the review approach adopted was largely a narrative one, and an attempt was made to simplify and tabulate themes of importance. This paper specifically stresses the overlapping factors of muscle related factors and their independent or contributory role to hip fracture injuries and their overall recovery rates and extent, and does not discuss the other multiple independent or associated hip fracture determinants or any cognitive correlates to any degree.

Results

General observations

As identified by a scan of the prevailing data base housed across time in PUBMED, the world's largest medical repository, and detailing various aspects of the topic of hip fractures that stress why hip fractures are serious life threatening health conditions, plus more specific muscle related attributes, as shown in table 1 the numbers of articles on muscle as a whole, are proportionately quite limited. At the same time, although considerable time and attention has been devoted to the importance of exercise as a primary, secondary and tertiary preventive approach, with 1706 exercise associated listed studies, the precise association between muscle- the target of exercise, has clearly attracted less attention as shown below. Topics included in the various muscle categories also tended to vary widely from aspects of muscle thickness, muscle adiposity and muscle degeneration to aspects of fostering muscle nutrition, muscle and physical performance, muscle and falls risk, muscle and rehabilitation post hip fracture, and effects of smoking on muscle function.

Key Search Terms Applied	Numbers of Associated Citations*
Hip Fractures	42,963
Hip Fractures and Disability	1213
Hip Fractures and Muscle	1464
Hip Fractures and Muscle Strength	535
Hip Fractures and Muscle Dysfunction	395
Hip Fractures and Sarcopenia	322
Hip Fractures and Muscle Atrophy	185
Hip Fractures and Proprioception	188
Hip Fractures and Quadriceps Muscles	64
Hip Fractures and Muscle Inflammation	60
Hip Fractures and Gluteal Muscles	51

Table 1: *Selected* ***PUBMED*** *listings in the context of hip fractures and muscle posted as of January 1 1953-April 30 2022 showing limited attention in this realm, compared to overall level of interest.*

Terms used in the literature to identify aspects of muscle structure and function that have been studied in hip fracture cohorts include, but are not limited to, the terms: muscle quality, muscle endurance, muscle mass, muscle strength, muscle force, peak muscle force, muscle power, muscle atrophy, muscle recovery, muscle asymmetry, muscle performance, and muscle metabolism.

In sum, among those published data reviewed, no consistent theme, low numbers of reports, and design variations are clearly more common than not, and thus precluded an effective estimation of the quality and specific implications of the research.

Selected noteworthy study findings

Several important findings that warrant attention in our view are summarized below in Box 1 and table 2 and the following narrative discourse.

Authors	Results	Conclusion
Aniansson *et al*. [17]	There was a more advanced reduction in muscle fiber size in the vastus lateralis, especially in the fast twitch fiber population compared to healthy subjects where the proportions of slow twitch and fast twitch fibers remained the same Well-maintained, enzymatic metabolic capacity, moderate neuropathic changes, and absence of myopathic changes indicate that the quality of the muscle tissue is relatively well preserved, even in elderly patients with hip fractures	Muscle fiber atrophy and weakness in muscle strength may be attributable in part to a low physical activity and are possibly reversible with exercise in some individuals
Malkov *et al*. [6]	Researchers found that decreased subcutaneous fat, measures of thigh muscle attenuation, and appendicular lean mass by height squared were associated with fracture risk in men In a similar model for women, only decreases in subcutaneous fat and muscle cross sectional area were associated with hip fracture risk	Dexa-derived subcutaneous fat thickness assessments are strong markers for hip fracture risk in both men and women
Bouten *et al*. [18]	In older adults with hip fractures, there were computerized tomographic findings of decreased thoracic paravertebral muscle size Muscle attenuation variables were associated with decreases in overall hip fracture survival	Spinal muscles should not be overlooked as hip fracture mediators
Chi *et al*. [19]	Gluteus medius and minimus tendon pathology and muscle atrophy increase with advancing age with progression of tendinosis to low-grade tendon tears to high-grade tendon tears	There is an associated progression in atrophy of these muscles, which may be important in fall-related hip fractures

Erinc *et al*. [20]	Subjects with hip fractures showed trends towards lower hip muscle cross sectional areas and greater fatty infiltration of the musculature than controls	Muscle atrophy and fat infiltration impact hip fracture risk
Kramer *et al*. [11]	Elderly female hip fracture patients show extensive Type II muscle fiber atrophy when compared with healthy young or age-matched healthy elderly controls	Type II muscle fiber atrophy in the elderly is an important hallmark of sarcopenia and may predispose to falls and (hip) fractures
Leboff *et al*. [21]	Women with extremely low vitamin D levels had reduced lower extremity muscle function and increased falls 1 year later	Vitamin D sufficiency after a hip fracture may improve function and reduce falls
Terraciano *et al*. [22]	Osteoporosis is associated with a preferential type II muscle fiber atrophy, which correlates with bone mineral density and reduced levels of Akt, a major regulator of muscle mass	Muscle mass and fiber type are possible hip fracture correlates

***Table 2**: Key findings from a scan of salient articles examining muscle sources of hip fracture pathology.*

- Anxiety and depression
- Asymmetrical muscle deficits
- Bone loss
- Fear of falling
- Frailty
- Functional task difficulties
- Increased falls risk
- Lack of energy
- Limited joint mobility
- Loss of independence
- Muscle fatigue
- Muscle weakness
- Pain and discomfort
- Poor balance
- Reduced life quality
- Significant impairments in self-care
- Sleep disturbances
- Reduced ability to work, socialize
- Walking difficulties

***Box 1:** Selected problems that may persist on return of the older hip fracture individual adult to the community for up to two years among survivors [Source: 3, 11-16].*

In addition to the abovementioned novel findings in table 2, other noteworthy observations that have emerged over time are highlighted in this next section as follows.

First, it does appear that there is an association between the status of muscle mass, and osteoporosis attributes, and the risk of fracturing a hip that may implicate both a loss of muscle mass and optimal overall mobility and functional ability [23]. Marzetti., *et al*. [10]

similarly note that the presence of sarcopenia or muscle mass declines with age is noteworthy because it clearly predicts a poor prognosis among older hip fracture cases, including a possible ongoing deterioration of muscle function, muscle composition, muscle aerobic capacity and metabolism, muscle fatty infiltration, insulin resistance, fibrosis and neural activation [24,25] even if it not causal. Additional research reveals that although disputed by Aniansson., *et al*. [17], elderly patients with hip fracture may indeed exhibit muscle metabolic alterations that may contribute to neuromuscular impairments that lead to hip fractures as well as possible attrition of bone [24], even though these may be amenable to therapy [26]. Another factor of note is muscle weakness by virtue of the idea that the presence of weak muscles heightens fracture risk because this potentially decreases the force required to fracture a hip [27]. As well, as mentioned above the surrounding muscle mass may be compromised and fail to provide adequate protection to the hip joint [28] or be too slow to protect the underlying bone [29]. The fatty degeneration of the gluteal minimus hip muscle may also predict a lower level of pelvic stability, plus a higher chance of falling and fracturing a hip [16].

Having low levels of muscle strength also increases the chances of sustaining a hip fracture [30], because this can hasten bone demineralization that leads to osteoporosis-a key risk factor for fracturing a hip [31]. Muscular factors also impact fall risk and mode of falling that often leads to hip fracture injuries [32]. Not surprisingly, an increased risk of falling and sustaining a hip fracture has been specifically noted in association with muscular impairments [33] at the hip and knee [34], poor ankle strength [35], and gluteus medius/minimus muscle density and size ratios [36].

Indeed, the role of muscle related aberrations of the lower limb, are increasingly evident possibly sufficiently crucial variables in explaining or contributing to hip fracture risk in the older adult as outlined by Wilson., *et al.* [37] who found the inability of an individual to lift a mass of 10 lbs (4.5 kg), was significantly associated with having an increased risk of incurring a hip risk. The extent of muscle density at a fractured hip site may also predict hip bone mineral density and the risk of a future second hip fracture [36].

Other observations indicate that in addition to the possible presence of adverse alterations in the bone mineral density and geometry of the proximal femur, the amount of adipose tissue of the upper thigh and the distribution of fat cells in these muscles appear significantly associated with the presence of an acute hip fracture [38], as well as influencing hip fracture outcomes in men [39]. The possibility has also been raised of the presence of possible damage to the actual vitamin D muscle receptor, and myocyte itself, which if present, is expected to foster sarcopenia and with this possibly greatly impede hip fracture recovery processes and reduced longevity post hip fracture [40,41].

Unsurprisingly hip fracture cases do appear to exhibit a high prevalence of having a lower than desirable muscle mass, as well as lower handgrip strength and sarcopenia [16,42], that can predictably foster a high susceptibility to future falls and possible hospital readmissions with surgical complications or secondary hip fractures. Pham., *et al*. [43] indicate that muscle weakness is indeed an independent determinant of fracture risk in men, and one that may negatively impact muscle-bone interactions and that should be further investigated in future studies. In addition, concerted efforts to specifically strengthen the hip abductor muscles, as well as overall muscle strength capacity is said to secure more effective hip bone protection, as well as functional outcomes than not [44-46], especially among frail malnourished older adults [47-50].

A further small body of research specifically points to a role for muscle asymmetries from side to side as both a possible pathogenic or contributory factor to hip fractures, as well as one requiring very insightful intervention approaches. For example, several authors report asymmetrical muscle strength recovery processes. While possibly consistent with the effect of disuse and inflammation in the affected limb along with training effects in the unaffected limb due to the favoring of this leg with ambulation during the post fracture period or differences between limb strength from side to side with aging [51], as well as conditions such as unilateral hip or knee osteoarthritis for example, the presence of persistent muscle strength asymmetries can predictably be expected to increase the risk of incurring an injurious fall and subsequent fracture [52,53], while posing various functional challenges that limit independence and possible bone protection even if muscle mass is not implicated [15,47,54-58]. As well, uncovering the sources of asymmetry may be key in this regard, for example, if these stem from asymmetrical vestibular deficits and a loss of vibration sense in the operated limb, this possibility should not be overlooked as one that can have considerable influence on the risk of falling and the sustaining of one or more hip fracture injuries in affected older adults [59].

In this regard, commonly recommended interventions for mitigating against hip fractures of: exercise, diet, and falls prevention education [60] must surely fail if they are not based on a systematic analysis of the specific muscular state and attributes of the individual in question. According to Chen., *et al*. [61] a very careful evaluation of the individual may not only help to develop more sound intervention plans, but with this there is a greater chance of averting any possible excess loss of muscle mass or persistently abnormal movement strategies that can greatly impair the attainment of the desired functional goals or markedly slow the functional recovery processes after surgery. In particular, the concept of targeted and tailored muscle interventions in this regard is strongly supported [62,63].

Discussion

Hip fractures, which are commonly highly debilitating injuries affecting many older adults in all parts of the world, continue to perpetuate tremendously costly public health medical and social costs, despite years of study and efforts to avert this injury. Unlike many health conditions affecting older adults, and where treatment can help to restore well being, once a hip fracture has occurred multiple challenges remain, including premature death, as well as the risk of sustaining further hip fractures, either on the same side or the opposite side. Thus, several notable researchers have concluded that the injury demands more be done to prevent it, rather than focusing solely on intervening to optimize the post hip fracture injury state [64].

This current mini-review was undertaken to examine what we know about possible muscle specific attributes that may predate or emerge consequent to hip fracture surgery that might be amenable to change, regardless of age, but when damaged, or atrophied, may heighten the risk for falling, as well as sarcopenia, while compromising hip fracture surgical recovery processes markedly and progressively [64].

To this end, this present review, while not encompassing all articles in the field, summarizes what appears to be the most pertinent data from the available peer reviewed literature that has examined the nature of the status of muscles at the spine, hip or knee and ankle as possible causal factors related to hip fractures or as factors mediating outcomes of surgery and related rehabilitation programs. A topic not often detailed or explored in the related literature, when compared to other topics (see Table 1), a role for various muscle properties, as well as muscle mass and function was sought.

In this regard, one can safely say, there is almost uniform consensus that muscular factors are likely to have high potential in this regard to advance the field significantly [eg., 65-67; Table 2). On the other hand, a retrospective analysis of hip fracture patients with and without muscle atrophy/weakness by Zhao., *et al*. [68] revealed that those exhibiting atrophy had significantly higher healthcare utilization and costs compared with hip fracture patients without atrophy. A loss of muscle strength that is not uncovered or addressed in a timely way can predictably lead to increases in muscle fat mass, reduced balance capacity, suboptimal muscle shock absorption ability, muscle fatigue, joint instability, poor co-ordination, and walking ability, plus poor further muscle mass and bone health declines and falls. In addition, a greater need for multiple health services and support is likely if muscular disturbances are not sought or assessed accurately, and treated accordingly [64-67]. A better understanding of the interaction of inflammation, malnutrition, vitamin D plus cognitive and comorbid status as this impacts muscle and possibly hip fracture risk should also be carefully studied. Why some hip fracture cases do improve or return to their pre fracture muscle status, but not others, which appears the rule rather than the exception, may also be worthwhile to examine closely from a muscular point of view.

In short, as proposed in figure 1, it is appears that efforts to preserve muscle mass and foster optimal muscle function across the lifespan is likely to offer more protection against hip fractures in later life, than not. Moreover, even if these injuries occur, the presence of a sound muscular system is likely to allow for more rapid recovery and desired outcomes than not, as well as bone health. However, emergent deficits in muscle mass and structure as well as function over time that may stem from multiple factors, and possible muscle fatigue damage and axial compressive forces generated by muscle [77,78], clearly warrants discovery sooner rather than later in the individual case. Indeed, what will work best to assist an older vulnerable adult to prevent an injuries hip fracture, may be quite unique, and may not work in another case, thus reliance on large scale trials that provide average outcomes at best may surely fail to capture what is needed and why to the same degree for an individual older adult if compared to careful case studies using single sample research designs and continuous as well as comprehensive muscular associated assessments over time.

To advance this line of inquiry, shortcomings and/or issues needing future attention include, but are not limited to examining the impact of the following on hip fracture risk and outcomes:

- Nutritional status and therapy
- Specific muscle enhancement and delivery methods
- Sampling strategies, sample size, and attrition
- Age, body mass, fracture and operation type, pre existing health status, and gender variations
- Nature of the hip fracture injury mechanism/its severity/extent
- Co-occurring chronic diseases and impaired balance and coordination
- The almost exclusive use of subjective, un validated, or possible unreliable outcome measurements
- The use/nature of any ongoing co-interventions
- Discrepant and poorly documented intervention protocols
- Wide variations in preventive and rehabilitation approaches [64].

Although every effort has been made in this review to reach an informed and coherent set of conclusions, limitations to the aforementioned ideas clearly include, the nature of the review, the failure to examine the quality of the most predominant studies, the use of a limited number of data bases, and possible omission of salient papers. However, the predominant discourse does not refute a very key role for sarcopenia as a major determinant of hip fragility fractures that warrants immediate attention, among others.

In this regard, and until more research emerges, the key themes presently examined do appear to favour a role for heightened hip fracture preventive efforts rather than focusing on post hip fracture interventions almost exclusively. Moreover, in recognition of the possible role muscular factors may play in fostering both hip fracture risk and the ensuing hip fracture injury outcomes where they occur, efforts to target at risk adults, especially those with one or more chronic health conditions [69] who may also exhibit multiple neuromuscular deficits, early on are generally more favoured than not. In addition, older adults with a low body mass [76] and low income [70], and those residing in institutions [71,72] who may be malnourished and experience sarcopenia might be targeted, in particular. Men too appear increasingly vulnerable to hip fracture and should probably not be neglected as a subgroup even though more women in general appear to incure hip fractures than men [73]. As such, young adults everywhere should be apprised of their risk for a later life hip fracture and its disability and be strongly encouraged to lead an active and healthy lifestyle [74] in light of the many observed post hip fracture muscle recovery challenges, even in the face of optimal and successful surgery [75].

Conclusion

This overview of the long history of efforts to better understand the etiology of hip fractures through a muscular lens seems to have revealed some highly valuable insights and leads us to conclude the following:

1. Hip fractures remain devastating injuries common among older population and injuries that are possibly rising in prevalence, and possibly even severity, as numbers of frail elders increase.
2. A multifaceted injury that is challenging to address uniformly, hip fractures appears to be strongly influenced, as well as a predictor of muscle changes as a result of one or more intersecting muscular factors.
3. Efforts to advance hip fracture prevention, a public health imperative of enormous importance, will tend to fail or remain suboptimal in our view if these focus solely on generic recommendations to exercise or alter the home environment without examining the multiple converging features of the aging muscular system that may require individualized interventions, and expert guidance, rather than compliance with generic exercises alone.
4. How emotions, stress, pain, social circumstances, living conditions, medication, food security and chronic health conditions interact or intersect to produce or perpetuate sarcopenia, plus an increased risk for falling, and suboptimal recovery post hip fracture in both femoral neck and inter-trochanteric fractures types, which is poorly studied, warrants more insightful attention.

In the interim, based on the past research of the hip fracture population over the last 70 years, muscle does appear to have emerged as a highly salient, but possibly overlooked modifiable hip fracture determinant, regardless of whether this is intrinsically or extrinsically derived, and deserves investments and prompt attention in both clinical research and practice realms.

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