



## Cover page

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## **PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF M.D. DEGREE IN GERIATRICS AND GERONTOLOGY**

**Title of the Protocol: Association between Sarcopenia, Fatigue and Orthostatic Intolerance in Geriatric Patients: A Case Control Study**

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**What is already known on this subject? AND  
What does this study add? (Maximum 6 lines) “References are not needed”**

Sarcopenia is emerging as one of the major age-associated health challenges of the twenty-first century, being prevalent among the elderly and associated with multiple adverse outcomes. Fatigue and orthostatic intolerance (OI) are also common in older adults and may share underlying mechanisms with sarcopenia, including impaired cardiovascular responses and autonomic dysfunction. Understanding the relationship between sarcopenia, fatigue, and OI can inform targeted interventions to improve geriatric care. In this study we are going to assess impact of sarcopenia on fatigue and orthostatic Intolerance in Geriatric Patients.

## 1. INTRODUCTION/ REVIEW (Maximum 1000 words) “References are needed”

Sarcopenia is a clinical syndrome that refers to a gradual and generalized loss of skeletal muscle mass, strength and physical performance. The decline of muscle mass is about 3–8% per decade after the age of 30 years and rises to 15% after 70 years of age. (*Vandewoude et al., 2017*)

Accumulating evidence suggests that sarcopenia is one of the central pathological processes driving physical frailty and it is implicated in a wide range of adverse health outcomes in older adults. Sarcopenia can cause an increase in the risk of falls and fractures due to falls, deterioration in activities of daily living, movement disorders, increased hospitalization, decreased quality of life, and even death. Additionally, it is associated with cardiovascular diseases including coronary artery disease, atrial fibrillation, and heart failure (*Iuliano et al., 2022*)

Fatigue can be defined as “an overwhelming, debilitating, and persistent feeling of burnout that reduces the person’s ability to perform activities of daily living, including working effectively and performing customary family and social duties” (*Riley et al., 2010*)

Fatigue is common, with a rate of approximately 20% in the general population. Researchers have investigated the relationship between fatigue and many diseases and revealed that this rate increases up to 50% in cancer, chronic infections, autoimmune, and neurological diseases in which the immune system is affected. The geriatric population is at higher risk of fatigue due to both physiological changes and comorbid conditions. (*Suzan et al., 2022*)

Orthostatic hypotension (OH) and delayed orthostatic blood pressure (BP) recovery on standing are disorders increasingly associated with falls and adverse clinical outcomes in older adults, and considered as part of orthostatic intolerance syndrome which include other symptoms as dizziness, inability to maintain balance and blurred vision. (*Keskin et al., 2021*)

Orthostatic hypotension, a chronic autonomic cardiovascular dysfunction that is characterized by inability to sustain adequate cardiac output to assuming an upright position, is defined in terms of a sustained drop in BP ( $\geq 20$  mmHg systolic and/ or  $\geq 10$  mmHg diastolic) at 3 min after standing, the prevalence of delayed BP recovery has been identified through the use of beat-to-beat orthostatic BP measurement in a number of population cohort studies. (*Saedon et al., 2020*)

Normally, in response to the venous pooling immediately after standing, a number of compensatory mechanisms such as increased venous tone and heart rate should come into play and normalize the blood pressure (BP) and thus the cerebral perfusion. Elderly patients are particularly prone to OH and related symptoms due to several comorbidities. (*Keskin et al., 2021*)

Since lower extremity muscle contraction is also a significant contributor for the venous blood to return to the heart, sarcopenic elderly patients owing to their low muscle strength along with impaired cardiovascular and nervous system functions may be prone to OH. (*Keskin et al., 2021*)

There is reason to suspect a pathophysiological link between sarcopenia and both delayed BP recovery and OH, given the role of the skeletal muscle pump in BP recovery and maintenance. The skeletal muscle pump is thought to aid venous return to the heart during exercise and standing, via rhythmic activity of the muscles of the lower limbs. (*Duggan et al., 2023*)

Loss of muscle strength and mass in sarcopenia could affect skeletal muscle pump function, leading to slower BP recovery and OH. This could then lead to falls, fractures, increased morbidity and even subsequent mortality. The clinical importance here is that unlike many other

causes of OH, sarcopenia is potentially preventable and/or reversible through physical exercise and nutrition interventions. (Negm *et al.*, 2022)

Due to the scarcity of research examining the links between fatigue, orthostatic intolerance (OI), and sarcopenia, this study seeks to explore their interrelationships.

## 2. AIM/ OBJECTIVES (Maximum 300 words)

To study the association between sarcopenia, fatigue and orthostatic intolerance in geriatric patients.



## 3. METHODOLOGY:

**Patients and Methods/ Subjects and Methods/ Material and Methods (Maximum 1000 words) “References may be needed”**

- **Type of Study:** Case-control study
- **Study Setting:** participants in the study will be recruited from AIN SHAMS UNIVERSITY HOSPITALS from the date of the approval of the study and till completing sample size, it will include elderly patients who can be included in the study.
- **Study Period:** till completion of sample size
- **Study Population:** elderly patients both males and females who are interviewed at AIN SHAMS UNIVERSITY HOSPITALS or at the hospital clinic.
- **Cases:** Elderly patients ( $\geq 65$  years) diagnosed with sarcopenia based on the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) criteria.
- **Controls:** Age- and sex-matched elderly patients without sarcopenia.
  
- **Inclusion Criteria:**
- *Patients (males or females) aged 65 or above years old.*

- *Participants who are willing to participate in the study.*
- **Exclusion Criteria:**
- *Patients who are not willing to participate in the study.*
- *patients with end organ damage (CHF NYHA III/IV), end-stage renal disease, Liver cell failure, respiratory failure.*
- *Patients with arrhythmia or using pacemakers*
- *patients diagnosed with parkinsonism, Diabetes mellitus, or peripheral neuropathy.*
- *Active infections or inflammatory conditions (e.g., sepsis, rheumatoid flare-up)*
- *Patient with acute stroke, Critically ill patients, Terminal illness, Bedridden or completely immobile patients,*
- *Medications Influencing Fatigue/OI: High-dose opioids, sedatives, or drugs causing significant orthostatic hypotension (e.g., alpha-blockers, diuretics without stable control)*

**Sampling Method:** simple random sampling from the patients admitted to AIN SHAMS UNIVERSITY HOSPITALS or interviewed at the hospital clinic.

**Sample Size:** using the PASS 15 program for sample size calculation, after reviewing results from the previous relevant studies, a medium effect size difference was assumed reading the frequency of orthostatic hypotension between cases and controls ( $d=0.6$ ) Duggan et al, 2023, and 2024 based on this assumption a sample size of at least 45 cases and 45 controls achieve 80% power to reject the null hypothesis of zero effect size when the population effect size is 0.60 and the significance level (  $\alpha$ ) is 0.050 using a two-sided z test.

#### **Study Tools:**

All participants will be subjected to:

-Informed written consent from the patients or the caregivers

#### **- COMPREHENSIVE GERIATRIC ASSESSMENT**

1. Full detailed history including comorbidities, medication use, history of fall.
2. Full physical examination.
3. Functional assessment through Activities of Daily Living (ADL) (*katz et al.,1963*) and Instrumental Activities of Daily Living (IADL): 8 items (*lawton et al.,1969*)
4. Mini Nutritional Assessment (MNA): 18 items, Arabic form (*Abd-Al-Atty et al., 2012*)
5. Assessment of cognitive decline using Arabic version of Mini -ACE. (*Qassem et al., 2021*)
6. Screening for depression by geriatric depression scale (GDS), Arabic version (*Sheata As et al., 1998*)

-**Assessment of sarcopenia** using a hand-grip test instrument with handheld dynamometer (*Roberts et al., 2011*), assessment of the muscle mass using bioelectrical impedance analysis (*Janssen et al., 2000*), assessment of physical performance by timed up and go test (TUGT). (*Podsiadlo et al., 1991*), SARC-F (*Woo et al., 2014*)

#### **- Assessment of Orthostatic intolerance:**

- History regarding the main symptoms of chronic orthostatic intolerance syndromes include light-headedness, syncope or near syncope, blurring of vision, headaches, problems with short-term memory and concentration, fatigue, intolerance of low impact exercise, palpitations, chest pain, diaphoresis, tremulousness, dyspnea or air hunger, nausea, and vomiting.
- The Orthostatic Hypotension Questionnaire (OHQ) (*Kaufmann et al., 2012*)
- Standing HR and BP measurements (by automated monitor) will be taken at 1, 3, 5,

and 10 minutes following a 20-min supine resting period.

- **Assessment of fatigue** using Arabic version of Fatigue Severity Scale (FSS). (*Al-Sobayel et al., 2016*)

-**physical activity assessment using** Incidental and planned questionnaire week version (*Delbaere et al., 2010*)

- **Ethical Considerations:**

1- An informed consent will be obtained from each participant prior to participation.

2- They will be oriented by nature of the study, safety and efficacy of the procedure to be used, and data extracted from this study.

3- Confidentiality and privacy of data will be ensured.

4- The participation will be on voluntary basis and the participants have the right to withdraw at any time.

5- Approval of the ethical committee of the faculty of medicine, Ain Shams University will be taken.

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