The Critical Role of Skeletal Muscle Health in Preventing Falls and Fractures

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Scenario

- A 71-year-old retired woman with no regular physical activity and a history of hypertension, Diabetes, and Obesity suffered an **Intertrochanteric Fracture** of the right femur.
- Losartan 50mg, Hydrochlorothiazide 12.5mg, Metformin 1000mg, Empagliflozin 12.5mg, Rosuvastatin 20mg
- Ca=8.7, Vit D=15, HbA1c=8.8, BUN=10, Cr=0.5
- **T score=-3.1**
- **SMI= 3.7 (normal=5.4)**

The Musculoskeletal Triad

Bone, muscle, and fat tissue work together as an integrated system to maintain structural integrity and metabolic health.

Bone Tissue

Provides structural framework and mineral storage. Responds to mechanical loading from muscle contractions.

Skeletal Muscle

Generates force for movement and stability. Protects bones during impact and maintains balance.

Adipose Tissue

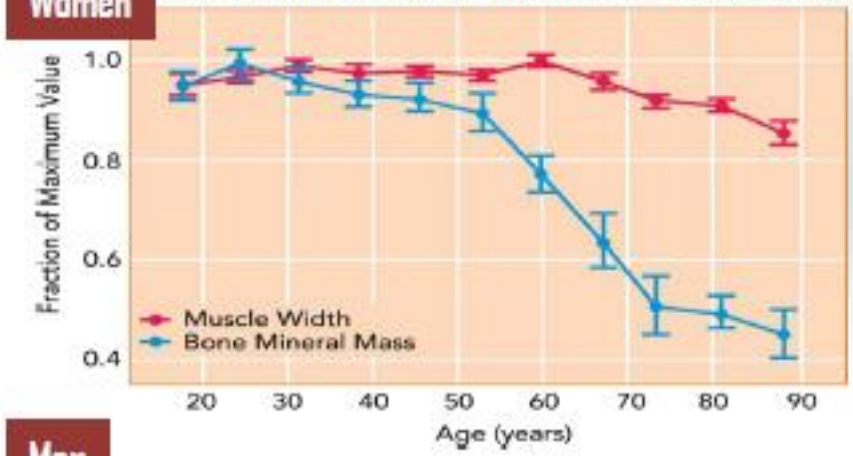
Secretes hormones affecting bone and muscle. Provides cushioning but excess amounts impair function.

Bone and muscle, similar temporal patterns

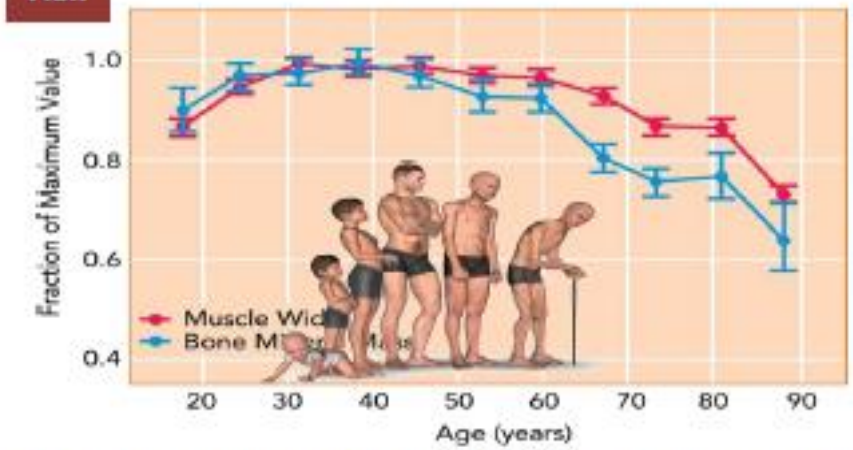
A parallel chronological evolution throughout life

Aging-related changes in BMD of the radius and muscle width in the forearm

Women



Men



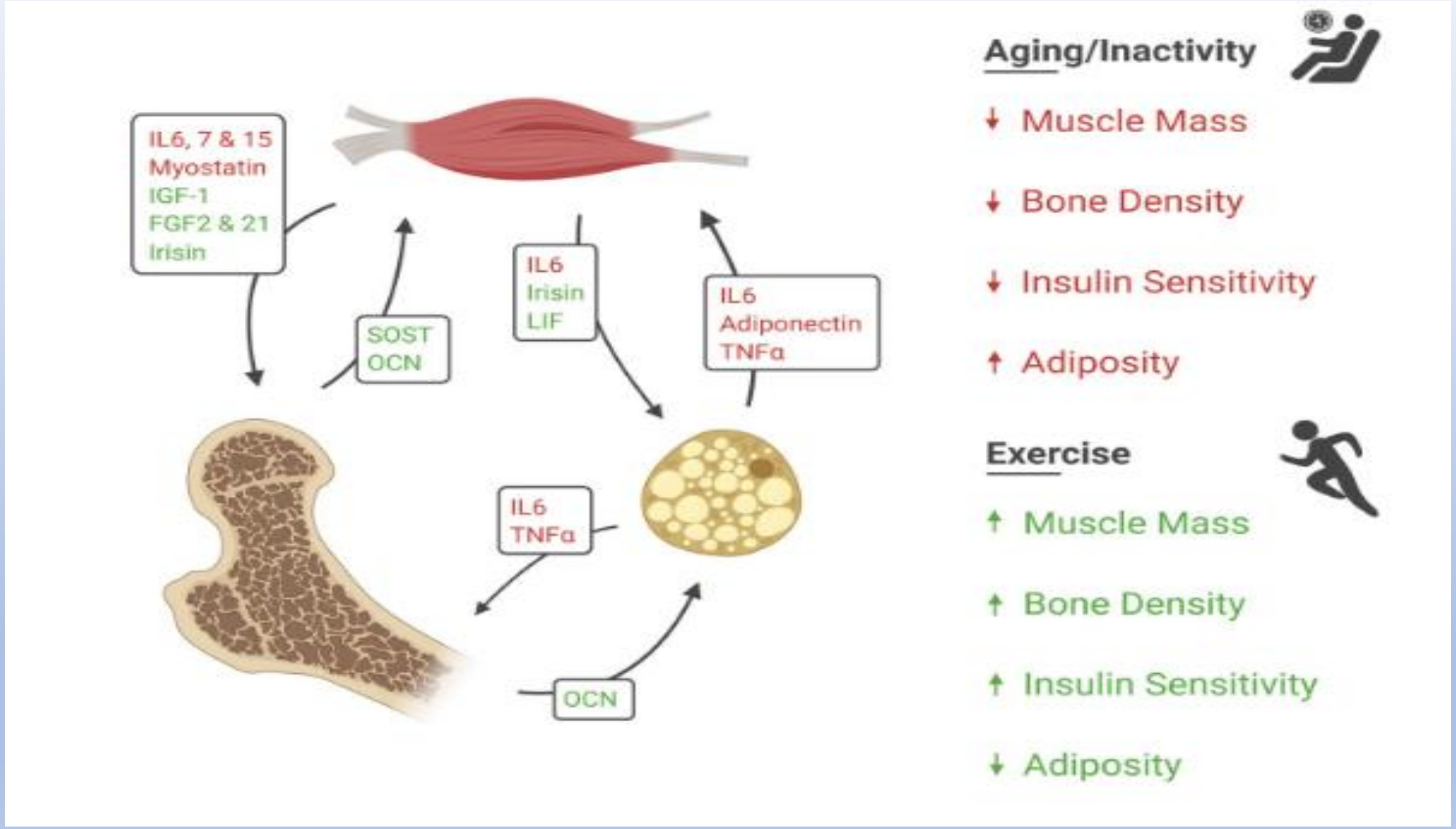
After 50 y

- **Muscle : mass ↘1-2% /y; strength loss 1.5-3% /y** *(Lang et al., Osteoporosis Int 2010)*
- **Bone : loss 1-2% /y** *(Riggs et al., J Bone Miner Res 2008)*

613 men and women across 11 different groups between the ages of 18–97 y

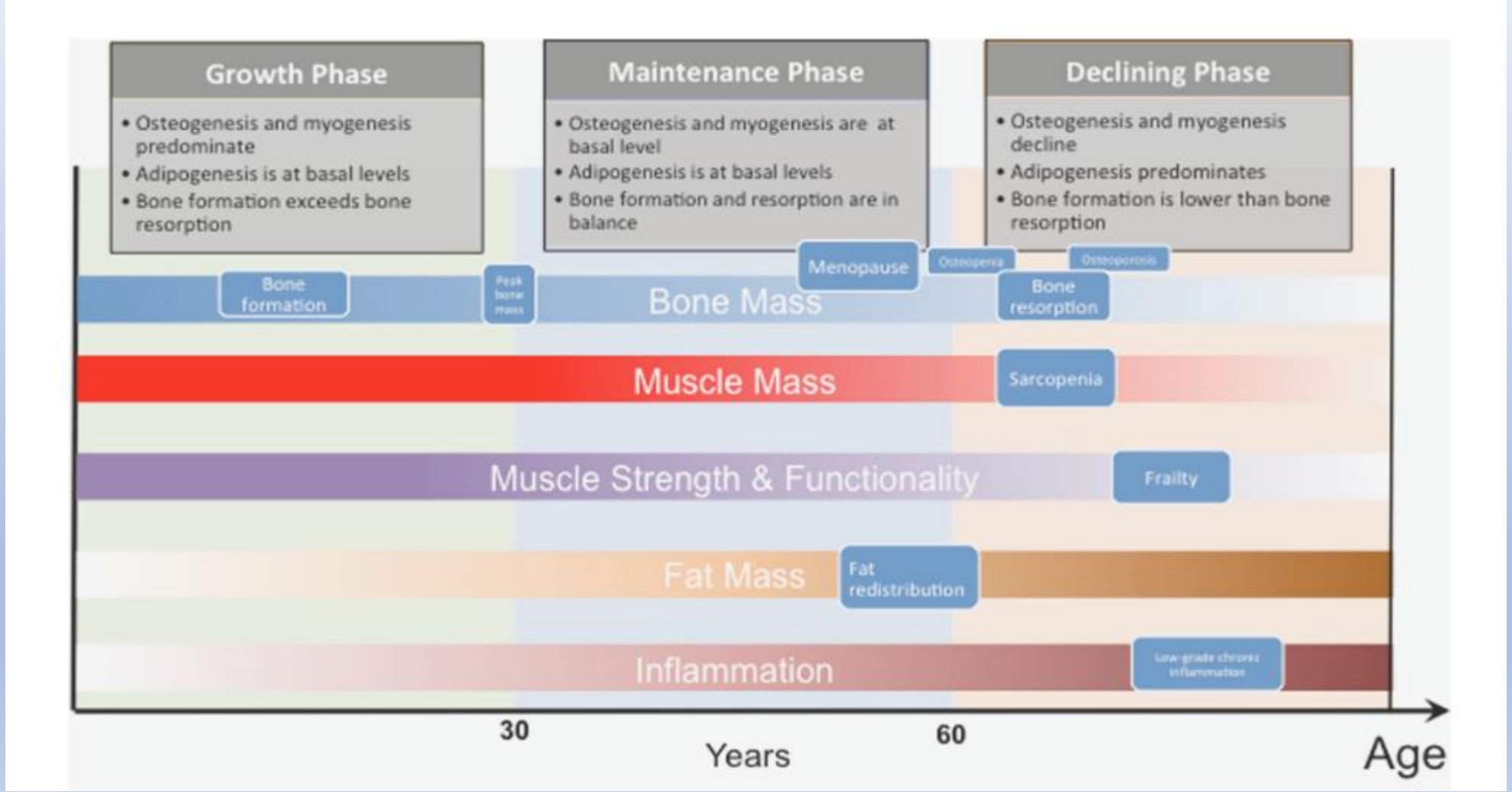
(Data were normalized to the peak value for bone and muscle across the lifespan)

The biological role of myokines, osteokines, and adipokines in muscle, bone, and fat crosstalk.

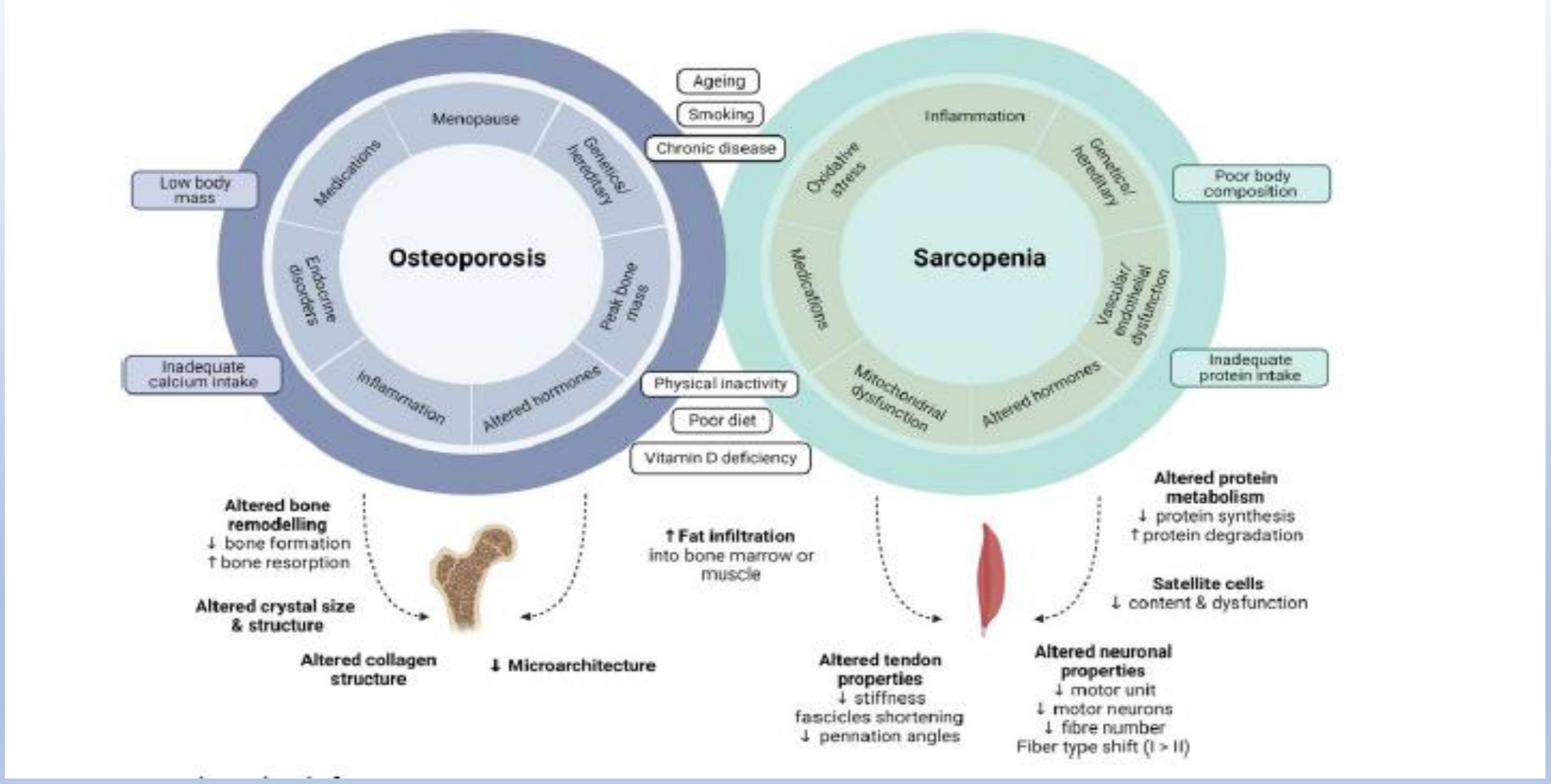


Muscle, Bone, and Fat Crosstalk: the Biological Role of Myokines, Osteokines, and Adipokines. Current Osteoporosis Reports (2020) 18:388–400

Changes in bone, muscle and fat tissues with increasing age and accompanying increase in low-grade chronic inflammation.



Shared Challenges for Ageing Bone and Muscle



Smith et al Calcif Tissue Int 2024

Sarcopenia

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.

Presence of any of the following clinical conditions:

- Functional decline or limitation; unintentional weight loss; depressive mood; cognitive impairment; repeated falls; malnutrition
- Chronic conditions (heart failure, chronic obstructive pulmonary disease, diabetes mellitus, chronic kidney disease, etc)

CRITERIA FOR THE DIAGNOSIS OF SARCOPENIA

LOW MUSCLE STRENGTH + **LOW MUSCLE MASS** = **SARCOPENIA**

SARCOPENIA + **LOW PHYSICAL PERFORMANCE**

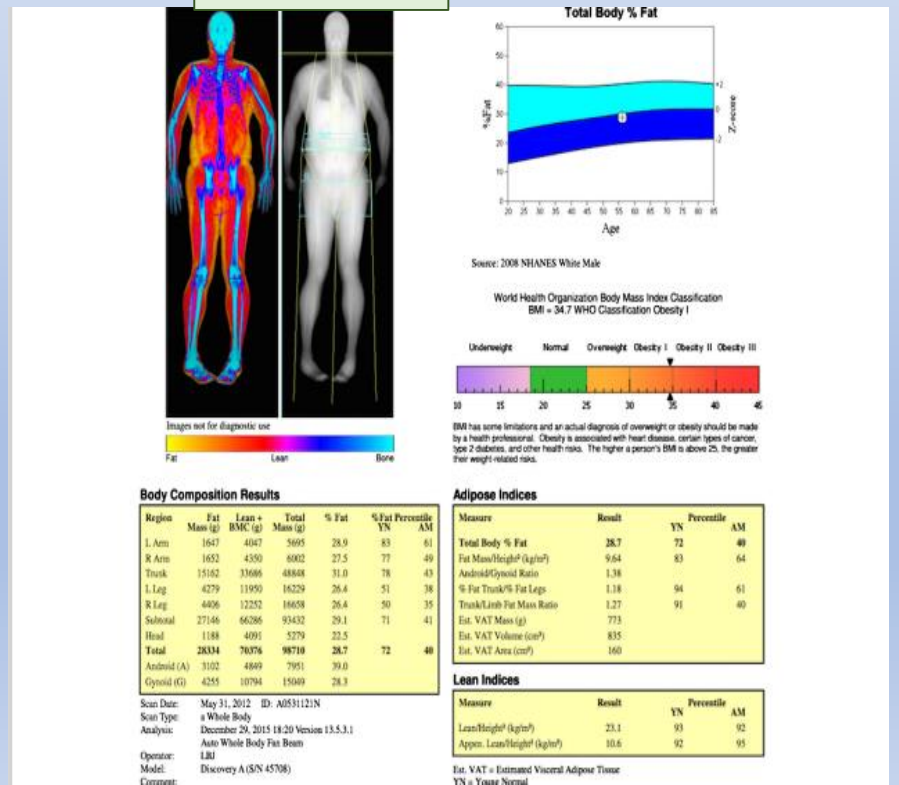
Severe Sarcopena

Cruz-Jentoft AJ et al. Sarcopenia: European consensus on definition and diagnosis. Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010

Measuring sarcopenia parameters

Muscle mass

DXA
BIA
CT
MRI

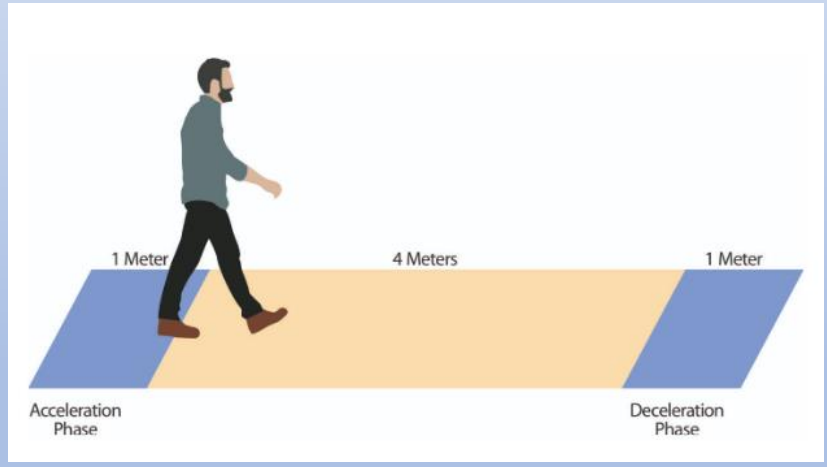


Muscle strength

- Handgrip dynamometer
- Chair stand test

Physical performance

- Gait speed
- SPPB
- TUG



Sarcopenia / Osteoporosis Interaction

- In post-menopausal women, those with sarcopenia had a 13 times higher risk of having osteoporosis vs. those without sarcopenia.
- Among community-dwelling older persons, those with sarcopenia had a 5-fold higher risk of developing osteoporosis.
- Cross-sectional and longitudinal studies showed that osteoporosis strongly increases the risk of sarcopenia and vice versa.

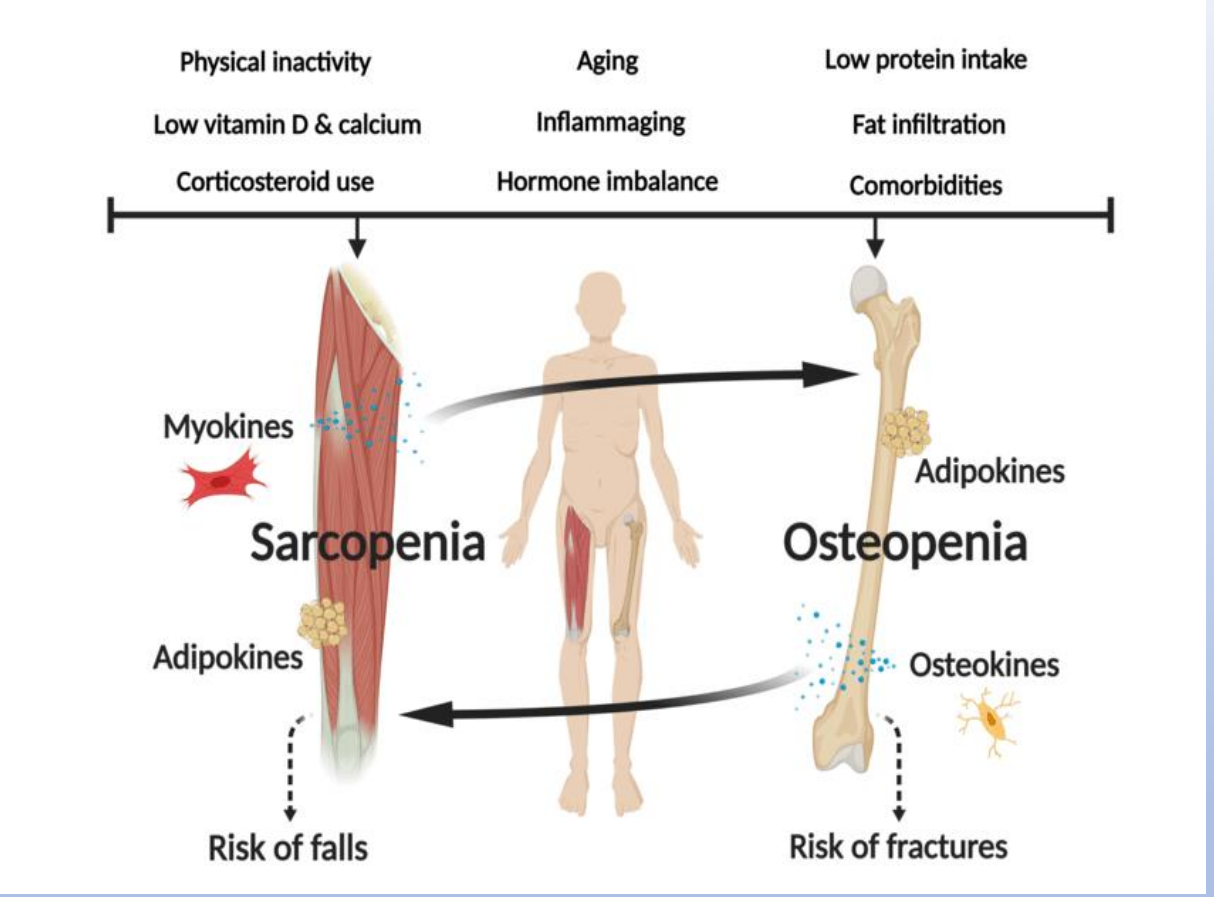
Sjöblom S, Suuronen J, Rikkonen T, Honkanen R, Kröger H, Sirola J. Relationship between postmenopausal osteoporosis and the components of clinical sarcopenia. Maturitas 2013;75:175–180.

Locquet M, Beaudart C, Reginster J-Y, Bruyère O. Association between the decline in muscle health and the decline in bone health in older individuals from the SarcoPhAge cohort. Calcif Tissue Int 2019;104:273–284.

Osteosarcopenia

- Osteosarcopenia is an increasingly recognized geriatric syndrome with a considerable prevalence which increases morbidity and mortality.
- **Osteosarcopenia:**

  Osteopenia/Osteoporosis + Sarcopenia
- These patients have greater risk of falls, fractures, institutionalization, and significant socioeconomic costs.



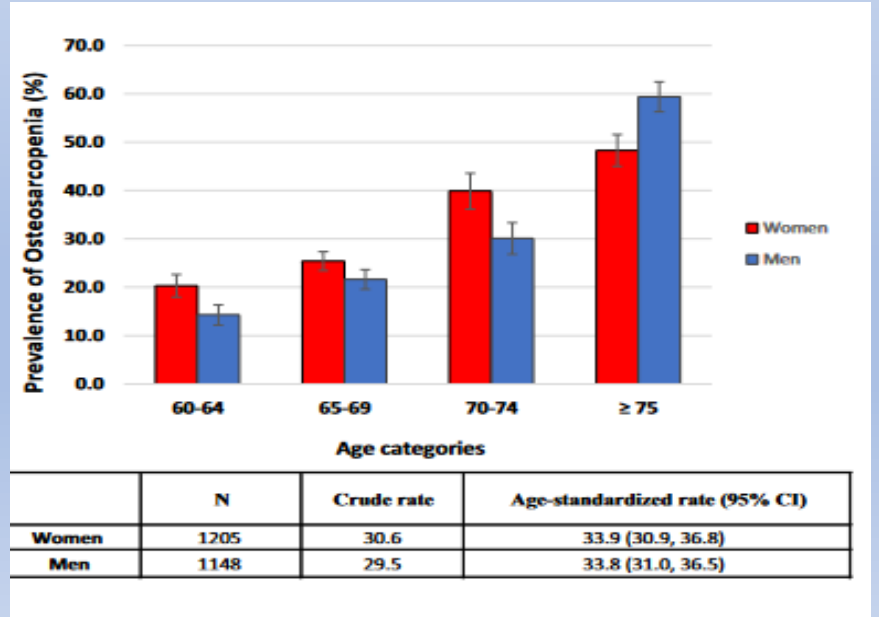
1. Kirk B, Zanker J, Duque G. Osteosarcopenia: epidemiology, diagnosis, and treatment-facts and numbers. J Cachexia Sarcopenia Muscle. 2020 Jun;11(3):609-618. doi: 10.1002/jcsm.12567. Epub 2020 Mar 22. PMID: 32202056; PMCID: PMC7296259.

2. Paintin J, Cooper C, Dennison E. Osteosarcopenia. Br J Hosp Med (Lond). 2018 May 2;79(5):253-258. doi: 10.12968/hmed.2018.79.5.253. PMID: 29727228; PMCID: PMC5963675.

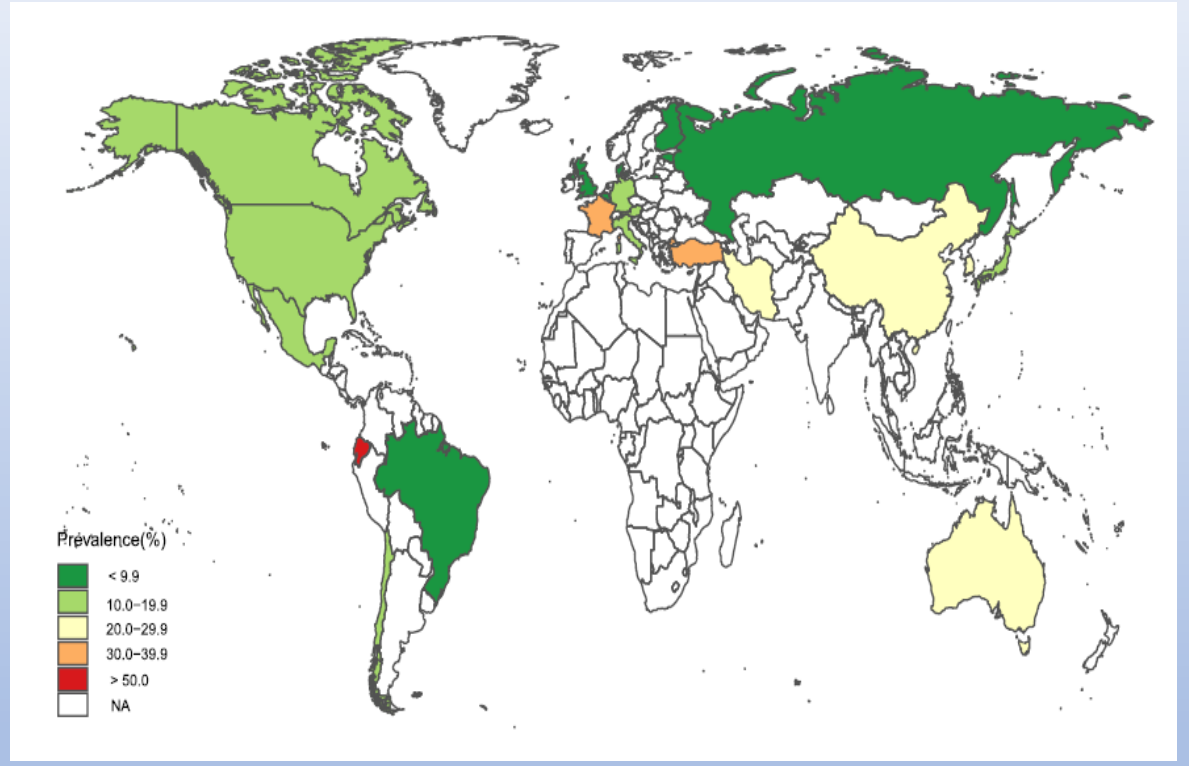
Geographical differences in the global prevalence of Osteosarcopenia

An overall prevalence of 21% (95% CI: 0.16–0.26).

In IRAN: The age-standardized prevalence of osteosarcopenia was **33.8** (95% CI 31.0–36.5) in men and **33.9** (30.9–36.8) in women.

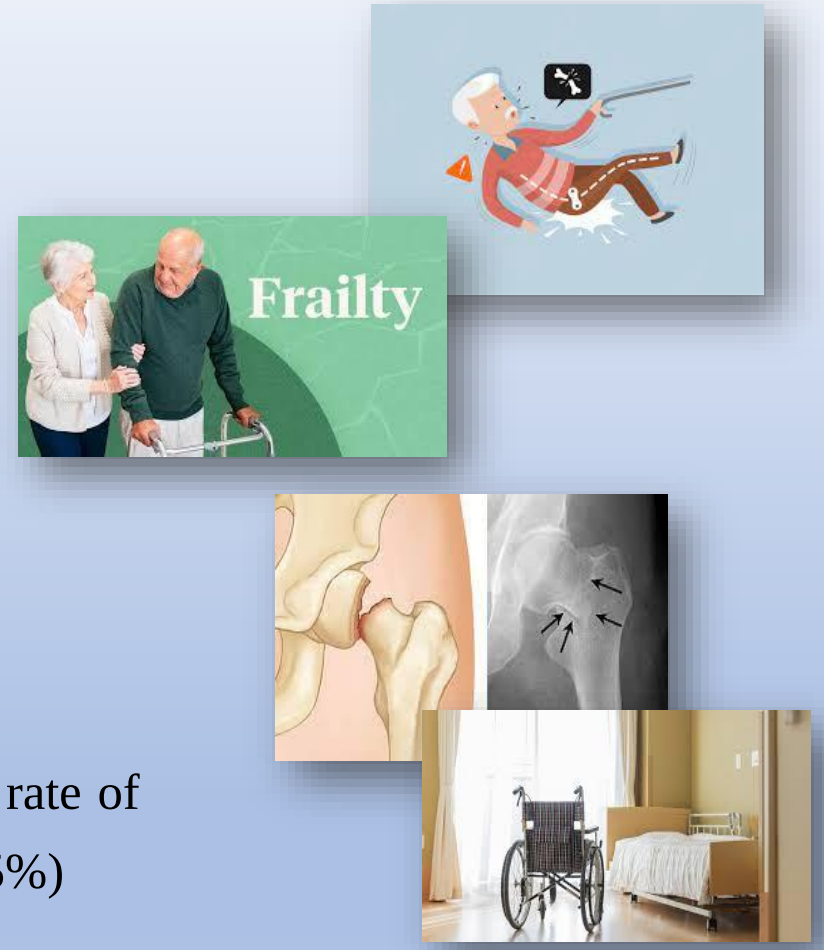


	N	Crude rate	Age-standardized rate (95% CI)
Women	1205	30.6	33.9 (30.9, 36.8)
Men	1148	29.5	33.8 (31.0, 36.5)

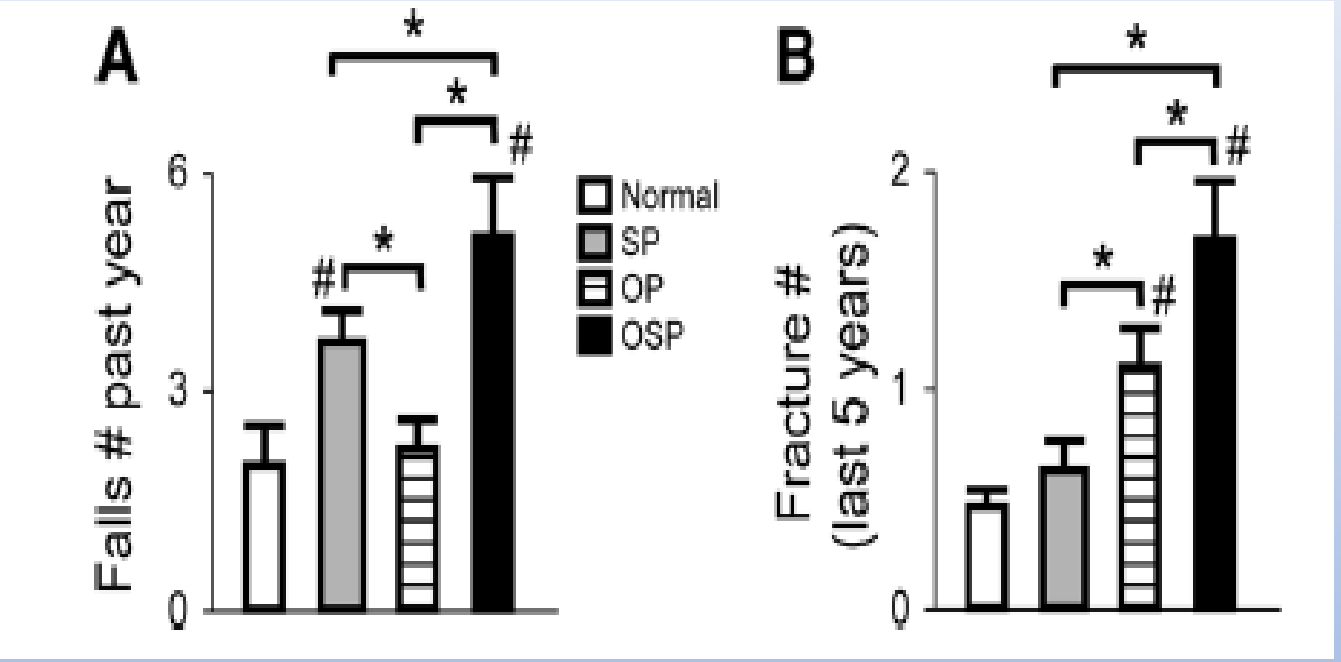


Osteosarcopenia Consequences

- Individuals with osteosarcopenia are at higher risk of:
  - **Falls,** (**ORs: 2.83–3.63**; P < 0.05),
  - **Frailty,**
  - **Fractures,** (**ORs: 3.86–4.38**; P < 0.05)
  - **Institutionalization.**
- It is also associated with significantly increased mortality:
  - Study on elderly Korean patients with hip fracture: 1-year mortality rate of 15% in the osteosarcopenic patients, more than that of osteoporotic (5%)
  - **Earlier death** [**hazard ratio (1-year follow-up): 1.84**, P = 0.023].



Prevalence of falls and fractures in osteosarcopenic subjects.

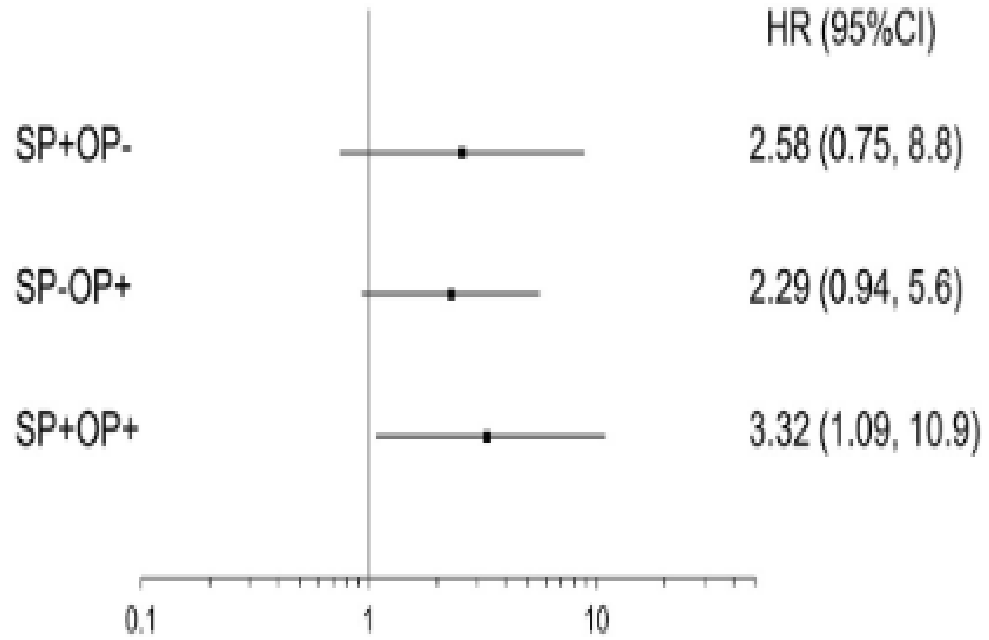


680 subjects (mean age=79, 65% female) assessed between 2008–2013. number of self-reported falls (past 6 months) (A) and fractures (last 5 years)(B)

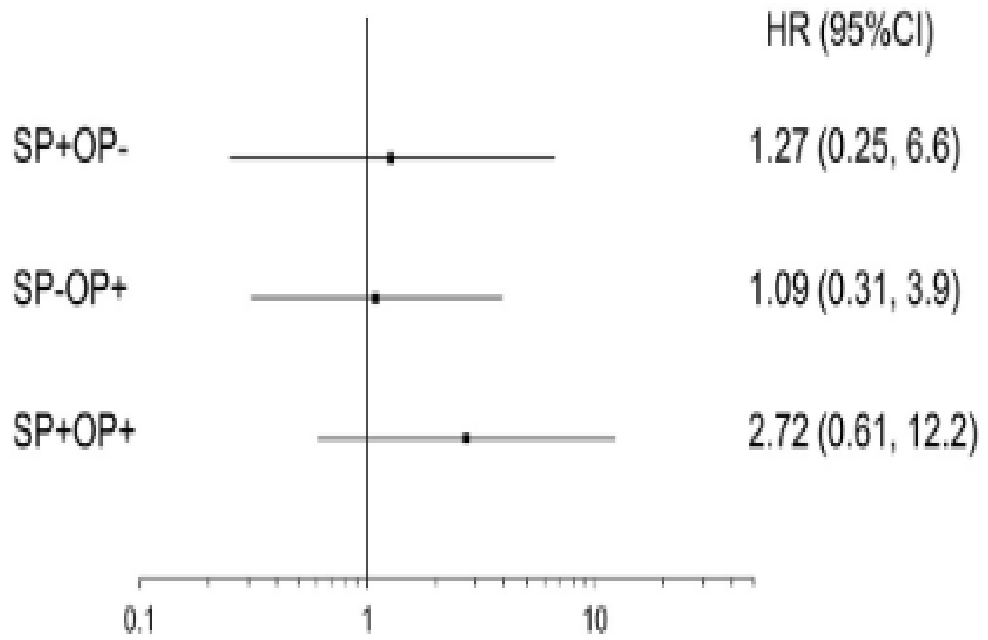
Comprehensive nutritional status in sarco-osteoporotic older fallers. The Journal of nutrition, health and aging. 2015

Osteosarcopenia synergistically increases the risk of falls and Fracures

Forest plots of HR for falls

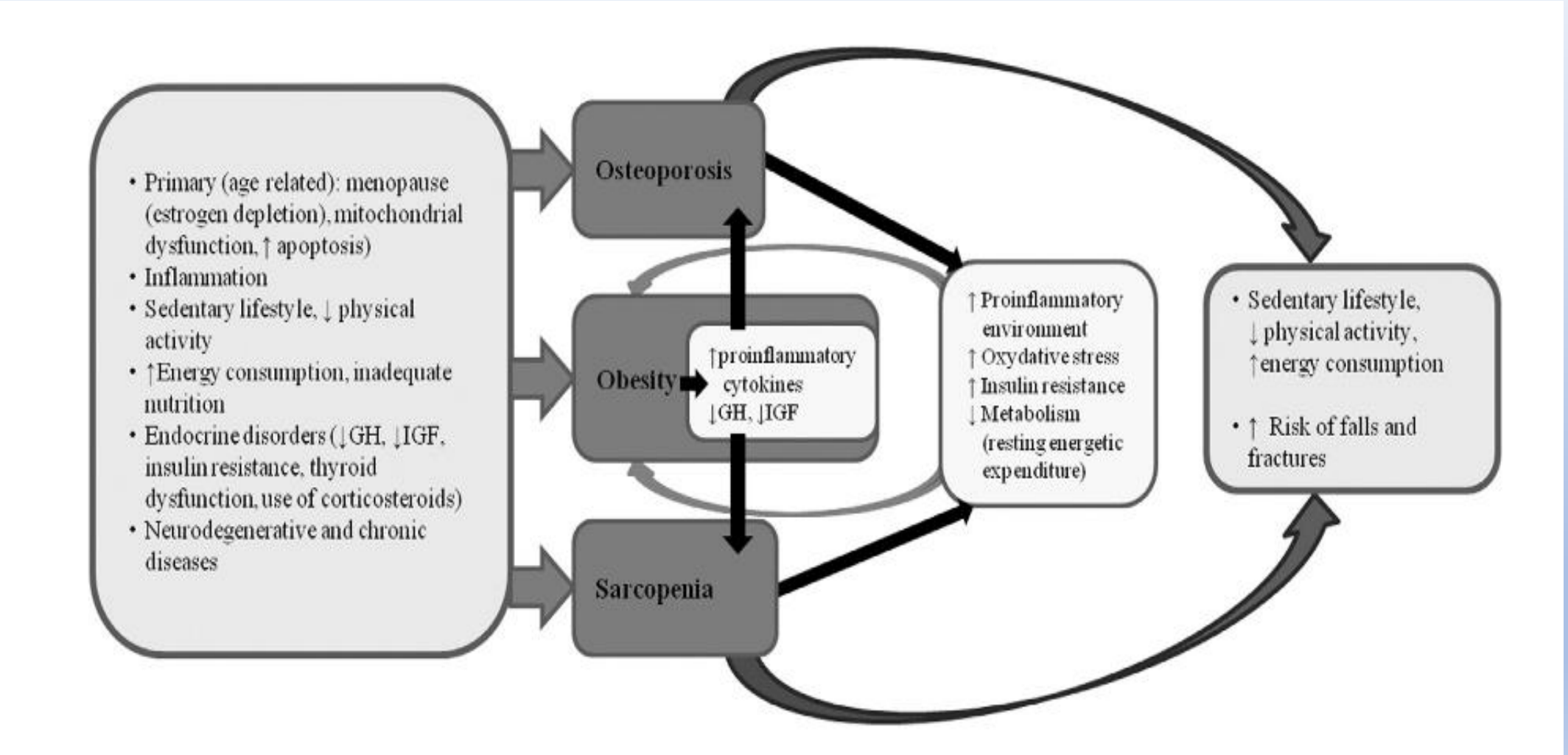


Forest plots of HR for fractures.



A total of 100 RA patients (SP-OP-: 44%, SP þ OP-: 17%, SP-OPþ: 28%, and SP þ OPþ: 11%) were enrolled; 37 patients had falls, and 19 patients had fractures.

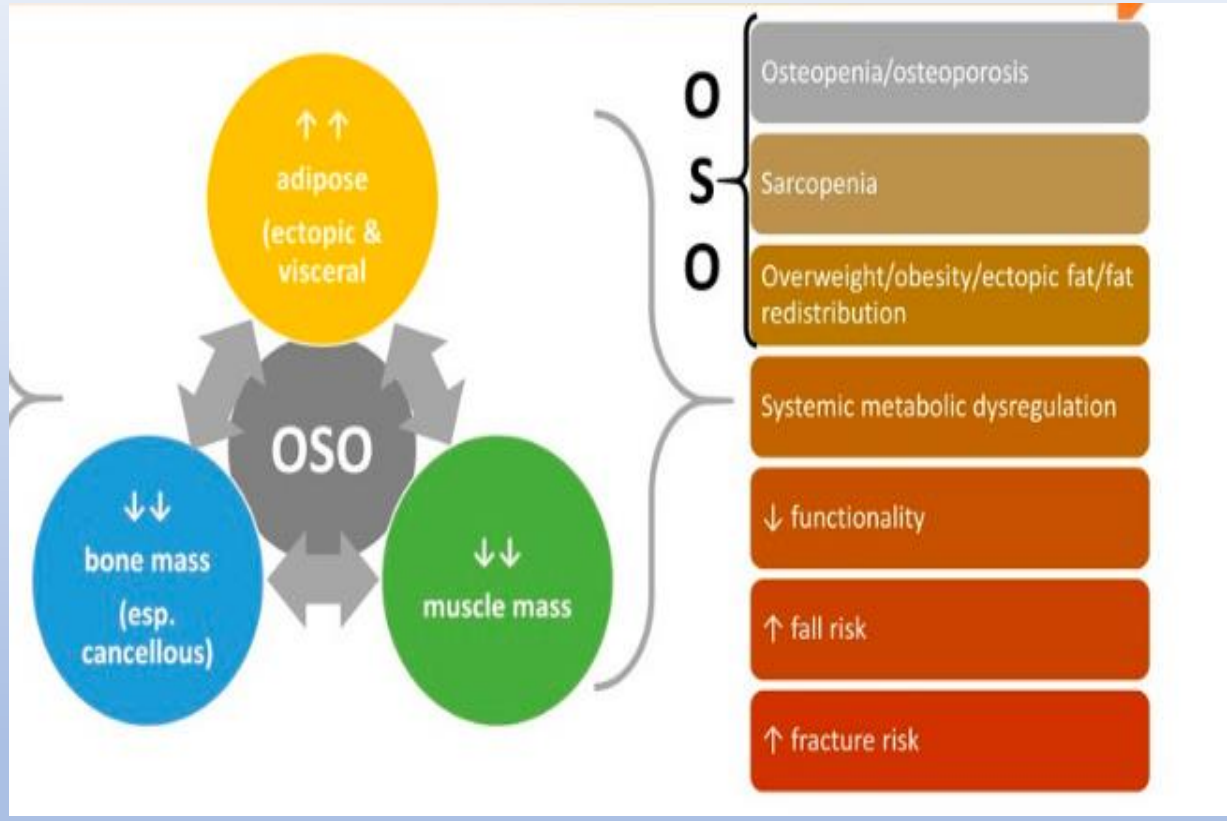
Relationships between obesity, sarcopenia and osteoporosis



Osteosarcopenic obesity and fall prevention strategies. Maturitas 80 (2015) 126–132

Osteosarcopenic Obesity

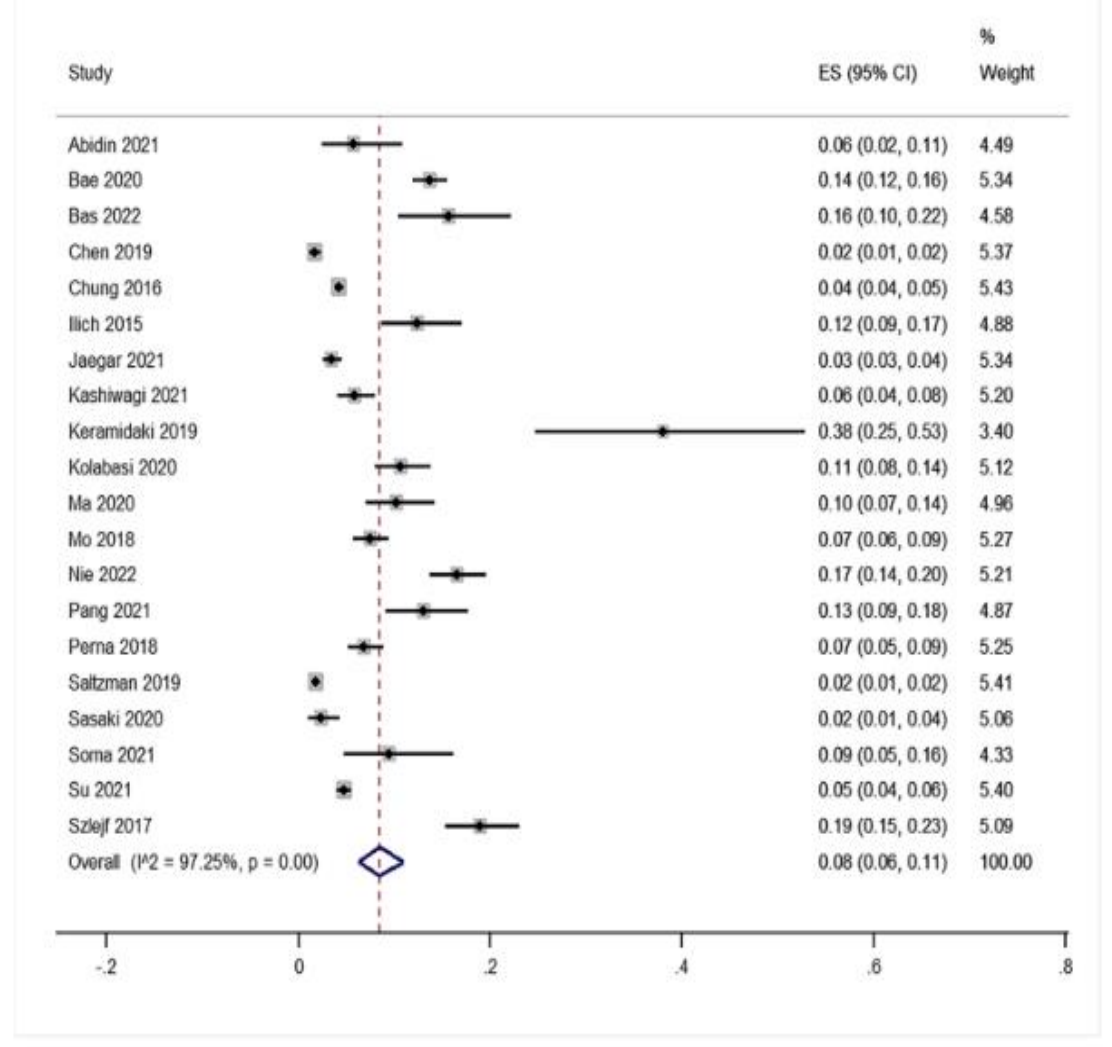
- OSO is the linked nature of the syndrome—from its cellular connections to the deterioration of bone (osteopenia/osteoporosis), muscle (sarcopenia) and excess adipose tissue (overweight/obesity, including the redistribution of fat into the visceral area and adipogenesis in bone and muscle tissues)



Owen J. Kelly , et al. Osteosarcopenic Obesity: Current Knowledge, Revised Identification Criteria and Treatment Principles. Nutrients 2019

Global prevalence of Osteosarcopenic Obesity

- The prevalence of OSO in middle-aged and older adults worldwide was **8%** (95% CI: 6%-11).
- Females (pooled prevalence = 9%) had a higher burden of OSO than males (pooled prevalence = 5%).
- The prevalence of OSO in the elderly population (pooled prevalence = **13%**; 95% CI: 9%-17%).



Ying Liu, et al. Global prevalence of osteosarcopenic obesity amongst middle aged and older adults: a systematic review and meta-analysis. 2023, Archives of Osteoporosis

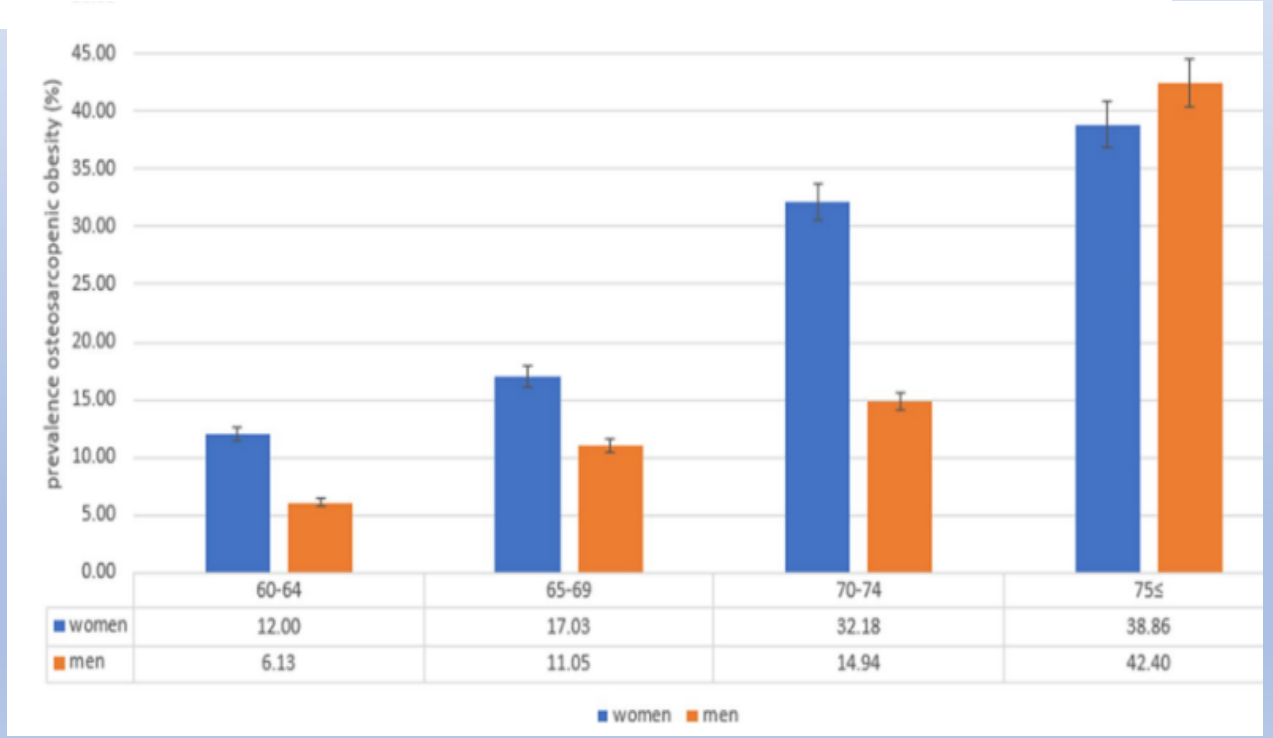
Archives of Osteoporosis (2023) 18:137
https://doi.org/10.1007/s11657-023-01340-9

ORIGINAL ARTICLE

Prevalence of osteosarcopenic obesity and related factors among Iranian older people: Bushehr Elderly Health (BEH) program

Mozhgan Ahmadinezhad[1] · Mohammad Ali Mansournia[2] · Noushin Fahimfar[3] · Gita Shafiee[4] · Iraj Nabipour[5] · Mahnaz Sanjari[6] · Kazem Khalagi[6] · Mohammad Javad Mansourzadeh[6] · Bagher Larijani[7] · Afshin Ostovar[6]

The standardized prevalence of OSO was **23.66%** (95% CI: 21.15-26.16) in women and **18.53%** (95% CI 16.35-20.87) in men.



Ahmadinezhad M, et al. Prevalence of osteosarcopenic obesity and related factors among Iranian older people: Bushehr Elderly Health (BEH) program. 2023. Archives of Osteoporosis

Logistic regression analyses of independent factors associated with fall and vertebra fracture

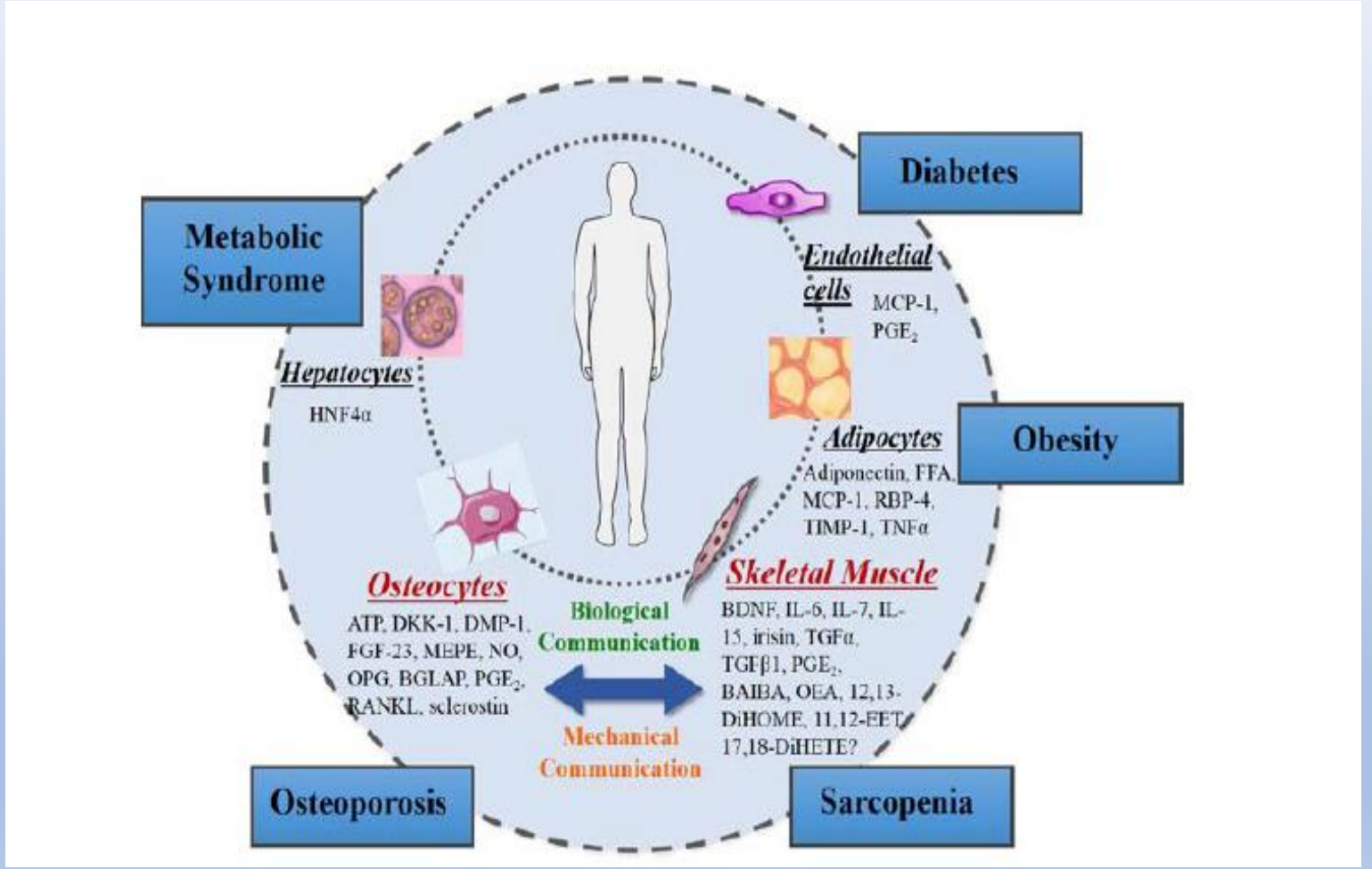
All 317 elderly people contributed to this research, with 12.2% (39 out of 317) identified as having OSO

	Odds ratio	95% CI	p
Fall			
Osteosarcopenic obesity	3.12	1.50–6.45	**0.002**
Age	1.02	0.98–1.05	0.342
ADL	1.49	0.79–2.80	0.223
IADL	1.10	0.64–1.87	0.735
Low physical activity	2.04	0.93–3.71	0.072
Presence of osteoporotic obesity	0.67	0.26–1.70	0.402
Vertebra fracture			
Osteosarcopenic obesity	3.36	1.58–7.12	**0.001**
Age	1.09	0.93–1.15	0.057
ADL	1.75	0.84–3.64	0.134
IADL	1.12	0.58–2.18	0.731
Low physical activity	0.79	0.39–1.62	0.520
Presence of osteoporotic obesity	0.69	0.24–1.03	0.061

Model 1 is adjusted for age, ADL, IADL, low physical activity, and only the presence of osteoporotic obesity.
Model 2 is adjusted for age, ADL, IADL, low physical activity, and only the presence of sarcopenic obesity.
ADL: Activities of daily living, IADL: Instrumental ADL, CI: Confidence interval

Osteosarcopenic Obesity's Role in Older Adults' Falls and Vertebral Fractures, Eur J Geriatr Gerontol 2025

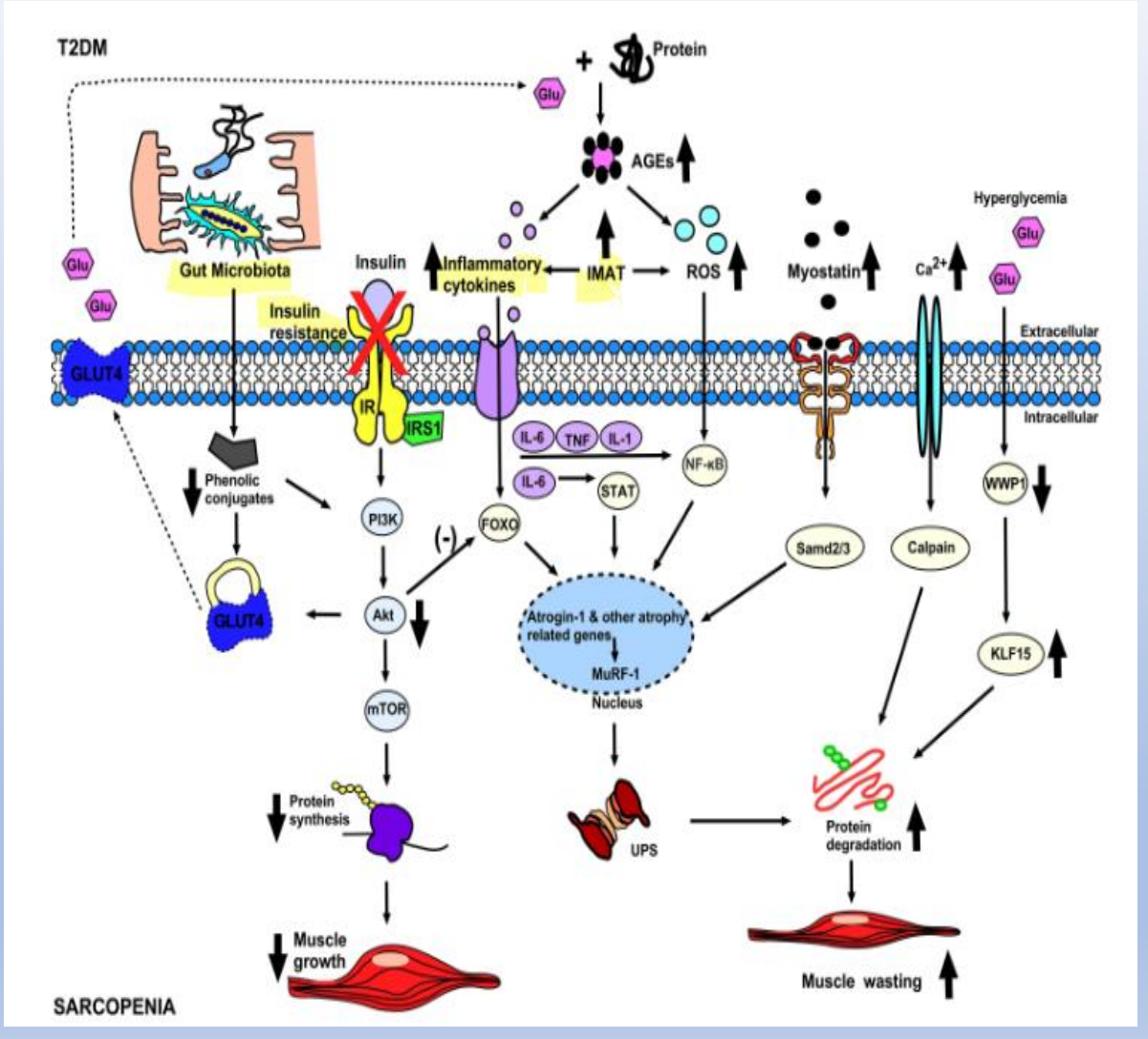
Bone-muscle crosstalk with other tissues, and impact on chronic diseases.



Cross-talk between muscle and bone .Chapter 4, 2019

The Metabolic Pathophysiology for Sarcopenia in T2DM

- **Insulin Resistance (IR)** the most important factor exacerbating sarcopenia in T2DM patients
- **Inflammatory Markers in T2DM**: IL-6, TNF-α, and C-reactive protein (CRP) /linked to insulin resistance
- T2DM increased **oxidative stress** , **hyperglycemia** in T2DM triggers increases associated with end production of ROS (Mitochondrial dysfunction, impairs muscle repair)
- A hallmark pathophysiology of diabetes is **obesity** and ectopic deposition of fat in many insulin target tissues including skeletal muscle((**Intramuscular Adipose Tissue (IMAT)**
- Dysbiosis of the **gut microbiota** has important role in pathogenesis of IR and T2D



Drugs that may cause sarcopenia and their direct effects on muscle

Antidiabetic drugs	Effect on Muscle Mass	Adverse Side Effects
Metformin	Increases	Digestive intolerance, dysgeusia, hyporexia, and vitamin b12 deficiency
Thiazolidinediones (Rosiglitazone, Pioglitazone)	Increases	Fractures and decompensated heart failure
Sulfonylureas (Glyburide, Glimepiride)	**Decreases**	Hypoglycemia, weight gain, Apoptosis ⬆, muscle protein⬇
Glinides (Repaglinide, Nateglinide)	**Decreases**	Potential hypoglycemia with combination therapy, Apoptosis ⬆, muscle protein⬇
DPP-Ivis (Sitagliptin, Saxagliptin,…)	Increases	Minimal risk of hypoglycemia
GLP-1 RA (Lira, Semaglutide, Tirzepatide)	**Decreases**	Muscle protein ⬇
SGLT-2i (Empa, Dapagliphlozine)	**Decreases**	Muscle protein ⬇
Insulin	Increases	Hypoglycemia,
Statin	**Decreases**	Mitochondrial function ⬇, coenzyme Q10 ⬇, apoptosis ⬆,muscle protein catabolism⬆
Loop diuretics	**Decreases**	Myoblast fusion ⬇

Scenario

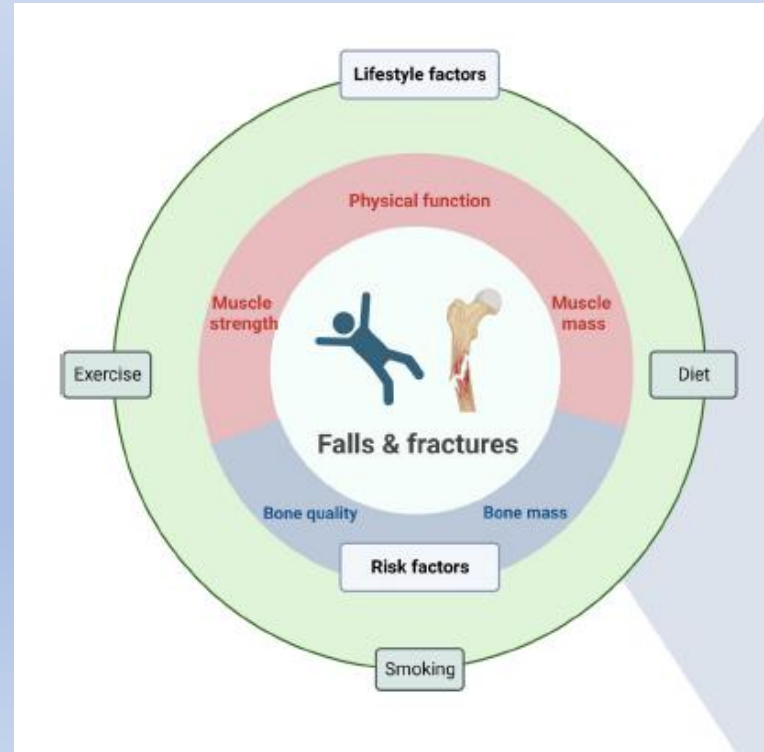
- A 71-year-old retired woman with no regular physical activity and a history of hypertension, Diabetes, and Obesity suffered an **Intertrochanteric Fracture** of the right femur.
- Losartan 50mg, Hydrochlorothiazide 12.5mg, Metformin 1000mg, Empagliflozin 12.5mg, Rosuvastatin 20mg
- Ca=8.7, Vit D=15, HbA1c=8.8, BUN=10, Cr=0.5
- **T score=-3.1**
- **SMI= 3.7 (normal=5.4)**

Management of Osteosarcopenic obesity

(Nutritional strategies to promote musculoskeletal health for fall and fracture prevention)

- Progressive **resistance and balance exercise**

  (2-3 times/ week , for 10-15 min)
- **Protein**: up to 1.5 g/kg
- **Vitamin D**: 800–1000 IU/day (higher doses for deficiency correction)
- **Calcium**: 1000–1200 mg/day from diet and/or supplements
- **Weight management**: a moderate-high caloric deficit (500–1000 kcal/day), initial goal of 5–10 % weight reduction over a period of 6 months



Conclusions

- Preserving Skeletal Muscle Health is Key to Preventing Falls and Fractures
- The combination of sarcopenia, osteoporosis, and obesity multiplies risks exponentially and requires special attention
- Screen for sarcopenia in older adults and patients with fractures (e.g., SARC-F, grip strength, gait speed)
- Through timely diagnosis and targeted interventions, we can preserve quality of life and independence in older adults
- Antidiabetic drugs impact muscle and bone health differently across drug classes and patient populations—personalized, risk-stratified therapy selection is essential for optimal outcomes
- Consider combined rehabilitation + Nutritional strategies for patients with osteosarcopenia and fracture.

Thanks