

2022.12.10.

제4회 비만대사증후군연구회 추계학술대회 및 전공의연수강좌

Session II. 비만의 역설과 근감소증 : 진단과 치료

왜 근감소증이 중요한가

- Sarcopenia & Sarcopenic Obesity

서울대병원

민경하

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2. Sarcopenia
3. Sarcopenic Obesity
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5. Conclusion

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Introduction

- Ageing Society
- Healthy ageing

-> 'Decade of healthy ageing 2021-30' by WHO

- Obesity

-> "major public health problem and a global epidemic" by WHO (1997)

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Sarcopenia

- **Sarcopenia** is a **progressive and generalized skeletal muscle disorder**

involving the accelerated **loss of muscle mass and function**

that is associated with increased adverse outcomes including falls, functional decline, frailty, and mortality.

- **From the Greek phrase** 'poverty of flesh'
- First described in the 1980s (**by Rosenberg, 1988**)
- **Age-related decline in lean body mass** affecting mobility, nutritional status, and independence

Cruz-Jentoft AJ, Sayer AA. Sarcopenia. The Lancet. 2019;393(10191):2636-46.

Rosenberg IH. Sarcopenia: origins and clinical relevance. The Journal of nutrition. 1997;127(5):990S-1S.

Sarcopenia

- It occurs commonly as an **age-related process in older people**,
influenced not only by contemporaneous risk factors,
but also by genetic and lifestyle factors operating across the life course.
- It can also occur in mid-life in association with a range of conditions.

Sarcopenia

- **Two recent milestones**

- 1) The introduction of **muscle function** into the concept in six consensus definitions since 2010

- new focus on muscle function (muscle strength, muscle power, or physical performance)
- more powerful predictor of clinically relevant outcomes than muscle mass alone

- 2) The Recognition of sarcopenia as an independent condition with an **International Classification of Diseases-10 code** in 2016 (M62.84)

- Yet, most clinicians remain unaware of the condition and the diagnostic tools needed to identify it

Definition of Sarcopenia

- **International definitions**

- 1) The European Working Group on Sarcopenia in Older People (EWGSOP) in 2010**

- defined sarcopenia using muscle mass, muscle strength, and physical performance (cutoffs not defined)

- 2) The International Working Group on Sarcopenia and Society of Sarcopenia, Cachexia and Wasting Disorders (SSCWD) in 2011**

- defined the disease using muscle mass and physical performance (cutoffs defined); SSCWD used

the phrase sarcopenia with limited mobility.

Definition of Sarcopenia

- **International definitions**

3) The Asian Working Group on Sarcopenia in 2014

- same definition as the EWGSOP and also defined cutoffs for Asia

4) The Foundation for the National Institutes of Health in 2014

- the disease using muscle mass and muscle strength, and also defined cutoffs; physical performance

was used as an outcome

Definition of Sarcopenia

- **International definitions**

5) EWGSOP updated their definition in 2019 (EWGSOP2)

- low muscle strength and low muscle mass or quality
- Acute (acute disease or sudden immobility) or chronic
- with cutoffs definition; physical performance was used to assess severity of the condition

Definition of Sarcopenia

- **From EWGSOP2**
 - Muscle mass and strength (in parallel with bone mineral density) peak in young adulthood and, after a plateau, start decreasing gradually with a faster decline in strength
- **WHO**
 - integrated care for older people from a disease-centered model to a function-centered model

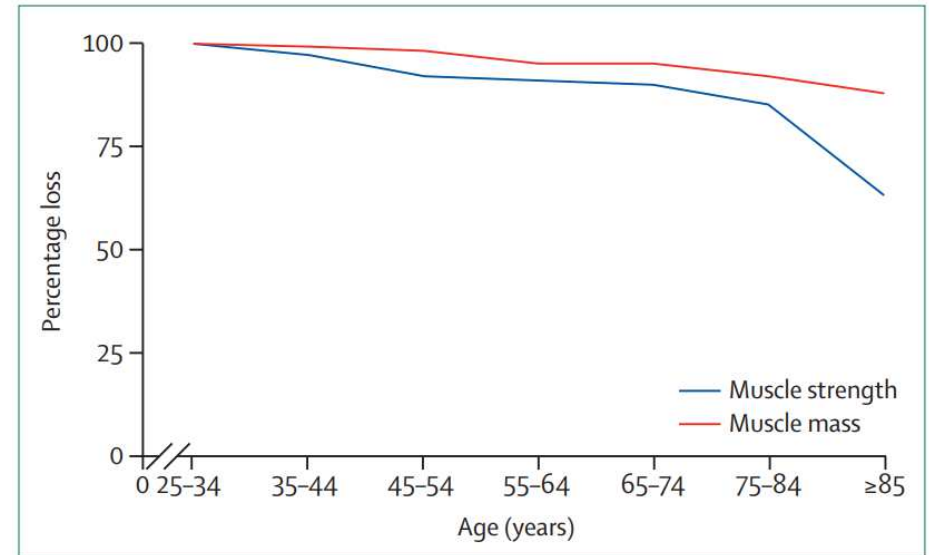


Figure 1: Percentage loss of muscle mass and muscle strength with age in men
Data from Ferrucci et al.¹⁷

Causes of Sarcopenia

- Nutritional
- Associated with inactivity
- Disease
- Iatrogenic

Panel 2: Frequent underlying causes of sarcopenia

Nutritional

- Low protein intake
- Low energy intake
- Micronutrient deficiency
- Malabsorption and other gastrointestinal conditions
- Anorexia (ageing, oral problems)

Associated with inactivity

- Bed rest, immobility, deconditioning
- Low activity, sedentary lifestyle

Disease

- Bone and joint diseases
- Cardiorespiratory disorders including chronic heart failure and chronic obstructive pulmonary disease
- Metabolic disorders (particularly diabetes)
- Endocrine diseases (particularly androgen deprivation)
- Neurological disorders
- Cancer
- Liver and kidney disorders

Iatrogenic

- Hospital admission
- Drug-related

Diagnosis of Sarcopenia

- Diagnosis requires measurement of a combination of **muscle mass, muscle strength, and physical performance**
- **EWGSOP2** proposed a stepwise approach to diagnosis
 - **Physical performance** : SARC-F
 - **muscle strength** : **grip strength**
 - **muscle mass** : **dual energy X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), CT, MRI**

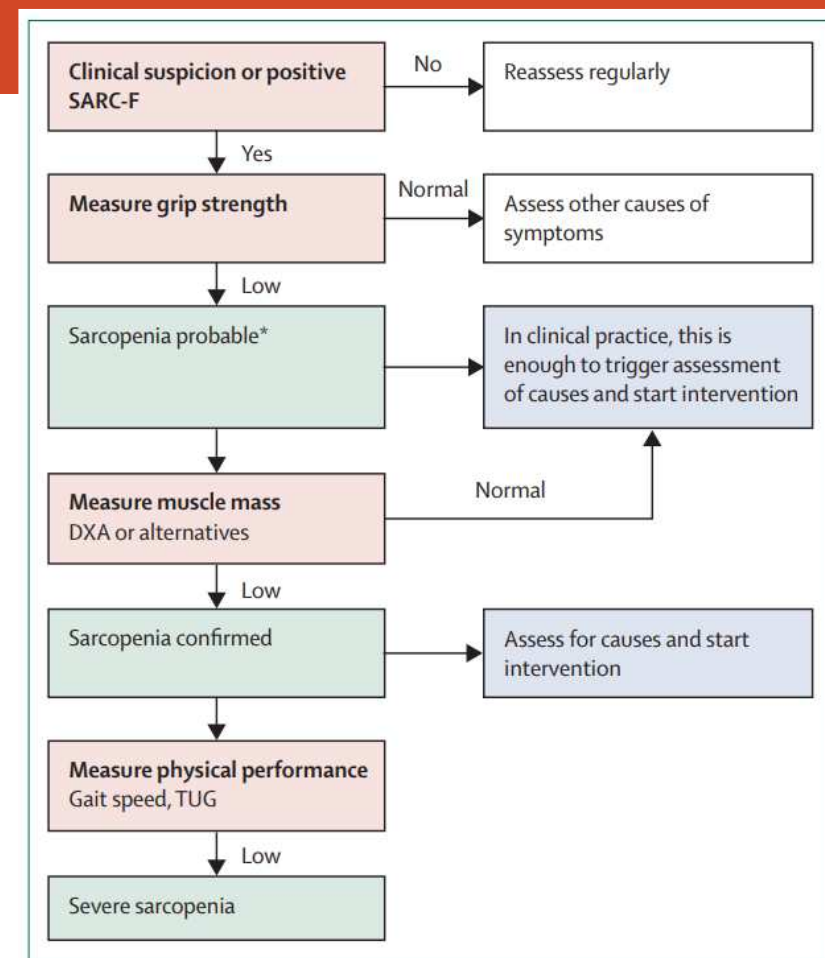


Figure 2: A simple algorithm to diagnose sarcopenia in clinical practice

Diagnosis of Sarcopenia

* SARC-F

: A Simple Questionnaire to
Rapidly Diagnose Sarcopenia
: total score 0-10
: ≥ 4 is predictive of sarcopenia
and poor outcomes.

Table 1
SARC-F Screen for Sarcopenia

Component	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None = 0 Some = 1 A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0 Some = 1 A lot, use aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0 Some = 1 A lot or unable without help = 2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None = 0 Some = 1 A lot or unable = 2
Falls	How many times have you fallen in the past year?	None = 0 1–3 falls = 1 4 or more falls = 2

Diagnosis of Sarcopenia

- **Muscle quality**

- two different concepts

: the association between strength and mass

: observable characteristics of muscle such as intermuscular or intramuscular adiposity

- yet is not sufficiently defined for use in clinical practice

- **Physical performance**

- gait speed, the 400m timed walk, Short Physical Performance Battery, the Timed Up and Go test

Diagnosis of Sarcopenia

- **Severity of sarcopenia**
 - Grading the severity of sarcopenia is important to predict outcomes and to choose the intensity of interventions
 - Severe vs. non-severe sarcopenia

Table 1. 2018 operational definition of sarcopenia

Probable sarcopenia is identified by Criterion 1.

Diagnosis is confirmed by additional documentation of Criterion 2.

If Criteria 1, 2 and 3 are all met, sarcopenia is considered severe.

1. Low muscle strength
2. Low muscle quantity or quality
3. Low physical performance

Diagnosis of Sarcopenia

- **Alternative or new tests and tools**
 - Blood biomarkers
 - Creatine dilution test : measuring skeletal muscle mass

Diagnosis of Sarcopenia

- **Differential diagnosis**

- malnutrition
- Cachexia
- frailty

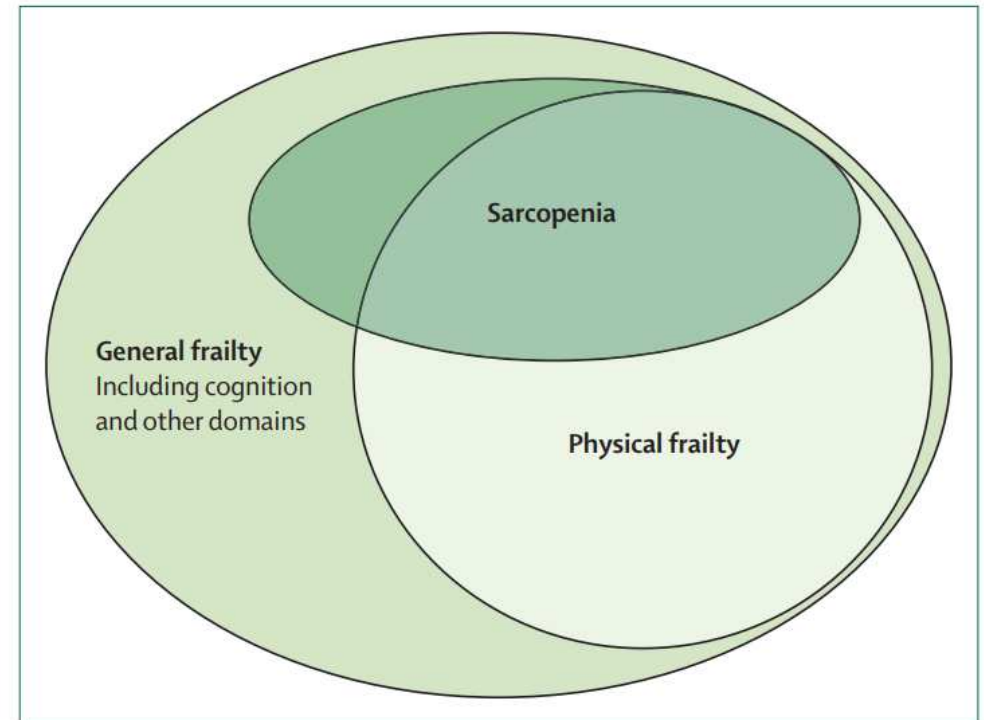


Figure 3: Schematic diagram showing the diagnostic overlap between sarcopenia and physical or general frailty

Pathophysiology of Sarcopenia

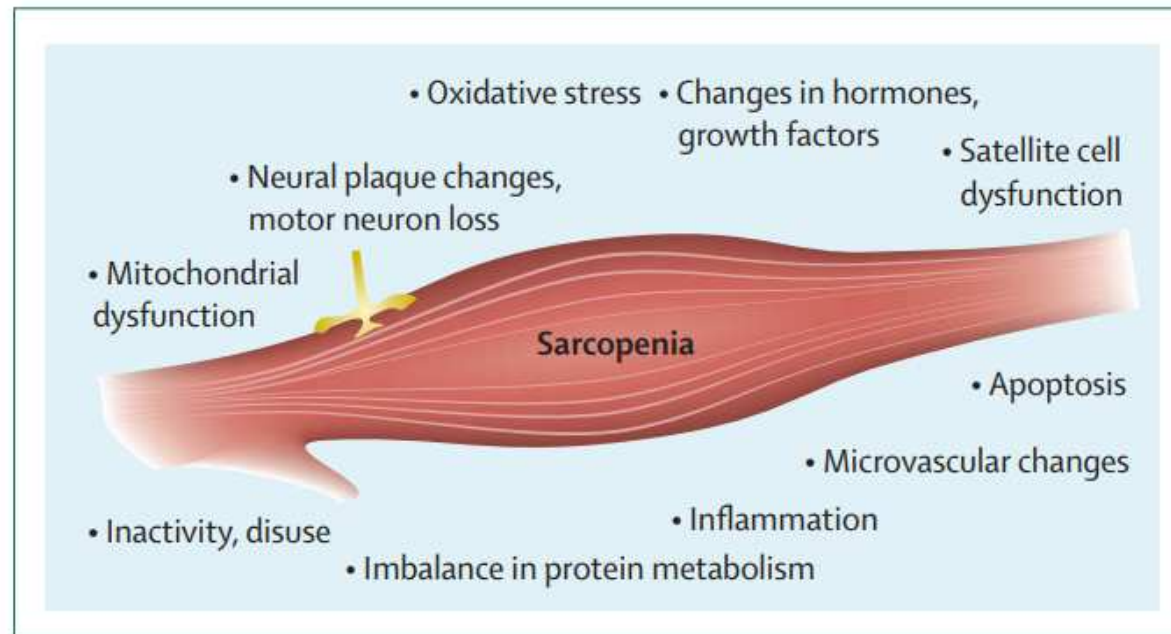


Figure 4: The multifactorial causes of sarcopenia

Health consequences of Sarcopenia

- Falls
- Physical frailty and disability
- Mortality

Marzetti E, Calvani R, Tosato M, Cesari M, Di Bari M, Cherubini A, et al. Sarcopenia: an overview. *Aging clinical and experimental research*. 2017;29(1):11-7.
Choi KM. Sarcopenia and sarcopenic obesity. *Endocrinology and metabolism*. 2013;28(2):86-9.

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Sarcopenic Obesity

- **Sarcopenic Obesity**
 - co-presence of sarcopenia and obesity
 - silent, progressive condition, tightly linked to aging
 - associated with deterioration in quality of life (QoL) and all-cause mortality

Definition of Sarcopenic Obesity

- **first defined by Baumgartner (In 2000)**
 - as a muscle mass index less than 2 SD below the sex-specific reference for a young, healthy population
 - * **muscle mass index** : appendicular skeletal muscle mass (ASM) divided by height squared (ASM/height²)
 - measured using dual X-ray absorptiometry.

- **defined by Davison et al. (In 2002)**
 - using anthropometrics and bioelectrical impedance

Stenholm S, Harris TB, Rantanen T, Visser M, Kritchevsky SB, Ferrucci L. Sarcopenic obesity-definition, etiology and consequences. *Current opinion in clinical nutrition and metabolic care*. 2008;11(6):693.

Kim TN, Yang S, Yoo H, Lim K, Kang H, Song W, et al. Prevalence of sarcopenia and sarcopenic obesity in Korean adults: the Korean sarcopenic obesity study. *International journal of obesity*. 2009;33(8):885-92.

Diagnosis of Sarcopenic Obesity

- at present, **no consensus on the definition** of sarcopenic obesity
- an appropriate definition would include the criteria for both sarcopenia and for obesity

- **Definition of Sarcopenia**
 - (a) low muscle mass, (b) low muscle strength, and (c) low physical performance

- **Definition of Obesity**
 - abnormal or excessive FAT accumulation that presents a risk to health
 - BMI, PBF, WC, etc.

Diagnosis of Sarcopenic Obesity

Author, year, and study name	Definition of Sarcopenia			Definition of obesity
	Muscle Mass	Muscle Strength	Physical Performance	
Baumgartner, 2000 [18]	DXA:ASM/ht ² < 7.26kg/m ² (M) ASM/ht ² < 5.45kg/m ² (F)	/	/	PBF > 27%(M) PBF > 38%(F)
Newman, 2003 [21]	DXA:ASM/ht ² < 7.23kg/m ² (M) ASM/ht ² < 5.67kg/m ² (F)	/	/	BMI ≥ 30kg/m ²
Baumgartner, 2004 [22] New Mexico Aging Process Study	DXA:ASM/ht ² < 7.26kg/m ² (M) ASM/ht ² < 5.45kg/m ² (F)	/	/	PBF > 27%(M) PBF > 38%(F)
Kim T.N, 2009, The Korean sarcopenic obesity study [23]	DXA:ASM/ht ² < 7.26 kg/m ² (M) ASM/ht ² < 5.45 kg/m ² (W)	/	/	PBF > 27%(M) PBF > 38%(F)
Cruz-Jentoft, 2010, EWGSOP [24]	DXA: ASM/ht ² < 7.26kg/m ² (M) ASM/ht ² < 5.50kg/m ² (F) (Rosetta Study) DXA: ASM/ht ² < 7.25kg/m ² (M) ASM/ht ² < 5.67kg/m ² (F) (health ABC study) DXA: ASM/ht ² < 7.23kg/m ² (M) ASM/ht ² < 5.67kg/m ² (F) (health ABC study) DXA: Residuals of linear regression on appendicular lean mass adjusted for fat mass as well as height: -2.29 (M), -1.73 (W) BIA: SM/ht ² < 8.87kg/m ² (W) SM/ht ² < 6.42kg/m ² (F) BIA: absolute muscle mass/ht ² severe < 8.50kg/m ² (W); < 5.75kg/m ² (F) Moderate 8.51-10.75 kg/m ² (W); 5.76-6.75kg/m ² (F)	Handgrip < 30 kg (M) Handgrip < 20 kg (F) Handgrip based on BMI category: Men: BMI ≤ 24 ≤ 29kg BMI 24.1-26 ≤ 30kg BMI 26.1-28 ≤ 30kg BMI > 28 ≤ 32kg Women: BMI ≤ 23 ≤ 17kg BMI 23.1-26 ≤ 17.3kg BMI 26.1-29 ≤ 18kg BMI > 29 ≤ 21kg	GS < 0.8 m/s (4 m) Or < 1.0 m/s (6 m) SPPB ≤ 8 points score	/

Ji T, Li Y, Ma L. Sarcopenic Obesity: An Emerging Public Health Problem. Aging and Disease. 2022;13(2):379..

Diagnosis of Sarcopenic Obesity

Fielding, 2011, IWGS [25]	DXA: $ASM/ht^2 \leq 7.23 \text{ kg/m}^2$ (M) $ASM/ht^2 \leq 5.67 \text{ kg/m}^2$ (F)	/	GS < 1.0 m/s (6 m)	/
Studenski, 2014, FNIH [26]	DXA: ALM < 19.75kg (W) ALM < 15.02kg (F) DXA: ALM/BMI < 0.789 (W) ALM/BMI < 0.512 (F)	Handgrip < 26 kg (M) Handgrip < 16kg (F) Handgrip: BMI < 1.0 (M) Handgrip: BMI < 0.56 (F)	/	/
Chen LK, 2014, AWGS [27]	DXA: $ASM/ht^2 < 7.0 \text{ kg/m}^2$ (M) $ASM/ht^2 < 5.4 \text{ kg/m}^2$ (F) BIA: $ASM/ht^2 < 7.0 \text{ kg/m}^2$ (M) $ASM/ht^2 < 5.7 \text{ kg/m}^2$ (F)	Handgrip < 26 kg (M) Handgrip < 18kg (F)	GS < 0.8 m/s (6 m)	/
Chuang 2015 [28]	DXA: $TSM/ht^2 < 11.45 \text{ kg/m}^2$ (M) $TSM/ht^2 < 8.51 \text{ kg/m}^2$ (F)	/	/	WC ≥ 90 cm (M) WC ≥ 80 cm (F)
Cruz-Jentoft, 2019, EWGSOP2 [29]	Use SARC-F questionnaire to find subjects with sarcopenia DXA/BIA: $ASM < 20 \text{ kg}$ (M) $ASM < 15 \text{ kg}$ (F) DXA/BIA: $ASM/ht^2 < 7.0 \text{ kg/m}^2$ (M) $ASM/ht^2 < 6.0 \text{ kg/m}^2$ (F)	Handgrip < 27 kg (M) Handgrip < 16kg (F) Chair stand > 15s for five rises	GS $\leq 0.8 \text{ m/s}$ (6 m) SPPB ≤ 8 point score TUG ≥ 20 s 400m walk test: non-completion or 6 min for completion	/

Diagnosis of Sarcopenic Obesity

Table 2. Different measurement methods of sarcopenic obesity.

Sarcopenia			Obesity	
Muscle Mass	Muscle Strength	Physical Performance	Adiposity	Fat Mass
DXA (ASM/h ² , ASM/wt, etc)	HGS	GS	Anthropometry	CT
Anthropometry (MAMC, calf circumference)	maximal knee extensor strength	TUG SPPB	(BMI, WC) DXA(PBF) BIA(PBF)	MRI
BIA (ASM/h ² , ASM/wt, etc)				
Ultrasonography, CT, MRI				

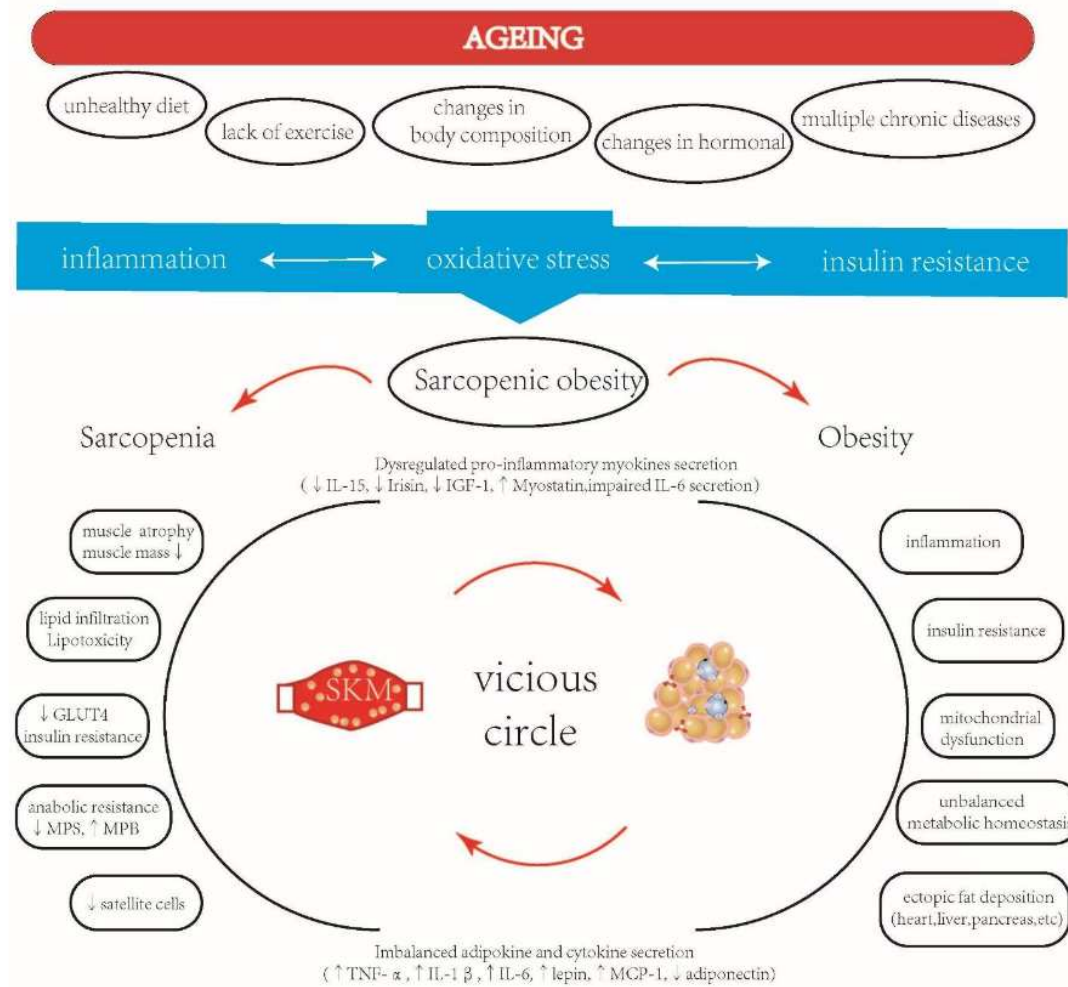
Abbreviations: DXA, dual-energy X-ray absorptiometry; ASM/wt, appendicular skeletal muscle divided by Weight; ASM/h², appendicular skeletal muscle divided by height in meters squared; MAMC, mid-arm muscle circumference; BIA, bioelectrical impedance analysis; CT, computed tomography scan; MRI, magnetic resonance imaging; HGS, hand grip strength; GS, gait speed; TUG, timed up-and-go; SPPB, short physical performance battery; PBF, percentage of body fat.

Pathophysiology of Sarcopenic Obesity

- Age-related changes in body composition
- Physical activity
- Inflammation
- Insulin resistance
- Growth hormone and testosterone
- Malnutrition and weight loss
- Association between obesity and muscle impairment

Stenholm S, Harris TB, Rantanen T, Visser M, Kritchevsky SB, Ferrucci L. Sarcopenic obesity-definition, etiology and consequences. *Current opinion in clinical nutrition and metabolic care*. 2008;11(6):693.

Pathophysiology of Sarcopenic Obesity



Ji T, Li Y, Ma L. Sarcopenic Obesity: An Emerging Public Health Problem. *Aging and Disease*. 2022;13(2):379.

Health consequences of Sarcopenic Obesity

Table 2 Potential consequences of sarcopenic obesity

Metabolic consequences

Higher IR

Higher rates of MetS

Increased arterial stiffness

Higher rates of dyslipidemia

Higher rates of arterial hypertension

Positive association with GGT

Physical capacity

Lower levels of physical fitness

Impaired physical functioning

Worse balance

Worse aerobic capacity

Higher rates of frailty

Positive association with osteoporosis

Higher rates of falls and fractures

Quality of life

Inverse association with QoL (controversial)

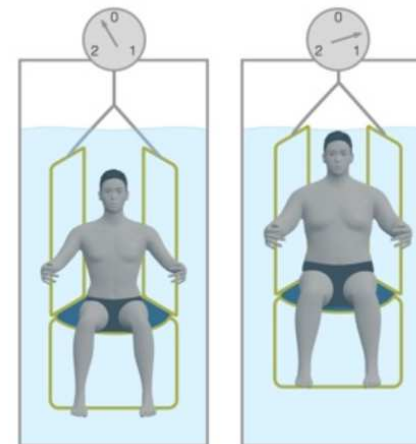
Inverse association with perceived stress and suicidal ideation

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Obesity

- **Definition :**
 - Overweight and obesity are defined as **abnormal or excessive FAT accumulation** that presents a risk to health (WHO)
- **Diagnosis :** Hydrostatic underwater weighing



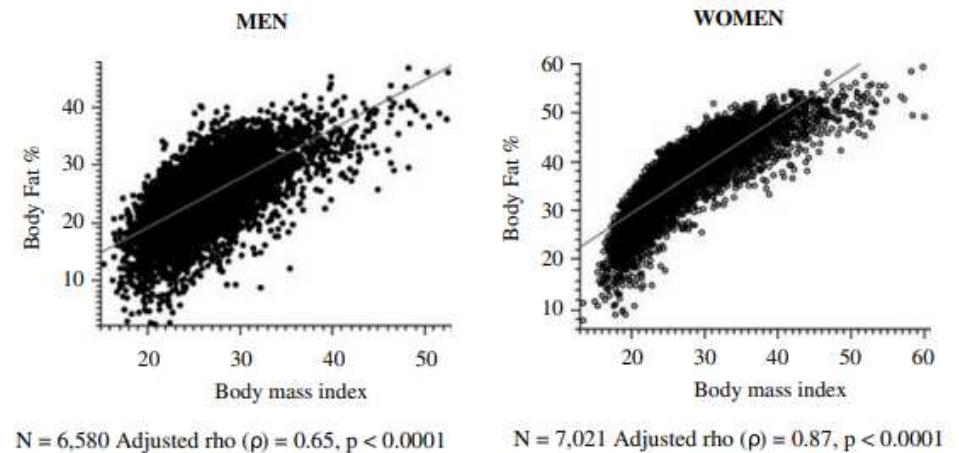
<https://support.fitdigits.com/health-through-fitness/a-healthy-living-weight/>
<https://dototetg.weebly.com/blog/body-composition1>

- **Diagnosis** : Body Mass Index, BMI
- $BMI = \text{Body weight(Kg)} / \text{Height(m)}^2$

Table I Obesity classification according to WHO and Asia-Pacific guidelines

	WHO (BMI)	Asia-Pacific (BMI)
Underweight	<18.5	<18.5
Normal	18.5–24.9	18.5–22.9
Overweight	25–29.9	23–24.9
Obese	≥30	≥25

Abbreviations: WHO, World Health Organization; BMI, body mass index.



Romero-Corral A, Somers VK, Sierra-Johnson J, Thomas RJ, Collazo-Clavell M, Korinek J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. *International journal of obesity*. 2008;32(6):959-66.

Lim JU, Lee JH, Kim JS, Hwang YI, Kim T-H, Lim SY, et al. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. *International journal of chronic obstructive pulmonary disease*. 2017;12:2465.

Obesity Paradox

Journal of the American College of Cardiology
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Published by Elsevier Science Inc.

Vol. 39, No. 4, 2002
ISSN 0735-1097/02/\$22.00
PII S0735-1097(01)01802-2

Interventional Cardiology

The Impact of Obesity on the Short-Term and Long-Term Outcomes After Percutaneous Coronary Intervention: The Obesity Paradox?

Luis Gruberg, MD, Neil J. Weissman, MD, FACC, Ron Waksman, MD, FACC, Shmuel Fuchs, MD, Regina Deible, RN, Ellen E. Pinnow, MS, Lanja M. Ahmed, MD, Kenneth M. Kent, MD, PhD, FACC, Augusto D. Pichard, MD, FACC, William O. Suddath, MD, Lowell F. Satler, MD, FACC, Joseph Lindsay, JR, MD, FACC
Washington, D.C.

- 9633 patients who underwent PCI (1994.01-1999.12)
- short-term outcome, long-term outcome & BMI -> better prognosis in obese group
- > "Obesity Paradox"

Gruberg L, Weissman NJ, Waksman R, Fuchs S, Deible R, Pinnow EE, et al. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? Journal of the American College of Cardiology. 2002;39(4):578-84.

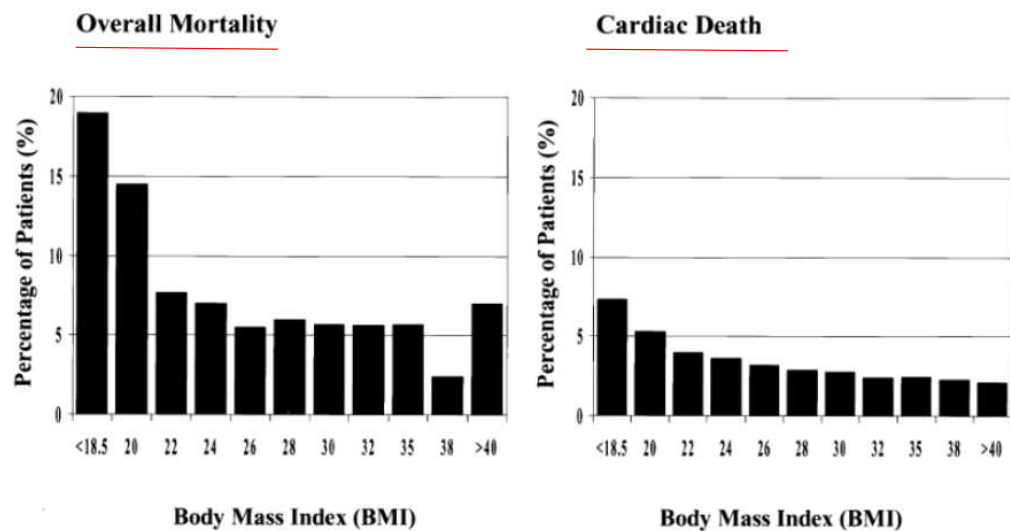


Figure 2. One-year overall and cardiac mortality rates among all patients according to body mass index (BMI).

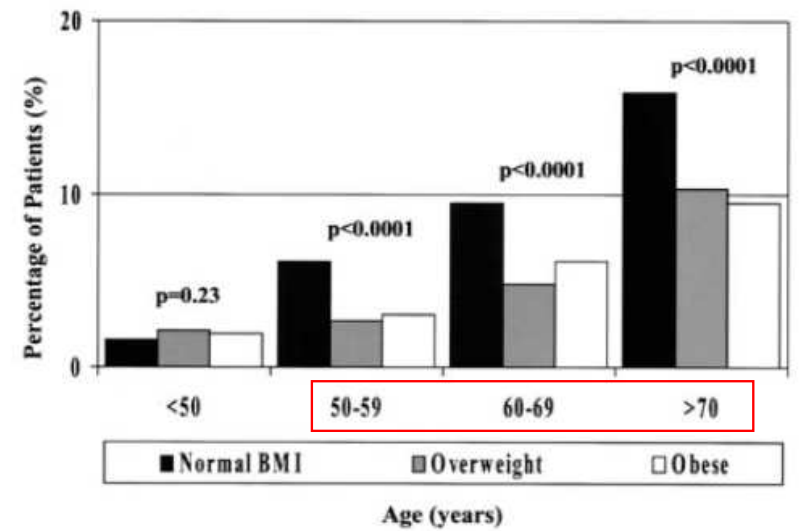


Figure 3. One-year mortality rates from all causes adjusted for age and body mass index (BMI) for all patients.

"obesity paradox"



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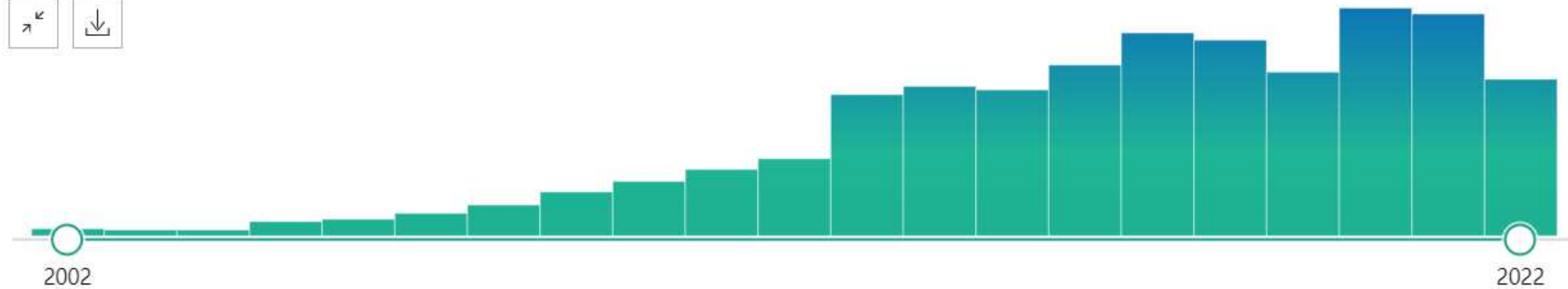
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RESULTS BY YEAR

1,442 results

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Obesity Paradox

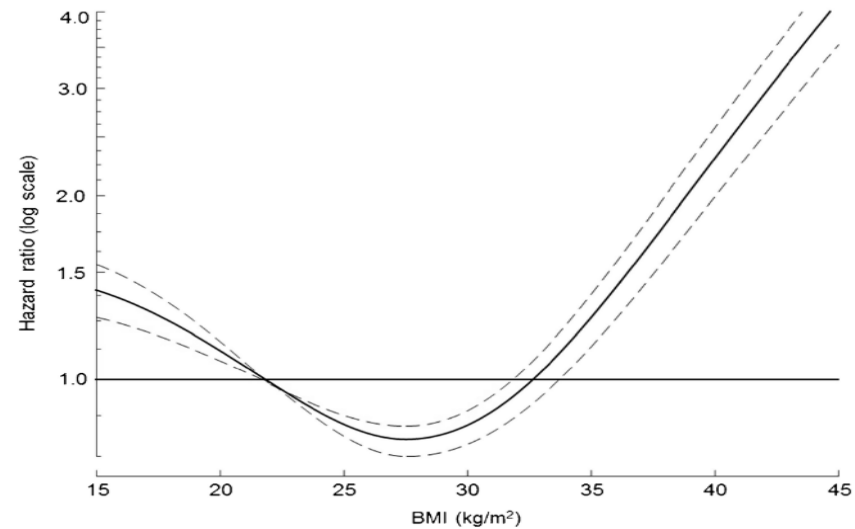


Fig. 1 An illustration of the obesity paradox. The *vertical axis* represents hazard ratio of mortality (log scale), compared with the baseline BMI of 22.5 kg/m². The *plot* represents a population in which the obesity paradox is observed, since the hazard ratio is below 1 in the overweight and obese range. The 95 % confidence intervals are shown with *dashed lines*

Obesity Paradox – Fact?

- **Biological Explanations**

- 1) Nutritional status
- 2) Muscle mass, muscle function
- 3) Role of Adipokine

Obesity Paradox – Bias?

- **Methodological Explanations**

- 1) BMI as an Inadequate Measure of Adiposity

- 2) Confounding

- 3) Selection Bias/ Collider Stratification Bias

- 4) Detection Bias

- 5) Reverse Causality

Obesity Paradox & Sarcopenic Obesity

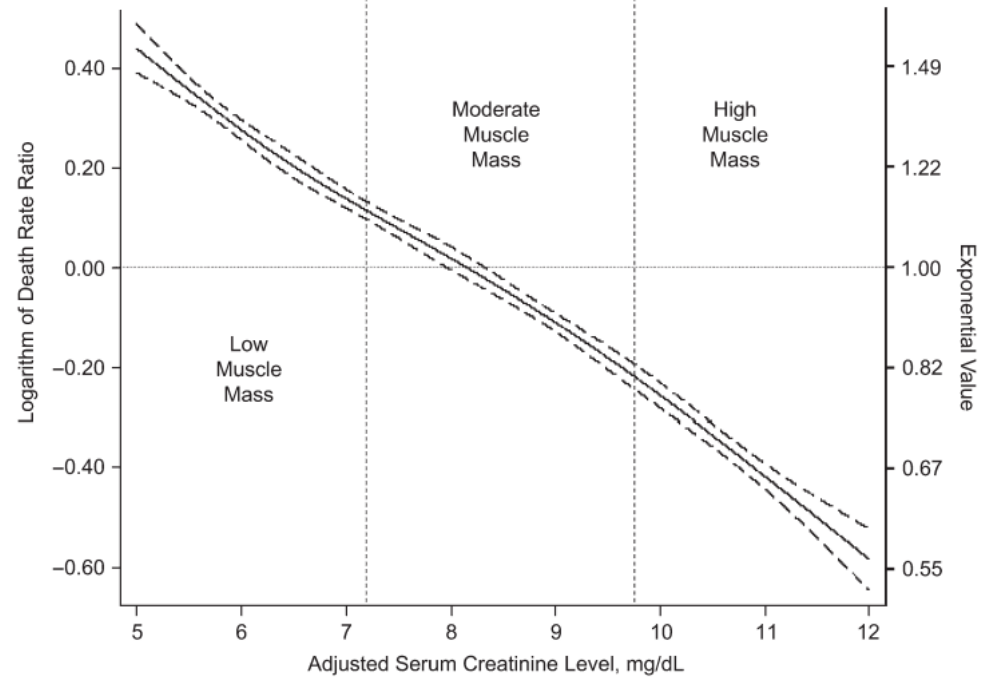
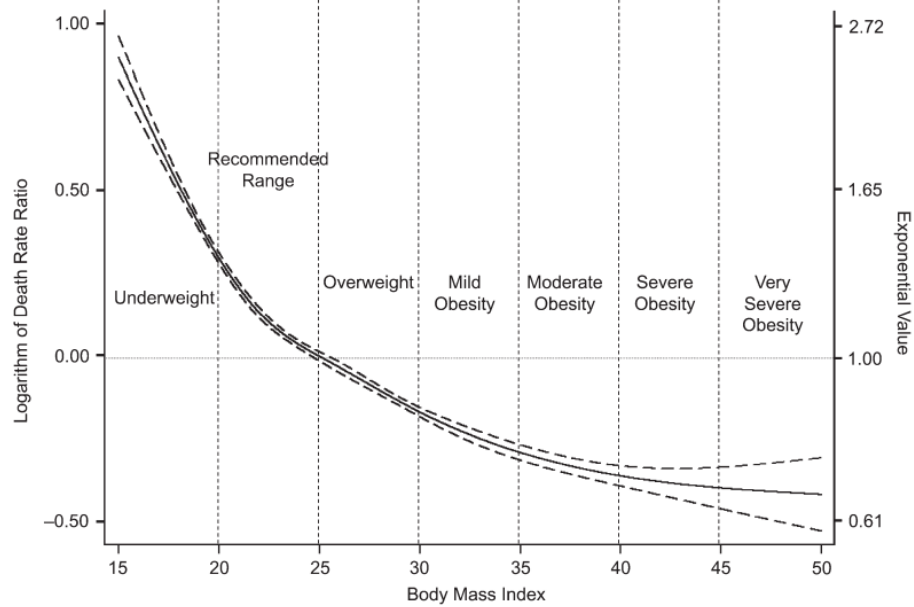
- Obesity Paradox
 - BMI as an Inadequate Measure of Adiposity
 - Lean mass vs. fat mass
 - Muscle mass?



Original Contribution

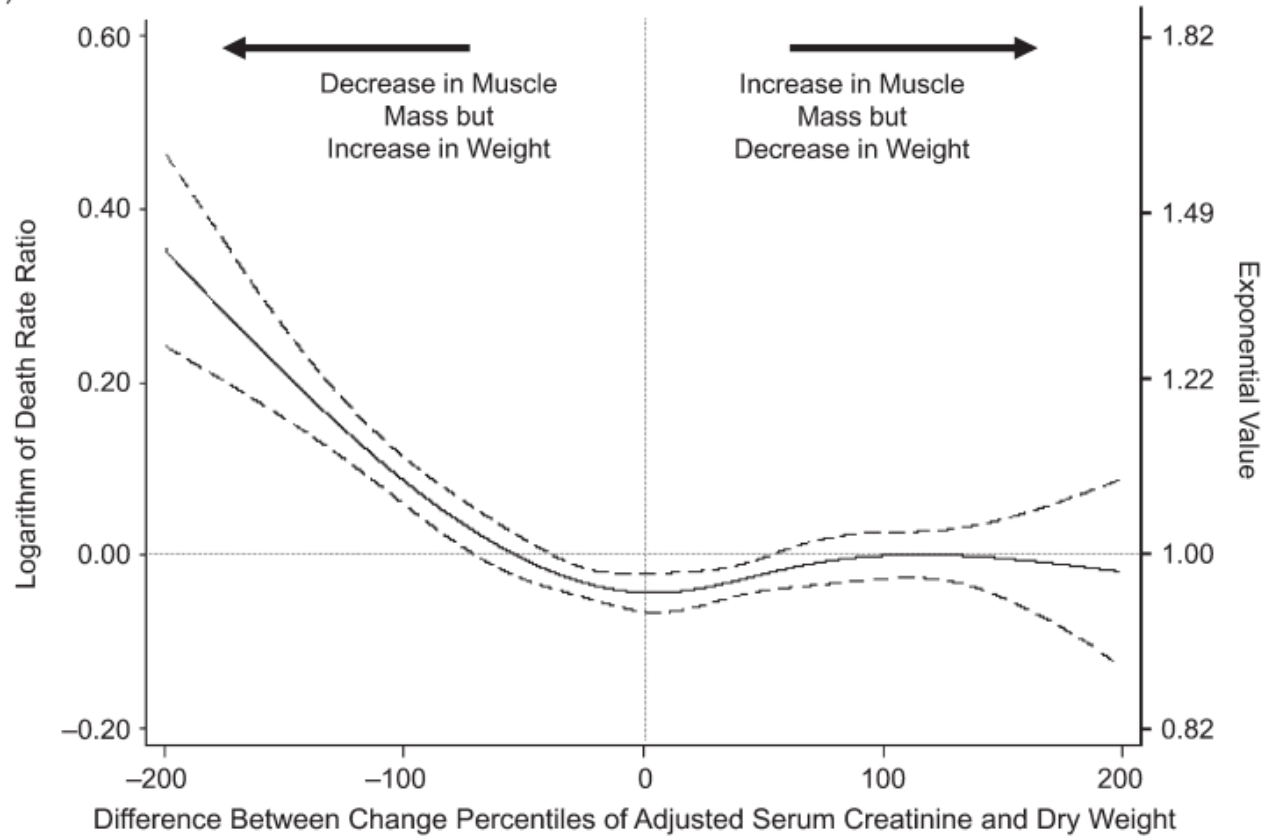
Mortality Prediction by Surrogates of Body Composition: An Examination of the Obesity Paradox in Hemodialysis Patients Using Composite Ranking Score Analysis

- 121,762 hemodialysis patients, BMI & mortality rate
- Lower BMI, higher mortality -> "obesity paradox"
- > d/t loss of muscle mass
- Check serum creatinine level (as a muscle-mass surrogate)
- > lower muscle mass and serum creatinine decline were associated with higher mortality



Kalantar-Zadeh K, Streja E, Molnar MZ, Lukowsky LR, Krishnan M, Kovesdy CP, et al. Mortality prediction by surrogates of body composition: an examination of the obesity paradox in hemodialysis patients using composite ranking score analysis. *American journal of epidemiology*. 2012;175(8):793-803.

B)



Kalantar-Zadeh K, Streja E, Molnar MZ, Lukowsky LR, Krishnan M, Kovesdy CP, et al. Mortality prediction by surrogates of body composition: an examination of the obesity paradox in hemodialysis patients using composite ranking score analysis. *American journal of epidemiology*. 2012;175(8):793-803.

Obesity paradox in cancer: new insights provided by body composition¹⁻³

Maria Cristina Gonzalez, Carla A Pastore, Silvana P Orlandi, and Steven B Heymsfield

- 175 cancer patients, BMI & mortality
- > obesity paradox
- FMI (fat mass index) vs FFMI (fat free mass index)
- > no obesity paradox
- Worst prognosis in sarcopenic obesity group

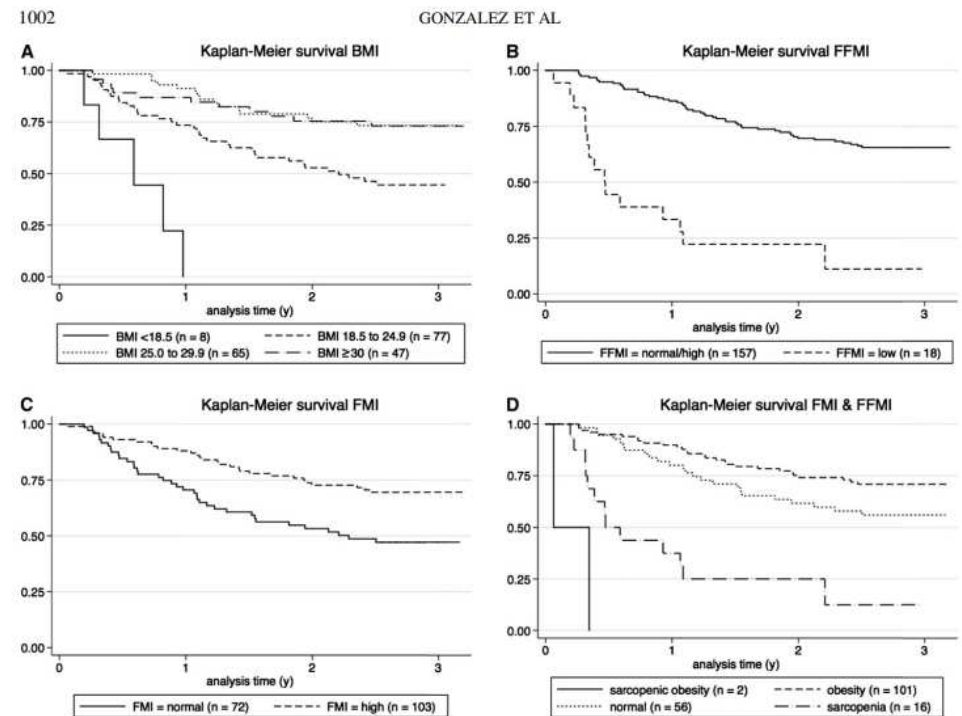


FIGURE 2. Kaplan-Meier survival curves according to BMI (in kg/m²) or body-composition analysis. A: Survival curves according to BMI groups. B: Survival curves according to a low FFMI or a normal or high FFMI. C: Survival curves according to FMI. D: Survival curves according to body-composition classification. FFMI, fat-free mass index; FMI, fat mass index.

Gonzalez MC, Pastore CA, Orlandi SP, Heymsfield SB. Obesity paradox in cancer: new insights provided by body composition. *The American journal of clinical nutrition.* 2014;99(5):999-1005.

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Conclusion

- “왜 근감소증이 중요한가?”

Conclusion

- “왜 근감소증이 중요한가?”
 - > **The importance of concept : Sarcopenia and Sarcopenic Obesity**
 - > **The importance of early diagnosis and appropriate intervention**
 - > **The importance of related research**

QnA

Thank you 😊