16th Congress of The Korean Society of Sarcopenia

2024년 대한근감소증학회
제16차 학술대회

| **일시** | 2024년 3월 16일(토) 09:00-17:00
| **장소** | 건국대학교병원 대강당
| **평점** | 대한의사협회 6평점

대한근감소증학회
The Korean Society of Sarcopenia

16th Congress of The Korean Society of Sarcopenia

2024년 대한근감소증학회 제16차 학술대회

2024년 3월 16일(토) 09:00–17:00 | 건국대학교병원 대강당 | 대한의사협회 6평점

- 프로그램 -

대학회장

08:50–09:00	Opening Remark				
Session Ⅰ Sarcopenia: How We Got Here and The Path Toward a Unified Definition	좌장: 김덕윤 경희의대, 김경민 연세의대				
09:00–09:30	Sarcopenia: Definition, Epidemiology, and Clinical Implications	원장원	경희의대	…	*3p*
09:30–10:00	Update of Mechanisms of Sarcopenia	최경묵	고려의대	…	*7p*
10:00–10:30	Changes in Sarcopenia Diagnosis Guidelines and Research Trends	백지연	울산의대	…	*9p*
10:30–10:40	Discussion				
10:40–10:55	Coffee Break				
Session Ⅱ Diagnosis Methods and Their Criteria for Sarcopenia	좌장: 김태년 인제의대, 홍성빈 인하의대				
10:55–11:20	Measurement of Skeletal Muscle Mass	전윤경	부산의대	…	*13p*
11:20–11:55	Measurement of Muscle Strength, Power and Physical Performance	김미지	경희의대	…	*17p*
11:55–12:20	Biomarkers of Sarcopenia	김범준	울산의대	…	*19p*
12:20–12:35	Discussion				
12:35–13:40	Lunch				
Session Ⅲ Sarcopenia and its Related Diseases	좌장: 하용찬 부민병원, 김태영 건국의대				
13:40–14:05	Sarcopenia and Frailty	정희원	울산의대	…	*25p*
14:05–14:30	Sarcopenic Obesity and Myosteatosis	김홍규	울산의대	…	*27p*
14:30–14:55	Osteosarcopenia	유준일	인하의대	…	*31p*
14:55–15:20	Cancer Cachexia: Targeting Pathophysiological Mechanisms	김영생	가천의대	…	*39p*
15:20–15:30	Discussion				
15:30–15:45	Coffee Break				
Session Ⅳ Management of Sarcopenia	좌장: 송욱 서울대, 이해정 가천대				
15:45–16:10	Nutritional Approaches to Treat Sarcopenia	박용순	한양대학교	…	*43p*
16:10–16:35	Exercise Interventions to Prevent and Improve Sarcopenia	이상기	충남대학교	…	*51p*
16:35–17:00	Rehabilitation Approaches in Patients with Sarcopenia	임재영	서울의대	…	*53p*
17:00–17:10	Discussion				

소학회장

Session Ⅴ Methodology of Muscle Research	좌장: 이윤실 서울대, 이승훈 원광대				
13:40–14:05	Primary Myoblast 분리와 활용	서준호	서울대 치의학대학원	…	*63p*
14:05–14:30	마우스 근육조직 분리 및 염색 방법	배주현	성균관의대	…	*67p*
14:30–14:55	마우스의 근기능과 운동능 측정 방법	김일영	가천의대	…	*69p*
14:55–15:20	근감소증의 in Vitro/in Vivo	강주희	인하의대	…	*71p*
15:10–15:30	Discussion				
15:30–15:40	Coffee Break				
Session Ⅵ Current and Upcoming Interventional Therapies for the Treatment of Sarcopenia	좌장: 이현승 충남의대, 류동렬 광주과학기술원				
15:45–16:10	Strategies for The Prevention of Sarcopenia and Frailty in Community-Dwelling Older Adults	박기수	경상의대	…	*75p*
16:10–16:35	Digital Healthcare and Sarcopenia	박현태	동아대학교	…	*79p*
16:35–17:00	The Future of Drug Treatments	권기선	한국생명공학연구원	…	*83p*
17:00–17:10	Discussion				
17:10	Closing Remark				

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Session I

Sarcopenia: How We Got Here and The Path Toward a Unified Definition

좌장: **김덕윤** 경희의대, **김경민** 연세의대

Curriculum Vitae

원장원

소속: 경희의대 가정의학교실

| 학력사항 |

서울대학교 의학과 학사
서울대학교 대학원 보건학 석사
고려대학교 대학원 예방의학 박사

| 경력사항 |

경희대학교병원 가정의학과 교수
경희대학교 노인노쇠연구센터장
경희대학교병원 어르신진료센터 소장
대한노인병학회 이사장
대한근감소증학회 명예회장

근감소증의 진단, 역학, 임상적 의의

경희의대
원장원

노화에 따라 근육량은 20~30세에 최대가 되었다가 이후 점차 감소하여, 40세 이후 70세까지는 10년에 8%씩 감소하다가 70세 이후에는 10년에 10% 가까이 감소하게 된다. 남성이 여성보다 근육량 자체는 더 많지만 나이에 따른 근육량 감소 속도는 남성이 더 빠르며, 상지보다 하지의 근육량 감소가 두드러지게 된다. 그런데 근력은 근육량보다 더 빨리 감소하여 70세 이후에는 10년에 25~35%가 감소하게 되며 여성보다 남성에서 더 빨리 감소한다.

근감소증의 진단

근감소증을 진단하려면 근육량 감소 외에도 근력 감소 또는 신체수행능력(예, 보행 속도 저하)이 동반되어야 한다. 2019년 아시아 지침(AWGS)은 사지 골격근량 측정을 위해 이중에너지 X선 흡수계측법(Dual-energy X-ray absorptiometry, DXA)이나 생체전기임피던스 측정기법(Bioelectrical impedance analysis, BIA)의 두 가지 모두 허용하고 있다. 물론 근육량을 가장 정확하게 측정하는 방법은 자기공명영상장치(Magnetic resonance imaging, MRI)와 전산단층촬영(Computed tomography, CT)이지만 이들은 비용이 비싸거나 방사선 노출 위험 증가로 임상에서 사용하기는 쉽지 않다. 반면에 DXA로 측정한 사지 골격근량에는 근육 외에도 근육 내 지방과 결합조직(섬유조직, 혈관 등)도 포함되어 측정된다는 단점이 있다.

최근엔 D3-Creatine dilution 방법을 이용한 전신의 근육량 측정방법이 실험적으로 사용되고 있다. 크레아틴(creatine)은 섭취하면 98%가 골격근에 분포되어 골격근에서 에너지를 만드는데 사용되고 크레아티닌(creatinine)으로 변형되어 소변으로 배출된다. 크레아틴의 수소기를 중수소(Deuterium = 2H)로 바꾸어 섭취하게 하고 일정 시간 뒤에 소변에서 중수소가 결합된 크레아티닌 농도를 측정함으로 체내 근육량을 계산해낼 수 있다.

이 방법의 장점은 근육 내의 지방을 포함하지 않는 근육량 측정이 가능하다는 것이다. 즉, 수축에 관여하

는 근육량만 측정하기 때문에 DXA 검사에 의한 근육량보다 근기능이나 예후와 더 잘 맞는다는 연구결과들이 있다.

근감소증의 위험 요인과 나쁜 건강결과

근감소증의 위험요인으로 가장 중요한 것은 나이(고령)이며, 생할 습관(흡연, 음주), 신체활동, 좋지않은 영양상태, 치아 상태, 그리고 각종 질환(골다공증, 갑상선질환, 당뇨병 등)이 있다.

근감소증은 치료하지 않으면 낙상과 골절 위험성을 증가시켜서 사망 위험을 증가시킬 뿐 아니라 심혈관질환(고혈압, 뇌출혈), 당뇨병, 골다공증, 폐렴, 인지기능 장애의 위험요인이며, 그 결과 요양시설 입소를 증가시키는 요인이 된다.

MEMO

Curriculum Vitae

최경묵

소속: 고려의대 내과학교실

| 학력사항 |

고려대학교 의과대학 졸업
고려대학교 의과대학 대학원 졸업

| 경력사항 |

고려의대 교수
대한내분비학회 연구이사
대한당뇨병학회 진료지침이사
대한비만학회 편집이사
대한지질동맥경화학회 학술이사

Update of Mechanisms of Sarcopenia

고려의대
최경묵

Aging results in a progressive loss of muscle mass and strength called "sarcopenia", which is Greek for ‘poverty of flesh’. Furthermore, the prevalence of obesity and osteoporosis in the elderly has markedly increased in advanced economy countries. A combination of excess body fat, and reduced muscle mass and/or strength, and osteoporosis is defined as "osteosarcopenic obesity". Muscle, bone, and fat mass are strongly inter-connected based on shared mechanism. Excess energy intake, physical inactivity, insulin resistance, hormonal changes, low-grade inflammation, oxidative stress, and impaired mitochondrial function may lead to the development of osteosarcopenic obesity. Recently, myokines, adipokines, and osteokines have been established as pivotal mediators to modulate cross-talk between muscle, adipose tissue, and bone.

We have performed a prospective cohort study named "Korean Sarcopenic Obesity Study (KSOS)" in Korean population. The purpose of KSOS was to examine the prevalence of sarcopenic obesity in Korean adults and to evaluate the effects of sarcopenic obesity on metabolic disorders. Moreover, our group have participated in the “Korean Frailty and Aging Cohort Study (KFACS)”, which is a national multicenter cohort study. KFACS have recruited community-dwelling adults aged 70-84 years from 10 medical centers nationwide. These efforts may support research to explore the pathophysiological mechanism and impact of sarcopenia and frailty in Korean population.

In this lecture, I would like to briefly summarize previous studies about mechanism of osteosarcopenic obesity and its implication with chronic metabolic diseases.

Curriculum Vitae

백지연

소속: 울산의대 내과학교실

| 학력사항 |

인제대학교 의학 학사
울산대학교 의학 석사
울산대학교 의학 박사

| 경력사항 |

서울아산병원 노년내과 촉탁임상전임강사
노인병 인정의
내분비-대사 분과 전문의

Changes in Sarcopenia Diagnosis Guidelines and Research Trends

울산의대
백지연

근감소증은 노화에 따라 발생하는 근육량 저하를 동반한 근육기능(근력) 또는 신체기능의 저하로 정의한다. 근감소증의 유병률은 인구 집단에서 연령 증가와 비례하며 아시아에서 Asian Working Group for Sarcopenia (AWGS) 2014 가이드라인에 따른 근감소증의 유병률은 5.5~25.7% 이고, 한국 연구를 기준으로는 적게는 4% 많게는 45% 이상까지도 관찰된다. 근감소증의 임상적 예후는 낙상, 사망, 기능저하에 의한 장기요양시설 입소 등 많은 노인의학적 나쁜 예후로 이어지기에, 전 세계의 인구 고령화와 함께 노인의학 분야에서 중요성이 증가되는 임상적 현상으로 간주되고 있다. 이에 따라 2016년 International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10 CM)에서는 근감소증을 질병으로 정의하였고, 한국에서도 2021년 제8차 한국표준질병 (KCD-8) 개정에서 근감소증을 M62.5로 분류하기 시작하였다.

근감소증은 노화자체와 연관된 여러가지 생물학적 기전이나 노화에 따라 축적되는 여러가지 질병에 따른 생리학, 생화학적 변화가 모두 더해져 초래되는 질환으로 그 자체로 노화 연관 질환이자 노인 증후군이다. 이러한 근감소증을 조작적으로 정의하기 위한 다양한 시도가 있어왔다. 최초에는 골다공증의 정의와 같은 방식으로 젊은 성인 인구의 근육량 분포에 기준을 두고 근육량이 일정정도 이하에 해당하는 경우 근감소증을 정의하였다. 그러나 점차 인구집단에서 근육량 뿐만 아니라 신체기능이 차지하는 임상적 중요성에 대한 연구 결과가 축적되면서 근감소증의 개념이 확장되었다. 대표적으로 2010년 유럽 근감소증 가이드라인 (European Working Group on Sarcopenia in Older People, EWGSOP)에서 근감소증을 근육량과 근육기능 두가지 기준을 바탕으로 정의하기 시작하였고, 이후 다양한 인구 집단과 환경에서의 역학 연구와 중재연구가 발표되었으며, 미국의 Foundation for the National Institutes of Health (FHIH), 유럽에서 EWGSOP를 개정한 EWGSOP2 정의, 2014년 발표된 아시아 근감소증 기준(Asian Working Group on Sarcopenia, AWGS)을 개정한 AWGS 2019 등이 차례로 발표되었다.

그러나 근감소증의 이러한 조작적 정의 자체가 전 세계적인 합의에 이르지 못하면서, 실제 임상현장에서

근감소증을 조기에 스크리닝, 진단하는 일이 잘 이루어지지 않고 있다. 이에 본 강의에서는 전체적인 근감소증 조작적 정의의 흐름을 소개하고, 향후 연구 방향에 대해 소개하고자 한다.

16th Congress of The Korean Society of Sarcopenia

2024년 대한근감소증학회 제16차 학술대회

Session II

Diagnosis Methods and Their Criteria for Sarcopenia

좌장: **김태년** 인제의대, **홍성빈** 인하의대

Curriculum Vitae

전윤경

소속: 부산의대 내과학교실

| 학력사항 |

부산대학교 의과대학 졸업
부산대학교 대학원 의학석사
부산대학교 대학원 의학박사

| 경력사항 |

부산대학교병원 내분비대사내과 기금부교수
대한비만학회 연수위원회 위원
대한내분비학회 수련위원회 위원
골대사학회 부울경지회 총무이사
골대사학회 국제협력이사, 학술위원회 위원

Measurement of Skeletal Muscle Mass

부산의대
전윤경

In the last years, there is an increasing interest in body composition assessment in the clinical practice as it can improve the clinical assessment of the patient and their impact on health. In this lecture, I intend to review to various method to measure skeletal muscle mass.

First, anthropometric measures are not body composition techniques; they could be considered as a marker of adiposity and muscularity. Mid-arm muscular circumference (MAMC) and calf circumference have shown to be correlated with muscle mass, and other anthropometric measures, as skinfold thickness, which can be used as a surrogate to estimate body fat through predictive equations when another body composition analysis is unavailable. Secondly, dual Energy X-ray absorptiometry (DXA) represented a reference method for the assessment of human body composition in the research field, considering its fast acquisition time, low radiation exposure, and relatively low cost when compared with other available techniques. However, DXA does not measure muscle mass specifically [19], and there is not acceptable evidence reporting the validity of DXA for lean mass assessment in any clinical population. Another doubly indirect method to estimate body compartments is the bioelectrical impedance analysis (BIA). BIA is based on the conductivity of the tissues according to their hydration and it estimates total body water volume and several other body compartments related to muscle mass (fat-free mass – FFM, skeletal muscle mass, and lean mass) through predictive equations. Ultrasound is a practical, noninvasive, and readily available method that has gained attention in recent years as a portable technique to assess body composition, especially muscle mass. Computed tomography (CT) is another image technique used for the body composition assessment. The muscle mass assessment by CT can be obtained by measuring the total area of skeletal muscle or psoas muscle at the level of

the third lumbar vertebra (L3), adjusted for the squared height (skeletal muscle index – SMI), through specific software. In regard to the magnetic resonance imaging (MRI), it is considered the gold standard for muscle mass and other body compartment evaluation but this method is too cumbersome and expensive for clinical practice, being restricted to research settings, and it is even rarely used in studies with large sample sizes. Biological methods, as the 24-h urinary creatinine excretion and D3-creatinine dilution in a single urine sample, can provide direct information about the muscle mass. There are various approaches to accurately detect muscle mass. More research is needed.

Curriculum Vitae

김미지

소속: 경희의대 융합의과학교실

| 학력사항 |

M.S University of Tsukuba, Japan Graduated School of Comprehensive Human sciences
Ph.D University of Tsukuba, Japan Graduated School of Comprehensive Human Sciences

| 경력사항 |

- National Research Foundation of Korea (NRF) grant-Sejong Science Fellowship (2023) Role: Supervisor
- National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) [grant numbers 2022R1A2C1012305]- Identification of circulating microRNA as novel early diagnostic and predictive biomarkers for aging-related sarcopenia
- The Research Program funded by the National Institute of Health, Korea Disease Control and Prevention Agency (2021-ER0605-00)- Korean Frailty and Aging Cohort Study (KFACS)
- Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Korea Ministry of Education [grant numbers 2017R1D1A1B03035192]- Elucidation of the Role and Digonosis of Ectopic Fat derived from Magnetic Resonance Imaging in Age-related Sarcopenia

Measurement of Muscle Strength, Power and Physical Performance

경희의대
김미지

근감소증의 임상적 정의는 근육량 감소와 더불어 근력의 약화 또는 보행속도와 신체활동 수행능력으로 대변되는 신체기능의 저하가 동반되는 경우를 의미한다. 현재 사용되고 있는 근감소증 진단 가이드라인에서 근육량 이외에, 근력 및 신체기능 평가가 근감소증 진단에 매우 중요하다는 견해가 우세하다.

2018년 개정된 유럽 노인 근감소증 워킹 그룹(European Working Group on Sarcopenia in Older People, EWGSOP 2)은 근육감소증의 1차 진단 변수로 낮은 근력(muscle strength)을 측정하여 “Probable sarcopenia”를 확인할 수 있으며, 근력측정 항목으로 악력과 의자 앉았다 일어서기(chair stand test)를 권고하고 있다. 또한, 중등도 결정(severity determination)에 사용할 수 있는 임상알고리즘(clinical algorithm)에서는 신체기능 저하를 진단할 수 있는 보행속도를 포함하여 신체기능 항목(short physical performance battery [SPPB], Timed-up-and-go test, 400-meter walk)들을 측정하도록 권고하고 있다. 또한, 개정된 아시아 근감소증 워킹 그룹(Asian Working Group for Sarcopenia, AWGS 2019)은 신체 기능 저하 (5-time chair stand test ≥12 seconds) 또는 낮은 근력(handgrip strength <28 kg for men and <18 kg for women)으로 정의되는 "possible sarcopenia " 개념을 소개하였다. 또한, 근육량 감소와 근력 감소 (악력), 그리고 신체 기능 저하(3가지 측정항목 중에서 하나라도 진단기준에 해당될 경우: gait speed <0.1m/s, SPPB ≤ 9 scores, chair stand test ≥12 seconds)를 모두 가진 환자를 "severe sarcopenia"으로 정의하였다. 2020년 미국 Sarcopenia Diagnostic and Outcomes Consortium (SDOC) 그룹에서는 악력과 보행속도의 평가로만 근감소증을 진단하고 있다. 최근 Global Leadership in Sarcopenia (GLIS) 그룹에서 임상 및 연구환경에서 국제적으로 근감소증 정의 및 진단에 대한 하나의 정의를 사용하기 위해서 합의점을 얻고자 노력 중이며, GLIS의 첫번째 단계로 공통 용어 정리하는 작업에서 신체기능 평가를 “objective physical performance”로, 근력 및 근파워는 “muscle function”로 분류하고 있다.

따라서, 본 강의에서는 최신 근감소증 진단 가이드라인의 근감소증의 진단을 위한 근 기능 및 신체기능 측정 프로토콜 및 진단 기준을 살펴보고, 의료기관 및 연구환경에 따라 가장 적합한 평가도구가 무엇인지 알아보고자 한다.

Curriculum Vitae

김범준

소속: 울산의대 내과학교실

| 학력사항 |

울산대학교 의학 학사
울산대학교 의학 석사
울산대학교 의학 박사

| 경력사항 |

울산의대 서울아산병원 교수
Medical College of Georgia 방문교수

Blood-Based Biomarker for Sarcopenia

울산의대
김범준

근감소증 혈액 바이오마커: Present

Recent Consensus Paper

Biochemical Markers of Musculoskeletal Health and Aging to be Assessed in Clinical Trials of Drugs Aiming at the Treatment of Sarcopenia: Consensus Paper from an Expert Group Meeting Organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the Centre Académique de Recherche et d'Expérimentation en Santé (CARES SPRL), Under the Auspices of the World Health Organization Collaborating Center for the Epidemiology of Musculoskeletal Conditions and Aging

Aurélie Ladang[1] · Charlotte Beaudart[2] · Jean-Yves Reginster[2,3] · Nasser Al-Daghri[3] · Olivier Bruyère[2] · Nansa Burlet[2] · Matteo Cesari[4,5] · Antonio Cherubini[6] · Mario Coelho da Silva[7] · Cyrus Cooper[8] · Alfonso J. Cruz-Jentoft[9] · Francesco Landi[10] · Andrea Laslop[11] · Stefania Maggi[12] · Ali Mobasheri[2,13,14,15] · Sif Ormarsdottir[16] · Régis Radermecker[17] · Marjolein Visser[18] · Maria Concepcion Prieto Yerro[19] · René Rizzoli[20] · Etienne Cavalier[1]

Abstract

In clinical trials, biochemical markers provide useful information on the drug's mode of action, therapeutic response and side effect monitoring and can act as surrogate endpoints. In pharmacological intervention development for sarcopenia management, there is an urgent need to identify biomarkers to measure in clinical trials and that could be used in the future in clinical practice. The objective of the current consensus paper is to provide a clear list of biochemical markers of musculoskeletal health and aging that can be recommended to be measured in Phase II and Phase III clinical trials evaluating new chemical entities for sarcopenia treatment. A working group of the European Society for Clinical and Economic Aspects of

Calcif Tissue Int. 2023 Feb;112(2):197-217

Two Sets of Biochemical Markers

- **The first category**: markers evaluating **musculoskeletal status**
  - muscle mass, neuro-muscular junction, muscle turnover and myokines
- **The second set**: markers evaluating **non-muscle-specific pathophysiological mechanisms**, referred to as causal factors
  - Three subclasses: adipokines, hormones, and inflammatory markers
- **At least one biochemical marker per subclass for each set** , except for muscle mass biochemical markers, **should be selected** if the pharmacological trial is a phase II or a phase III trial

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Recommended Musculoskeletal Markers

	Phase II		Phase III	
	Recom-mendation	Time point assessment	Recom-mendation	Time point assessment
Assessment of musculoskeletal status				
Muscle mass				
D3creatine dilution test	N		N	
Myokines				
Myostatin – Follistatin	M	Every 3 months	M*	Every 3 months
Activin A	FRN		FRN	
GDF-15	O	Baseline	O	Baseline
Irisin	FRN		FRN	
Neuro-muscular junction				
CAF	N		N	
BDNF	M	Every 3 months	M	Every 3 months
Others				
PIIINP	M	Every 3 months	M	Every 3 months
Sarcopenia index	M	Baseline	M	Baseline

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Recommended Causal Factors

	Phase II		Phase III	
	Recom-mendation	Time point assessment	Recom-mendation	Time point assessment
Assessment of causal factors				
Adipokines				
Adiponectin	O*	Every 3 months	O*	Every 6 months
Leptin	O*	Every 3 months	O*	Every 6 months
Hormones				
IGF-1	M	Every 3 months	M	Every 6 months
DHEAS	M*	Every 3 months	O*	Every 6 months
Cortisol	M*	Every 3 months	O*	Every 6 months
Testosterone	O*	Every 3 months	O*	Every 6 months
Inflammatory markers				
CRP	M	Every 3 months	M	Every 6 months
IL-6	M	Every 3 months	O	Every 6 months
TNF-α	M	Every 3 months	O	Every 6 months

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Weakness of Musculoskeletal Factors

Assessment of musculo-skeletal status	Modification in sarcopenia	Evidence	Weakness	Associated disease	Mechanism
Muscle mass					
D3creatine dilution test	Decreased	Direct measurement of muscle mass [15]	Most data on the same male cohort [155]	Unknown	Exogenous biomarker
		Associated with physical performance, handgrip strength but not systematically with walking speed [16, 156]	Raw studies in female [155]		
		Predictive of major outcome (Falls, fracture, mobility, mortality) [18–20]	Longitudinal studies only available in rats [157]		
Myokines					
Myostatin	sex dependent	Increased with higher muscle mass [26, 158, 159]	Conflicting data [25]	Decreased upon inflammation [26, 160]	Muscle protein turnover
		Gender dependent association with gait speed [161]		Increased with obesity and heart failure [23, 162]	
		Probably decreased in long-term training [33]		Increased with renal insufficiency [26, 158]	
Follistatin	Increased	Associated with muscle mass and function in women [28, 31]	Conflicting data between men and women [28]	Unknown	Muscle protein turnover
		Increased in long-term training [33]			
Activin A	Unknown	Target same receptors as myostatin [163]	Limited number of studies [163]	Unknown	Muscle protein turnover
GDF-15	Increased	Correlate with muscle mass and performance tests [42–44]	Limited number of studies [163]	Increased with renal insufficiency [49]	Muscle protein turnover
		Not modified by exercise in long-term interventional studies [52, 53]			
Irisin	Decreased	Associated with muscle mass and strength [56, 164]	No interventional studies [30]	Unknown	Muscle protein turnover
		Increased by exercise [30]			
Neuro-muscular junction					
CAF	Increased	Associated with muscle mass and handgrip strength [58–62]	Limited number of interventional studies [30]	Unknown	Remodelling of neuro-muscular junction
		Decreased with exercise [63, 165]			
BDNF	Decreased	Accurate for diagnosis of sarcopenia [66, 69]	Limited number of studies [8O]	Unknown	Remodelling of neuro-muscular junction
		Correlate with CAF [68, 69]			

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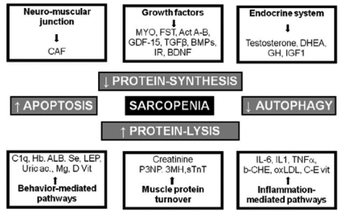
일반적인 근감소증 혈액 바이오마커 발굴 전략

Based on Pathophysiology of Sarcopenia



근감소증 기전을 완전히 이해하지 못하고 있다

→ Untargeted approach의 필요성

Curico F et al., Experimental Gerontology 85 (2016)

Biomarkers Only for Sarcopenia?

Weakness of Possible Causal Factors

Assessment of causal factors	Modification in sarcopenia	Evidence	Weakness	Associated disease	Mechanism
Adipokines					
Adiponectin	Increased	Associated with physical performance tests [167]	Results are influenced by the ratio male/female [113]	Pro-inflammatory factor [160]	Muscle-fat crosstalk
		Modified by non-pharmacological interventions [106, 109]	Conflicting data [107]	Decreased in coronary heart disease [166]	
		Predictive of major outcome (all-cause mortality) [110]		Decreased in obesity and type 2 diabetes [168]	
Leptin	Increased	Associated with appendicular lean mass [103, 106, 115]	Studies in sarcopenic obesity and insulin resistance cohorts rather than normal aging [103, 116, 119]	Influenced by level of adiposity [53]	Muscle-fat crosstalk
		Modified by non-pharmacological interventions [106, 116]	Highly relevant in sarcopenic obesity [80]		
Hormones					
IGF-1	Decreased	Associated with muscle mass, handgrip strength and gait speed [30, 125]	Not accurate enough for diagnosis [122]	Decreased with hepatic disorder [170]	Anabolic
		Increased by long-term resistance training [126]			
DHEAS	Decreased	DHEAS treatment improve muscle strength and function when combined with exercise [124]	Modified secretion is part of aging [171]	Modified by diseases of the endocrine system [171]	Anabolic
		Modified by non-pharmacological interventions [123]			
Cortisol	Increased	Associate with muscle mass [130, 172]	Modified secretion is part of aging [171]	Modified by diseases of the endocrine system [171]	Anabolic
		Modified by non-pharmacological interventions [123, 135]			
Testosterone	Probably decreased	Testosterone treatment improve muscle strength and mass [136]	Mostly studied as pharmacological target rather than biomarker [134, 173]	Modified by diseases of the endocrine system [171]	Anabolic
Inflammatory markers					
CRP	Increased	Increase is associated with lower handgrip strength and muscle mass [139, 157]	Unspecific biomarker of frailty and aging [155]	Increased by chronic or acute inflammation [140]	Low grade chronic inflamation
		Associated with future decline of muscle strength [141, 172]			
		Modified by non-pharmacological interventions [135, 144]			
IL-6	No basal modification	Increase is associated with lower handgrip strength and muscle mass [139]	Unspecific biomarker of frailty and aging [155]	Increased by chronic or acute inflammation [140]	Low grade chronic inflamation

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No Optimal Biomarkers for Sarcopenia

Ageing Research Reviews 93 (2024) 102148
Contents lists available at ScienceDirect
Ageing Research Reviews
journal homepage: www.elsevier.com/locate/arr

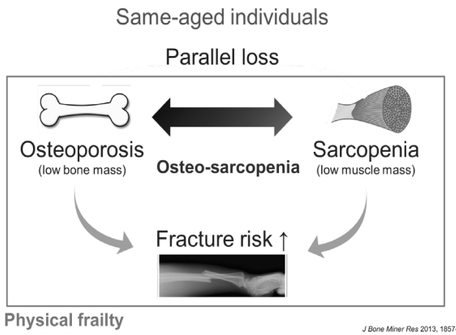
Review article

Blood biomarkers for sarcopenia: A systematic review and meta-analysis of diagnostic test accuracy studies

ABSTRACT

Biomarkers are emerging as a potential tool for screening or diagnosing sarcopenia. We aimed to summarize the current evidence on the diagnostic test accuracy of biomarkers for sarcopenia. We comprehensively searched Ovid MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials up to January 2023 and only included diagnostic test accuracy studies. We identified 32 studies with 23,840 participants (women, 58.26%) that assessed a total of 30 biomarkers. The serum creatinine to cystatin C ratio (Cr/CysC) demonstrated a pooled sensitivity ranging from 51% (95% confidence interval [CI] 44–59%) to 86% (95% CI 70–95%) and a pooled specificity ranged from 55% (95% CI 38–70%) to 76% (95% CI 63–86%) for diagnosing sarcopenia defined by five different diagnostic criteria (11 studies, 7240 participants). The other 28 blood biomarkers exhibited low-to-moderate diagnostic accuracy for sarcopenia regardless of the reference standards. In conclusion, none of these biomarkers are optimal for screening or diagnosing sarcopenia. Well-designed studies are needed to explore and validate novel biomarkers for sarcopenia.

Bone-Muscle Interaction & Frailty



J Bone Miner Res 2013, 1857–65

Effects of Lumican on Muscle & Bone

[Muscle: Animal and In Vitro research]

Article

Lumican, an Exerkine, Protects against Skeletal Muscle Loss

Han Jin Cho [1], Young-Sun Lee [1], Da Ae Kim [1], Sung Ah Moon [1], Seung Eun Lee [2], Seung Hun Lee [3] and Jung-Min Koh [3,*]

[Bone: Animal and In Vitro research]

Muscle-Derived Lumican Stimulates Bone Formation via Integrin α2β1 and the Downstream ERK Signal

Jin Young Lee [#], So Jeong Park [#], Da Ae Kim [1], Seung Hun Lee [2], Jung-Min Koh [3] and Beom-Jun Kim [2]*

Article

Lumican Inhibits Osteoclastogenesis and Bone Resorption by Suppressing Akt Activity

Jin-Young Lee [1], Da-Ae Kim [1], Eun-Young Kim [2], Eun-Ju Chang [2], So-Jeong Park [1,+] and Beom-Jun Kim [3,*]

기존 근감소증 바이오마커

연구의 문제점 및 연구방향

일반적인 근감소증 혈액 바이오마커 발굴 전략

Based on Pathophysiology of Sarcopenia

Curico F et al., Experimental Gerontology 85 (2016)

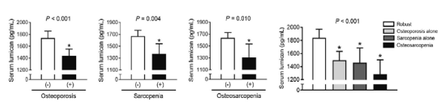
Lumican as a Biomarker for Osteo-Sarcopenia


Contents lists available at ScienceDirect
Bone
journal homepage: www.elsevier.com/locate/bone

Full Length Article

Circulating lumican as a potential biomarker for osteosarcopenia in older adults

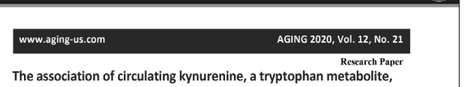
Sex, age, and BMI adjusted



Risk of osteoporosis, sarcopenia, and osteosarcopenia according to decrease in serum lumican level by logistic regression analysis.

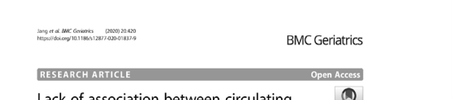
Adjustment	Osteoporosis		Sarcopenia		Osteosarcopenia	
	OR (95 % CIs) per serum lumican 1 SD decrease	P	OR (95 % CIs) per serum lumican 1 SD decrease	P	OR (95 % CIs) per serum lumican 1 SD decrease	P
Unadjusted	**2.15 (1.34–3.47)**	**0.002**	**3.36 (1.71–6.21)**	**<0.001**	**3.64 (1.68–7.57)**	**0.001**
Sex, age, and BMI adjusted	**2.31 (1.39–3.86)**	**0.001**	**3.45 (1.58–7.52)**	**0.002**	**4.17 (1.64–10.6)**	**0.003**

Circulating Biomarker for Frailty


www.aging-us.com AGING 2020, Vol. 12, No. 21
Research Paper

The association of circulating kynurenine, a tryptophan metabolite, with frailty in older adults

Il-Young Jang [1,*], Jin Hoon Park [2,*], Jeoung Hee Kim [2], Seungjoo Lee [2], Eunju Lee [1], Jin Young Lee [3], So Jeong Park [3], Da Ae Kim [3], Mark W. Hamrick [4], Beom-Jun Kim [5]


Jang et al. BMC Geriatrics (2020) 20:420
https://doi.org/10.1186/s12877-020-01837-9
BMC Geriatrics
RESEARCH ARTICLE Open Access

Lack of association between circulating apelin level and frailty-related functional parameters in older adults: a cross-sectional study

Il-Young Jang [1*], Seungjoo Lee [2*], Jeoung Hee Kim [2], Eunju Lee [1], Jin Young Lee [3], So Jeong Park [3], Da Ae Kim [3], Mark W. Hamrick [4], Jin Hoon Park [2*] and Beom-Jun Kim [5*]

Summary

- 혈액 시료를 활용한 중개연구의 의미
- Suggested biochemical markers for musculoskeletal health
- No definite serologic biomarkers for sarcopenia
- 기존 근감소증 바이오마커 연구의 문제점 및 연구방향
- 바이오마커 연구의 첫걸음: 코호트 구축
- 근감소증 바이오마커 확립 전략
- Osteo-sarcopenia, Frailty & Aging 바이오마커로의 확대

16th Congress of The Korean Society of Sarcopenia

2024년 대한근감소증학회 제16차 학술대회

Session III

Sarcopenia and its Related Diseases

좌장: **하용찬** 부민병원, **김태영** 건국의대

Curriculum Vitae

정희원

소속: 울산의대 내과학교실

| 학력사항 |

서울대학교 의학 학사
서울대학교 의학 석사
KAIST 이학 박사

| 경력사항 |

서울대학교병원 진료조교수(내과/입원의학센터)
서울아산병원 노년내과 촉탁임상전임강사
서울아산병원 노년내과 임상조교수

Sarcopenia and Frailty

울산의대
정희원

정희원

Curriculum Vitae

김홍규

소속: 울산의대 내과학교실

| 학력사항 |

한양대학교 의학 학사
울산대학교 의학 석사
울산대학교 의학 박사

| 경력사항 |

가천의대 길병원 내분비내과 전임강사, 조교수
미국 국립보건원(NIH)방문교수
서울아산병원 건강의학과(내분비내과) 임상교수

Sarcopenic Obesity and Myosteatosis (근감소성 비만과 근지방증)

울산의대
김홍규

Sarcopenic obesity (SO, 근감소성 비만)은 sarcopenia(근감소증)와 obesity(비만)이 함께 존재하는 것을 특징으로 하는 상태를 의미한다. 이러한 상태는 비만이 근육에서 myosteatosis(근지방증) 등을 유발하고 근육량을 감소시키는데 영향을 주고, 근감소증도 myokine의 변경, 활동 부족 및 의존적 상태 등으로 비만에 악영향을 끼치면서 그 상태가 더욱 악화되는 현상으로 유발될 수 있다고 설명하고 있다. 또한 근감소성 비만은 사망, 심혈관질환과 같은 다양한 질환 및 geriatric syndrome과 같은 poor health outcome과 연관이 된다는 연구들이 있어왔다. 그러나 최근까지도 널리 인정을 받는 진단 기준이 마련되어있지 않아서 환자의 진단 및 관리가 어렵고, 예방 및 예후에 대한 좀 더 객관적인 연구가 잘 이루어지고 있지 못하였다.

최근 2022년 유럽영양학회(ESPEN)와 유럽비만학회(EASO)를 중심으로 16개국의 비만과 근감소증 등의 전문가들이 모여 consensus statement를 발표하였는데 강의의 전반부에서는 이에 대해서 살펴볼 예정이다. 이에 따르면, 진단 과정을 screening, 진단, 그리고 staging으로 나누고 있다. Screening에서는 비만과 근감소증의 위험이 있는 대상을 선정하고, 진단 1단계는 악력 또는 하지 근력의 측정 또는 chair stand test¸¦ 사용해서 근육의 기능을 평가하는 것으로, 이러한 검사에서 이상이 있는 경우에만 진단 2단계인 체성분 분석을 진행하는 것으로 되어있다. '비만'은 체지방률을 사용하여 진단하고 'low muscle mass'는 골격근을 체중으로 나눈 'relative reduction'를 적용하는 것으로 되어있는데, 이는 키로 보정하는 이전의 진단 방법과 차이가 있다.

또한, 본 consensus statement에서는 비만인에서 myosteatosis(근지방증)이 흔하고 근감소성 비만의 기전에 매우 중요하다고 강조하여 언급하고 있는데, 이는 근육 사이에 지방이 축적되는 현상으로 강의의 후반부에서는 이에 대한 내용을 다룰 예정이다. 본 연구자는 2018년부터 인공지능(artificial intelligence, AI)을 이용하여 복부 CT에서 내장지방 및 골격근량의 자동측정방법(automated measurement) 개발에 참여하면서 골격근(skeletal muscle)을 질(quality)를 구분하여 측정하는 프로그램을 개발하는 데 참여하였다. 즉,

측정한 전체 복부둘레근육을(total abdominal muscle area, TAMA)을 골격근(skeletal muscle area, SMA)과 지방(inter- or intra muscular adipose tissue, IMAT)으로 구분하고, 골격근을 density에 따라서 Normal attenuation muscle area (NAMA; good quality muscle)와 Low attenuation muscle area (LAMA; fatty muscle)로 구분하여 측정하는 방법이다. 이를 이용하여 대규모의 건강검진 코호트에서 각각의 측정 값들을 연령대별 분포를 분석하였는데 골격근을 그 질을 구분하지 않고 측정한 것과는 매우 차이가 나는 결과를 얻을 수 있었다. 또한, 본 연구자는 근육내 지방이 증가되는 근지방증(myosteatosis)의 정도를 정의할 수 있는 새로운 지표인 NAMA/TAMA index를 고안하였고, 이를 사용하여 myosteatosis의 연령별 유병률도 조사하였는데 연령이 증가함에 따라서 그 유병률이 급격히 증가되는 것을 알 수 있었다. 따라서 골격근을 평가할 때에, 특히 노년에서는 단지 그 양만을 측정하고 평가하는 것에는 많은 문제가 있을 가능성이 있다는 것을 시사하였다.

마지막으로 골격근을 키로 보정한 이전의 진단 기준과 체중으로 보정한 새로운 기준으로 근감소성 비만을 진단했을 때의 그 유병률과 문제점을 서울아산병원 건강검진수진자의 자료와 최근 발표된 호주의 연구를 통해서 살펴보았는데 비만인에서는 키로 보정한 경우에 근감소증의 진단률이 지극히 낮다는 것을 알 수 있었다. 이는 비만인에서 키로 보정하는 골격근량을 기준으로 근감소증을 진단하는 것이 적절하지 않다는 것을 시사한다. 따라서, 대한근감소증학회에서도 '근감소성 비만'의 진단에 대한 논의 및 Korean Working Group on Sarcopenia (KWGS)의 guideline에도 이를 반영 하는 것의 필요성에 대한 논의가 진행되어야 할 것으로 생각되었다.

Curriculum Vitae

유준일

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| 학력사항 |

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충북대학교 의학과 석사
중앙대학교 의학과 박사

| 경력사항 |

경상국립대병원 정형외과 부교수
경상국립대병원 융합연구센터장, 개방형실험실 부단장
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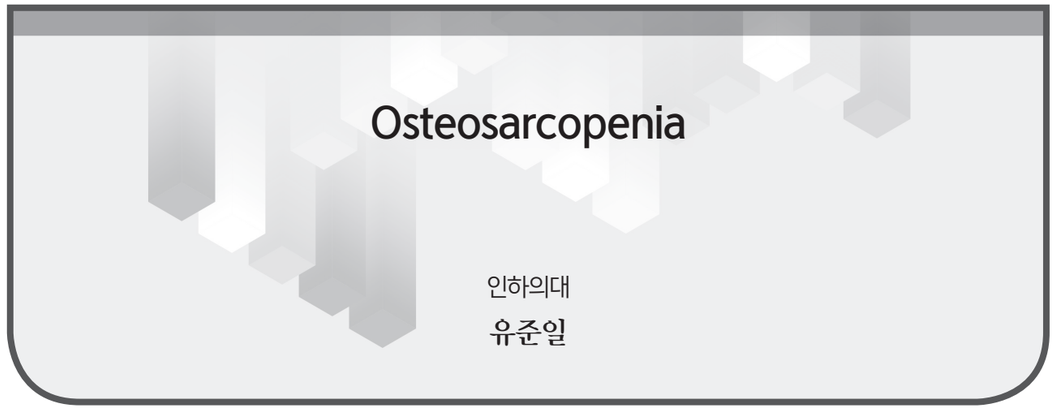
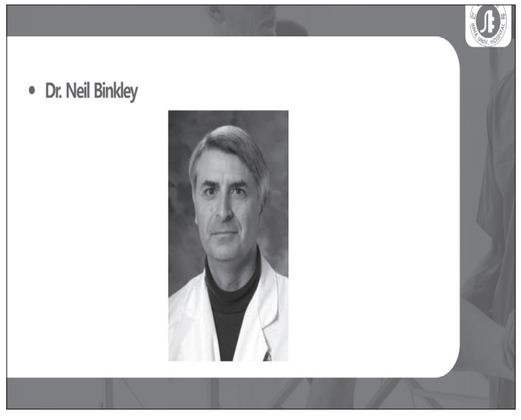
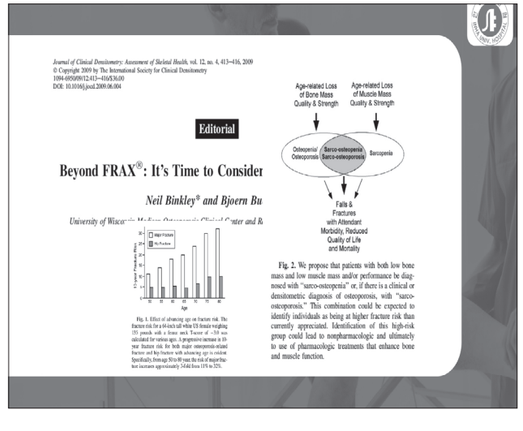
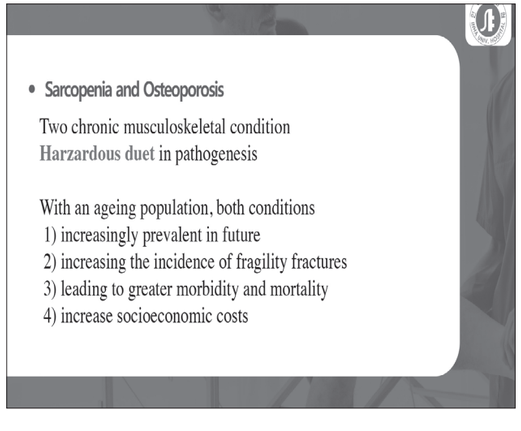
대한근감소증학회 총무이사









- **Definition of osteosarcopenia**
  - Sarco-ostepenia
  - Osteosarcopenia
  - Controversial of definition of osteosarcopenia
  - T-score < -1 and sarcopenia
    Huo et al JAMDA 2015
    Drey et al ACER 2016
  - T-score < -2.5 and sarcopenia
    Yoshimura et al OI 2017
    Yoo & Ha JKMS 2018

Journal of Cachexia, Sarcopenia and Muscle 2024; 15: 8–20
Published online 12 December 2023 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/jcsm.13392

REVIEW

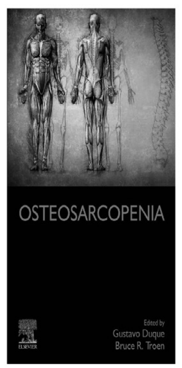
Global epidemiological features and impact of osteosarcopenia: A comprehensive meta-analysis and systematic review

Shanping Chen[1,2,3], Xiao Xu[4,5,6], Huping Gong[7], Ruzhao Chen[4,5,6], Lijuan Guan[1,2,3], Xuedan Yan[1,2,3], Lihua Zhou[1,2,3], Yongxue Yang[1,2,3], Jiang Wang[4,5,6], Jianghua Zhou[8], Chuan Zou[2,3,9]* & Pan Huang[10]*

[1]Department of Gerontology and Geriatric, Chengdu Fifth People's Hospital, Chengdu, China; [2]The Second Clinical Medical College, Affiliated Fifth People's Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu, China; [3]Geriatric Diseases Institute of Chengdu, Chengdu, China; [4]Affiliated Hospital of Jinggangshan University, Center for Clinical Medicine Research of Jinggangshan University, Ji'an, China; [5]Department of Medicine, Jinggangshan University, Ji'an, China; [6]Online Collaborative Research Center for Evidence-Based Medicine Ministry of Education, Jinggangshan University Branch, Ji'an, China; [7]College of Nursing, Gannan Medical University, Ganzhou, China; [8]Department of Cardiology, The First Affiliated Hospital, Wenzhou Medical University, Wenzhou, China; [9]Department of General Practice, Chengdu Fifth People's Hospital, Chengdu, China; [10]College of Nursing, Wenzhou Medical University, Wenzhou, China

- Osteosarcopenia is defined as the <u>concurrent occurrence of osteopenia/osteoporosis and sarcopenia</u>.

- **Dr. Gustavo Duque**



2. Prevalence

Osteosarcopenia

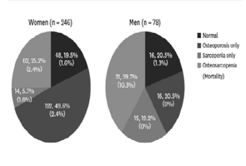
- **Osteosarcopenia Prevalence Varies by Definition and Population**
  - Cohort of 680 Australian older adults (65% women) referred to a falls and fracture clinic
  - Needed to have fall, low BMD or fragility fracture history to be included
  - Mean age : 79 years
  - Osteopenia/Osteoporosis prevalence (T-score < 1.0) was 65%
  - Sarcopenia prevalence using the EWGSOP was 51%

Osteosarcopenia prevalence
40%

Huo. JAMDA 2015. 16(4): 290-5

- **Osteosarcopenia Prevalence in Korea**
  - Patients ≥ 50 years admitted following hip fractures
  - 83 men and 259 women
  - Sarcopenia prevalence was defined using AWGS (grip strength cut offs, ALM/height2, and no gait speed)
  - Osteoporosis : T-score < -2.5

Osteosarcopenia prevalence
37% in men, 24% in women



Yoo and Ha. JKMS. 2018

- **Epidemiology of Osteosarcopenia**

Table 1. Epidemiological studies of the osteosarcopenia

References	Country	Year	Subjects	Prevalence of osteosarcopenia
Yoo et al.[15]	Korea	2018	Hip fracture patients	27.2%
Huo et al.[16]	Australia	2015	Community dwelling older people	40.0%
Wang et al.[17]	China	2015	Community dwelling older people	10.4% in men, 15.1% in women
Drey et al.[18]	Germany	2016	Pre-frail elderly	28.0%

Yoo and Ha. JBM. 2018

- **Epidemiology of Osteosarcopenia**

- 18.5 % (63 articles, 63369 subjects)
- 1.5 % ~ 64.3 %
- Female, hospital cohort, Oceania, retrospective study ↑

Chen et al. JCSM. 2024

- **Relationship with osteoporosis and sarcopenia**

Relationship between postmenopausal osteoporosis and the components of clinical sarcopenia

Samu Sjöblom*, Juha Suuronen, Toni Rikkonen, Risto Honkanen, Heikki Kröger, Joonas Sirola

Table 3
Risk of osteoporosis related to sarcopenia and its components according to logistic regression (N = 590).

Variables	Unadjusted model OR (95% confidence interval)	Adjusted model* OR (95% confidence interval)
Sarcopenia		
Sarcopenia	12.9 (3.1–53.5)§§	9.4 (2.1–41.4)§
Presarcopenia	6.5 (1.5–28.6)*	3.7 (0.8–18.2)*
Non-classified	5.7 (1.6–21.2)§	6.5 (1.7–25.5)§
Normal	Reference group	Reference group
Grip strength		
1st quartile	11.7 (2.6–53.4)§§	10.7 (2.3–50.3)§
2nd quartile	3.6 (0.7–18.4)	2.4 (0.4–13.1)
3rd quartile	1.6 (0.26–9.9)	1.3 (0.2–8.3)
4th quartile	Reference group	Reference group
RSMI		
1st quartile	7.5 (1.6–34.6)§	7.7 (1.3–47.7)*
2nd quartile	4.1 (0.8–20.7)	6.1 (1.0–37.1)*
3rd quartile	2.2 (0.4–12.4)	3.0 (0.5–18.7)
4th quartile	Reference group	Reference group
Walking time		
1st quartile	5.1 (1.1–23.4)*	9.3 (1.8–48.3)§
2nd quartile	3.1 (0.6–15.3)	4.8 (0.9–25.3)
3rd quartile	2.5 (0.5–13.6)	1.3 (0.8–2.2)
4th quartile	Reference group	Reference group

Adjusted for: age, body mass index (BMI), physical activity hormone therapy (HT), consumption of alcohol and smoking.
* $p < 0.05$.
§ $p < 0.01$.
§§ $p < 0.001$ in comparison to reference group.

Sarcopenic women had a 12.9 times higher odds of having osteoporosis when compared to non-sarcopenic women.

- **Relationship with osteoporosis and sarcopenia**

Table 3
Binary logistic regression analysis: factors associated with the presence of osteoporosis.

	B	OR (95% CI)	p
Age	0.047	1.048 (1.013–1.085)	0.008
Presence of sarcopenia	0.588	1.8 (1.073–3.018)	0.026
Interval fracture–DXA scan	−0.027	0.973 (0.943–1.005)	0.097

Notes: The dependent variable was the presence of osteoporosis (conventionally attributed a value of 1, whereas the absence of osteoporosis was conventionally attributed a value of 0). The independent variables included in the regression model are listed in the Table. The presence of sarcopenia was conventionally attributed a value of 1 (the absence of sarcopenia was attributed a value of 0).

Hip fracture women with sarcopenia have higher risk of osteoporosis than hip fx. women without sarcopenia (adjusted OR=1.8)

- **Relationship with osteoporosis and sarcopenia**

Sarcopenia and its relationship with bone mineral density in middle-aged and elderly European men

S. Verschueren · E. Gielen · T. W. O'Neill · S. R. Pye · J. E. Adams · K. A. Ward · F. C. Wu · P. Szulc · M. Laurent · F. Claessens · D. Vanderschueren · S. Boonen

Osteoporos Int (2013) 24:87–98

Table 4 The association between sarcopenia and osteoporosis

	Number	Osteoporsis[a] OR (95 % CI)
RASM (per SD)[b]	674	0.7 (0.5, 0.9)**
Sarcopenia[c]		
RASM at ≥7.26 kg/m²	594	Referent
RASM at <7.26 kg/m²	80	3.0 (1.6, 5.8)**
Leuven cohort only[d]		
Sarcopenia[e]		
Normal	321	Referent
Pre-sarcopenia	41	3.8 (1.6, 9.1)**
Sarcopenia	14	2.0 (0.4, 10.0)
Severe sarcopenia	0	–

Results expressed as odds ratios (OR) and 95 % CI
RASM relative appendicular skeletal muscle mass
*$p<0.05$; **$p<0.01$; ***$p<0.001$
[a] Osteoporosis: T-score ≤ −2.5 at femoral neck, total hip or lumbar spine
[b] Adjusted for age and centre
[c] Sarcopenia using definition of Baumgartner et al. [18]: RASM at <7.26 kg/m²
[d] Adjusted for age
[e] Sarcopenia using definition of EWGSOP [19]: presarcopenia—RASM at <7.26 kg/m², sarcopenia—RASM at <7.26 kg/m² +low muscle strength (grip strength, ≤29 kg if BMI is ≤24; ≤30 kg if BMI is 24.1–28; and ≤32 kg if BMI is >28 [33]) or low physical performance (walking speed <1.0 m/s [34]) and severe sarcopenia—all three criteria

Sarcopenia (RASM<7.26 kg/m²) was 3-fold higher risk of osteoporosis.

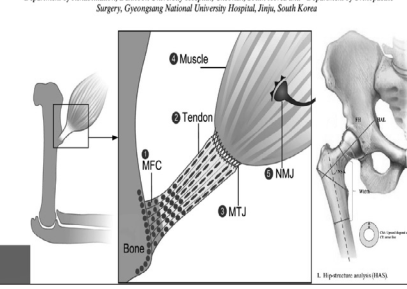
Sarcopenia (by EWGSOP) was twice as likely to have osteoporosis.

- **Relationship with osteoporosis and sarcopenia**

Sarcopenia and Hip-Structure Analysis Variables in Korean Elderly Population

Hana Choi,[1] and Jun-Il Yoo[2,]*

[1] Department of Rehabilitation, Dankook University Hospital, Cheonan, South Korea and [2] Department of Orthopaedic Surgery, Gyeongsang National University Hospital, Jinju, South Korea



1. Hip-structure analysis (HAS).

Choi and Yoo. JCD. 2018

• Relationship with osteoporosis and sarcopenia in Korea

ORIGINAL ARTICLE
Musculoskeletal Disorders

JKMS

High Prevalence of Sarcopenia in Korean Patients after Hip Fracture: A Case-Control Study

Jun-Il Yoo,[1] Yong-Chan Ha,[2] Hyeok-Bin Kwon,[1] Young-Kyun Lee,[1] Kyung-Hoi Koo,[1] and Moon-Jib Yoo[3]

Sarcopenia-related falls and fractures are increasing worldwide due to the aging population. The purpose of this study was to 1) evaluate anthropometric characteristics related to hip fracture in Korean patients, 2) investigate sarcopenia prevalence in hip

Table 4. Stepwise logistic regression analysis for hip fracture

Variables	B	OR	95% CI	*P* value
Age	0.14	1.15	1.13-1.17	< 0.001
Presence of sarcopenia	1.87	6.52	4.67-9.09	< 0.001
Presence of osteoporosis	0.62	1.87	1.35-2.58	< 0.001

OR, odds ratio; CI, confidence interval.

Yoo and Ha. JKMS. 2016.

3. Clinical significance

Osteosarcopenia

• Comprehensive nutritional status in sarco-osteoporotic older fallers

- Cross-sectional study.
- Falls and Fractures Clinic, Nepean Hospital (Penrith, Australia).
- 680 subjects (mean age=79, 65% female) assessed between 2008-2013.
- Sarcopenia was present in 47.4% of those with osteopenia (167/352) and 62.7% in those with osteoporosis (91/145).
- BMI< 25, MNA score <12, serum folate <20 nmol/L, hemoglobin <120g/L, Hypoalbuminemia (<35 g/L)

J Nutr Health Aging. 2015

• The relationship between sarcopenia and fragility fracture

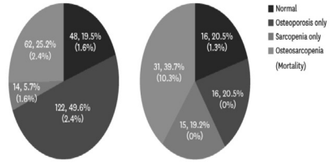
- The prevalence of sarcopenia after fracture
  12.4 to 95% in males and 18.3 to 64% in females.
- Higher prevalence of sarcopenia in elderly men with fragility fracture
- Increased risk of fragility fracture in man with sarcopenia and low BMD

Wong et al. Osteopros Int, 2019

• Osteosarcopenia is associated with poor health outcomes

- Compared to patients without osteosarcopenia
- Patients with osteosarcopenia reported impaired mobility more frequently (Huo, JAMDA, 2015)
- Patients with hip fracture and sarcopenia and have decreased ability to perform ADL(Di Monaco 2015)

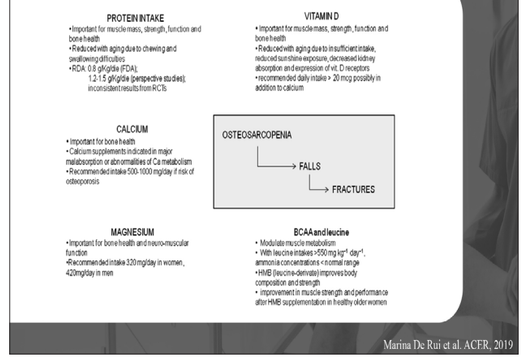
• Prevalence of osteosarcopenia and 1- year mortality



Yoo and Ha. JKMS. 2018

4. Treatment

Osteosarcopenia



Marina De Rui et al. ACER. 2019

• Frailty is more common in patients with osteosarcopenia

- 250 women from the Women's Health and Aging Studies II
- Mean age : 79.6 (76-86)
- Frailty (defined by Fried/Cardiovascular Health Study criteria) prevalence was 6.8%
- Sarcopenia(defined by ALM/height2 only)prevalence was 42.4% in the entire cohort and 52.9% in frail adults
- Osteoporosis (defined by WHO T-score < -2.5) prevalence was 18.4%
- Osteosarcopenia prevalence was 10.7%
- Frailty odds ratio was 6.4 for those with osteosarcopenia.

Frisoli Bone. 2011 48(2011) 952-957.

• Phenotype in patients with osteosarcopenia

- 68 prefrail adults between 65 and 94 years
  Hand grip strength ⇩ Chair rising time ⇧

  Drey M. Aging Clin Exp Res. 2016
- Total of 680 people (mean age; 79 year)
  Older, mostly women, are at high risk for depression and malnutrition, have body mass index lower than 25, and showed a higher prevalence of peptic disease, inflammatory arthritis, hip fracture, history of atraumatic fracture, and impaired mobility.

  HuoYR. J Am Med Dir Assoc. 2015

• Protein rich foods intakes are known to decline with age

- Food preference in older people
- Poor chewing ability
- More concerned about food texture compared to younger adults
- The loss of chemosensory acuity due to medications and aging

• Protein rich foods intakes are known to decline with age

- RDA for protein, as promulgated by the Food and Nutrition Board of the United States National Academy of Science, is 0.8 g protein/kg body weight/day for adults, regardless of age.
- Prospective studies showed that intake of up to at least **1.2–1.5 g protein/kg body weight/day** seems to be safe in old people.

Wolfe RR et al. Clin Nutr. 2008
Pedersen AN et al. Food Nutr Res. 2014

- **Protein rich foods intakes are known to decline with age**
  - Vitamin D deficiency is a very common condition in old people caused by reduced sunshine exposure, kidney hydroxylation, vitamin D receptors' expression and insufficient vitamin D intake.
    → muscle atrophy, reduced muscular strength and power, impaired balance and consequent increased risk of recurrent falls and fractures.
    → **800 IU (20 μg) of vitamin D** from all sources should be consumed every day to prevent falls in men and women older than 60 years.

Cramer JT, et al. J Am Med Dir Assoc, 2016

- **Calcium**
  - The **"bone nutrient"**, because nearly 99% of the Ca in the adult human body is contained in bones as hydroxyapatite.

→ The current recommendations for Ca intakes are **1000–1200 mg/day in older people.**

→ Considering that calcium intake in **elderly men and women** is lower than recommended (approximately **750 mg/day**), a supplementation of about 500 mg calcium per day could be sufficient, avoiding side effects that could impair pharmacological compliance.

Inelmen EM, et al. J Nutr Health Aging, 2000

- **Magnesium**
  - **Mg is located approximately at 60% in bone** and is essential for organic bone matrix synthesis.
  - Mg is essential for **normal neurological and muscular function**.
  - The recommended daily intake of Mg necessary for **bone health** in older age is **320 mg in women and 420 mg in men**.

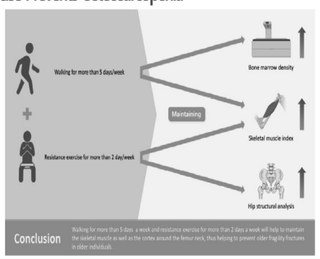
→ Although Mg deficiency can affect the quality of bone, the relationship between Mg and fractures is uncertain and results are conflicting.

Veronese N., et al. Br J Nutr, 2017

- **Branched-chain amino acids (BCAAs)**
  - **The BCAAs are quite popular among bodybuilders to promote skeletal muscle hypertrophy.**
  - **Leucine** → muscle metabolism,
    > 550 mg/kg/day
  - Supplementation of beta-hydroxy-beta-methylbutyrate (HMB)
    →positive effect on body composition and body strength in the elderly.

Luckose F., et al. Crit Rev Food Sci Nutr, 2015

- **Daily Walking Accompanied with Intermittent Resistance Exercise Prevents Osteosarcopenia**



Lee and Yoo et al. JBM. 2022

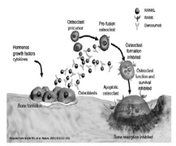
- **Pharmacological Tx for Osteosarcopenia**

JCI The Journal of Clinical Investigation

RANKL inhibition improves muscle strength and insulin sensitivity and restores bone mass

Nicolas Bonnet, ... , Eleni Douni, Serge Ferrari

In conclusion, RANKL deteriorates while its inhibitors improve muscle strength and insulin sensitivity in osteoporotic mice and humans. Hence, denosumab could represent a novel therapeutic approach for sarcopenia.



Lee and Yoo et al. JBM. 2022

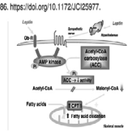
- **Pharmacological Tx for Osteosarcopenia**

JCI The Journal of Clinical Investigation

Low-dose leptin reverses skeletal muscle, autonomic, and neuroendocrine adaptations to maintenance of reduced weight

Michael Rosenbaum, ... , Ellen Murphy, Rudolph L. Leibel

J Clin Invest. 2005;115(12):3579-3586. https://doi.org/10.1172/JCI25977.



Lee and Yoo et al. JBM. 2022

요 약

- 골근감소증 정의와 유병률
- 골근감소증 임상적 의의
- 골근감소증 치료

Curriculum Vitae

김영생

소속: 가천의대 내과학교실

| 학력사항 |

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대한종양내과학회 보험정책위원

Cancer Cachexia: Targeting Pathophysiological Mechanisms

가천의대
김영생

Cancer cachexia is a complex systemic syndrome marked by muscle wasting, characterized by a state of catabolism. It impacts various remote organs, and their interactions with cancer cells collectively create the cancer cachexia environment. During the development and progression of cancer cachexia, the interactions between dysfunctional organs and cancer cells, or other organs within the cancer cachexia environment, trigger a series of stress responses, leading to the deterioration of several organs such as the liver, heart, pancreas, intestines, brain, bones, and spleen. These effects disrupt the balance of metabolism, neural activity, and immune function. The roles of these organs shift from inhibiting tumor growth to promoting cancer cachexia as cancer advances. This presentation provides an overview of recent advancements in treatment and delves into the molecular mechanisms and clinical studies related to cancer cachexia, focusing on metabolic, neurological, and immunological irregularities across various organs. Updated understanding of cancer cachexia might facilitate the exploration of biomarkers and novel therapeutic targets of cancer cachexia.

MEMO

16th Congress of The Korean Society of Sarcopenia
2024년 대한근감소증학회 제16차 학술대회

Session IV

Management of Sarcopenia

좌장: 송욱 서울대, 이해정 가천대

Curriculum Vitae

박용순

소속: 한양대학교

| 학력사항 |

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워싱턴주립대학교,임상영양학박사

| 경력사항 |

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한양대학교 의과대학 내부겸직교수
Korean Food and Drug Administraion Consultant
한양대학교 식품영양학과 교수
한국과학기술한림원(The Korean Academy of Science and Technology, KAST) 정회원

Nutritional Approaches to Treat Sarcopenia

한양대학교
박용순

Contents

1. Sarcopenia
2. Energy
3. Protein
4. Vitamin D
5. n-3 PUFA
6. Other nutrients
7. Dietary pattern
8. Summary

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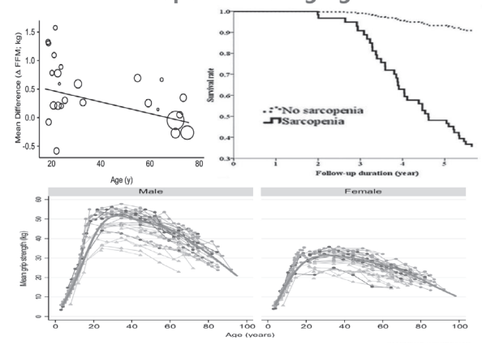
3

Sarcopenia and Aging



Bauer et al, JAMDA 2013; Moon et al. PlosOne 2016; Musumeci, J Funct Morphol Kinesiol 2017

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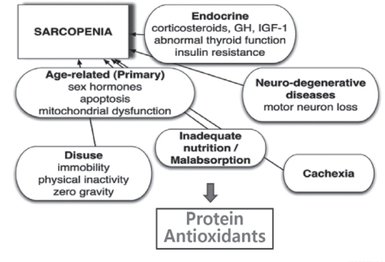
Sarcopenia and Nutrition

- Inadequate nutrient intake secondary to the "anorexia of aging" is considered an important risk factor in the development and progression of sarcopenia



Cruz-Jentoft et al. Age and Ageing 2010;39:412–423

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Sarcopenia and Dietary Intake

- Participant with ≥ 65 y (n=3656) from KNHANES 2008, 2009, 2010, and 2011
- Sarcopenia was defined in accordance with the criteria of the Asia Working Group for Sarcopenia (SMI <5.4 kg/m² in women and <7.0 kg/m² in men)

Variables	Men			Women		
	Normal (n=1112)	Sarcopenia (n=470)	*P* value	Normal (n=1851)	Sarcopenia (n=223)	*P* value
Total energy (kcal/d)	1956.7±695.6	1735.4±684.0	<0.001	1435.9±538.9	1273.9±445.5	<0.001
Total proteins (g/d)	66.1±32.3	55.5±26.4	<0.001	45.2±23.1	40.0±19.3	<0.001
Vitamin D (ng)	22.3±7.6	20.8±7.8	0.003	19.2±7.6	18.7±7.4	0.409
Fasting glucose	104.6±26.5	105.9±34.2	0.375	103.1±22.4	103.4±33.3	0.868

Yoo et al, Nutrition 2018;53:38-42

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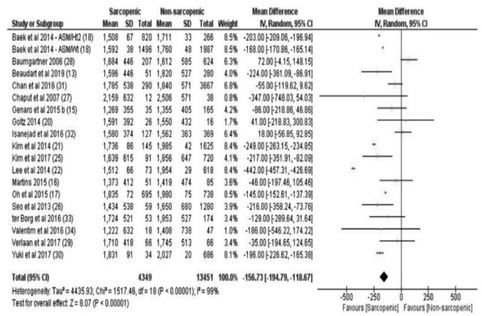
Prevalence of Malnutrition in Korean: KFACS

	Nonfrail (n = 1,329)	Frail (n = 106)	p
Age (years)	75.6 ± 3.8	78.9 ± 3.5	<.001
Women, n (%)	680 (51.2)	65 (61.3)	.044
BMI (kg/m²)	24.5 ± 3.0	24.4 ± 3.9	.946
Smoking status, n (%)			.642
Never	810 (60.9)	67 (63.2)	
Former	439 (33.0)	31 (29.2)	
Current	80 (6.0)	8 (7.5)	
Alcohol, n (%)[a]			.909
Never	1069 (80.7)	86 (81.1)	
Ever	256 (19.3)	20 (18.9)	
Education (year), n (%)			<.001
0–6	553 (41.6)	70 (66.0)	
≥7	776 (58.4)	36 (34.0)	
Low economic status, n (%)[b]	83 (6.3)	13 (12.4)	.016
Marital status, n (%)			.008
Married	946 (71.2)	59 (55.7)	
Divorced/separated	351 (26.4)	44 (41.5)	
Widowed	30 (2.3)	3 (2.8)	
Single	2 (0.2)	0 (0.0)	
Comorbidity, n (%)[c]			.001
0	334 (25.1)	14 (13.2)	
1	510 (38.4)	35 (33.0)	
≥2	485 (36.5)	57 (53.8)	
Number of medications[d]	3.7 ± 5.4	7.3 ± 13.2	<.001
Cognitive impairment, n (%)[e]	233 (17.5)	50 (47.2)	<.001
Nutritional status[f]			<.001
Normal	1131 (85.1)	64 (60.4)	
At risk of malnutrition	191 (14.4)	32 (30.2)	
Malnutrition	7 (0.5)	10 (9.4)	
hs-CRP mg/L, n (%)			.005
<1.0	862 (64.9)	63 (59.4)	
1.0–3.0	345 (26.0)	23 (21.7)	
>3.0	122 (9.2)	20 (18.9)	

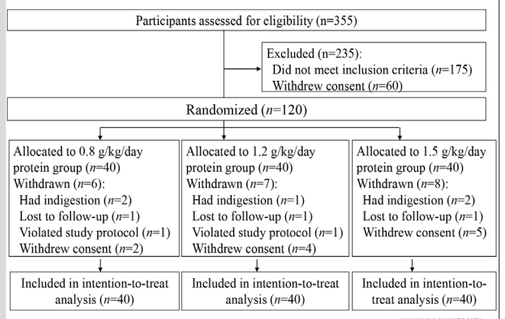
Kim et al, J Gerontol Med Sci 2021;78:499

Energy Intake and Sarcopenia



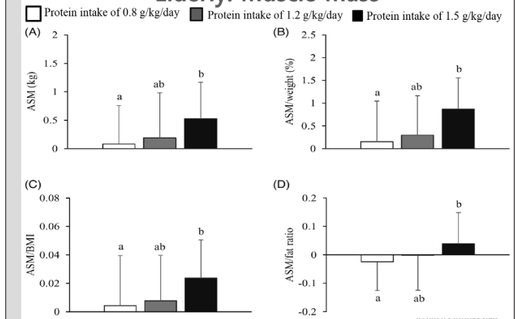
Santiago et al. Nutr Rev 2021;79:1338–1352

Protein and Sarcopenia in Korean Elderly



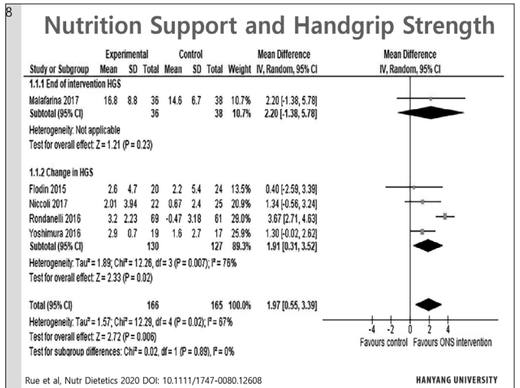
Park et al, Am J Clin Nutr 2018;108:1026-1033

Protein and Sarcopenia in Korean Elderly: Muscle Mass



Park et al, Am J Clin Nutr 2018;108:1026-1033

Nutrition Support and Handgrip Strength



Rue et al, Nutr Dietetics 2020 DOI: 10.1111/1747-0080.12608

Protein and Lean Mass: Health ABC

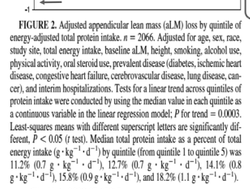


FIGURE 2. Adjusted appendicular lean mass (aLM) loss by quintile of energy-adjusted total protein intake. n = 2066. Adjusted for age, sex, race, study site, total energy intake, baseline aLM, height, smoking, alcohol use, physical activity, oral steroid use, prevalent disease (diabetes, ischemic heart disease, congestive heart failure, cerebrovascular disease, lung disease, cancer), and interim hospitalizations. Tests for a linear trend across quintiles of protein intake were conducted by using the median value in each quintile as a continuous variable in the linear regression model; P for trend = 0.0003. Least-squares means with different superscript letters are significantly different, $P < 0.05$ (*t* test). Median total protein intake as a percent of total energy intake (g · kg^{-1} · d^{-1}) by quintile (from quintile 1 to quintile 5) was 11.2% (0.7 g · kg^{-1} · d^{-1}), 12.7% (0.7 g · kg^{-1} · d^{-1}), 14.1% (0.8 g · kg^{-1} · d^{-1}), 15.8% (0.9 g · kg^{-1} · d^{-1}), and 18.2% (1.1 g · kg^{-1} · d^{-1}).

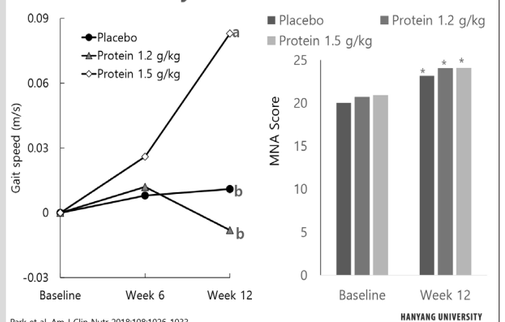
TABLE 2
Adjusted regression coefficients (and SE) for change in total lean mass (LM) and appendicular LM (aLM) per unit of energy-adjusted protein intake[1]

	LM		aLM	
	β (SE)	P	β (SE)	P
Total protein				
Model 1	9.02 (2.99)	0.003	5.43 (1.64)	0.0009
Model 2	8.76 (3.00)	0.004	5.31 (1.64)	0.001
Model 3	6.38 (2.74)	0.02	4.10 (1.51)	0.007
Animal protein[2]				
Model 1	8.98 (3.00)	0.003	5.32 (1.65)	0.001
Model 2	8.82 (3.01)	0.003	5.26 (1.65)	0.001
Model 3	6.58 (2.75)	0.02	4.13 (1.52)	0.006
Vegetable protein[3]				
Model 1	9.92 (7.08)	0.16	8.24 (3.89)	0.03
Model 2	7.23 (7.14)	0.31	6.55 (3.92)	0.10
Model 3	1.08 (6.52)	0.87	3.28 (3.61)	0.36

[1] n = 2066. LM, aLM, and energy-adjusted protein intake were measured in grams. Multiple linear regression models. Model 1 was adjusted for age, sex, race, study site, total energy intake, baseline LM or aLM, and height. Model 2 was adjusted for variables in model 1 plus smoking, alcohol use, physical activity, oral steroid use, prevalent disease (eg, diabetes, ischemic heart disease, congestive heart failure, cerebrovascular disease, lung disease, or cancer), and interim hospitalizations. Model 3 was adjusted for variables in model 2 plus change in fat mass.
[2] Models for animal protein were also adjusted for vegetable protein intake.
[3] Models for vegetable protein were also adjusted for animal protein intake.

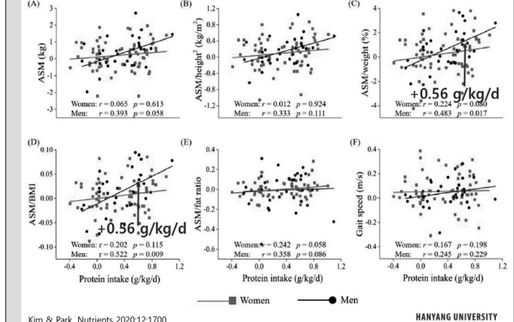
Am J Clin Nutr 2008;87:150-5

Protein and Sarcopenia in Korean Elderly: Muscle Function



Park et al, Am J Clin Nutr 2018;108:1026-1033

Change of Protein and Muscle Mass



Kim & Park, Nutrients 2020;12:1700

Meat Consumption and Muscle

	RT+Meat		CRT					
	Baseline (n = 53)	Change (n = 48)	Baseline (n = 47)	Change (n = 43)	Net difference	Group	Time	Group × time
Body composition								
Total body FM (kg)	30.1 ± 8.2	−0.5 (−0.9, −0.03)	28.9 ± 9.6	−0.3 (−0.7, 0.2)	−0.2 (−0.4, 0.8)	0.651	0.042	0.179
Percentage of body fat	42.6 ± 5.9	−0.8 (−1.3, −0.3)	41.2 ± 7.7	−0.4 (−0.8, 0.1)	−0.4 (0.3, −1.1)	0.436	0.005	0.071
Total body LTM (kg)	37.3 ± 4.3	0.6 (0.3, 0.8)	37.3 ± 3.5	0.1 (−0.4, 1.1)	0.5 (0.1, 0.8)	0.758	0.005	0.007
Femur muscle CSA (mm²)	4047 ± 835	5.4 (3.7, 7.1)	4075 ± 623	4.0 (2.2, 5.8)	1.4 (−1.0, 3.9)	0.565	0.001	0.397
Femur sFat CSA (mm²)	8148 2163	0.2 (−1.2, 1.5)	8112 ± 2945	0.7 (−1.0, 2.3)	−0.5 (−2.6, 1.6)	0.971	0.441	0.684
Femur MD (mg/cm³)	740 ± 2.4	0.8 (0.0, 1.6)	74.4 ± 3.1	0.4 (−0.6, 1.5)	0.4 (−0.9, 1.7)	0.973	0.074	0.588
Muscle strength								
Leg extension (kg)	32.0 ± 11.2	28 (18, 39)	28.1 ± 10.1[a]	10 (−1, 21)	18 (3, 34)	0.014	0.005	0.010
Muscle function								
4-square step test (s)	7.7 ± 1.5	5.4 (1.6, 9.2)	7.7 ± 1.6	6.5 (1.4, 11.7)	−1.1 (−7.4, 5.1)	0.915	0.001	0.274
Timed-up-and-go test (s)	9.1 ± 3.3	−14.4 (−19.5, −9.1)	9.1 ± 2.4	−16.4 (−23.7, −9.1)	−2.0 (−6.6, 10.6)	0.667	0.001	0.788
30-s sit-to-stand test	13.1 ± 3.1	10.5 (11.1, 25.8)	12.5 ± 3.0	27.0 (19.4, 34.5)	−8.4 (−18.9, 1.9)	0.472	0.001	0.190
Bone mineral density								
Femoral neck (g/cm²)	0.815 ± 0.107	0.2 (−0.5, 0.9)	0.852 ± 0.147	−0.5 (−1.1, 0.04)	0.71 (−0.1, 1.6)	0.205	0.573	0.092
Total hip (g/cm²)	0.866 ± 0.134	0.2 (−0.4, 0.9)	0.897 ± 0.152	−0.2 (−0.9, 0.4)	0.4 (−0.5, 1.4)	0.593	0.937	0.164
Lumbar spine (g/cm²)	1.073 ± 0.177	−0.3 (−1.1, 0.4)	1.105 ± 0.184	−0.3 (−1.0, 0.4)	0.0 (−1.0, 1.0)	0.980	0.091	0.880

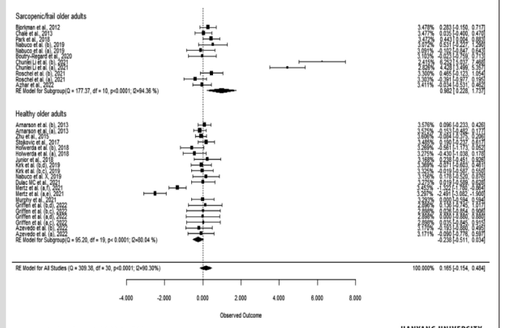
- In 4-mo RCT, 100 women aged 60–90y in 15 retirement villages receive resistance training (RT) with lean red meat (~60g) 6d/wk [RT+Meat group; n=53] or control [1 serving pasta or rice/d; control RT (CRT) group; n=47]. All undertook RT 2 times/wk with 1000 IU vitD
- A protein-enriched diet equivalent to ~1.3g/kg/d achieved through lean red meat is safe and effective for enhancing the effects of RT on lean tissue mass and muscle strength and reducing circulating IL-6 concentrations in elderly women

Daly et al. Am J Clin Nutr 2014;99:899–910

Protein Recommendation for Sarcopenia

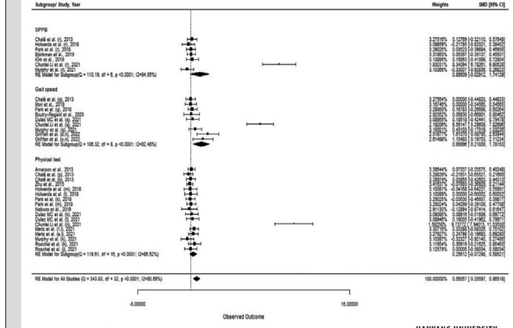
- PROT-AGE Study Group and ESPEN Expert Group suggest that daily protein intake should be at least 1.0 to 1.2 g/kg body weight for healthy older people to maintain and regain lean body mass and function,
- and 1.2 to 1.5 g/kg body weight for geriatric patients with acute and chronic diseases.

Whey Protein on Lean Mass



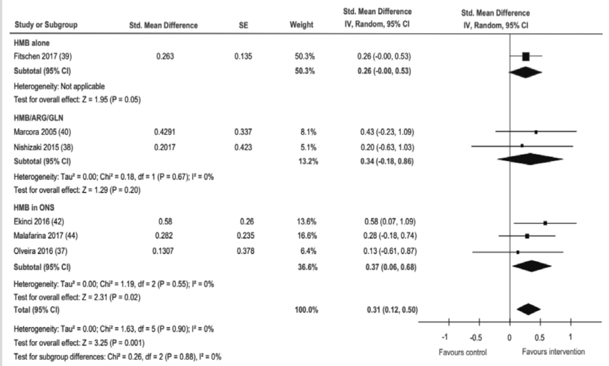
Nasimi et al. Adv Nut 2023;14:762

Whey Protein on Physical Function



Nasimi et al. Adv Nut 2023;14:762

β-Hydroxy-β-Methylbutyrate (HMB) and Muscle Strength



Bear et al. Am J Clin Nutr 2019;109:1119–1132

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Vitamin D and Sarcopenia

Study Design	Patient Characteristics	N Included in Analyses	Intervention	Control Group	Duration	Conclusions
RCT *	Institutionalized people ≥ 60 y	56	1000 mg calcium/day + 150.000 IU vitamin D/month (after 2 months: 90.000 IU/month)	1000 mg calcium/day + placebo/month	6 months	Strength muscle: improvement of hip flexors and knee extensors strength
RCT	Community-dwelling people ≥ 70 y with 25(OH)D ≤ 78 nmol/L	242	1000 mg calcium/day + 800 IU vitamin D/day	1000 mg calcium/day	12 months	Muscle strength and physical performance: improvement of hand grip strength and knee isometric extension strength, SPPB, TUG and 4-m walking speed
PCS	Post-menopausal women ≥ 50 y with osteoporosis and/or vitamin D deficiency	113	800IU/day 20 µg vitamin D/day	-	6 months	Muscle strength and physical performance: improvement of isometric leg extension strength and TUG
RCT	Sarcopenic older adults	380	20 g protein (3 g leucine) + 3 g fat + 9 g carbohydrates + 800 IU vitamin D twice daily	Iso-caloric control product twice daily	13 weeks	Muscle mass and physical performance: improvement of BIA and chair-stand test
RCT	Frail older people, after hospital discharge	243	Single dose of 300.000 IU	Placebo (single dose)	10 weeks	Physical performance: no improvement of quadriceps resistance exercise
RCT	Sedentary men 65–90 y with 25(OH)D < 30 ng/mL and SPPB ≤ 9	130	4.000 IU vitamin D/day	Placebo/day	9 months	Physical performance: no improvement of SPPB or gait speed
RCT	Community-dwelling people ≥ 60 y with 25(OH)D ≤ 20 ng/mL	100	858 (+800) IU vitamin D/day	Placebo/day	1 year	Lower-extremity power, strength and lean mass: no improvement of Keiser pneumatic leg press, backward tandem walk test, SPPB, dual X-ray
RCT	Home-dwelling women 70–80 y with at least 1 fall in the previous year and no use of vitamin D supplements	409	800 IU vitamin D/day ± exercise	Placebo/day ± exercise	2 years	Mass muscle, muscle strength and physical performance: no improvement of BIA and SPPB, TUG, 4-m walking speed and 5 times chair stand

Remelli et al, Nutrients 2019:11:2861

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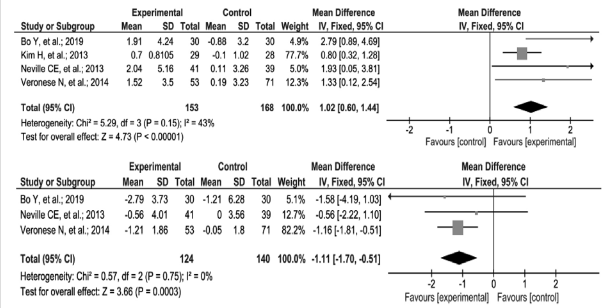
Antioxidant with Handgrip Strength and Time to Complete 5 Stands

1) 900 mg/d of Mg for 12 wks; 2) 218 mg/d of vitamin E + 1404 IU/d of vitamin D + 44 g/d of protein for 6 mon; 3) 540 mg/d of catechin for 3 mon; 4) 5 portions/d of fruit and vegetable consumption for 16 wks



Besora-Moreno et al. Clin Nutr 2022;41:2308e2324

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Lean Mass and Carnitine

Authors/Title/Year	Type of Study	L-Carnitine Supplementation	Sample	Duration	Results
Sawicka Angelika K et al. 2018	Randomized study	Yes 1500 mg once a day	28	24 weeks	Evident better preservation of lean mass in those taking L-carnitine.
Malaguarnera M. 2007	Randomized, double-blind, placebo-controlled study.	Yes 2 g once a day	66 centenarians	6 months	Patients taking L-carnitine had a reduction in fat mass and an increase in lean mass.

Rondanelli et al, Nutrients 2020:12:307

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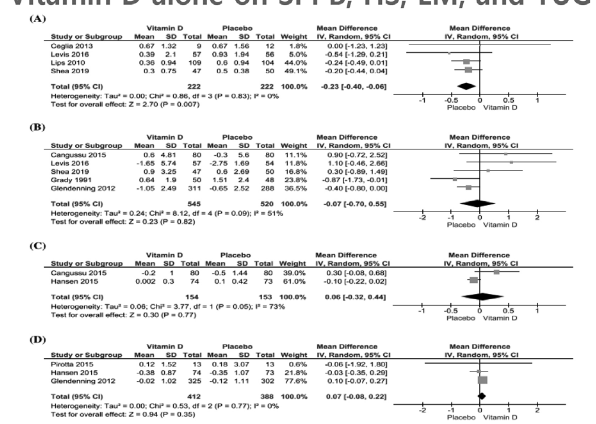
Vitamin D alone on SPPB, HS, LM, and TUG



Prokopidis et al. J Cachexia, Sarcopenia Muscle 2022:13:1642

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Frailty Risk and RBC n-3 PUFA : KFACS

	Quintiles of Fatty Acid Levels						Fatty Acid Continuous[a]	
	Q1	Q2	Q3	Q4	Q5	p for Trend	OR (95% CI)	p
20:5n3								
Frail/nonfrail, n	32/266	33/265	20/266	12/266	9/266			
Cutoff, %	≤1.48	1.48<to≤1.90	1.90<to≤2.30	2.30<to≤2.86	>2.86			
OR (95% CI)	1.0	1.34 (0.74–2.42)	0.78 (0.40–1.50)	0.62 (0.30–1.30)	0.33 (0.14–0.77)*	.002	0.59 (0.44–0.80)	.001
22:6n3								
Frail/nonfrail, n	35/265	20/267	21/265	17/267	13/265			
Cutoff, %	≤8.30	8.30<to≤9.17	9.17<to≤9.87	9.87<to≤10.78	>10.78			
OR (95% CI)	1.0	0.83 (0.44–1.58)	0.58 (0.30–1.10)	0.74 (0.37–1.45)	0.42 (0.20–0.87)*	.018	0.81 (0.70–0.94)	.006

Note: OR (Odd ratios) and 95% CIs (confidence intervals) were presented. Estimates of p for trend values for linear trends were based on linear scores derived from the medians of quintiles of erythrocyte levels of n-3 PUFA among nonfrail participants. Logistic regression was adjusted for sex, age, body mass index, smoking, alcohol drinking, medications, cognitive impairment, nutritional status, and high-sensitivity C-reactive protein. p-value of < .025 was regarded as statistically significant by Bonferroni correction. *p < .025 compared to the first quintile by logistic regression analysis.

[a]Each point corresponds to a 1-unit increment in erythrocyte levels of n-3 PUFA.

Kim et al, J Gerontol Med Sci 2021;78:499

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Muscle Strength and Functional Food

기능성	성분	효과	근거논문
근력 개선에 도움을 줄 수 있음	오미자추출물	대퇴사두근력, 악력	Am J Clin Nutr 2021;113:1440; In J Environ Res Public Health 2020;17:2475
	발효굴추출물	대퇴사두근력, 악력	In J Environ Res Public Health 2022;19:16450
	저분자유청단백 가수분해물	대퇴사두근력, 근파워	
	강황추출물	대퇴사두근력, 악력, 우측족저굴곡, Timed Up & Go	

https://www.foodsafetykorea.go.kr

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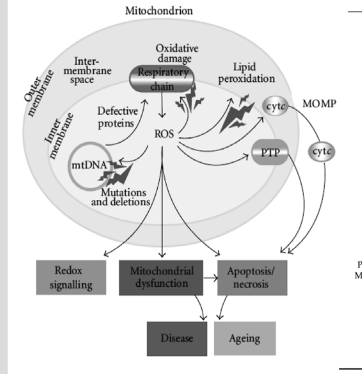
Dietary Inflammation Index (DII)



Dietary Parameters	Inflammatory Effect Score [1]
Carbohydrate (g)	0.097
Total fat (g)	0.298
Protein (g)	0.021
Fiber (g)	−0.663
Vitamin A (µg RE)	−0.401
Vitamin D (µg)	−0.446
Vitamin E (mg)	−0.419
Vitamin C (mg)	−0.424
Beta carotene (µg)	−0.584
Thiamin (mg)	−0.098
Riboflavin (mg)	−0.068
Niacin (mg)	−0.246
Vitamin B_6 (mg)	−0.365
Folate (µg)	−0.190
Vitamin B_{12} (mg)	0.106
Magnesium (mg)	−0.484
Iron (mg)	0.032
Zinc (mg)	−0.313
Selenium (µg)	−0.191
n-3 fatty acids (g)	−0.436
n-6 fatty acids (g)	−0.159
Cholesterol (mg)	0.110
Saturated fat (g)	0.373
Polyunsaturated fatty acids (g)	−0.337
Monounsaturated fatty acids (g)	−0.009
Garlic (g)	−0.412
Ginger (g)	−0.453
Onion (g)	−0.301
Turmeric (mg)	−0.785
Green/black tea (g)	−0.536
Pepper (g)	−0.131
Alcohol (g)	−0.278
Caffeine (g)	−0.110

Kim & Park, Nutrients 2018;10;1363

Oxidative Medic Cell Longevity 2012

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Muscle Function in Frailty Criteria and n-3 PUFA : KFACS

	Weight Loss/ Nonweight Loss (n = 61/1,374)		Exhaustion/ Nonexhaustion (n = 445/990)		Low PA/ Non-low PA (n = 126/1,309)		Slow WS/Non-slow WS (n = 340/1,095)		Low HGS/ Non-HGS (n = 229/1,206)	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
20:5n3										
OR (95% CI)	1.05 (0.77–1.42)	.669	0.89 (0.77–1.03)	.101	0.78 (0.61–0.98)	.036	0.84 (0.72–0.99)	.022	0.83 (0.69–0.99)	.032
22:6n3										
OR (95% CI)	0.97 (0.81–1.16)	.729	0.89 (0.82–0.97)	.005	1.06 (0.93–1.20)	.382	0.86 (0.79–0.94)	.001	0.94 (0.85–1.04)	.197

Note: ORs (odds ratio) and 95% CIs (confidence intervals) were presented. Each point corresponds to a 1-unit increment in erythrocyte levels of n-3 PUFA. Logistic regression was adjusted for sex, age, body mass index, smoking, alcohol drinking, medications, cognitive impairment, nutritional status, and high-sensitivity C-reactive protein. p-value of < .025 was regarded as statistically significant by Bonferroni correction. PA = physical activity; WS = walking speed; HGS = handgrip strength.

Kim et al, J Gerontol Med Sci 2021;78:499

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Sarcopenia and n-3 PUFA Supplementation

References	Year	Sample size, age (years)	Sarcopenia defining parameter(s)	Methodology	Findings
Omega-3 PUFAs supplementation alone					
Hutchins-Wiese [80]	2011	126 postmenopausal women, 64–96 years (mean 75 ± 6 years)	Gait speed, hand grip strength, chair rise time	RCT, 1.2 g EPA + DHA vs olive oil placebo daily for 6 months	Increase in walking speed with 0.03–0.05 m/s in omega-3 PUFAs group. No significant benefit for hand grip strength of chair rise time
Smith et al. [55]	2011	16 healthy older adults, ≥ 65 years (mean 71 ± 2 years)	Muscle protein synthesis	RCT, 1.86 g EPA + 1.50 g DHA vs corn oil placebo daily for 8 weeks	Omega-3 PUFAs supplementation increased the muscle protein synthesis in response to a hyperaminoacidemic-hyperinsulinemic clamp
Smith et al. [56]	2015	60 healthy older adults, 60–85 years (mean control group 69 ± 7 year; omega-3 group 68 ± 5 years)	Thigh muscle volume, hand grip strength, one-repetition maximum (1-RM) strength	RCT, 1.86 g EPA + 1.50 g DHA vs corn oil placebo daily for 6 months	Omega-3 PUFAs supplementation increases thigh muscle volume and muscle strength
Krzyminska-Siemaszko et al. [83]	2015	735 community-dwelling older adults, ≥ 65 years (mean 74.6 ± 8 years)	Muscle mass, gait speed, TUG	RCT, 660 mg EPA + 440 mg DHA + 200 mg other omega-3 PUFAs + 10 mg vitamin E vs 11 mg vitamin E alone daily for 12 weeks	No significant effect on muscle mass, muscle strength or gait speed
Omega-3 PUFAs supplementation combined with physical exercise					
Cornish and Chilibeck [58]	2009	51 subjects, > 60 years (mean 65.4 ± 0.8 years)	Muscle thickness (knee and elbow), muscle strength (1-RM)	RCT, 14 g/day ALA vs corn oil daily combined with resistance training program (3days/week) for 12 weeks	ALA supplementation gave a larger increase in knee flexor muscle thickness
Rodacki et al. [84]	2012	45 women (mean 64 ± 1.0 years)	Muscle strength (knee flexor/extensor, plantar extensors, dorsiflexors), chair rise time, TUG	RCT, fish oil containing 0.4 g EPA + 0.3 g DHA daily as supplementation, 3 arms: strength training (ST) alone for 90 days, ST 90 days + 90 days supplementation vs ST 90 days + 150 days supplementation	All groups increased strength due to the strength training, but the association of a supplement caused greater improvements in muscle strength and functional capacity. There was no extra increase due to an additional 60 days of supplementation (90 vs 150 days)
Da Boit et al. [57]	2012	50 subjects, ≥ 65 years (mean men 70.6 ± 4.5 years; women 70.7 ± 3.3 years)	Muscle strength (knee extensor), SPPB, muscle quality (strength per unit muscle area)	RCT, 2.1 g EPA + 0.6 g DHA vs safflower oil placebo daily, combined with resistance training 2×/w for 18 weeks	Omega-3 PUFAs supplementation augments increases in muscle function and quality in older women but not in older men after resistance exercise training

Dupont et al, Aging Clin Exp Res 2019;31:825

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DII and Frailty Risk

	Total (n = 321)	Good Nutritional Status (n = 103)	Poor Nutritional Status (n = 218)
Non-frail/pre-frail, n	92/187	53/47	39/140
Crude OR (95% CI)	1.15 (1.02–1.29) *	1.01 (0.83–1.23)	1.11 (0.94–1.30)
Adjusted OR (95% CI) [1]	1.01 (0.85–1.19)	0.86 (0.65–1.14)	1.10 (0.87–1.39)
Non-frail/frail, n	92/42	53/3	39/39
Crude OR (95% CI)	1.89 (1.55–2.31) **	2.15 (1.16–3.97) *	1.73 (1.38–2.19) **
Adjusted OR (95% CI) [1]	1.64 (1.25–2.17) **	3.13 (0.96–10.20)	1.68 (1.21–2.34) **

[1] Adjusted for age, chewing ability, and energy intake; OR, odds ratio; CI, confidence interval. * p-value < 0.05; ** p-value < 0.01.

Kim & Park, Nutrients 2018;10;1363

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DII and Muscle Function in Frailty Criteria

	Total (n = 321)	Good Nutritional Status (n = 103)	Poor Nutritional Status (n = 218)
Weight loss/non-weight loss, n	38/283	4/99	34/184
Crude OR (95% CI)	1.15 (1.02–1.29) *	1.26 (0.82–1.94)	1.09 (0.93–1.28)
Adjusted OR (95% CI) [1]	1.29 (1.03–1.60) *	1.50 (0.82–2.74)	1.26 (0.99–1.60)
Exhaustion/non-exhaustion, n	184/137	31/72	153/65
Crude OR (95% CI)	1.16 (1.05–1.27) **	0.96 (0.78–1.17)	1.11 (0.98–1.26)
Adjusted OR (95% CI) [1]	1.04 (0.90–1.20)	0.89 (0.67–1.19)	1.08 (0.89–1.30)
Low physical activity/non-low physical activity, n	43/278	6/97	37/181
Crude OR (95% CI)	1.41 (1.21–1.63) **	1.50 (1.04–2.18) *	1.33 (1.13–1.58) **
Adjusted OR (95% CI) [1]	1.16 (0.94–1.45)	1.52 (0.90–2.57)	1.08 (0.85–1.37)
Low walking speed/non-low walking speed, n	65/256	11/92	54/164
Crude OR (95% CI)	1.43 (1.25–1.62) **	1.45 (1.08–1.95) *	1.37 (1.18–1.59) **
Adjusted OR (95% CI) [1]	1.33 (1.10–1.61) **	1.35 (0.90–2.02)	1.33 (1.07–1.65) *
Low grip strength/non-low grip strength, n	74/247	22/81	52/166
Crude OR (95% CI)	1.28 (1.14–1.44) **	1.25 (1.00–1.55)	1.33 (1.15–1.54) **
Adjusted OR (95% CI) [1]	1.34 (1.13–1.60) **	1.28 (0.94–1.74)	1.37 (1.11–1.70) **

[1] Adjusted for age, chewing ability, and energy intake; OR, odds ratio; CI, confidence interval. * p-value < 0.05; ** p-value < 0.01.

Kim & Park, Nutrients 2018;10;1363

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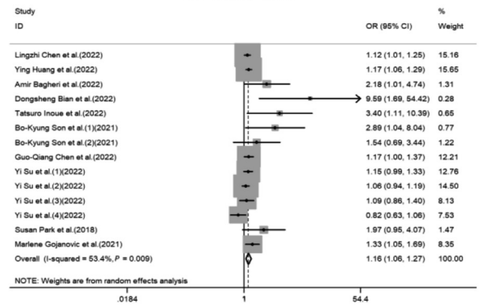
Sarcopenia Risk in Subjects with a High vs Low DII



Diao et al. Nutrients 2023;15:219

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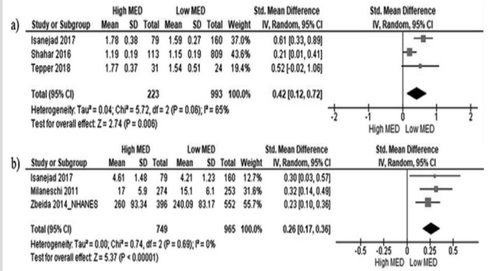
Mediterranean Diet with Walking Speed (a) and Knee Extensor Muscle Strength (b)



Coelho-Júnior et al. Ageing Res Rev 2021; 101395

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Summary

- Malnutrition and energy intake are associated with risk of sarcopenia, and nutrition support can improve sarcopenia.
- Supplementation of protein, vitamin D, and n-3 PUFA can have beneficial effect on sarcopenia, based on clinical trials.
- There are some clinical trials suggesting that supplementation of carnitine and antioxidants improve sarcopenia.
- Dietary patterns such as DII and Mediterranean Diet are associated with risk of sarcopenia, based on epidemiological studies.

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Curriculum Vitae

이상기

소속: 충남대학교

| 학력사항 |

고려대학교 이학박사

| 경력사항 |

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충남대학교 스포츠과학과 교수

Review: Exercise Interventions to Prevent and Improve Sarcopenia

충남대학교
이상기

The Purpose of this study is to analyze the details of the exercises/exercise program prescribed for prevention and improvement of muscle mass/muscle strength/physical performance among sarcopenic older adults. A systematic literature search was conducted in three electronic databases and the details of exercises such as single component or multicomponent exercise program, frequency/week, intensity, duration of the exercise program, type of exercises, progression, adverse events reported, outcome measures used, and whether technology or other educational aids were used to deliver the program were extracted. In summary, we recommend multimodal training (RE+AE, RE+Balance) and resistance training for old adults with sarcopenia. Aerobic training (walking, bicycle ergometer ex, and aquatic ex) should be performed with moderate (5~6 CR10/RPE, 30~60 m/day, 5 days/week) to high intensity (7~8 CR10/RPE, 30 m/day, 3 days/week), and 500 MET-min/week. RE training is included with large muscle groups (performing activities of daily living; lower-walking, rising from a chair and climbing stairs, upper-dressing, self-care) with progressive intensity (70~80% RM or 7~8 CR10/RPE), 1~3 sets of 8~12 repetitions, 2 times per week, and at least 12 weeks.

Curriculum Vitae

임재영

소속: 서울의대 재활의학교실

| 학력사항 |

서울대학교 의학과 학사
서울대학교 의학과(해부학전공) 의학석사
서울대학교 의학과(재활의학전공) 의학박사

| 경력사항 |

서울대학교의과대학 재활의학교실, 분당서울대학교병원 교수
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분당서울대학교병원 의학자료정보센터장
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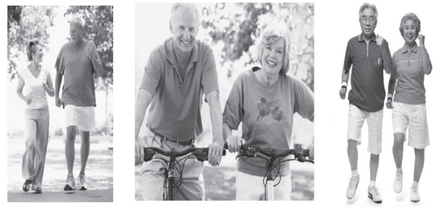
Rehabilitation Approaches in Patients with Sarcopenia

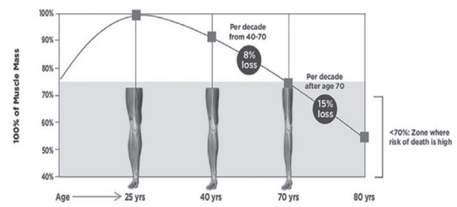
서울의대
임재영

건강 노화 Healthy aging

튼튼한 근골격계



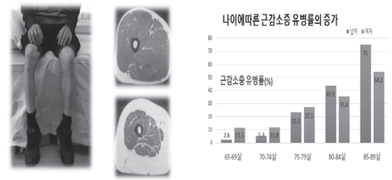
Loss of Muscle Mass over Time



Baier S, et al. *JPEN J Parenter Enteral Nutr.* 2009;33(1):71-82.
Flakoll P, et al. *Nutrition.* 2004;20(5):445-451.
Grimby G, et al. *Acta Physiol Scand.* 1982;115(1):125-134.
Janssen I, et al. *J Appl Physiol.* 2000;89(1):81-88.

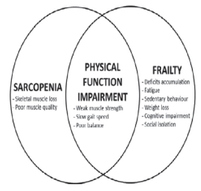
근감소증 (Sarcopenia)

- 근감소증이란: 노화에 따라 골격근육량이 감소하고 신체기능이 저하되는 현상. 의료비, 장기요양비용을 급증하게 하는 매우 중요한 건강문제(**Geriatric Giant**)로 대두.
- 2018년도 유럽 근감소증 진단/관리 지침, 2019년 아시아 근감소증 진단/관리 지침의 수정 및 새로운 합의.
- 국제표준질병분류(ICD-11)와 한국표준질병사인분류에 근감소증 (M62.5) 포함: 진단 알고리즘과 진단 기준에 대한 국제적 합의와 공식 질병으로 인정됨에 따라 근감소증의 중요성과 가치에 대해 전세계적으로 주목.



근감소증 (Sarcopenia)

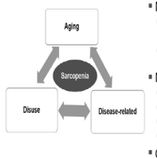
- 노화에 따른 골격근육량의 감소로 근력 저하와 함께, 각종 신체기능이 저하되는 현상.
- Physical marker or component of frailty



Cesari M, Front Aging Neurosci 2014

How to manage older patient with sarcopenia

Clinical features of sarcopenia



- Musculoskeletal
  - Osteoporosis, fragility fracture
  - Arthritis
- Medical diseases
  - Endocrine
  - Respiratory
  - Renal
  - Cardiac
- Cancer-related

- In chronic degenerative/geriatric disease/cancer-related sarcopenia, acute/recovery phase due to exacerbation of the underlying disease, injury, or disuse
- Continuous, chronic progression of sarcopenia related to chronic degenerative/geriatric disease/cancer – Maintenance phase
- Age-related sarcopenia - mainly in the very old age or late life.

Fragility fracture (Hip fracture) | Metabolic syndrome related | Cancer-related

Core evaluations

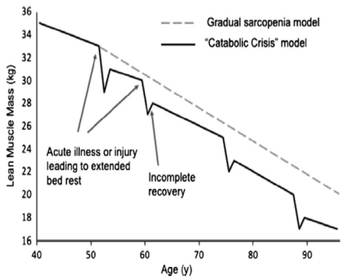
- Lab including 25 OH vitamin D, radiologic exams of spine, knee, shoulder, DEXA, body composition, etc)
- Comprehensive geriatric assessment (다약제복용, 낙상위험도, 우울, 섬망 등)
- Mobility : comprehensive geriatric performance battery (FAC, BBS, KOVAL, 보행속도, 근력, 근파워, 근지구력, etc)

Sarcopenia: wide spectrum based on functional level

Severe	Moderate	Mild	Non-sarcopenia
Sarcopenia with disability	Sarcopenia	Pre-sarcopenia	Robust

Steffi M et al. J Nutr Health Aging. 2016

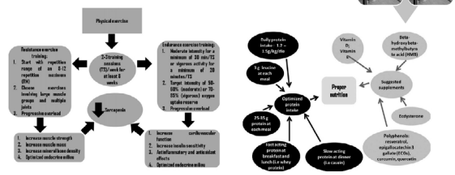
Potential model of age associated muscle loss (sarcopenia)



Kirwan et al. GeroScience 1550 (2020) 42:1547–1578

Current status of therapeutic interventions for sarcopenia

- Interventions for sarcopenia
  - Exercise, nutrition, or combined interventions to prevent or treat sarcopenia
  - Rehabilitation therapy and exercise for the impairment related to sarcopenia
  - Pharmacologic interventions – *not available yet*
  - Assistive technologies to assist gait and ADL in sarcopenia patients



Exercise intervention

Nutritional intervention Sgro et al. 2019

Rehabilitation approach: patients with sarcopenia

Functional rehabilitation (Gait and ADL training)	Medical and nutritional management	Exercise interventions

Exercise interventions

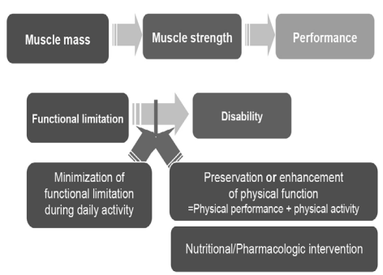
Sarcopenia with disability	Sarcopenia	Sarcopenia at risk	Robust

Rehabilitation exercise - Modality-specific - Full supervised - Institution-based	Habitual exercise Self-directed Community based

Depending on the delivery, combined interventions if necessary

- Full Supervised/Semi-supervised/Self directed
- Institution based/Community based/Home bound
- Smart system, wearable, IoT

Management strategy to prevent and manage sarcopenia



Management strategy for sarcopenia

- Evaluation of functional decline of physical function and mental function
- Diagnosis of secondary sarcopenia-related medical or neurologic conditions
- Comprehensive approach for frailty, sarcopenia, osteoporosis, and nutritional problems
- Ambulation and ADL evaluation
- Specific management planning based on the evaluation
- Development of effective modality specific interventions

Modality-specific Exercise interventions

- Task specific power-oriented
- Eccentrically biased training
- Blood flow restriction exercise: Kaatsu (加圧)
- Computer assist devices (interactive software)
- Motor driven
- Hybrid (movement + electric stimulation)
- Vibration training
- Exercise robotics

Eccentrically biased exercise | Hybrid (voluntary/ electrical stimulation) exercise | Blood flow restriction exercise | Vibration exercise

근감소증 중재 한계점과 고려사항

AS-IS	TO-BE
• 운동 및 영양 중재: 근감소증 예방에 긍정적 효과 • 근감소증으로 진행한 노인 환자에게 운동과 영양 중재의 이해 부족 • 근감소증 노인 환자에게 일반적인 운동과 영양 단독 중재 효과에 대한 근거 부족 • 근감소증 시기별, 중증도에 따른 관리 체계 미흡	▪급성기 근감소증 환자와 회복기 및 유지기에 속한 환자에 따른 시기별, 기능수준별 다요소 운동 프로그램 적용 ▪각 단계별 순응도를 고려한 복합 프로그램 적용. ▪영양평가에 따른 근거기반 영양 중재와 운동과 영양 중재 결합. ▪의료기관(원인질환 치료전략), 운동전문가, 임상영양사가 포함된 다학제 중재 필요

17

Multidisciplinary combined Exercise and Nutrition inTervention fOR Sarcopenia, MENTORS

Patient-Centered Clinical Research

Evidence Generation Research on Health Technologies

SNUH 분당서울대학교병원 서울부민병원 경희대학교병원

Objectives

- To develop standardized multidisciplinary Combined Exercise and Nutrition Intervention for sarcopenia (MENTORS)
- To conduct multicenter clinical trial to comparative effectiveness of MENTORS in comparison with conventional medical care in sarcopenia older patients.
- To establish the dissemination strategy to the community
- To test the feasibility of MENTORS by implementing that to the representative community hospitals and clinics.

Power/eccentric exercise

Make the movement as quickly as possible (power exercise), and slowly return while feeling the resistance of the band (eccentric contraction)

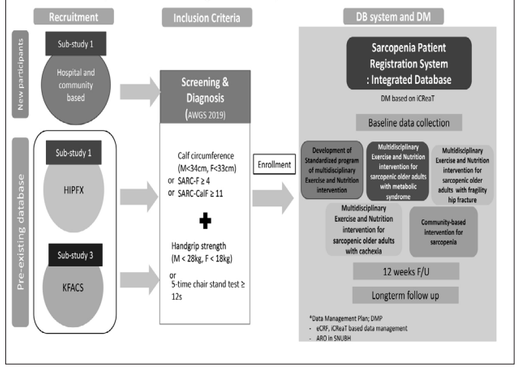
Straighten your one leg as quickly as possible or within 1 sec.

Then, slowly return to original position for 3~ 5 sec.

Resistance exercise

Upper	Trunk	Lower
☐ Biceps Curl	☐ Back extension	☐ Leg lateral rotation
☐ Dips	☐ Curl up	☐ Leg extension
☐ Front raise	☐ Bridge (supine)	☐ Hip abduction
☐ Chest press	☐ Bridge (side)	☐ Squat
		☐ Heel raise

Korean Sarcopenic Patient Registration System



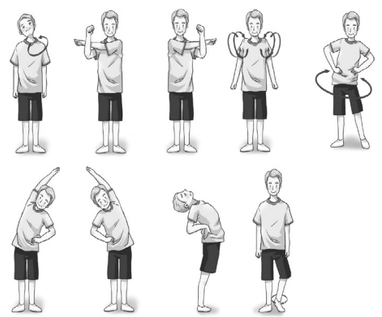
Multidisciplinary combined Exercise and Nutrition inTervention fOR Sarcopenia, MENTORS

- Hip fracture-related, metabolic syndrome related, cancer-related → Standard intervention method universally applicable for sarcopenia related to major diseases.
- Initial assessment for early detection and management of sarcopenia-related comorbidities and risk factors.
- Evidence-based exercise/nutrition complex intervention method.
- Customized complex intervention based on the patient's physical function and nutritional status: goal of proper nutrition and recovery and maintenance of optimal physical activity.
- Modular customized interventions for each patient's disease, phase, and functional status.
  - Underlying disease (hip fracture, metabolic syndrome, cancer, etc.)
  - Timing (acute, post-acute, maintenance)
  - Level of exercise and nutrition intervention (beginning, intermediate (default), advanced)
- Goal setting and selection of specific intervention protocol.

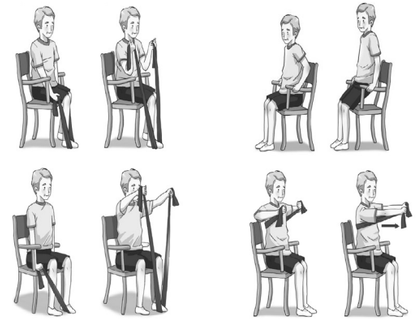
Discussion and consensus by multidisciplinary experts

Endorsed by National Academic Societies

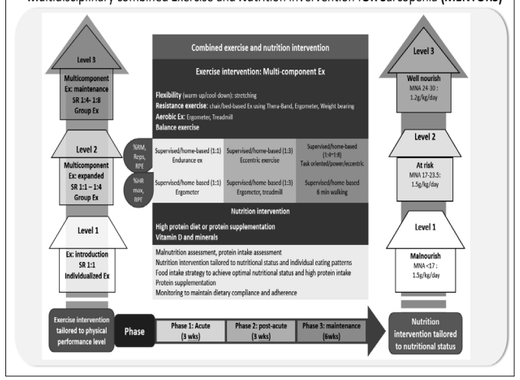
Warm up & Cool down



Upper body



Multidisciplinary combined Exercise and Nutrition inTervention fOR Sarcopenia (MENTORS)



Exercise intervention

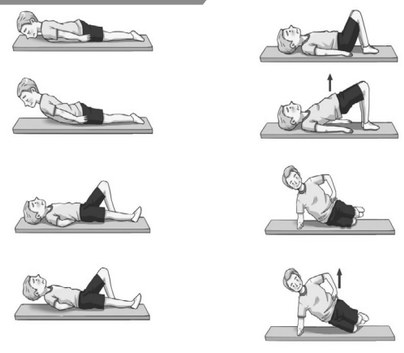
	Introductory(3wks) 2 visits/wk	Expanded (3wks) 2 visits/wk	Maintenance (6 wks) 1 visits/wk
Stretching	Warm up / Cool down	Warm up / Cool down	Warm up / Cool down
Resistance	Conventional resistance training@chair/bed-based elastic band Ex)	*Eccentric exercise (chair/bed-based elastic band Ex)	**Power/eccentric exercise (stand position with chair)
Aerobic	Stationary bicycle (RPE 9-11 or HRmax 60) 10 min	Stationary bicycle (RPE 11-13 or HRmax 70) 15 min	Stationary bicycle (RPE 11-13 or HRmax 70) 20 min
Intensity	8~10 rep 3 sets Upper theraband yellow (F) Red (M) Lower loop band red (F) green (M)	10~12 rep 3~4 sets Upper theraband yellow~red (F) Red~green (M) Lower loop band red-green (F) green~blue (M)	15 rep 3~4 sets Upper theraband red (F) green (M) Lower loop band green (F) blue (M)

➢Conventional resistance training : Concentric contraction

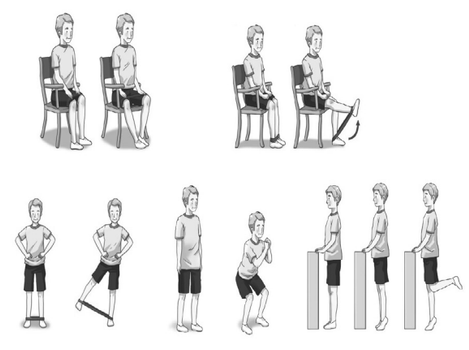
➢**Eccentric exercise** : Eccentrically biased training

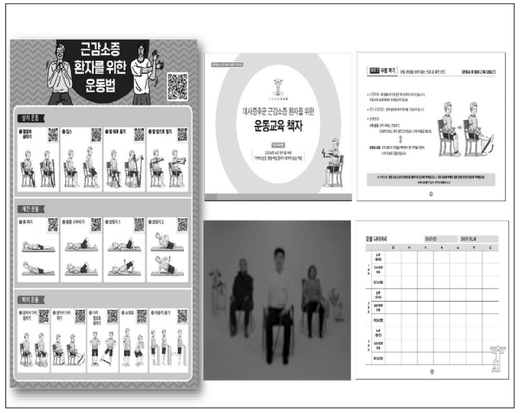
➢Power/eccentric exercise: Make the movement as fast as possible (power exercise), and slowly return while feeling the resistance of the band (eccentric contraction)

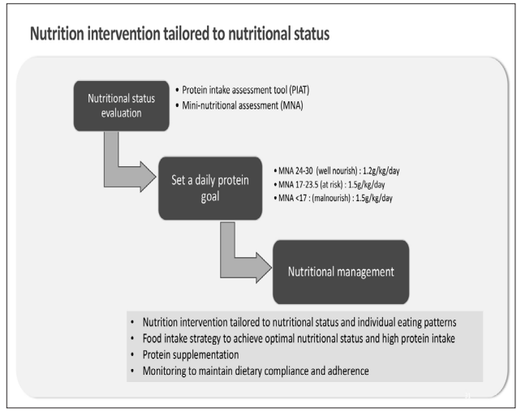
Trunk

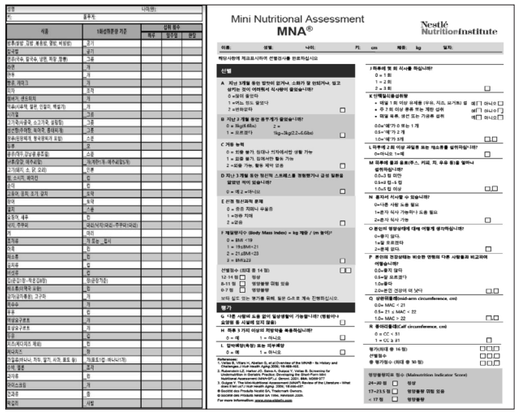


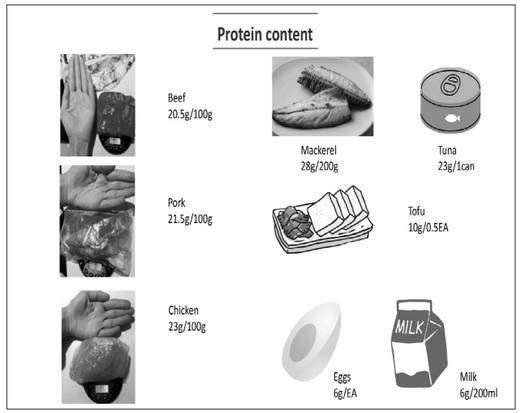
Lower Body

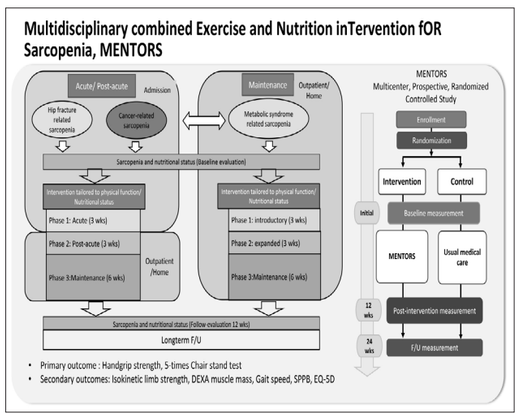


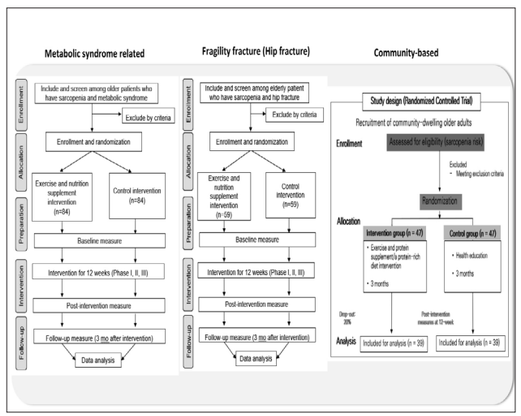




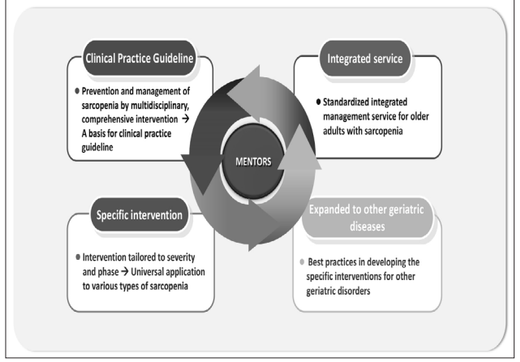








기대효과 및 활용 방안 (Utilization Planning)



요약 Summary

- 근감소증 – 초고령사회의 매우 중요한 건강문제 (Geriatric Giant)
- 근감소증 재활 전략
  - 영양 및 운동 중재, 재활치료 및 재활운동, 근감소증 약물치료, 근감소증 환자를 위한 보조기기
  - 다학제, 통합적 접근
  - 중증도, 시기에 따라 맞춤형
- 근감소증 다학제 운동·영양 복합 중재: 시기와 중증도에 따라 맞춤 제공이 가능한 효과적인 치료 방법

MEMO

16th Congress of The Korean Society of Sarcopenia

2024년 대한근감소증학회 제16차 학술대회

Session V

Methodology of Muscle Research

Session V

좌장: **이윤실** 서울대, **이승훈** 원광대

수학회장

Curriculum Vitae

서준호

소속: 서울대 치의학대학원

| 학력사항 |

Ph.D. Seoul National University School of Dentistry
Cell and Developmental Biology
B.S. KAIST

| 경력사항 |

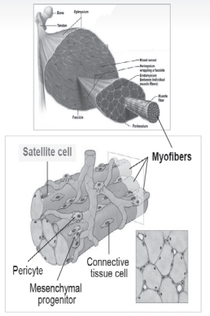
Postdoctoral Fellow, Seoul National University Dental Research Institute

Primary Myoblast 분리와 활용

서울대 치의학대학원
서준호

Introduction

Myoblasts: Activated Muscle Stem Cells

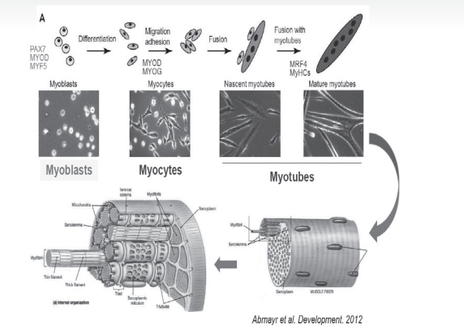


- **Muscle stem cells (satellite cells)** are located outside the myofiber membrane and beneath the basal lamina.
- **Satellite cells** remain quiescent (inactive) under normal conditions.
- Myofiber damage → **Activation of satellite cells into** myoblasts (PAX7+, MYOD+) → Proliferation → Fusion into new myotubes or with host myofibers for regeneration.

Pannerec et al. Trends Mol Med. 2012

Introduction

Myogenic Differentiation

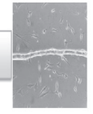


Abmayr et al. Development. 2012

Protocols for Isolation of Muscle Stem Cells

Part I Direct isolation by mincing the muscle tissue

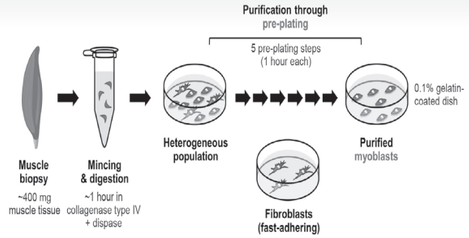
- Pre-plating technique
- Fluorescence-activated cell sorting (FACS)



Part II Isolation by culturing myofibers

Part I

Pre-plating Method: An Overview



- Requires purification (pre-plating) steps to remove fast-adhering fibroblasts.
- Pre-plating: the transfer of supernatant to a fresh culture dish after **1 hour** (supernatant contains myoblasts that take longer to adhere to the dish).

Part Ⅰ

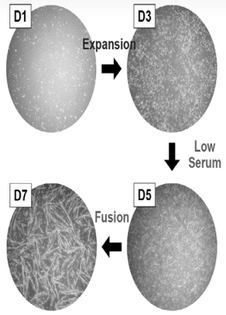
Expansion & Differentiation

➢**Expansion:**

- **Expansion Medium**: F-10 with 20% HI-HS, 1% P/S, and 2.5 ng/mL final concentration of basic FGF.
- Replenish half the medium every 2 days.

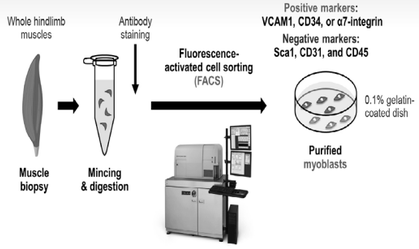
➢**Fusion:**

- Fusion Medium: DMEM with 5% HI-HS and 1% P/S.
- Start differentiation when the cells reach 70% confluence.
- Replenish half the medium every 2 days.



Part Ⅰ

Isolation by FACS: An Overview



➢ Yields highly pure muscle stem cell populations.

➢ Requires FACS device and specific antibodies for positive and negative selection.

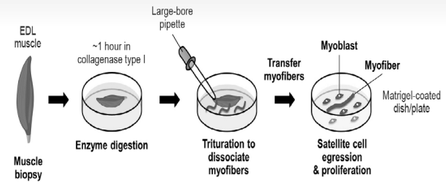
Part Ⅰ

Important Notes for Part Ⅰ

1. Older mice yield less muscle stem cells with lower purity and higher fibroblast content (**neonatal mice give the greatest yield** of myogenic cells).
2. Do not grow myoblasts at less than 10% confluence, but also do not allow them to become too crowded, or they may differentiate or die. Recommended seeding density: 5,000-10,000 myoblasts/cm^2.
3. **Pre-plating steps can be repeated** after trypsinization for passaging. **Using diluted trypsin (1:5-1:10)** will detach myoblasts while leaving many fibroblasts attached to the dish.
4. Avoid overcrowding the well with cells when plating for differentiation (the cells still proliferate a bit after differentiation induction).

Part Ⅱ

Myofiber Culture: An Overview



➢ Yields a highly pure, but relatively small satellite cell population.

➢ More difficult compared to other methods (myofibers must be very carefully manipulated while observing under a stereo microscope.

➢ Long EDL myofibers are generally cultured.

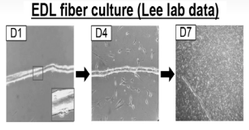
Keire et al. Methods Mol. Biol. 2013

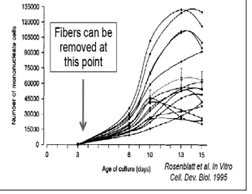
Part Ⅱ

Myofiber Culture

1. After transferring myofibers to a matrigel-coated dish (fibers are submerged in a small drop of pure DMEM), incubate at 37°C, 5% CO_2 for at least 1 hr to allow the fibers to attach.
2. When the fibers attach, **slowly add warm culture medium** (DMEM with 20% HS and 1% P/S).
3. Change medium every 2-3 days.

EDL fiber culture (Lee lab data)



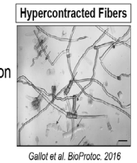


Rosenblatt et al. In Vitro Cell. Dev. Biol. 1995

Part Ⅱ

Important Notes for Part Ⅱ

1. **Avoid over-digestion of myofibers.** Generally, 1 hour digestion works well.
2. Myofibers must be very carefully manipulated, or they will hyper-contract or die. Sudden changes in temperature may also result in hypercontraction. Always use pre-warmed media.
3. If examining satellite cell behavior under quiescence conditions, too much agitation/shaking during digestion may activate satellite cells.



Gallot et al. BioProtoc. 2016

Summary

	Isolation by mincing the muscle		Culturing myofibers
	Mincing (5 min)		Enzyme digestion (1 hr)
	Enzyme digestion (45 min)		Fiber dissociation (10 min)
	Antibody staining & **FACS** (3 hrs)	**Pre-plating** & seeding (5 hrs)	**Fiber transfer** & seeding (10 min)
Purity	High	Medium	High
Yield	Medium	High	Low
Difficulty	Medium	Easy	Hard

Curriculum Vitae

배주현

소속: 성균관의대

| 학력사항 |

건양대학교 해부병리학과 석사
성균관의대 분자세포생물학 박사

| 경력사항 |

성균관의대 연구원
Emory University, School of medicine
Atlanta, GA, Department of Orthopedics

마우스 근육조직 분리 및 염색 방법

성균관의대
배주현

골격근은 생체내의 대사 및 병리학적 상태에 따라 형태학적 변화가 매우 다양하다. 오늘날, 근육 연구자들은 연구 초기 단계에서 근육의 형태학적 변화를 바탕으로 연구 방향을 결정한다. 대표적으로, 노화성 근감소증에서 보이는 근육양의 감소와 세포소기관들의 변화과정은 1차적으로 해부학적, 조직학적 및 면역조직학적 분석에 의존한다. 또한, 연구자가 설계한 실험 모델에서 나타나는 근육의 형태학적 변화는 결과적으로 분자 신호전달 메커니즘 연구의 바탕이 된다. 하지만, 골격근은 뇌와 같이 부드러운 조직은 아니기에, 근육 분리과정 및 면역화학 염색과정에서 많은 연구자들이 어려움을 겪는다. 따라서, 연구 목적에 따른 적합한 골격근을 선정하고 올바르게 분리하여, 최종적인 형태학적 변화를 규정하기 위해서는 올바른 실험 방법이 요구된다.

오늘날, 유전체학 및 단백질체학의 발달로 인해 근육 내 세포 신호전달의 통합적인 이해가 점점 발전하고 있다. 하지만, 관련된 세포신호전달 체계가 유도하는 골격근의 최종적인 변화는 결국 조직학적 분석에 기반할 수밖에 없다. 이에 본 연자는 기본적인 조직학적 분석을 소개하고 골격근의 연구과정에서 발생하는 다양한 실험적인 오류와 이에 대한 문제해결 방식을 제안하고자 한다.

Curriculum Vitae

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Assessments of Muscle Performance, Functional Muscle Mass and Muscle Protein Dynamics

가천의대
김일영

ABSTRACT

Sarcopenia, the loss of muscle mass and strength that occur with aging, results from rates of protein breakdown exceeding synthesis in skeletal muscle over an extended period, thereby worsening other clinical conditions such as type 2 diabetes mellitus, obesity, osteoporosis, and cancer and ultimately the quality of life in older adults. Despite significant research efforts, effective therapeutics have not been successfully developed and/or discovered yet. In this regards, accurate assessments of changes in muscle function or performance and dynamic nature of muscle are crucial in understanding aging muscle and evaluations of efficacy of potential therapeutics, thus facilitating the discovery and development of effective therapeutics for reversing sarcopenia. Herein, I will discuss experimental methods that deals with 1) muscle performance, i.e., strength (grip strength, ladder climbing, and weight pulling) and endurance (treadmill running), 2) functional muscle mass (using D3 creatine dilution) and 3) muscle protein turnover (protein synthesis and breakdown) using stable isotope tracers with its effect on other tissues, all being currently used in my lab.

Keywords: Heavy water labelling, D3-creatine dilution, Skeletal muscle, Stable isotope tracers

Curriculum Vitae

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근감소증의 in Vitro/in Vivo 모델

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MEMO

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Session VI

Current and Upcoming Interventional Therapies for the Treatment of Sarcopenia

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Curriculum Vitae

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Strategies for the Prevention of Sarcopenia and Frailty in Community-dwelling Older Adults

경상의대
박기수

노인 대상 다양한 보건, 복지 사업들이 국가 및 지역사회 단위에서 진행되고 있다. 그렇지만 아직까지 노인들의 신체적, 정신적 그리고 사회적 기능을 회복, 유지하기 위한 프로그램, 즉, 노쇠 예방보다는 질병 중심, 사회 경제적 지원으로 이루어지고 있다. 여기서는 이에 대한 각각의 사업들을 고찰하고 지역사회 노쇠 예방사업을 위한 것에 대해서 논의하고자 한다

노쇠 및 근감소증은 입원, 조기사망 등과 밀접한 관련이 있어 이를 예방 관리하는 것은 국가적 차원에서도 중요하다. 이를 일으키는 인자는 여러 가지 알려져 있는데, 생활 습관에서는 신체활동과 영양 공급 그리고 사회적 요인으로 자기 효능감, 사회적 고립, 우울감, 탈진 등이 관련이 있어, 이를 예방, 관리하는 것은 중요하다. 결과적으로 지역 보건사업에서는 이러한 것에 대한 개입이 필요할 것이다.

국가 및 지역사회 차원에서 하는 노인 대상 사업은 우선 국민건강증진종합계획 2030에 노인 분야 세부 추진 계획으로 허약, 노쇠 등 보편적 건강관리서비스 체계로 개편을 포함하고 있다. 보건소의 통합건강증진사업에서는 신체활동과 영양에서 노인 대상 사업들이 있기는 하지만 노쇠 또는 근감소증에 대한 평가 등은 고려되고 있지 못하다. 방문건강관리사업에서는 총 28문항으로 구성된 허약노인 건강면접 조사가 있지만 문항 수가 너무 많고 보행 평가에서도 TUG로 평가하고 있어 좀 더 간단한 도구가 필요하다. 그리고 치매안심센터에서 하는 사업이 노쇠 예방사업과 연계되어 있음을 보건소 실무진 교육 시 함께 진행되어야 한다.

노인복지사업 중 노인맞춤돌봄서비스에서도 생활교육이 포함되어 있고 신체건강분야와 정신건강분야에 서비스를 제공하고 있으며, 장기요양보험제도에서 재가 노인 대상으로 돌봄을 제공하고 있지만 쉽게 비의료인들도 개입할 수 있는 도구의 부재로 아직 노쇠 예방과 관리를 위해서는 진행되지 못하고 있다.

한편, 국내 연구에서도 지역사회 노쇠 관리 모형으로 노쇠 의심 군을 대상으로 포괄적 평가와 개입이 필요하며 모형을 제시하였다. 세계보건기구 역시 포괄적 노인인구 개입 전략을 발표하였고 가까운 싱가포르에서는 국가노쇠전략을 발표하여 일차의료기관과 보건소 차원에서의 노쇠 전략을 실시하고 있다.

연구진은 남해군 보건소와 함께 소지역 간(읍면동간) 건강 격차를 줄이고자 면 단위에서 노쇠 관리 사업을 하고 있다. 2020-2022년 3년간 질병관리청의 기원으로 사업을 하였고 현재는 남해군 자체 사업을 면 단위에서 노쇠예방사업을 하고 있다. 노인을 대상으로 노쇠 평가로서는 한국형 FRAIL로 평가하고 있고, 신체활동, 영양중재, 방문간호 등을 중재에 포함하여 하고 있다. 신체활동은 주민 참여 사업으로 하며, 영양은 단백질 보충제를 지원받아 배포하고 있고, 방문보건은 간단한 평가 후 지역사회 연계를 하고 있다. 2023년에는 303명을 대상으로 전, 후 평가(SARC_F, 의자에서 5회 일어서기, 최대악력, 노인영양지수 등)를 하였으며, 최대악력을 제외하고는 모든 지표들이 향상되었다.

지역사회 노인 대상 사업에서 노쇠의 중요성에 대한 인식 개선과 함께 보건기관, 복지기관에서 실용적으로 사용할 수 있는 도구 보급, 개입 컨텐츠 개발 보급 그리고 인력 교육 등이 앞으로 학회 차원에서 적극적으로 개입하여야 할 것이다.

MEMO

Curriculum Vitae

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Digital Healthcare and Sarcopenia: Focusing on Community-Based Exercise and Digital Health Technologies

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Sarcopenia is a major problem in the older population and is caused by a variety of factors. These include physical aging, lack of exercise, chronic disease, nutritional imbalances, fractures, neurodegenerative diseases, arthritis, and internal medical conditions. Despite the importance of early detection and management, it can be difficult to effectively intervene with nutrition or exercise therapy in cases of excessive loss of muscle mass, joint deterioration due to muscle weakness, decreased general well-being, and reduced ability to maintain activities of daily living.

Over the past 20 years, there have been nearly 14,000 research papers on sarcopenia, of which randomized controlled trial (RCT) interventions and clinical trial studies, including exercise and nutrition, account for about 11%. Nevertheless, there are still many challenges in managing sarcopenia early and providing sustainable community-based solutions, which require further discussion and research and development in this area. In 2021, Korea recognized sarcopenia as a disease by assigning it a disease code (M62.5) for the first time in the 8th revision of the Korean Standard Diagnostic Classification of Diseases. However, no treatment has been developed yet.

Advances in digital health technologies and digital therapies have the potential to provide innovative approaches to sarcopenia management. Wearable sensors and mobile applications can enable early detection, diagnosis, and personalized interventions, and can provide personalized exercise programs and nutritional guidance to optimize muscle health. Digital health technologies also have the potential to improve access to sarcopenia management through remote monitoring and intervention, and to increase patient engagement and adherence to treatment regimens.

Our research team is conducting studies of digital healthcare-based living lab-based and wearable

sensor and virtual reality-based interventions, as well as traditional exercise-based interventions for sarcopenia prevention, and we have found evidence that digital healthcare-based interventions are more effective than traditional interventions in improving muscle function and cognitive function over a shorter period of time, and are more effective in terms of subject motivation and sustainability, suggesting that digital healthcare technologies may play an important role in creating new challenges in sarcopenia management.

Major countries around the world, including the U.S., have recognized the potential of digital healthcare early on and have been implementing policies to foster the industry, and Korea has been working to create an ecosystem by quickly preparing related policies such as the Biohealth Industry Innovation Strategy. Of course, like any other innovative technology or industry, there is a debate about the appropriate line of regulation, but as digital healthcare is directly related to human health and life, the world is making every effort to find a balance. In addition, the first digital cure was announced in Korea in early 2023.

Therefore, integrating digital healthcare into sarcopenia management has the potential to enhance patient-centered care and improve outcomes, but there are many challenges to digital healthcare-based sarcopenia prevention. These include lack of digital literacy, usability issues for professionals, lack of scientific evidence based on real-world evidence (RWE), and regulatory approval. Nevertheless, as one of the countries with the fastest growing aging population and digital technology use, there is promise that Korea can overcome these challenges and create a new paradigm that can play a leading role in digital healthcare-based sarcopenia prevention and management. In this lecture, we will discuss our challenges and future for the fighting of sarcopenia based on digital healthcare technology for healthy community.

MEMO

Curriculum Vitae

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The Future of Drug Discovery for the Treatment of Sarcopenia

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Sarcopenia, or age-related decline in muscle mass and function, has a variety of drug targets. The etiologies of sarcopenia are not fully understood. An imbalance between muscle protein synthesis (anabolism) and degradation (catabolism) may cause the onset of the sarcopenia. Both intrinsic factors within skeletal muscle (e.g., inflammation, apoptosis, autophagy, mitochondria, neuromuscular junction, and calcium metabolism) and extrinsic factors in systemic environments (e.g., endocrine, nutrition, immobility) contribute to defective satellite cell maintenance, myogenesis, and myotube atrophy as well as neuromuscular coordination. Understanding the mechanisms in sarcopenia is essential to identify a variety of molecular targets for pharmacological treatment.

The integrity and function of the neuromuscular junction (NMJ), the junction between the nervous and muscular systems, is important for neural control of muscle strength production. Although aged rodents have consistently shown features of NMJ endplate fragmentation and denervation, the existence of NMJ changes in aged humans remains controversial. Evidences support failure of NMJ transmission as a possible causal factor for sarcopenia. Morphometric studies showed a weak association between nerve terminals and motor units in the elderly NMJ. Additionally, in vivo assessment of single muscle fiber action potentials using single-fiber electromyography and nerve stimulation muscle strength measurements revealed NMJ failure in aged mice and rats. Possible mechanisms for this failure include simplification of postsynaptic folding and altered AchR clustering and their function. Although clinical data investigating single synaptic function in the context of aging are limited in humans, these NMJ transmission defects offer a well-defined pathway for clinical implementation. Investigation of small molecules that are currently clinically available or being clinically tested for other muscle degenerative disorders may provide a rapid pathway for the development of interventions for sarcopenia.

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