Anna VerMeulen

Sarcopenia: Causes, Implications, and Rehabilitation

Sarcopenia was originally described as an age-associated decline in skeletal muscle mass. More recently, the sarcopenia definition also includes decreased strength and functional impairment. These associated declines increase the risk for falls, fractures, dependency, hospitalization, and mortality in older adults.[1–3] Some researchers and medical professionals refer to sarcopenia as "age related muscle mass" and use a different term, dynapenia as "muscle strength and functional decline."[4] For the remainder of this paper, sarcopenia will encompass the two definitions and indicate a decrease in muscle mass, strength, and function with increased age. Sarcopenia occurs typically around the age of 70 in both genders and prevalence is reported from 1% to 29% in community-dwelling elderly, 14% to 33% of elderly in long-term care, and 10% in acute hospital populations.[3] An individual's muscle mass peaks around age 20 to 30 and declines about 30% to 50% from age 40 to 80; furthermore, after age 60, a 3% annual decline in muscle functional capacity is typical.[1] However, there is a difference between typical muscular decline with aging and excessive loss of strength, function, and independence that is associated with sarcopenia. Decades of research conclude that this condition is a diagnosis common among older individuals, but it can be prevented or managed by nonpharmacologic and maybe pharmacologic means.[3] Sarcopenia does not have to be a definite process of aging.

Multiple clinical paradigms exist for identifying patients with sarcopenia or at risk for sarcopenia. A summary list of implications for screening of sarcopenia includes: patients with recurrent falls, unintentional weight loss, other chronic conditions, patients who are non-ambulatory or have difficulty rising from a chair; or anyone over the age of 65.[1] A common screening tool used in the clinic is the SARC-F.[3] The SARC-F is a questionnaire including strength, assistance, walking, rise from chair, climbing stairs, and falls. Scores range from 0-10 with lower scores indicating less risk for adverse outcomes from sarcopenia.[5] See Table 1 for the SARC-F Questionnaire and scoring sheet. Diagnosing sarcopenia is also multifactorial. An individual must exhibit the following: low muscle mass, low physical performance, and low muscle strength to be diagnosed with sarcopenia.[1] The gold standard for analyzing muscle mass is CT or MRI, but due to high cost of these tests, Dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) are more often used. CT determines muscle cross sectional area, muscle density, and fatty infiltration. MRI assesses muscle cross sectional area and volume. DXA estimates total lean tissue but does not directly measure muscle mass. BIA measures fat-free mass.[6] Body mass index is also sometimes used for diagnostic criteria. Since low muscle mass is compatible with low physical performance; gait speed and the Short Physical Performance Battery (SPPB) are also included as diagnostic tools.[1] The SPPB includes gait speed, 5 time chair stand, static balance and the Timed Up and Go test.[6] Hand grip strength is often the best diagnostic tool to measure muscle strength; however, its appropriateness has been questioned since a lower extremity strength test may be more indicative of function and mobility.[6] Table 2 includes diagnostic values of sarcopenia for the tools mentioned.

Sarcopenia is a predictor of all-cause mortality among community-dwelling older adults and nursing home residents.[2] Older adults with sarcopenia who are admitted to the hospital have an increased risk of 1 year mortality than those without sarcopenia.[7] Risk factors of sarcopenia include advanced age, genetics, low body mass index, malnutrition, comorbidities such as cerebrovascular disease or others that decrease activity, and low physical activity.[1–3] Age related factors include hormonal decline, decreased muscle mass, and decreased muscle contractility.[3,8] Testosterone in men typically declines 1% each year after the age of 30 demonstrating a steady decline in muscle mass. Women see a drastic decline in muscle mass after age 55 suggesting involvement of decreased estrogen after menaupause.[1] Growth hormone is also known to decrease with age. Growth hormone is used by the body to make myotubes and IGF-1 which is a regulator of bone and muscle growth.[1] Extreme muscle loss with age is often caused by diminishing hormonal anabolic signals in combination with increased catabolic signals via pro-inflammatory cytokines such as tumor necrosis factor alpha and interleukin-6. These cytokines are common in skeletal muscles of older adults and produce inflammation and tissue destruction as well as increase risk for morbidity and mortality.[9] Malnutrition and physical inactivity are modifiable risk factors which will be discussed in more detail later in this paper. Nutritional factors influenced by aging include decrease in appetite, decrease in sense of taste and smell, loss of teeth or use of dentures, gastrointestinal changes, and/or dependency on others to provide meals.[3] In addition to decrease in appetite, the ability to synthesize protein decreases with age.[8] "Decreased protein intake in particular has adverse consequences for muscle health" in individuals at any age.[3] This decrease in protein synthesis in older adults combined with common inadequate nutrient intake increases the risk of muscle breakdown and consequently decreased strength and impaired function.[8] Physical activity also typically declines in older adults, especially with illness or presence of comorbidities. Furthermore, inactivity is believed to be the most important risk factor for developing sarcopenia.[8] "Linear sarcopenic declines in muscle mass and strength are … punctuated by transient periods of muscle disuse that can accelerate losses of muscle and strength."[10] See Figure 1. These transient periods of disuse can include illness, injury, hospitalization, or even a reduction in daily steps. "Reports have documented that 2-3 weeks of reduced daily steps may induce: negative changes in body composition, reductions in muscle strength and quality, anabolic resistance, and decrements in glycemic control in older adults."[10] These reduced periods of activity are harder to recover from with age. “In healthy older adults, 10 days of bed rest results in loss of leg strength, power, and aerobic capacity … resulting in reduction in muscle mass and strength.”[3] A 2015 study linked sitting time with risk of sarcopenia in 60 to 86 year old community-dwelling individuals. They found that for each 1-hour increment of sitting, risk of sarcopenia increased by 33%. This finding was independent of physical activity.[11] Muscle mass is positively correlated with bone strength as bone deposition relies on loading and pull from muscles. As muscle mass declines with age, so does the quality of bone, therefore sarcopenia and osteopenia/osteoporosis are common comorbidities.[1] Other common comorbidities include frailty, sarcopenic obesity, cachexia, and type 2 diabetes. Frailty and sarcopenia have similar impacts on physical function and independence, both causing muscle weakness.[3] “Sarcopenic obesity is defined as the combination of low lean body mass and high fat mass.”[1] This causes a “double metabolic burden” affecting cardio-metabolic and physical functions.[3] Type 2 diabetes is common with sarcopenia due to its effect of insulin resistance.[12] Insulin stimulates protein synthesis including muscle synthesis; therefore, defects in insulin signaling can lead to decreased muscle mass.[13] “Cachexia is a syndrome where loss of muscle mass and strength are associated with an underlying disease state.”[1]

Sarcopenia can lead to fatigue, increased risk of falls, fractures, disability, impairment in activities of daily living, decreased quality of life, and mortality.[1,3] “Patients aged 80 or older diagnosed with sarcopenia were three times more likely to report a fall within 2 years when compared to non-sarcopenic patients.”[1] Increased femoral neck fractures and vertebral fractures occur with a comorbidity of osteoporosis leading to hospitalization, further weakness, decrease in function, and increased risk of death. Prevalence of sarcopenia in individuals who suffer a hip fracture is 17-74%.[14] Surgical complication and length of hospital stay are also affected by sarcopenia with patients showing around a five-fold increased risk of postoperative complications, longer hospital stay, higher likelihood of discharge to rehabilitation or nursing facility and therefore higher healthcare costs.[1] Mortality rates also increase with sarcopenia. Acutely ill, hospitalized patients who were malnourished or at-risk for malnourishment are more likely to die in 3 months compared to patients without sarcopenia.[15] Patients undergoing general surgery in the lowest quartile of core muscle size showed a 75% three-year survival rate.[1] Individuals undergoing liver transplant have an increased risk of morbidity and mortality both before and after transplant, increased risk of sepsis, and increased risk of post-transplant metabolic syndrome.[16]

Since the two major modifiable risk factors for sarcopenia are adequate nutrition and exercise, these are considered the two most important factors for preventing sarcopenia in older adults. There have been many studies over the years that support exercise in the aging population. “Although exercise can’t avoid the aging process, physical activity can minimize the physiological effects of a sedentary behavior and increase active life expectancy by limiting the development and progression of chronic disease and disabling conditions.”[17] In addition to improving aerobic capacity and muscular strength, exercise has shown to decrease risk of developing or progressing cardiovascular disease, type 2 diabetes, hypertension, obesity, and certain cancers as well as reduces risk of falls and fall related injuries.[17] General exercise recommendations for the elderly do not differ from younger adults and include a minimum of 150 minutes of moderate intensity exercise or 60 minutes of vigorous exercise each week.[17] Initiating exercise at any age is beneficial, one study found that individuals who began exercising at age 85 increased survival compared to individuals who were sedentary.[17] However, as discussed earlier, an individual’s muscle mass peaks around age 20 to 30 and declines with age due to the effects of hormonal decline. Additionally after age 60, a 3% annual decline in muscle functional capacity is typical.[1] Adequate exercise and nutrition throughout an individual's whole life might be best prevention method for sarcopenia. A recent article in the New York Times titled "Regular Exercise May Keep Your Body 30 Years 'Younger'" reported on a study of 70-year-old men and women who have exercised for decades. They found these individuals had higher aerobic capacities than others their age and compared to individuals 30 years younger. Also, muscular capillaries and enzymes were found to be 40% higher than their inactive peers.[18] A Canadian study investigated the effects of aerobic exercise on progressive decline of muscle strength, muscle mass, and aerobic capacity in younger adults and an older adults. They recruited individuals of all ages who were either sedentary or highly aerobically active. They discovered that grip strength and knee extension strength decreased with age but was greater in the active group compared to the control group for all ages. Further, knee extension strength was associated with greater lean mass in the active subjects. This shows that "long-term aerobic exercise may attenuate age-related reductions in muscle strength in addition to its cardiorespiratory and metabolic benefits."[19] Additionally, aerobic exercise has been shown to attenuate chronic inflammation, increase muscle fiber cross-sectional area and can reduce intramuscular fat infiltrate which improves the function of muscle relative to body weight.[17]

Resistance training is the method found to most effectively increase muscle size and strength in the general population. There are many studies and systematic reviews showing resistance training at any age, even the elderly, increases muscle mass and muscle strength. Resistance training also improves cardiorespiratory fitness, increases flexibility, decreases falls risk, increases bone mineral density and tendon strength, reduces blood pressure, and improves insulin sensitivity which are all prevalent in individuals with sarcopenia.[17] Studies have shown a significant dose-response relationship of volume and intensity of exercises. However, there is little evidence showing a superior effect of exercise performed to failure over lower intensity exercise performed at 20-30 repetition maximum. Resistance training for older adults should involve all major muscle groups and focus on functional strength and mobility training. However, "due to the disproportionate degree of muscle atrophy and strength decline of the lower limb musculature during aging" … an emphasis on lower extremity strengthening is important to improve mobility and function.[17] General guidelines for a typical older adult suggest at least 2 or more days per week using 8-10 exercises at moderate to vigorous effort for 8-12 repetitions.[17]

"Several studies have identified protein intake as a key factor for sarcopenia prevention in older people, especially during resistance training."[20] However, about 38% of adult men and 41% of adult women do not eat enough protein. The recommended daily amount of protein is 0.8g/kg/day; however, experts agree that this is too low for the aging population and recommend 1.2-2.0g/kg/day or higher for the elderly.[21] Note that this elevated intake does not affect renal function.[22] They recommend this higher amount due to older adults are less responsive to low doses of amino acid, and this can be overcome by higher levels of consumption. A recent systematic review with meta-analysis, the largest on this subject to date, compiled data from 49 studies with 1863 healthy older adults and determined that dietary protein supplementation significantly enhanced muscle strength and size when combined with resistance training. Significant improvements were found in one-repetition-maximum (see Figure 2), fat-free mass, and muscle cross-sectional area; however, changes in fat free mass was less effective with increasing age. The study also found that protein supplementation beyond intake of 1.62g/kg/day did not result in a further increase of muscle size after resistance training.[23] (see Figure 3). Other studies have shown that consuming whole proteins such as whey or casein after resistance training improves muscle protein synthesis, but type of protein and its effects on muscle growth are beyond the scope of this paper.[12] There have also been studies finding positive association between nutritional supplementation alone (without exercise) and prevention and/or treatment of sarcopenia. One study looked at the effects of supplementation of carbohydrates and essential amino acids during 28-day bedrest in 13 healthy male adults. The group that consumed 16.6g essential amino acids and 30g carbohydrate in addition to their usual meal maintained more leg mass and strength compared to the group who just consumed their usual meal. See Figures 4 and 5 respectively. While this is a low powered study, it suggests that supplementation may ameliorate loss of lean muscle mass and strength that typically occurs during bedrest.[24] Another study investigated 2,000 older adults and found an inverse relationship between loss of muscle mass and dietary protein intake over a 3 year period. The study adjusted for other dietary intake and physical activity suggesting protein intake was the catalyst for improved muscle mass.[12]

Resistance training and nutritional supplementation are also primary methods for treating older adults who are diagnosed with sarcopenia.[1] In sarcopenic muscles, metabolic changes have been associated with a key regular of protein synthesis called mammalian target of rapamycin (mTOR). Loss of type 2 muscle fibers are also present, along intramuscular fat infiltration, and increase in inflammation from pro-inflammatory cytokines discussed previously. Exercise has an effect on all of these processes. Mechanical loading activates mTOR, decreases fat infiltration, and decreases inflammation via reducing cytokines such as C-reactive protein and interleukin-6.[25] Many of the concepts discussed previously related to sarcopenia prevention can also be applied to treatment of individuals diagnosed with sarcopenia. There is no absolute consensus protocol of physical activity for individuals with sarcopenia; however, there have been many studies proving useful in attenuating sarcopenia. In addition to the general exercise guidelines, older adults with sarcopenia can benefit from gradual increase in intensity to improve strength and hypertrophy. Increased resistance by 5% up to 40% of 1RM for arm exercises and up to 60% for leg exercises are recommended.[17] Furthermore, studies have shown that resistance training 2-3 times per week for 3-6 months improved outcomes for patients.[1] A recent randomized control study of 72 seventy year old men and women with pre-sarcopenia found a that a "functional resistance training program was effective in maintaining functional strength and increasing muscle mass…"[20] Training included eight exercises which were able to increase intensity using weight or decrease load using a support band (TRX) if needed. These exercises included squats, calf raises, chair stands, lunges or half lunges, TRX rows, pushups, and bridges. Each session began with a 5-10 minute warm-up. For the first week, exercises were performed in 2 sets of 12 repetitions each without additional weight to learn the movements. For weeks 2-4, exercises were performed in 3 sets of 10 and weeks 5-10 were performed in 4 sets of 10 repetitions. Participants were encouraged to increase weight as able with each exercise using resistance bands, weighted vests, weight belts, or water bottles. The intervention group showed significant improvement in all functional outcomes including SPPB, TUG, and handgrip strength. The control group showed improvement in only the TUG, but not at a significant difference. Lean body mass in the intervention group increased significantly by 2.8% while fat mass decreased 2.4%.[20] This indicates an improvement in muscle mass, muscle strength, and physical function. A study also found that physical activity plus nutritional supplementation in older adults diagnosed with sarcopenia increased fat-free mass, strength, improved activities of daily living, and lowered C-reactive protein.[26] In this randomized, double-blind, placebo-controlled study, 130 sarcopenic older adults with average age of 80 years participated in a 12 week physical activity program including strength and balance exercises with supplementation of whey protein, essential amino acids, and vitamin D. The placebo group did not receive supplementation. This shows that appropriate exercise and nutrition is beneficial in improving strength and physical function in older adults with diagnosed sarcopenia.[26]

Currently, there are no pharmacological therapies approved by the FDA for treatment of sarcopenia. Supplementation of growth hormone and IGF-1 have shown little to no effect. Supplemental testosterone and anabolic steroids have shown increases in strength and muscle mass but are accompanied by increased risk of prostate cancer, virilization in women, and cardiovascular events. Studies are being done using various agents as treatment such as androgen receptor modulators, myostatin inhibitors, vitamin D, and angiotensin-converting enzyme inhibitors.[8] Supplementation with vitamin D has shown to improve muscle strength in patients over 65 and creatine supplementation combined with resistance training has shown to improve muscle strength.[1]

Physical Therapists can play a direct and vital role in preventing, identifying, and/or treating sarcopenia in older adults. While they do not have direct access to the gold standard diagnostic tools such as CT or MRI, physical therapists are experts in the diagnostic tools of grip strength, gait speed, and the SPPB. They could also implement the SARC-F to screen for older patients meeting the clinical paradigm discussed previously. If sarcopenia is suspected, they have the ability to properly refer to the needed health professional for further diagnostic testing. Physical therapists are most capable providers, along with nutritionists to treat sarcopenia. PTs are experts in improving functional independence and mobility and are able to use the exercise interventions discussed above to provide older patients with appropriate intervention. In the clinic, physical therapists may also discuss general nutritional guidelines with patients and refer to a nutritionist if sarcopenia is suspected. A 6-month randomized control trial found that individualized, patient-centered physical therapy was effective and cost-effective for individuals ages 70 or older with mobility problems. The study interventions included motivational interviewing, physical examination, goal setting, self-management coaching, and exercise training. Among conclusion of therapy, frailty decreased and quality of life increased.[27]

Declines in strength, muscle mass, function, and independence are expected with aging; however, these consequences are not inevitable. There is ample evidence to suggest regular physical activity including strength training and proper nutrition throughout life and especially as one ages can have a positive impact on muscle mass and strength. Studies have also found that individuals with pre-sarcopenia have the ability to improve muscle strength and size with appropriate resistance training intervention. Additionally, once sarcopenia is diagnosed in an individual, studies have shown that improvement in muscle mass, strength, and function can occur with introduction of a progressive resistance training and proper nutrition and ultimately a reversal of sarcopenia may occur. Developing a customized program and constantly encouraging increased load and proper nutrition intake is key to improve muscle strength and muscle mass in these individuals as intensity, frequency, and protein have shown to correlate with benefit.[20,25]

Appendix:

Table 1: SARC-F Questionnaire and Scoring[3]

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

Table 2: Diagnostics for Sarcopenia
(low muscle mass, physical performance, and muscle strength)

	DXA score	BIA score	6-meter gait speed	SPPB score	TUG	Hand grip strength
Men	<7.00-7.23 kg/m^2	< 7.00-8.87kg/m^2	<0.8-1.0 m/s	<8-9/12	>12 seconds indicates falls risk	<26-30kg
Women	< 5.40-5.67 kg/m^2	< 5.70-6.42kg/m^2				<16-20kg

*Adapted from International Working Group on Sarcopenia, Asian Working Group on Sarcopenia, European Working Group on Sarcopenia in Older People, and Foundation for the National Institutes of Health[1]

Figure 1: Normal and disuse-accompanied sarcopenic loss of muscle mass and function for adults after the age of 50 years.[10]

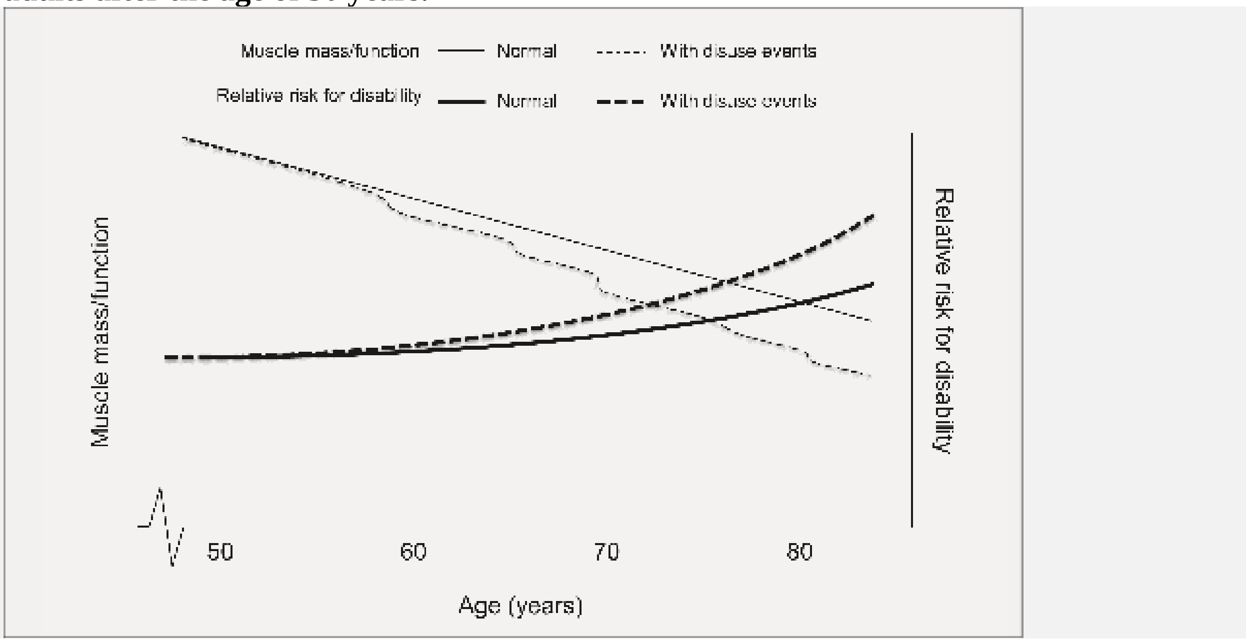


Figure 2: Forest plot of results of one-repetition maximum in untrained and trained participants who supplemented with protein.[23]

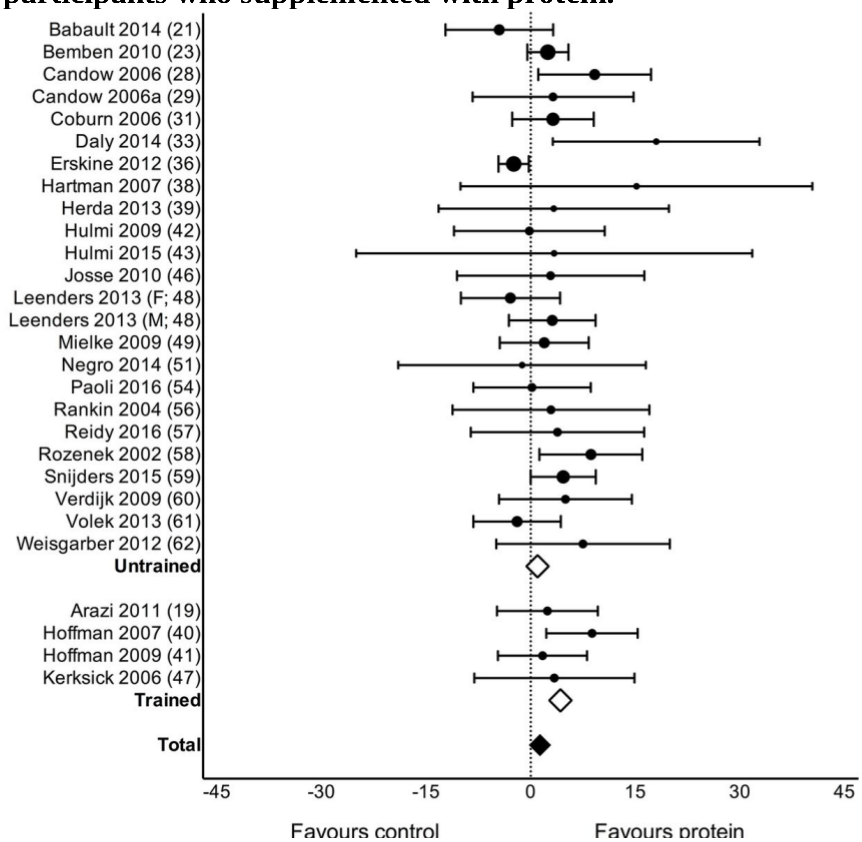


Figure 3: Linear regression between relative total protein intake and change in fat-free mass measured by DEXA[23]

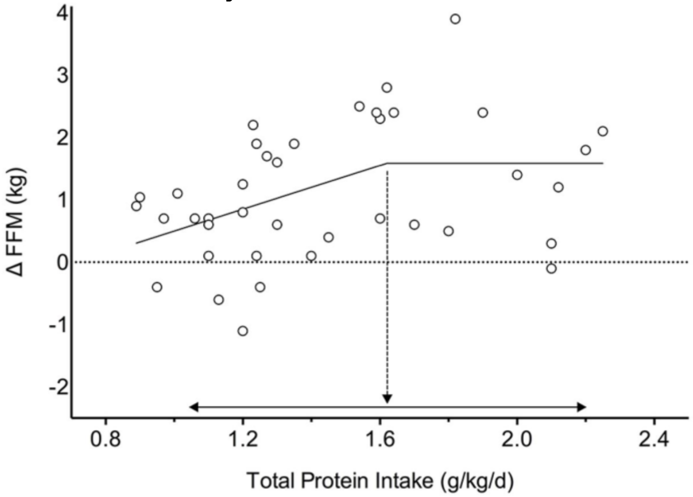


Figure 4: Change in lean leg mass after bedrest. P<0.05. Determined by DEXA[24]

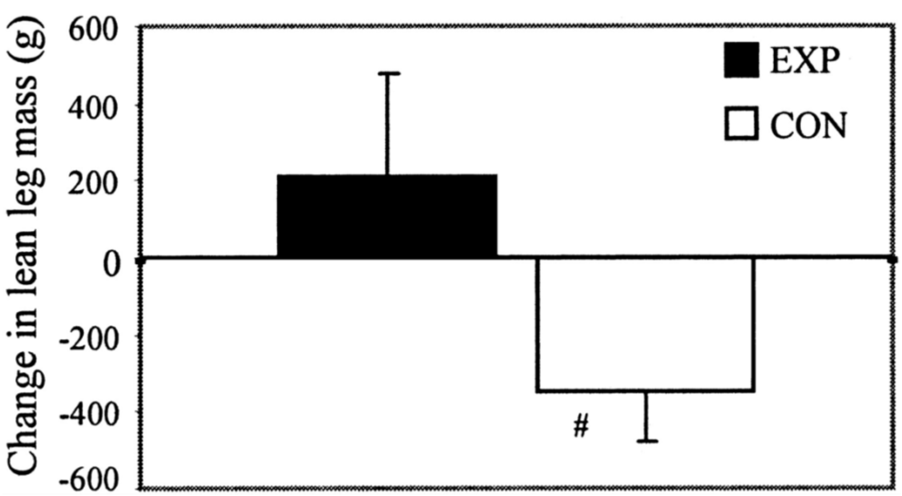
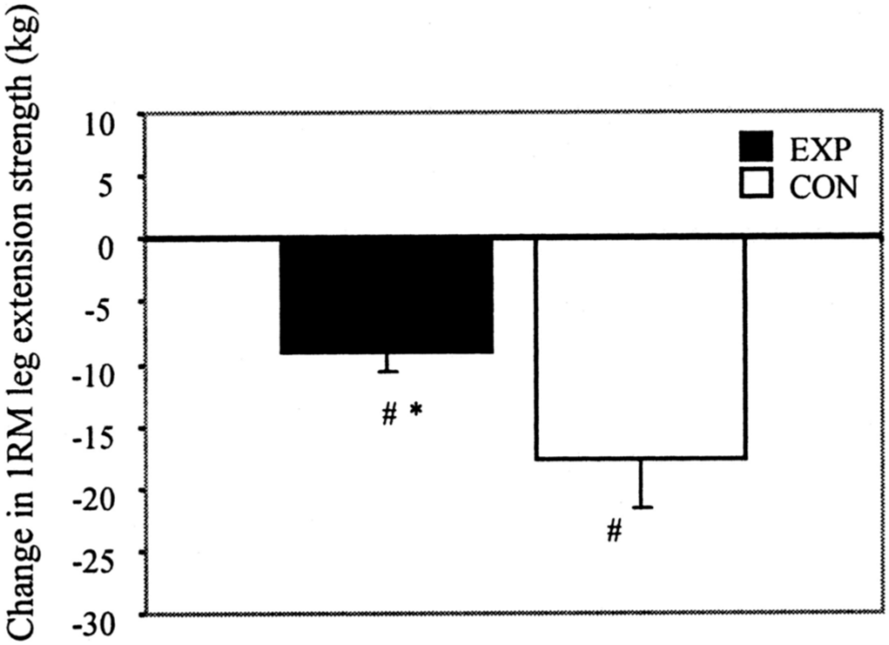


Figure 5: Change in 1RM leg extension strength after bedrest. *Significant difference between groups P<0.05[24]



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