Skeletal Muscle as a Metabolic, Endocrine, and Functional Organ

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Narrative review

This manuscript is an evidence-informed narrative review. It is not a systematic review, a clinical practice guideline, or a substitute for individualized medical, nutrition, or exercise care.

Abstract

Skeletal muscle is commonly viewed as a locomotor tissue, yet it is also the body's largest insulin-responsive organ, a major glycogen and amino-acid reservoir, a site of oxidative metabolism, and a source of contraction-responsive signaling molecules. Age-related muscle decline is therefore not a single problem of size. Muscle quantity, tissue quality, force production, movement velocity, and real-world physical performance represent related but distinct dimensions of muscle health. This distinction is clinically important because strength and power generally decline faster than muscle mass, and prospective studies more consistently associate low strength, lower-extremity function, and reduced muscle power with disability, hospitalization, and all-cause mortality than low muscle mass alone. At the same time, muscle mass remains metabolically important because it provides potential capacity for insulin-stimulated glucose disposal, glycogen storage, amino-acid reserve, and mitochondrial content. The effective metabolic role of muscle, however, depends not only on how much tissue is present but also on insulin sensitivity, perfusion, contractile activation, fat infiltration, neuromuscular integrity, and mitochondrial function. This narrative review integrates evidence on sarcopenia, dynapenia, muscle quality, glucose regulation, mitochondrial aging, myokine signaling, anabolic resistance, and exercise and protein interventions. Contemporary diagnostic frameworks prioritize low strength as the first clinical signal of sarcopenia and use low muscle quantity or quality to confirm the diagnosis. The evidence supports an integrated strategy: preserve muscle quantity, improve tissue quality, maintain maximal strength, train power and functional capacity when appropriate, and combine resistance exercise with aerobic activity and adequate protein. Muscle mass is metabolic infrastructure; strength and power reveal whether that infrastructure can generate useful force quickly enough to protect mobility, independence, and physiological reserve.

Keywords: skeletal muscle; sarcopenia; dynapenia; muscle quality; muscle power; insulin resistance; mitochondria; myokines; anabolic resistance; healthy aging

Key conclusions

- Muscle quantity and muscle function should not be treated as interchangeable. Strength and power are only partly explained by muscle size.

- Low strength and poor physical performance are stronger and more consistent predictors of disability and mortality than low mass alone, although observational associations do not prove causation.
- Muscle mass still matters because it provides metabolic and physiological reserve, but glucose disposal depends on active, insulin-sensitive muscle rather than tissue quantity alone.
- Muscle quality is multidimensional and includes force per unit tissue, fat infiltration, architecture, neuromuscular activation, excitation-contraction coupling, perfusion, and mitochondrial function.
- Aging increases vulnerability, but inactivity and disuse are powerful, modifiable accelerators of anabolic resistance, mitochondrial decline, weakness, and loss of function.
- Resistance exercise is the central intervention for strength and lean tissue; high-velocity training can target power; aerobic exercise supports mitochondrial and cardiometabolic function; adequate protein supports adaptation and recovery.

1. Scope and Evidence Approach

This paper is a narrative synthesis of peer-reviewed literature on skeletal-muscle metabolism, aging, physical function, exercise, and protein nutrition. Evidence was drawn from key consensus statements, systematic reviews, meta-analyses, prospective cohort studies, randomized trials, and mechanistic human studies. Human evidence was prioritized; animal and cell studies are used only where they clarify mechanisms that cannot be measured directly in humans. Because the search and selection process was not prospectively registered and does not meet formal systematic-review standards, this paper does not claim exhaustive coverage.

The paper also separates four levels of inference: (1) biological plausibility, (2) acute physiological response, (3) long-term change in muscle or function, and (4) association with disability or mortality. These levels should not be collapsed. For example, an acute rise in muscle protein synthesis does not by itself prove long-term hypertrophy, and an observational association between strength and survival does not prove that increasing strength directly reduces mortality.

2. Skeletal Muscle Is More Than a Locomotor Tissue

Skeletal muscle is a large, adaptable organ that integrates mechanical loading, neural activation, nutrient availability, endocrine signals, and cellular energy metabolism. Under insulin-stimulated postprandial conditions, skeletal muscle accounts for the majority of glucose uptake from the circulation, commonly estimated at approximately 70-80% in metabolically healthy people (Merz &

Thurmond, 2020; Sjøberg et al., 2021). Muscle also stores glycogen, contains a large share of the body's amino acids, houses an extensive mitochondrial network, and releases contraction-responsive signals that communicate with adipose tissue, liver, bone, immune cells, and other organs (Schnyder & Handschin, 2015; Hoffmann & Weigert, 2017).

These functions make muscle loss clinically relevant even before a person appears frail. Nevertheless, the phrase “more muscle means better glucose control” is incomplete. Muscle glucose uptake depends on the amount of available tissue, but also on insulin signaling, GLUT4 translocation, capillary perfusion, glycogen status, recent contraction, mitochondrial flexibility, and lipid infiltration. Resistance and aerobic exercise can improve glucose handling before a large increase in muscle mass occurs, demonstrating that tissue quality and activation matter alongside quantity (Merz & Thurmond, 2020; Park et al., 2006).

3. Five Dimensions of Muscle Health

Research and clinical practice often use “muscle health” as if it were a single variable. It is more accurately understood as a set of related constructs.

Construct	What it represents	Common assessments	Why it matters	Important limitation
Muscle quantity	Amount of lean or contractile tissue	DXA appendicular lean mass; CT/MRI cross-sectional area or volume; BIA estimates	Metabolic reserve, glycogen and amino-acid storage, potential force-producing and mitochondrial capacity	DXA lean mass is not identical to contractile muscle and does not measure function
Muscle quality	Function or tissue integrity relative to quantity	Strength per unit mass/area; CT attenuation; ultrasound echo intensity; phase angle; intramuscular fat	Explains why people with similar mass can differ greatly in force, insulin sensitivity, and mobility	No single accepted definition or gold-standard measure
Strength	Maximum force or	Grip strength;	Independence, task	Affected by pain,

Construct	What it represents	Common assessments	Why it matters	Important limitation
	torque	knee-extension torque; one-repetition maximum; chair-rise ability	capacity, fall recovery, mortality and disability risk marker	motivation, joint disease, neural activation, and technique
Power	Rate of performing work: force multiplied by velocity	Sit-to-stand power; stair-climb power; leg-press power; jump or dynamometer tests	Rapid balance correction, stair climbing, rising from a chair, crossing a street	Testing methods vary and some require specialized equipment
Physical performance	Integrated ability to complete real-world tasks	Gait speed; Short Physical Performance Battery; Timed Up and Go; chair stands	Closest to mobility, disability, and independent living	Reflects multiple systems beyond muscle, including balance, cognition, pain, and cardiopulmonary capacity

Muscle quality is especially important because it explains the gap between muscle size and performance. The term has been used for strength per unit lean mass, radiologic density, fat infiltration, tissue architecture, cellular composition, or combinations of these measures. A recent scoping review found substantial variation in definitions and methods, reinforcing that “quality” should always be operationally defined in research reports (de Lucena Alves et al., 2023).

4. Sarcopenia Versus Dynapenia: Why Function Matters as Much as Mass

The original use of sarcopenia referred primarily to age-related loss of muscle mass. Dynapenia was later proposed to describe age-related loss of strength and power that cannot be explained by atrophy alone (Manini & Clark, 2012). The distinction arose because longitudinal studies repeatedly showed that strength declines more rapidly than muscle size and that preserving or even gaining lean mass does not necessarily prevent loss of force. In the Health, Aging and Body Composition cohort, changes in muscle area explained only a minority of the variation in strength loss, while strength

declined several times faster than mass in many participants (Goodpaster et al., 2006; Manini & Clark, 2012).

Modern clinical definitions have partly absorbed this insight. The revised European Working Group on Sarcopenia in Older People framework (EWGSOP2) identifies low muscle strength as the primary characteristic that makes sarcopenia probable. Low muscle quantity or quality confirms the diagnosis, and poor physical performance indicates severe sarcopenia (Cruz-Jentoft et al., 2019). Thus, contemporary sarcopenia is not synonymous with low mass. It is a muscle-failure syndrome in which strength is the first clinical signal, quantity or quality confirms the structural deficit, and performance establishes severity.

Dynapenia remains a useful concept because it directs attention to neural drive, motor-unit loss, excitation-contraction coupling, tendon properties, fiber composition, myosteatosis, and movement velocity. These factors can reduce force and power even when DXA-measured lean mass appears relatively preserved. However, dynapenia and sarcopenia should not be treated as mutually exclusive diagnoses. They are overlapping ways of describing different components of age-related muscle failure.

The central distinction

Muscle mass describes how much tissue is present. Strength describes how much force the neuromuscular system can produce. Power describes how quickly that force can be expressed. Physical performance shows whether the entire system can complete meaningful tasks.

5. Strength and Power Predict Mortality and Disability; Mass, Less Consistently

5.1 Strength as a prognostic marker

The clinical importance of strength extends well beyond gym performance. Strength reflects the integrated status of skeletal muscle, motor neurons, central drive, joints, pain, cardiovascular reserve, inflammation, nutrition, and chronic disease. It therefore functions as a broad marker of physiological reserve.

Prospective cohort evidence consistently associates lower grip strength and knee-extensor strength with higher all-cause mortality. In the Health ABC cohort, strength was associated with mortality after adjustment for muscle size, whereas muscle size itself was not strongly associated with mortality in the same models (Newman et al., 2006). A systematic review and meta-analysis involving approximately two million adults likewise found that higher upper- and lower-body strength was associated with lower all-cause mortality risk (García-Hermoso et al., 2018). More recent evidence in 5,472 ambulatory women aged 63-99 years showed graded inverse associations between grip strength and mortality after adjustment for objectively measured physical activity, sedentary time, walk speed, clinical factors, and inflammation (LaMonte et al., 2026).

5.2 Lower-extremity strength and power

Lower-extremity function is particularly important because standing, stair climbing, gait acceleration, balance recovery, and fall avoidance depend on the ability to produce force rapidly. Muscle power - the product of force and contraction velocity - generally declines earlier and more steeply with age than maximal strength and often relates more closely to mobility tasks (Reid & Fielding, 2012; Byrne et al., 2016). In a prospective study of 1,928 older adults, very low relative sit-to-stand power was independently associated with hospitalization, and with all-cause mortality in men after multivariable adjustment; the mortality estimate in women was attenuated after adjustment (Losa-Reyna et al., 2022). These findings support lower-extremity power as a clinically informative marker while also showing why sex-specific estimates and residual confounding must be considered.

5.3 Muscle mass predicts risk less consistently, but is not irrelevant

Meta-analytic evidence indicates that strength and physical performance predict future activities-of-daily-living limitations more consistently than muscle mass (Wang et al., 2020). Dose-response analyses in community-dwelling older adults likewise show that strength and gait speed carry important prognostic information for disability and mortality (Seino et al., 2022). This does not make mass irrelevant. Low appendicular muscle mass is associated with mortality in pooled analyses,

and some cohorts report better survival with higher relative muscle mass (de Santana et al., 2021; Li et al., 2018; Srikanthan & Karlamangla, 2014). The balanced interpretation is that muscle mass provides structural and metabolic reserve, whereas strength, power, and performance more directly reveal whether that reserve is functional.

5.4 Prognostic association is not proof of causation

These mortality findings are observational. Low strength may partly reflect occult disease, undernutrition, inflammation, neurological decline, or frailty that also raises mortality risk. Therefore, strength should be described as a strong prognostic marker and modifiable physical capacity, not as a proven independent cause of longevity. Randomized exercise trials demonstrate improvements in strength and function, but most are not designed or powered to establish reductions in all-cause mortality.

6. Why Muscle Mass Still Matters: Glucose Disposal, Reserve, and Mitochondria

The stronger prognostic value of function should not lead to the opposite error of dismissing muscle mass. Muscle quantity remains metabolically and clinically important for at least four reasons.

6.1 Potential capacity for glucose disposal and glycogen storage

Skeletal muscle is the principal site of insulin-stimulated glucose uptake after a meal. A larger pool of metabolically active muscle provides more potential surface area for glucose transport and more total glycogen-storage capacity. Cohort studies associate lower muscle indices and muscle loss with insulin resistance, metabolically unhealthy phenotypes, and future type 2 diabetes, although body fat, activity, and reverse causality complicate interpretation (de Carvalho et al., 2021; Xue et al., 2023; Liu & Zhu, 2023).

The key word is potential. A larger muscle compartment that is inactive, infiltrated with fat, poorly perfused, or insulin resistant may dispose of glucose less effectively than a smaller but active and insulin-sensitive muscle compartment. Aging, inactivity, myosteatosis, mitochondrial alterations, and impaired insulin-signaling pathways can all reduce glucose uptake per unit of tissue (Merz &

Thurmond, 2020; Shou et al., 2020; Hong & Choi, 2020). Contraction itself stimulates glucose uptake through pathways partly independent of insulin, which explains why exercise can improve glycemic control before measurable hypertrophy occurs (Merz & Thurmond, 2020; Sjøberg et al., 2021). A more accurate conceptual model is that whole-body muscle glucose disposal reflects the interaction of muscle quantity, tissue quality, perfusion, insulin sensitivity, glycogen status, and recent contractile activity.

6.2 Amino-acid reserve during illness and disuse

The body has no inert storage depot for protein comparable with adipose triglyceride or glycogen. Skeletal muscle therefore functions as a large, mobilizable amino-acid reserve during fasting, trauma, infection, surgery, immobilization, and inadequate intake. This reserve supports hepatic protein synthesis, immune activity, wound healing, and gluconeogenesis, but prolonged mobilization produces negative net muscle-protein balance and loss of function. Greater pre-illness muscle reserve may provide a buffer during catabolic events, although reserve does not prevent rapid disuse atrophy (McKendry et al., 2024).

6.3 Mitochondrial “real estate”

Muscle fibers contain mitochondria that oxidize carbohydrate and fat and generate ATP. More muscle tissue can provide more total mitochondrial volume - a useful concept that may be described as metabolic “real estate.” The metaphor has limits: mitochondrial density, respiratory capacity, substrate flexibility, and quality control vary substantially between individuals, and additional muscle mass does not automatically guarantee superior oxidative function.

Earlier literature often attributed lower mitochondrial content and respiratory capacity directly to chronological aging (Johnson et al., 2013). More recent studies show that habitual physical activity and cardiometabolic health are major confounders. In active adults, mitochondrial respiration can be preserved across much of the lifespan, whereas inactive adults generally show poorer energetics (Distefano et al., 2017; Grevendonk et al., 2021). In 139 men aged 20-93 years, physical activity was

associated with better physical performance and mitochondrial energetics, while age itself was not associated with lower mitochondrial respiratory capacity or greater reactive oxygen species production. Mitochondrial calcium-retention capacity nevertheless declined with age regardless of activity and was related to muscle mass and performance, indicating that activity does not fully prevent every age-related mitochondrial change (Cefis et al., 2025).

6.4 Reserve against disuse and acute stress

Older adults lose muscle rapidly during step reduction, limb immobilization, bed rest, and hospitalization and often recover more slowly than younger adults. A larger initial reserve may delay the point at which muscle loss produces disability, even though it does not eliminate the underlying anabolic resistance of disuse. This is one reason muscle quantity remains relevant even when strength is the stronger predictor of immediate function (McKendry et al., 2024).

7. Muscle Quality: The Link Between Mass, Metabolism, and Function

Muscle quality describes the capacity and integrity of muscle relative to its quantity. In functional studies, it is often calculated as force or torque per unit of muscle mass or cross-sectional area. In imaging studies, it may refer to CT attenuation, ultrasound echo intensity, fascicle architecture, or intramuscular adipose infiltration. At the cellular level, it can include fiber-type composition, myofibrillar density, capillary supply, mitochondrial function, motor-unit recruitment, and excitation-contraction coupling (de Lucena Alves et al., 2023).

Aging can reduce muscle quality through multiple pathways. Motor-neuron loss and incomplete reinnervation reduce the number and precision of motor units. Type II fibers, which support rapid force and power, are preferentially lost or atrophied. Myosin concentration and specific tension can decline, while tendon and connective-tissue changes alter force transmission. Myosteatosis and lipid intermediates can impair insulin signaling, and neuromuscular activation and calcium handling may become less efficient (Manini & Clark, 2012; Mitchell et al., 2012; Hong & Choi, 2020; Cefis et al., 2025).

Type 2 diabetes illustrates why quality matters. Older adults with diabetes can have lower muscle strength and lower strength per unit regional lean mass than peers without diabetes, even after accounting for muscle quantity (Park et al., 2006). This may reflect neuropathy, microvascular impairment, myosteatosis, inflammation, mitochondrial alterations, and impaired insulin signaling. Resistance exercise can improve strength, insulin sensitivity, and muscle quality without requiring large changes in total mass (Brooks et al., 2007).

The clinical implication is that a body-composition scan should not be interpreted in isolation. Two people with the same appendicular lean mass can differ markedly in force, power, gait, insulin sensitivity, and resilience. Assessment should pair quantity with at least one functional measure, such as grip strength, chair-rise performance, gait speed, or knee-extensor testing.

8. Skeletal Muscle as an Endocrine and Signaling Organ

Contracting skeletal muscle releases peptides and metabolites that act locally and systemically. These signals are often grouped under the terms myokines and exerkines. Well-studied examples include contraction-associated interleukin-6, interleukin-15, myostatin-related pathways, apelin, and other signals involved in substrate mobilization, tissue remodeling, and immune-metabolic communication (Schnyder & Handschin, 2015; Hoffmann & Weigert, 2017).

This field requires careful language. The same molecule can have different effects depending on its source, concentration, duration, and physiological context. The transient IL-6 response to exercise differs from chronically elevated inflammatory IL-6. Irisin, BDNF, and several proposed muscle-brain signals remain active areas of research, but their measurement, tissue source, dose-response relationships, and clinical importance are not fully resolved. Lactate is better described as a metabolite and exerkine than as a myokine. Therefore, skeletal muscle can confidently be described as a signaling organ, but specific claims that an individual myokine prevents dementia, treats inflammation, or independently explains exercise benefits generally exceed current human evidence.

Loss of muscle or loss of contractile activity may reduce this signaling capacity, but it is difficult to separate the effect of less tissue from the effect of less exercise. Contraction is the major stimulus. Preserving muscle without using it is not biologically equivalent to maintaining an active muscle organ.

9. Aging, Disuse, and Anabolic Resistance

Muscle mass is determined by the long-term balance between muscle protein synthesis (MPS) and muscle protein breakdown. In many healthy older adults, fasting MPS is not dramatically lower than in younger adults; the more consistent difference is a reduced response to protein feeding and sometimes exercise. This blunted responsiveness is termed anabolic resistance (Breen & Phillips, 2011; Wall et al., 2015).

Anabolic resistance is heterogeneous and context dependent rather than an inevitable fixed state. Physical inactivity, step reduction, bed rest, inflammation, insulin resistance, reduced perfusion, low energy intake, inadequate protein, and chronic disease can all contribute. In older adults, only two weeks of step reduction has been shown to lower leg lean mass and blunt the postprandial MPS response (Breen et al., 2013). Disuse during illness or hospitalization can accelerate muscle loss and compound pre-existing age-related vulnerability (McKendry et al., 2024).

Resistance exercise is a potent countermeasure because it increases MPS and sensitizes muscle to dietary amino acids. Exercising before protein intake increases the use of dietary protein-derived amino acids for new muscle protein in both younger and older men (Pennings et al., 2011). The interaction is important: protein supplies substrate, while mechanical loading directs adaptation and maintains neuromuscular function.

10. Protein Requirements Across the Adult Lifespan

The adult protein Recommended Dietary Allowance of 0.8 g/kg/day is a population-level estimate intended to meet the needs of nearly all healthy adults, not a disease-treatment target or a

guarantee of optimal muscle preservation in every older or physically active person. Expert groups commonly recommend approximately 1.0-1.2 g/kg/day for healthy older adults and 1.2-1.5 g/kg/day during acute or chronic illness, with higher intakes considered in selected severe illness or rehabilitation contexts under clinical supervision (Bauer et al., 2013; Deutz et al., 2014). Active adults performing resistance exercise may benefit from intakes toward the upper end of evidence-based ranges, but kidney disease, medically prescribed restrictions, total energy intake, and individual tolerance must be considered.

Per-meal dose also matters because MPS responds to discrete feeding events. Controlled studies estimate that older adults require a larger relative protein dose than younger adults to maximize acute myofibrillar MPS under the specific conditions tested - approximately 0.4 g/kg per meal in older men versus approximately 0.24 g/kg in younger men (Moore et al., 2015). These values are estimates, not universal thresholds. Body size, protein quality, exercise, health status, meal composition, and habitual intake modify the response.

Leucine contributes to mTORC1 signaling, but the “leucine threshold” should be treated as a heuristic rather than a binary switch. Leucine can help initiate anabolic signaling, while the full complement of essential amino acids supplies the substrate required to synthesize new protein. Systematic reviews show that the relationship between postprandial leucinemia and MPS is real but variable and does not explain all responses across age groups and conditions (Zaromskyte et al., 2021).

Protein distribution across meals may create repeated opportunities to stimulate MPS, particularly when breakfast and lunch are chronically low in protein. Long-term evidence that a perfectly even distribution is superior to every other pattern remains less definitive than the evidence for adequate total intake, sufficient meal-level doses, and resistance exercise. The practical priority is

therefore to avoid chronically low total intake and repeated meals that contribute too little high-quality protein to daily needs (Morgan et al., 2025).

11. Exercise Countermeasures: Quantity, Quality, Strength, Power, and Mitochondria

11.1 Progressive resistance training

Progressive resistance training is the most direct intervention for increasing or preserving strength and lean tissue. It improves neuromuscular recruitment, force production, muscle quality, insulin sensitivity, and functional capacity, including in very old and clinically vulnerable adults. Meta-analysis shows that protein supplementation can modestly augment resistance-training gains when baseline protein intake or training stimulus leaves room for improvement, but training remains the primary stimulus (Morton et al., 2018).

Expert consensus recommends that older adults perform individualized, progressive muscle-strengthening exercise at least twice weekly, alongside aerobic and balance training. Load, volume, range of motion, and exercise selection should be adapted to health status, pain, fall risk, training history, and supervision needs (Izquierdo et al., 2021).

11.2 Power and movement velocity

Because power declines faster than strength and is closely linked to mobility, training should eventually include the intent to move appropriate loads quickly, provided the person has adequate foundational strength and can do so safely. High-speed power training can improve the velocity component of power and may be especially relevant for rapid balance correction and daily tasks (Sayers & Gibson, 2014).

Current evidence does not show that high-velocity training is universally superior to traditional resistance training. A 2023 systematic review of 19 randomized trials found generally similar functional outcomes, with small advantages for the Short Physical Performance Battery and Timed Up

and Go that were based on low-quality evidence and of uncertain clinical importance (Morrison et al., 2023). The practical conclusion is to train strength first and add appropriately supervised power work when function and safety allow, rather than replacing all traditional resistance exercise.

11.3 Aerobic exercise and mitochondrial quality

Aerobic exercise is the dominant stimulus for mitochondrial biogenesis, capillary adaptation, and cardiorespiratory fitness. Moderate-intensity continuous exercise and interval training can increase mitochondrial density and oxidative enzyme activity. This complements resistance training: resistance exercise preserves or increases the amount and force-generating capacity of tissue, while aerobic exercise improves the oxidative quality and vascular support of that tissue. The strongest healthy-aging strategy is therefore not “cardio versus weights,” but a combined program with balance and functional practice (Izquierdo et al., 2021; Cefis et al., 2025).

11.4 Disuse prevention and rapid response

Periods of illness, hospitalization, immobilization, or major step reduction should be treated as high-risk events for muscle loss. Where medically appropriate, early mobilization, resistance exercise before and after planned procedures, adequate energy and protein, and rehabilitation can reduce the depth and duration of disuse-related decline. Resistance bands, body-weight exercise, and lower-load training can provide scalable options when conventional equipment is unavailable (McKendry et al., 2024).

12. An Integrated Model: Mass Is Infrastructure; Function Is Output

The evidence supports an integrated rather than competitive view of muscle mass and muscle function. Muscle quantity provides the physical substrate: fibers, glycogen capacity, amino-acid reserve, contractile proteins, and mitochondrial space. Muscle quality determines how effectively each unit of tissue responds to insulin, oxidizes fuel, receives neural input, and generates force. Strength

and power express the output of the neuromuscular system. Physical performance translates that output into walking, standing, stair climbing, fall avoidance, and independent living.

Conceptual heuristic - not a validated equation

Whole-body functional-metabolic capacity can be thought of as the interaction of muscle quantity × tissue quality × neural activation × habitual use. A deficit in any one component can constrain the entire system.

This framework explains several observations that otherwise appear contradictory. A person can have normal lean mass but severe weakness because neural and tissue quality are poor. Another can have low mass yet retain good function because quality and activity are high. Resistance training can improve glucose control before hypertrophy because activation and insulin sensitivity improve. Aerobic training can preserve mitochondrial function without adding much mass. The best outcome is not maximum mass at any cost, but sufficient quantity combined with high quality, strength, power, and regular use.

13. Practical and Clinical Implications

A research-informed assessment should avoid relying on body weight, BMI, or lean mass alone. Depending on the setting, a practical muscle-health screen may include grip strength, a five-times chair stand, gait speed, and questions about falls, stairs, rising from the floor, and recent activity reduction. DXA, BIA, CT, MRI, or ultrasound can add information about quantity or tissue composition when clinically indicated, but each method has limitations and should be interpreted with function.

For prevention and healthy aging, the priorities are:

- Progressive resistance training at least twice weekly, scaled to the individual and covering major muscle groups.

- Aerobic activity sufficient to support cardiorespiratory fitness, insulin sensitivity, perfusion, and mitochondrial adaptation.
- Balance, gait, and task-specific practice, especially for people with fall risk or functional limitation.
- Power-focused movements only after an appropriate strength and safety foundation, with supervision when needed.
- Adequate total energy and protein, with attention to meals that are chronically low in protein.
- Rapid action during and after illness, immobilization, or hospitalization to minimize disuse-related loss.

These are educational principles rather than individualized prescriptions. People with cardiovascular disease, diabetes, kidney disease, neurological disorders, severe osteoporosis, recent surgery, significant pain, or medically prescribed dietary restrictions should obtain individualized medical, exercise, and nutrition guidance.

14. Limitations and Research Gaps

Several limitations shape interpretation of this literature. First, sarcopenia and muscle quality are measured with heterogeneous definitions, devices, normalization methods, and cut points, which complicates comparison across studies. Second, DXA lean mass includes non-contractile tissue and cannot directly measure fiber quality or intramuscular fat. Third, strength and mortality studies are observational and remain vulnerable to reverse causality and residual confounding. Fourth, acute MPS studies are useful mechanistically but do not guarantee long-term changes in muscle, strength, or disability. Fifth, many exercise and protein trials are short, include relatively healthy volunteers, and are not powered for hospitalization or mortality. Sixth, studies of mitochondrial aging often differ in participant activity, sex, muscle sampled, and laboratory technique. The 2025 lifespan study of mitochondrial energetics, for example, included men only and was cross-sectional (Cefis et al., 2025).

Important research priorities include standardized measures of muscle quality and power, trials that combine strength, power, aerobic, and nutrition interventions, better inclusion of women and adults over 80 years, longitudinal measurement rather than single baseline testing, and studies that connect changes in muscle physiology to patient-important outcomes such as falls, hospitalization, cognition, independence, and survival.

15. Conclusion: Protect the Metabolic Engine and the Functional Output

Skeletal muscle is simultaneously a metabolic organ, an endocrine-signaling tissue, an amino-acid and glycogen reserve, a mitochondrial compartment, and the machinery of movement. Age-related muscle failure is therefore not captured by a single scan or a single strength test.

Strength and power deserve special emphasis because they decline faster than mass and more consistently predict disability, hospitalization, and all-cause mortality. Lower-extremity strength and power are especially relevant to standing, gait, stair climbing, balance recovery, and independent living. Yet the evidence does not support abandoning muscle mass. Muscle quantity provides metabolic infrastructure and reserve; low mass is associated with adverse outcomes in several cohorts and pooled analyses, even if the association is less consistent than for strength.

The most defensible conclusion is that muscle mass and muscle function answer different questions. Mass asks how much tissue and reserve are available. Quality asks how well that tissue is built and metabolically regulated. Strength asks how much force the neuromuscular system can produce. Power asks how quickly force can be expressed. Performance asks whether the whole organism can translate these capacities into daily life.

Healthy aging requires attention to all of them. Progressive resistance training preserves the structure and force-producing capacity of muscle; appropriately introduced power training preserves speed; aerobic exercise supports mitochondrial and vascular function; and sufficient protein provides the

substrate for adaptation and recovery. The goal is not simply to carry more muscle, but to maintain muscle that is metabolically active, neurologically connected, strong, fast, and repeatedly used.

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Interpretive note

Mortality, hospitalization, and disability findings discussed in this review are primarily observational. They support the prognostic importance of muscle strength, power, quantity, and performance, but do not establish that changing any single measure in isolation will necessarily change survival. Intervention evidence is strongest for improving strength, power, mobility, insulin sensitivity, and physical function.

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