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Clinical anabolism: a conceptual framework for preserving morphology and function in chronic disease, aging, and catabolic states

Anabolismo clínico: uma estrutura conceitual para a preservação da morfologia e da função em doenças crônicas, envelhecimento e estados catabólicos

Lucas Caseri Câmara[1]

Abstract

Chronic diseases and aging often converge toward a shared biological phenotype characterized by loss of skeletal muscle mass, bone mass, strength, endurance, physical performance, and functional reserve. These changes are not merely secondary consequences of illness; in many patients, they become active determinants of frailty, disability, falls, fractures, reduced treatment tolerance, hospitalization, and mortality. We propose the term **clinical anabolism** as a conceptual framework to describe a medical, therapeutic, monitored, and functionally oriented approach aimed at preserving or restoring structurally and metabolically relevant tissues, particularly skeletal muscle and bone. This concept requires a clear distinction between testosterone replacement in documented androgen deficiency, therapeutic anabolic strategies in selected catabolic or rehabilitation-related conditions, and nonmedical anabolic-androgenic steroid use. Clinical anabolism should not be understood as cosmetic enhancement or indiscriminate pharmacological intervention, but as a multimodal strategy integrating resistance training, rehabilitation, nutrition, treatment of the underlying disease, and, in selected cases, pharmacological anabolic

[1] Director of the Brazilian College of Exercise and Sports Medicine
E-mail: lucascc_med@hotmail.com
https://orcid.org/0000-0001-6329-2897

agents. Future studies should prioritize patient-centered outcomes such as strength, gait speed, falls, independence, hospitalization, treatment tolerance, and quality of life, rather than lean mass alone.
Keywords: Sarcopenia; muscle strength; anabolic agents; anabolic steroids

Resumo

As doenças crônicas e o envelhecimento frequentemente convergem para um fenótipo biológico comum, caracterizado pela perda de massa muscular esquelética, massa óssea, força, resistência, desempenho físico e reserva funcional. Essas alterações não são meramente consequências secundárias da doença; em muitos pacientes, tornam-se determinantes ativos de fragilidade, incapacidade, quedas, fraturas, redução da tolerância ao tratamento, hospitalização e mortalidade. Propomos o termo anabolismo clínico como uma estrutura conceitual para descrever uma abordagem médica, terapêutica, monitorada e funcionalmente orientada, destinada a preservar ou restaurar tecidos estrutural e metabolicamente relevantes, particularmente o músculo esquelético e o osso. Esse conceito exige uma distinção clara entre reposição de testosterona em deficiência androgênica documentada, estratégias anabólicas terapêuticas em condições catabólicas ou relacionadas à reabilitação selecionadas, e o uso não médico de esteroides anabolizantes androgênicos. O anabolismo clínico não deve ser compreendido como aprimoramento estético ou intervenção farmacológica indiscriminada, mas como uma estratégia multimodal que integra treinamento resistido, reabilitação, nutrição, tratamento da doença de base e, em casos selecionados, agentes anabólicos farmacológicos. Estudos futuros devem priorizar desfechos centrados no paciente, como força, velocidade da marcha, quedas, independência, hospitalização, tolerância ao tratamento e qualidade de vida, em vez de apenas massa magra.

Palavras-chave: Sarcopenia; força muscular; agentes anabólicos; esteroides anabolizantes.

Chronic diseases and aging often converge toward a common biological outcome: progressive morphological and functional loss [1-3]. Reduced skeletal muscle mass, bone mass, strength, endurance, physical performance, and body composition

quality are clinically relevant because they are associated with frailty, disability, falls, fractures, reduced tolerance to treatment, hospitalizations, and mortality [1-3]. These changes should not be interpreted merely as secondary consequences of disease and, in many patients, they become active components of the disease trajectory itself [1,3].

In this context, we propose the term **clinical anabolism** to describe a medical, therapeutic, monitored, and functionally oriented approach aimed at preserving or restoring structurally and metabolically relevant tissues, particularly skeletal muscle and bone [1,4,5]. This approach is intended for patients with, or at risk for, loss of lean mass, bone mass, strength, physical performance, or functional reserve [1,3,4]. Its central goal is not cosmetic improvement or nonspecific performance enhancement, but preservation of autonomy, resilience, and clinically meaningful function [1,3].

The starting point of clinical anabolism should be the clinical phenotype, not the pharmacological agent. Patients with different diagnoses may share similar patterns of structural and functional decline [1,4]. An older adult with frailty, a patient with chronic kidney disease, a patient with chronic obstructive pulmonary disease, a postmenopausal woman with osteoporosis, a patient with cancer, a person living with HIV/AIDS, a severe burn patient, a patient receiving long-term glucocorticoids, or an individual undergoing a major surgery or rapid weight loss may all develop loss of muscle, bone, strength, endurance, and exercise tolerance through distinct pathophysiological pathways [1,4,5]. Recognizing this shared phenotype is essential if morphological and functional decline are to be treated as legitimate therapeutic targets [1,3,4].

Importantly, this proposal requires a strict conceptual distinction among three clinical scenarios involving anabolic agents [4,10,11]. The first is hormonal replacement in patients with documented androgen deficiency, for which current guidelines emphasize compatible symptoms, biochemical confirmation, assessment of contraindications, and monitoring [10,11]. The second is therapeutic anabolism in selected catabolic, sarcopenic, frail, or rehabilitation-related conditions, in which the therapeutic target is not only a hormone concentration, but also loss of tissue, strength, and function [1,4,11]. The third is nonmedical, aesthetic, recreational, or sports-related anabolic-androgenic steroid use, which is often associated with supratherapeutic doses, multiple substances, uncertain drug sources, and limited

medical supervision [4,10,11]. These categories share some pharmacological agents, but they differ in indication, dose, goal, risk profile, monitoring, and ethical justification [4,10]. Conflating them weakens scientific reasoning and obstructs responsible clinical investigation [4].

Sarcopenia illustrates this shift in perspective, and the revised European consensus defines it as a muscle disease in which low muscle strength is the primary parameter, low muscle quantity or quality confirms the diagnosis, and poor physical performance indicates severity [1]. This definition moves the discussion from muscle volume alone to clinically relevant function [1]. The patient is harmed not simply because muscle mass decreases, but because rising from a chair, walking, preventing falls, tolerating illness, and maintaining independence become progressively compromised [1,3].

Aging is also associated with progressive body composition changes, including increases in fat mass and decreases in fat-free mass during adult life [2]. However, morphological and functional loss is not explained by chronological aging alone [1,3]. Chronic inflammation, anabolic resistance, immobility, inadequate protein and energy intake, functional hypogonadism, pain, hospitalization, glucocorticoid exposure, and chronic disease may accelerate the same process [1,4,5]. Therefore, treating only the primary disease may be insufficient when structural and functional reserve has already been lost [1,3,4].

The prognostic relevance of strength supports this argument, as seen in the Prospective Urban Rural Epidemiology study, where grip strength was inversely associated with all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, and incident disability [3]. Muscle strength, muscle mass, and bone mass should therefore not be viewed as merely athletic or aesthetic variables [1-3]. They are clinical variables related to survival, independence, and biological resilience [1-3].

The biological rationale for anabolic interventions is not new and dates back to the 1940s [4,5,12]. Classic experimental and clinical work on anabolic-androgenic steroids described effects on nitrogen retention, protein metabolism, skeletal muscle, bone, erythropoiesis, and debilitated states [4,5]. Kochakian's work (the *Handbook of Experimental Pharmacology 43: Anabolic Androgenic Steroids* - 1976), explicitly framed anabolic-androgenic steroids beyond sexual androgenic functions, emphasizing their

metabolic actions and the need for careful clinical application in selected metabolic diseases and wasting conditions [5]. Later academic works, including Taylor's *Anabolic Therapy in Modern Medicine (2002)*, also discussed therapeutic anabolic strategies across several medical contexts [12].

The distinction between therapeutic use and nonmedical supraphysiological use remains important, particularly in clinical medicine, where the objective is often not to induce hypertrophy, but to prevent or reverse deterioration [4,5,12]. Several clinical conditions have historically been discussed or investigated as potential contexts for therapeutic anabolic strategies, particularly when they involve wasting, muscle loss, bone loss, impaired recovery, or functional decline. These conditions should not be interpreted as formal indications for anabolic-androgenic steroid therapy, but as clinical scenarios historically discussed or potentially relevant to the framework of clinical anabolism (**Table 1**).

Table 1. Clinical conditions historically discussed or investigated in relation to therapeutic anabolic strategies

Kochakian CD - Handbook of Experimental Pharmacology 43: Anabolic Androgenic Steroids (1976) **Taylor WN - Anabolic Therapy in Modern Medicine (2001)**	
1. Sarcopenia and Frailty	14. Cancer
2. Corticosteroid-Induced Osteoporosis	15. Cardiovascular Diseases and Rehabilitation
3. Postmenopausal Osteoporosis	16. Chronic Obstructive Pulmonary Disease
4. Osteoporosis and Male hypogonadism	17. Stroke
5. Autoimmune Diseases	18. Diabetes Mellitus
6. Amyotrophic Lateral Sclerosis	19. Chronic Kidney Disease
7. Chronic Fatigue	20. Muscular Dystrophies and Myopathies
8. Multiple Sclerosis	21. Spinal Cord Injury
9. Rheumatoid Arthritis	22. Alzheimer's Disease and Cognitive Deficit
10. Sjögren's Syndrome	23. Osteoarthritis
11. Systemic Lupus Erythematosus	24. Immobility and Gravity-Related Changes
12. AIDS and HIV Infection	25. Nutritional and metabolic therapy
13. Thermal Injury / Burn Patients	26. Dermatological Diseases / Wound Healing

Basaria, Wahlstrom, and Dobs reviewed anabolic-androgenic steroid therapy in chronic diseases characterized by weight loss and muscle catabolism, discussing effects on lean mass, body weight, erythropoiesis, quality of life, and physical performance in selected populations [4]. This review is particularly relevant because it frames anabolic

therapy as a potential intervention on disease-related catabolic trajectories, rather than as a simple strategy for increasing muscle size [4].

Controlled human studies demonstrate the biological capacity of androgens to affect muscle [6,7]. In healthy men, supraphysiological testosterone increased fat-free mass, muscle size, and strength, especially when combined with resistance training [6]. This model should not be directly extrapolated to frail or chronically ill patients, but it confirms the androgen-responsive nature of muscle mass and strength [6]. In patients receiving hemodialysis, nandrolone decanoate increased lean body mass and improved selected functional measures in a randomized trial [7]. In HIV-associated wasting, testosterone therapy has been associated with increases in lean body mass [8]. In severe burns, oxandrolone has been associated in systematic review evidence with reduced weight loss and improved recovery of lean mass or selected clinical outcomes [9].

These findings do not justify broad or indiscriminate prescription. They indicate that legitimate clinical questions exist [4,7-9,12]. In selected diseases, therapeutic anabolic strategies may act not only on low body weight or wasting, but also on components of the disease trajectory, such as anemia, lean mass loss, bone fragility, exercise intolerance, delayed recovery, impaired rehabilitation response, and reduced quality of life [4,7-9,12]. Clinical anabolism should therefore be conceptualized as an intervention on a morphological and functional trajectory, not as a cosmetic intervention [1,4,12].

Adequate clinical safety does not mean the absence of adverse effects; it means an acceptable risk-benefit relationship within a precise indication, with appropriate drug selection, dose, route, duration, patient selection, and monitoring [4,10,12]. Potential adverse effects include lipid changes, fluid retention, hypertension, erythrocytosis, acne, alopecia, virilization in women, hepatotoxicity with 17-alpha-alkylated compounds, gonadal suppression, infertility, and possible cardiovascular events in susceptible patients [4,10,12]. This is another point at which therapeutic use differs from abuse: therapeutic use requires indication, proportionality, follow-up, and predefined safety surveillance [4,10,12].

In practice, clinical anabolism should be multimodal. Resistance training, integrative rehabilitation, nutritional support, adequate protein intake, pain

management, sleep optimization, treatment of inflammation, correction of hormonal deficiency when present, correction of vitamin D deficiency when present, and control of the primary disease are central components [1,4]. Pharmacological anabolic agents, when considered, should be complementary rather than substitutes for these measures [1,4,12]. An anabolic drug prescribed without a functional plan reduces a complex medical strategy to incomplete pharmacology [1,4,12].

Physicians caring for patients with chronic disease should therefore be attentive to the morphological and functional axis of illness. The clinical question should not be limited to “What is the diagnosis?” It should also include: how much muscle, bone, strength, endurance, and autonomy has this patient lost [1-3]? Is this loss progressing [1,3]? Does it change prognosis [3]? Is there a therapeutic window to interrupt or reverse this trajectory [1,4]? These questions are consistent with contemporary concepts of sarcopenia, frailty, androgen deficiency, and rehabilitation medicine, all of which require attention to symptoms, target tissues, function, and clinical risk rather than isolated laboratory values [1,3,10].

For the field to advance, minimum criteria are needed. Clinical anabolism should require an objective indication, baseline assessment of body composition, strength, physical performance, and bone risk when appropriate, integration with nutrition and exercise, monitoring of efficacy and safety, informed consent, and predefined criteria for continuation or discontinuation [1,4,10,12]. Future studies should prioritize patient-centered functional outcomes, such as strength, gait speed, falls, independence, treatment tolerance, hospitalization, and quality of life, rather than changes in lean mass alone [1,3,4,12].

In summary, clinical anabolism proposes that loss of structure and function should be recognized as a legitimate therapeutic target in chronic disease, aging, and catabolic states [1,4]. Between neglect of functional deterioration and indiscriminate anabolic drug use, there is a scientific, clinical, and ethical space for careful investigation [4,10,12]. This is the space in which physicians and researchers should develop a prudent, monitored, and outcome-oriented approach to preserving muscle, bone, strength, and autonomy [1,3,4,12].

Conflict of interest statement

The author declares no commercial or financial conflicts of interest related to this manuscript. The views expressed herein are academic and conceptual in nature and should not be interpreted as an endorsement of the indiscriminate, aesthetic, recreational, or nonmedical use of anabolic-androgenic steroids.

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