USE OF ANABOLIC HORMONE THERAPIES IN SARCOPENIA IN OLDER ADULTS: CURRENT EVIDENCE AND PROGNOSIS

USO DE TERAPIAS HORMONAIS ANABÓLICAS NA SARCOPENIA EM IDOSOS: EVIDÊNCIAS ATUAIS E PROGNÓSTICO

USO DE TERAPIAS CON HORMONAS ANABÓLICAS EN LA SARCOPENIA EN ANCIANOS: EVIDENCIA ACTUAL Y PRONÓSTICO

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ABSTRACT
Sarcopenia is a multifactorial condition associated with aging, characterized by the progressive loss of skeletal muscle mass and function, with significant impact on physical performance and quality of life in older adults. In this context, anabolic hormone therapies have been investigated as potential strategies to mitigate this process. This study aimed to critically analyze the current scientific evidence regarding the use of these therapies in the management of sarcopenia in older individuals. This is a narrative literature review conducted using PubMed, ScienceDirect, and SciELO databases, including publications from 2016 to 2026. A total of 17 studies were selected, addressing testosterone replacement therapy (TRT), selective androgen receptor modulators (SARMs), and other hormonal approaches. The findings indicate that TRT consistently improves lean body mass and body composition; however, its effects on physical function remain heterogeneous. SARMs show promising anabolic effects in experimental models, but clinical evidence is still limited. Additionally, relevant concerns persist regarding the safety of these interventions, particularly in relation to cardiovascular risk and long-term outcomes. In conclusion, despite favorable effects on structural parameters, anabolic hormone therapies do not yet have sufficient evidence to support their use as standard treatment for sarcopenia, highlighting the need for further studies focusing on functional outcomes and long-term safety.

Keywords: Sarcopenia. Hormone Therapy. Testosterone. Aging. Skeletal Muscle.

RESUMO
A sarcopenia é uma síndrome multifatorial associada ao envelhecimento, caracterizada pela perda progressiva de massa e função muscular, com impacto significativo na funcionalidade e na qualidade de vida de idosos. Nesse contexto, terapias hormonais anabólicas têm sido investigadas como estratégia potencial para atenuar esse processo. O presente estudo teve como objetivo analisar criticamente as evidências científicas acerca do uso dessas terapias na sarcopenia em idosos. Trata-se de uma revisão narrativa da literatura, realizada nas bases de dados PubMed, ScienceDirect e SciELO, contemplando publicações entre 2016 e 2026. Foram incluídos 17 estudos que abordaram a terapia de reposição de testosterona (TRT), os moduladores seletivos do receptor androgênico (SARMs) e outras abordagens hormonais. Os resultados demonstraram que a TRT apresenta efeitos consistentes sobre o aumento da massa muscular e melhora da composição corporal, embora seus impactos sobre a função física sejam heterogêneos. Os SARMs mostraram potencial promissor em modelos experimentais, porém com evidência clínica ainda limitada. Adicionalmente, persistem incertezas relevantes quanto à segurança dessas intervenções, especialmente em relação a riscos cardiovasculares e efeitos em longo prazo. Conclui-se que, apesar dos efeitos favoráveis sobre parâmetros estruturais, as terapias hormonais anabólicas ainda não apresentam evidência suficiente para sua utilização como tratamento padrão da sarcopenia, sendo necessárias investigações adicionais com foco em desfechos funcionais e segurança clínica.

Palavras-chave: Sarcopenia. Terapia Hormonal. Testosterona. Envelhecimento. Músculo Esquelético.

RESUMEN
La sarcopenia es un síndrome multifactorial asociado al envejecimiento, caracterizado por la pérdida progresiva de masa y función muscular, con un impacto significativo en la funcionalidad y la calidad de vida de los adultos mayores. En este contexto, se han investigado las terapias con hormonas anabólicas como una estrategia potencial para mitigar este proceso. Este estudio tuvo como objetivo analizar críticamente la evidencia científica sobre el uso de estas terapias en la sarcopenia en adultos mayores. Se trata de una revisión narrativa de la literatura, realizada en las bases de datos PubMed, ScienceDirect y SciELO,

que abarca publicaciones entre 2016 y 2026. Se incluyeron diecisiete estudios que abordaron la terapia de reemplazo de testosterona (TRT), los moduladores selectivos del receptor de andrógenos (SARMs) y otros enfoques hormonales. Los resultados demostraron que la TRT tiene efectos consistentes en el aumento de la masa muscular y la mejora de la composición corporal, aunque sus impactos en la función física son heterogéneos. Los SARMs mostraron un potencial prometedor en modelos experimentales, pero con evidencia clínica aún limitada. Además, persisten importantes incertidumbres con respecto a la seguridad de estas intervenciones, especialmente en lo que respecta a los riesgos cardiovasculares y los efectos a largo plazo. Se concluye que, a pesar de sus efectos favorables sobre los parámetros estructurales, las terapias con hormonas anabólicas aún carecen de evidencia suficiente para su uso como tratamiento estándar para la sarcopenia, y se requieren más investigaciones centradas en los resultados funcionales y la seguridad clínica.

Palabras clave: Sarcopenia. Terapia Hormonal. Testosterona. Envejecimiento. Músculo Esquelético.

1 INTRODUCTION

Sarcopenia is a complex geriatric syndrome, characterized by progressive loss of muscle mass and function, strongly associated with adverse clinical outcomes, including functional disability, frailty, and increased mortality. Although widely recognized as a multifactorial condition, recent literature emphasizes the central role of endocrine dysfunction in the imbalance between muscle anabolic and catabolic pathways (CHO et al., 2022; MINNETTI et al., 2026). In this scenario, the reduction of anabolic hormones such as testosterone, growth hormone, and IGF-1 has been consistently associated with deterioration in body composition. However, despite the biological plausibility, the magnitude and clinical relevance of these hormonal changes remain heterogeneous among studies, suggesting that their isolated contribution to sarcopenia may be overestimated in certain contexts (BATSIS; VILLAREAL, 2018; SHIN; JEON; KIM, 2018).

The progressive drop in testosterone levels in aging, often linked to late hypogonadism, has been pointed out as one of the main therapeutic targets in an attempt to reverse muscle loss. Although evidence indicates an association between low androgen levels and worsening muscle mass and strength, the causal relationship remains incompletely established, being influenced by multiple clinical and metabolic factors (TAKAYAMA, 2017; AMANO, 2025). In addition, observational studies and clinical interventions show inconsistent results regarding the direct impact of testosterone on physical functionality, suggesting that gains in muscle mass do not always translate into significant clinical improvement (SHIN; JEON; KIM, 2018).

In this context, testosterone replacement therapy (TRT) emerged as one of the main pharmacological strategies investigated. Although clinical trials demonstrate consistent increases in lean mass and improvement in body composition parameters, the effects on functional outcomes, such as mobility and physical performance, remain controversial (BHASIN et al., 2023; NIGHTINGALE et al., 2018). In addition, there are still relevant uncertainties regarding the long-term safety of TRT, especially with regard to cardiovascular risk and possible prostatic implications, which limits its clinical applicability in elderly populations (WANG; SWERDLOFF, 2022; KHODAMORADI et al., 2020). These inconsistencies highlight a critical gap between the observed physiological effects and the clinical benefits actually achieved.

At the same time, new pharmacological approaches, such as selective androgen receptor modulators (SARMs), have been proposed as potentially safer alternatives, due to their selective tissue action. Despite promising results in experimental models and initial studies, demonstrating increased muscle mass and favorable metabolic effects, the absence

of robust evidence in large-scale clinical trials significantly limits their incorporation into clinical practice (CHRISTIANSEN et al., 2020; BORECKI et al., 2025; MORIMOTO et al., 2020). In addition, the extrapolation of preclinical data to elderly populations with multiple comorbidities remains a substantial challenge, reinforcing the need for caution in the interpretation of these findings (SPRINGER; SPRINGER; ANKER, 2017).

Despite advances in the understanding of the hormonal mechanisms involved in sarcopenia, there is no consensus regarding the role of anabolic therapies in its management, especially with regard to its functional efficacy and long-term safety. While non-pharmacological interventions, such as resistance exercise and nutritional support, remain consolidated strategies (KILGORE, 2016; CHO, 2025), hormonal therapies still occupy an uncertain space between therapeutic promise and clinical limitation. In this context, there is a significant gap in the literature regarding the real applicability of these interventions in geriatric clinical practice. Thus, the present study aims to critically analyze the current evidence on the use of anabolic hormonal therapies in sarcopenia in the elderly, focusing on their efficacy, safety, and prognostic implications.

2 METHODOLOGY

This is a narrative review of the literature, with a qualitative approach, oriented to the critical analysis of scientific evidence on the use of anabolic hormonal therapies in the management of sarcopenia in the elderly. The bibliographic search was conducted in a structured manner in the PubMed, ScienceDirect and SciELO databases, including publications in the period from 2016 to 2026. English descriptors were used, combined by Boolean operators (AND, OR), including: *"sarcopenia", "anabolic hormone therapy*", *"testosterone replacement therapy", "selective androgen receptor modulators"* and *"aging".* The search strategy was designed to encompass studies that investigated both the pathophysiological mechanisms associated with sarcopenia and hormonal therapeutic interventions, prioritizing evidence with clinical applicability.

The eligibility criteria were previously defined. Original articles, reviews, and experimental or clinical studies with a direct relationship to the topic were included. The inclusion criteria included: (i) publications in the last ten years; (ii) availability of full text or structured abstract; and (iii) relevance to the use of anabolic hormonal therapies in sarcopenia in the elderly. Duplicate studies, non-peer-reviewed publications, articles with divergent thematic focus, and studies with no clinical relevance to the target population were excluded.

The study selection process was conducted in sequential stages. Initially, screening was performed by reading the titles and abstracts identified in the databases, excluding studies that did not meet the established criteria. Then, the eligible articles were read in full, when available, for further evaluation of methodological adequacy and scientific relevance. The final inclusion of the studies considered the consistency of the designs, the clarity of the outcomes analyzed, and the contribution to the understanding of the theme. At the end of this process, 17 articles were selected.

Data extraction and organization were carried out in a standardized manner, including information such as the type of study, the population investigated, the proposed intervention, the main outcomes related to muscle mass and function, as well as safety aspects associated with hormonal therapies. These elements supported the qualitative synthesis of the evidence.

The analysis of the studies was conducted from a descriptive-analytical perspective, with emphasis on the identification of patterns of evidence, convergences and divergences between the results, in addition to the critical evaluation of methodological limitations. Particular consideration was given to the efficacy of interventions on functional outcomes, the consistency of results between different designs, and uncertainties regarding long-term safety. The interpretation of the findings was oriented towards the integration of the available data and the problematization of the gaps in the literature, especially with regard to the clinical applicability of hormonal therapies in the elderly population.

3 RESULTS

We included 17 studies published between 2016 and 2026, covering narrative reviews, clinical and experimental studies, and mechanistic analyses. Overall, evidence focuses on evaluating the effects of anabolic hormone therapies on body composition, muscle function, and safety in elderly or hormone-deficient individuals.

Testosterone replacement therapy (TRT) was the most frequently investigated intervention, with consistent results regarding increased lean body mass and reduced fat mass, especially in individuals with hypogonadism (BHASIN et al., 2023; NIGHTINGALE et al., 2018). In addition, improvements in muscle strength parameters were observed, although the magnitude of these effects varies between studies. On the other hand, the outcomes related to physical function and functional performance were heterogeneous, with divergent evidence regarding their effectiveness in improving mobility and functional capacity (SHIN; JEON; KIM, 2018). With regard to safety, the studies point to relevant uncertainties, particularly related to cardiovascular risk and possible prostate implications, aspects that

remain inconclusive in the available literature (WANG; SWERDLOFF, 2022; KHODAMORADI et al., 2020).

Selective androgen receptor modulators (SARMs) emerge as a promising therapeutic approach, characterized by selective anabolic effects on muscle tissue. Evidence from experimental studies demonstrates an increase in muscle mass and improvement in metabolic parameters, with a potentially more favorable profile in terms of adverse effects when compared to traditional androgens (CHRISTIANSEN et al., 2020; MORIMOTO et al., 2020). In addition, recent reviews indicate the development of compounds in the clinical investigation phase, with preliminary results suggesting positive effects on lean mass (BORECKI et al., 2025). However, the literature still shows a predominance of preclinical data or initial studies, with limited evidence from robust clinical trials in elderly populations.

At the same time, other hormonal axes have been implicated in the pathophysiology and management of sarcopenia. Studies highlight the role of growth hormone (GH), insulin-like growth factor type 1 (IGF-1), and sex steroids in the regulation of muscle mass, showing that the decline of these hormones with aging contributes to the loss of muscle mass and function (MINNETTI et al., 2026; BATSIS; VILLAREAL, 2018). Additional therapeutic approaches, such as myostatin inhibitors, ghrelin analogues, and other hormone modulators, are in experimental stages, with still limited evidence regarding their clinical efficacy (CHO et al., 2022; CHO, 2025).

Regardless of the pharmacological approach, the studies analyzed consistently reinforce the central role of non-pharmacological interventions, particularly resistance exercise and nutritional support, as fundamental strategies in the management of sarcopenia (KILGORE, 2016).

In summary, the findings indicate that anabolic hormone therapies have more consistent effects on body composition parameters than on functional outcomes, while new approaches, such as SARMs, remain in the scientific consolidation phase.

4 DISCUSSION

The findings of this review show that, although anabolic hormone therapies have consistent effects on body composition parameters, their translation into relevant clinical benefits remains uncertain. Testosterone replacement therapy (TRT), for example, relatively uniformly demonstrates increased lean mass and reduced body fat (BHASIN et al., 2023; NIGHTINGALE et al., 2018). However, the heterogeneity of the results related to physical function suggests that structural gains do not necessarily translate into functional improvement, a central aspect in the clinical definition of sarcopenia. This dissociation raises

questions about the real effectiveness of TRT as an isolated therapeutic intervention, especially considering that functionality, and not only muscle mass, is the main prognostic determinant in the elderly (SHIN; JEON; KIM, 2018).

In addition, the absence of consensus regarding the safety of TRT represents a critical limitation for its clinical application. Although some studies indicate a relatively safe profile when used under controlled conditions, concerns persist regarding cardiovascular risk and possible prostatic repercussions, especially in elderly populations with multiple comorbidities (WANG; SWERDLOFF, 2022; KHODAMORADI et al., 2020). The lack of long-term clinical trials, with adequate statistical power to evaluate adverse events, makes it difficult to consolidate robust clinical recommendations, keeping TRT in a zone of therapeutic uncertainty.

Regarding selective androgen receptor modulators (SARMs), the available results reinforce their potential as a more specific and theoretically safer pharmacological alternative. Experimental studies demonstrate significant anabolic effects, with a positive impact on muscle mass and metabolic parameters (CHRISTIANSEN et al., 2020; MORIMOTO et al., 2020). However, the predominance of preclinical data and the scarcity of robust clinical trials substantially limit the extrapolation of these findings to clinical practice. In addition, the absence of consistent data on long-term safety and effects in frail elderly populations reinforces the need for caution, especially in view of the history of hormonal therapies whose risks only became evident after expanded use (BORECKI et al., 2025; SPRINGER; SPRINGER; ANKER, 2017).

Another relevant point refers to the complexity of the pathophysiology of sarcopenia, which cannot be attributed exclusively to hormonal decline. Although alterations in axes such as testosterone, GH, and IGF-1 play a relevant role, the interaction with inflammatory, metabolic, and functional factors suggests that isolated therapeutic approaches tend to have limited efficacy (MINNETTI et al., 2026; BATSIS; VILLAREAL, 2018). In this context, the literature analyzed consistently reinforces the central role of non-pharmacological interventions, particularly resistance exercise, as a fundamental strategy in the management of the disease (KILGORE, 2016). This indicates that hormonal therapies, when used, should be understood as adjuvants, and not as primary interventions.

The integrated analysis of the studies shows, therefore, a significant gap between the physiological effects of hormonal therapies and their effective clinical applicability. Although there are advances in the development of new approaches, such as SARMs and other hormone modulators, the absence of robust evidence, especially regarding relevant clinical outcomes and long-term safety, prevents the consolidation of these strategies as a

therapeutic standard. Thus, the current scenario is marked by consistent biological promises, but not yet fully translated into measurable clinical benefits.

Thus, the available literature does not support a consensus regarding the routine use of anabolic hormone therapies in the treatment of sarcopenia in the elderly, evidencing the need for more robust clinical studies, focusing on functional outcomes and long-term safety. The definition of the role of these interventions in clinical practice depends, therefore, on more consistent evidence that allows overcoming the current methodological limitations and reducing the uncertainties that still exist.

5 CONCLUSION

The evidence analyzed indicates that anabolic hormone therapies, particularly testosterone replacement therapy, have consistent effects on body composition parameters, such as increased muscle mass and reduced adiposity. However, these benefits do not translate uniformly into improved physical function, the main clinical outcome in sarcopenia, evidencing a relevant dissociation between structural and functional effects.

In addition, significant uncertainties persist regarding the safety of these interventions, especially in relation to cardiovascular risk and prostate implications, which limits their broad application in the elderly population. In the case of selective androgen receptor modulators, although initial results are promising, the predominance of preclinical evidence and the scarcity of robust clinical trials prevent their incorporation into clinical practice at the present time.

The multifactorial complexity of sarcopenia reinforces that isolated therapeutic approaches, based exclusively on hormonal modulation, have limited efficacy. In this context, non-pharmacological interventions, such as resistance exercise and nutritional support, remain fundamental strategies and supported by more consistent evidence.

Thus, anabolic hormonal therapies cannot yet be considered the therapeutic standard for sarcopenia in the elderly, currently occupying a potentially adjuvant role and restricted to specific clinical contexts. The consolidation of its use depends on the performance of high-quality clinical studies, focusing on functional outcomes and long-term safety, capable of reducing the uncertainties that are still present and guiding its applicability in clinical practice.

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