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Anorexia of aging: from diagnosis to treatment

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Abstract

Anorexia of aging is characterized by reduced appetite and/or food intake in older adults, leading to negative outcomes such as malnutrition, frailty, sarcopenia, and increased mortality. Despite its high prevalence, anorexia of aging has often been underdiagnosed and undertreated due to a lack of consensus on diagnostic criteria and effective interventions. This narrative review provides an updated general perspective on anorexia of aging, highlighting its challenges and potential therapeutic approaches. Articles were selected from international databases over a 40-year period, focusing on biological mechanisms, clinical outcomes, and management strategies. The main factors associated with anorexia of aging in the literature include changes in appetite regulation, sensory decline, social isolation, depression, and comorbidities. The Simplified Nutritional Appetite Questionnaire is the most widely used screening tool to identify anorexia of aging risk. Early identification allows early interventions, including dietary modifications and nutritional supplementation. Pharmacological strategies, such as ghrelin receptor agonists, have shown promise. Given the significant impact of anorexia of aging, addressing this condition is essential to promote healthier aging and reduce health risks. It is essential for caregivers and professionals to receive updated knowledge so that effective measures can be implemented.

Keywords: anorexia; older adult; appetite; food intake; weight loss.

INTRODUCTION

Anorexia of aging (AA) is a relevant geriatric condition related to reduced appetite and/or decreased food intake in older people.[1] This multifactorial syndrome is associated with several negative health outcomes, including malnutrition, weight loss, frailty, depression, sarcopenia and increased risk of disability and mortality.[2-5]

A number of factors can contribute to AA, which highlights the complex interactions between physiological, metabolic, and social changes associated with the aging process.[6] Major physiological factors include a lower basal metabolic rate, changes in body composition (ie, increased body fat and loss of skeletal muscle mass) and changes in gastrointestinal function.[4] These physiological changes are often accompanied by reduced perception of taste and smell, which can reduce the pleasure of eating.[6] Psychosocial factors, such as social isolation, loneliness and grief, also play a crucial role, often aggravating the effects of the syndrome.

AA is a complex condition that involves multiple aspects of human aging. Its identification and management remain challenging due to the limited literature on specific diagnostic criteria,[7,8] effective treatments,[9] and robust preventive strategies. This knowledge gap hampers early interventions that could mitigate the effects of this syndrome.

Because the challenges associated with AA have been underestimated, there is a need to disseminate relevant and up-to-date information on the topic, which could increase understanding of the syndrome and help predict its effects. Therefore, this narrative review aimed to synthesize the current knowledge on AA, focusing on key clinical outcomes, the biological regulation of appetite, and strategies for diagnosis and treatment that are grounded in the most recent evidence.

METHODS

This narrative review is based on a search of the scientific literature on AA, supplemented by insights from clinical practice. The search was conducted non-systematically in the PubMed, SciELO and LILACS databases from 1980 to September 2024. We selected 1980 as the starting point because that was the year Morley coined the term "anorexia of aging."[10] The search strategy consisted of the descriptors "anorexia of aging" and "elderly person", combined with the Boolean operator "AND".

Studies addressing AA as a primary or secondary condition were included and grouped to explore the disorder's effects on health, its biological mechanisms, and treatment strategies. Given the heterogeneity and lack of consensus on the definition of the syndrome, an operational definition based on loss of appetite, reduced food intake and weight loss, whether alone or in combination, was considered. No language restrictions were determined to expand the scope of the results, although we did not consider grey literature (theses, dissertations, book chapters, or books).

Definitions and importance

AA, a common condition among older adults, involves an exacerbated physiological adaptation of aging-related appetite control mechanisms. It is defined as the loss of appetite and/or food intake due to a decrease in basal metabolic rate and proportion of lean body mass.[2] AA may be considered a geriatric syndrome because multifactorial conditions contribute to its onset, it has heterogeneous pathophysiological mechanisms, and it has a high prevalence.[4,5]

AA has been associated with several adverse outcomes, such as the risk of falls, fractures, and hospitalizations, and it is an independent risk factor for high morbidity and mortality.[11] Understanding and diagnosis of AA are essential, as it is a key factor in weight loss, malnutrition, sarcopenia, and frailty. AA must be prevented and identified to reduce negative outcomes.[12,13]

Essentially, the loss or alteration of appetite is central to AA, and its etiology can be understood through 3 primary contributing factors.

1. Physiological factors: hormonal changes, such as a reduction in ghrelin and neuropeptide Y and an increase in cholecystokinin and leptin, play a crucial role in decreasing hunger and food intake in older adults.[14,15] Additionally, changes in gastrointestinal motility and sensory perception further affect appetite.[16]
2. Behavioral factors: studies indicate that older adults often experience reduced pleasure in eating due to changes in taste and smell, which can negatively influence food intake.[17]
3. Environmental and social factors: social isolation and depression are associated with lower caloric intake, and the institutionalized are at higher risk of anorexia than community-dwellers.[3,18]

Appetite loss in AA is often related to abnormalities identified by the individual, family members, or a health care provider. These abnormalities are often based on a comparison of current and previous dietary habits. Thus, AA results in reduced energy and nutrient intake, including protein, fiber, and micronutrients, potentially leading to malnutrition.[14]

Health care professionals face several challenges in addressing AA among older adults, as highlighted by Takagi et al. The primary difficulty is related to the assessment of appetite, as many participants perceived appetite loss as inevitable

and often relied on subjective interviews and clinical judgment for evaluation. Takagi et al. also found that the lack of robust evidence on effective treatments posed a significant barrier to intervention. However, health care professionals with greater awareness of AA were more likely to use screening tools to assess appetite, emphasizing the important role of knowledge and training in management.[19]

The lack of a consensus definition of AA presents makes diagnosis and management challenging. Health care providers often rely on subjective assessments, leading to inconsistent care. Additionally, the absence of clear treatment guidelines complicates effective intervention. These issues not only affect the health of older adults but also have broader implications for families, society, and health care systems, underscoring the need for standardized approaches to improve care and reduce associated costs.

Epidemiology of anorexia of aging

The prevalence and incidence of AA have been evaluated in several studies around the world and vary significantly, with rates ranging from 0.20[20] to 63%,[21] depending on the population studied.

In May 2025, a systematic review and meta-analysis[22] synthesized the global prevalence and incidence of AA across different populations and settings. An overall prevalence rate of 22.7% was estimated from 29 864 296 older adults in 36 studies across 17 countries,[22] with a higher prevalence among inpatients (13 to 63%) and nursing home residents (5.8 to 61%) than among community-dwellers (0.20 to 55%).[22] This variability in prevalence, observed previously in systematic reviews by Malafarina et al.[6] and Fielding et al.,[3] can be attributed to the lack of specific diagnostic criteria, ie, when general self-assessment methods are used, the prevalence of AA varies. In studies using the Simplified Nutritional Appetite Questionnaire (SNAQ) to assess AA, the prevalence ranged from 9.8 to 53.8%.[23] Fernandez et al. found that the SNAQ was the most used tool in this context.[22] However, when other subjective measures are used, such as the Comprehensive Nutritional Appetite Questionnaire, the prevalence can reach 79.3%.[24]

While most studies focus on the prevalence of AA, research on its incidence remains limited, with the majority concentrating on cross-sectional data within specific populations. For instance, studies have found an AA found incidence rates of 39% in community participants,[15] 25.4% in intensive care unit patients,[16] and 0.9% in Medicare fee-for-service data.[17] Fernandez et al.[22] estimated the overall incidence of at 3.78% using 3 population-based studies from North America and Europe involving different diagnostic tools.

In summary, although the prevalence of AA has been widely studied in diverse populations, research on its incidence remains scarce. Most studies rely on cross-sectional data, and there is a need for longitudinal studies following the syndrome's progression over time. The variable results highlight the importance of standardized diagnostic criteria and the need for further research to better understand the impact of AA on health.

Etiology of anorexia of aging

There are a variety of medical conditions that become more frequent with age, and they may be associated with loss of appetite and weight, potentially leading to AA. These conditions include gastrointestinal diseases (malabsorption syndromes, eg, bacterial overgrowth, gluten enteropathy, and pancreatic insufficiency) and abnormalities in gastric motility that cause early satiety.[18]

Furthermore, swallowing disorders (eg, dry mouth, tooth loss, lesions or sores in the mouth), dyspepsia (eg, gastritis and ulcers),[18,25] neurodegenerative and neurological diseases (such as stroke with residual swallowing deficits, dementia and Alzheimer's disease), acute and chronic infections (eg H. pylori, tuberculosis, and recurrent urinary tract infections),[26] endocrine disorders (eg, hypercalcemia), and micronutrient deficiencies may cause nutrient malabsorption, gastrointestinal symptoms, and loss of appetite.[27]

Certain chronic diseases that involve increased energy expenditure, such as congestive heart failure, chronic obstructive pulmonary disease and Parkinson's disease, are also associated with AA.[18,26]

Another factor that contributes to delayed gastric emptying and, hence, appetite loss is circulating levels of interleukin-1, interleukin-6 and tumor necrosis factor alpha, which are typically higher in older adults. This increase is independent of specific diseases or multimorbidity and is due to chronic low-grade inflammation, a hallmark of the aging process.[18] These cytokines enhance circulating leptin levels and directly stimulate leptin mRNA expression. Besides their direct effects, pro-inflammatory cytokines also stimulate the production of hypothalamic corticotropin releasing factor, an orexigenic neurotransmitter that mediates leptin action.[26]

There is also a range of routinely prescribed medications that can suppress the appetite, including: digoxin, amiodarone and spironolactone, phenothiazines, lithium, amitriptyline, fluoxetine, and other selective serotonin reuptake inhibitors and non-steroidal anti-inflammatory agents. Specific mechanisms can be highlighted, such as proton pump inhibitors, which can cause hypochlorhydria (further delaying gastric emptying),[18] laxatives, which can cause malabsorption, and

theophylline, which can increase metabolism, thus contributing to weight loss.[18,28]

Psychological, social, and physical factors can also contribute to AA. Some examples in the psychological context are bereavement and mental health issues, such as depression.[27] The association between depression and AA is important, as demonstrated by Aprahamian et al.,[2] who found that 30.7% of older outpatients with major depression experienced AA. Cox et al.[14] confirmed that appetite and mood are significantly affected by aging. Functional magnetic resonance imaging has identified changes in the brain's reward centers[29] in older individuals suffering from depression, suggesting that depression has a neurobiological impact on appetite regulation.

In addition to the above mentioned factors, older individuals with dementia are also at an increased risk of AA. This is partly due to the loss of appetite and weight, as well as a decline in physical activity levels as the syndrome progresses.[30] As highlighted by Fostinelli et al.,[30] a comprehensive assessment of eating behavior is essential in this population. In support of this, Dagenais et al.[4] found that 38.3% of older adults with dementia experienced anorexia within a 12-month period.

Social factors include poverty and difficulties with shopping, meal preparation, and self-feeding, in addition to living alone, social isolation, and loneliness.[27] However, depression may be a secondary factor in AA, since Hsieh et al.[31] observed that 23.7% of older adults who lived alone had AA, suggesting that loneliness and AA could precede depression. Furthermore, loneliness itself may be an independent risk factor for AA, as evidenced by Bolus et al. in rural Lebanon,[32] who found that lonely older adults had a 1.15 times higher likelihood of malnourishment.

Finally, the physical factors include immobility, impaired vision, and poor dentition, which results in chewing problems.[27]

Given the multifactorial nature of AA, it is crucial to recognize its contributing factors, including medical, psychological, social and physical conditions. Early identification and comprehensive assessment are essential to reduce the adverse outcomes associated with AA, such as malnutrition, weight loss, and increased morbidity. Preventing the onset and progression of AA requires addressing psychosocial factors such as loneliness and depression. Further research and the development of improved clinical protocols are necessary to enhance our understanding and management of this complex syndrome.

Outcomes of anorexia of aging

Previous studies have identified several adverse outcomes associated with AA, including functional impairment,[33] reduced immunocompetence,[33] malnutrition,[18] and lower overall quality of life.[34] These associations help explain why AA is often linked to reduced physical performance, including slower gait speed, poorer endurance, decreased mobility, lower muscle mass, and reduced exercise capacity.[3] Additionally, AA is associated with difficulties in activities of daily living, frailty, falls,[3] sarcopenia and an increased risk of hospitalization, nursing home admission, and mortality.[15] Specifically, sarcopenia increases the risk of falls, fractures, functional impairment, and hospital admission.[35] Sarcopenia is also more prevalent among individuals who are malnourished or at risk of malnutrition.[36,37] Severe weight loss, a key component of frailty, is strongly associated with poor health care outcomes, highlighting the importance of addressing these interrelated conditions.[38,39]

Compared to younger adults (26 – 27 years), healthy older adults (70 – 74 years) have reduced appetite and energy intake, including a 16–20% lower energy intake, 25 – 39% lower hunger, and 37% more satiety. These age-related differences in healthy adults establish lower food intake as a common feature of aging.[31] Loss of appetite and/or reduced food intake after 65 years of age is not desirable, especially due to the increased vulnerability to nutritional deficiencies and malnutrition in this population.[2] An example of appetite loss in clinical practice occurred in a large study of community-dwelling Americans aged ≥ 65 years, 17% of whom lost 5% of their body weight over 3 years, which was associated with a 70% increase in mortality, irrespective of initial weight.[31]

Identifying individuals with poor appetite is an opportunity for early intervention, potentially preventing weight loss and mitigating these significant health challenges.[15] This is especially important because many of the above mentioned factors are at least partially responsive to treatment.[31]

Recognizing the significant risks associated with AA highlights the need for timely identification and early intervention. Addressing key factors, such as malnutrition, frailty, and sarcopenia, can substantially improve health outcomes and prevent further decline. Since many of these issues are at least partially responsive to treatment, early action can help postpone AA's effects on physical and mental health. Ultimately, prioritizing recognition of AA and its associated conditions in clinical practice is essential for promoting better aging and reducing the syndrome's long-term consequences.

Biological appetite regulation

Appetite regulation plays a central role in AA, with appetite loss being the primary factor, while weight loss and reduced intake are subsequent components. We believe that understanding the physiological mechanisms behind appetite

regulation, including neurobiological and hormonal factors, is key to comprehending AA. This approach provides a clearer understanding of its underlying causes, enabling more effective intervention strategies.

Appetite, the desire for food, is a complex process involving both physiological and psychological components. While primarily a physiological response, appetite is influenced by external factors, such as the eating environment,[40] and internal factors, including the psychological reward of eating, gut microbiota,[41] resting metabolic rate, and total energy expenditure.[40]

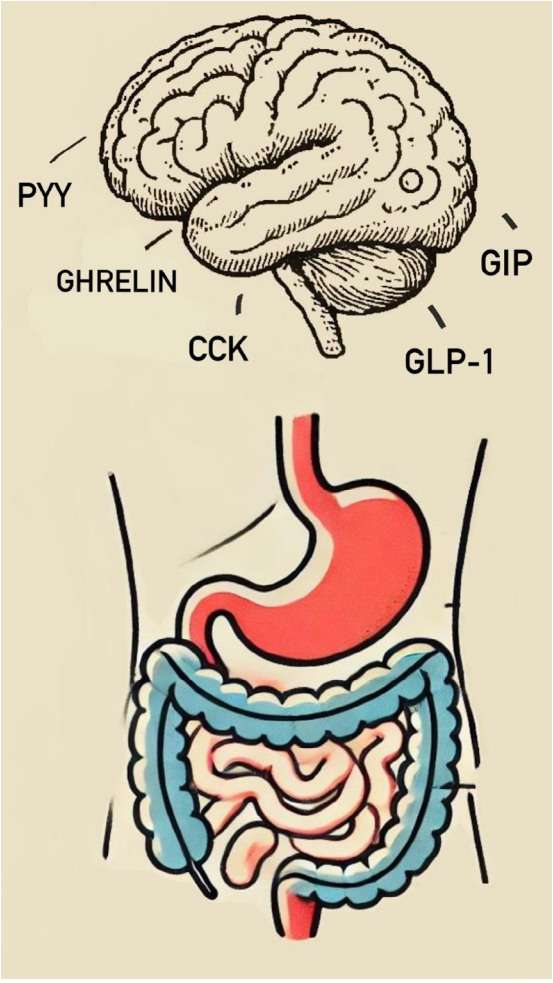
Aging is associated with a decline in both resting metabolic rate and total energy expenditure, with a reduction of approximately 13 – 20% in resting metabolic rate between 30 and 80 years of age.[40] This decrease is partly due to a reduction in Na-K-ATPase activity and a decrease in skeletal muscle protein turnover, which contribute to the intrinsic loss of metabolic function with age. In a cross-sectional cohort study of 358 well-phenotyped Dutch community-dwelling older adults from the Longitudinal Aging Study Amsterdam, Fluitman et al.[41] demonstrated that gut microbiota is significantly associated with poor appetite and undernutrition. In this cohort, participants with either poor appetite or undernutrition had significantly lower fecal acetate levels, which correlated with a reduced abundance of Blautia, a potent acetate producer.

From a physiological perspective, appetite is regulated by a complex interplay of stimuli (eg, hunger) and inhibitory signals (eg, satiety), mediated through both peripheral and central pathways (Figure 1). These processes are primarily coordinated by the arcuate nucleus of the hypothalamus, often referred to as the appetite control center.[42] Peripherally, appetite is largely influenced by basal metabolic rate and hormonal signals originating from the gastrointestinal tract, pancreas, and adipose tissue.[15] Specifically, appetite and energy intake depend on the coordinated function of gastric mechanisms, such as gastric motility and plasma ghrelin levels, and small intestinal processes, including pyloric motility and the secretion of gut hormones such as cholecystokinin, glucagon-like peptide-1, peptide YY, and gastric inhibitory polypeptide.

The biological mechanisms that regulate appetite and energy intake are particularly influenced by the aging process. In older adults, gastric emptying tends to be somewhat delayed, partly due to the increased frequency and amplitude of pyloric motility.[2,11] Additional physiological changes include an enlarged gastric antral area, greater antral stretch, reduced perception of gastric distension, diminished maximal gallbladder contraction, gastric atrophy, and decreased fundal compliance.[40] These alterations are often accompanied by changes in gastrointestinal motility and reduced sensitivity to gastrointestinal tract distension.[14]

Sensory decline is also common with aging, particularly in olfactory and gustatory functions, due to a reduction in both the number and structural integrity of taste buds.[15,40] Such sensory impairments may diminish the enjoyment of food and weaken sensory-specific satiety, potentially increasing the risk of micronutrient deficiencies.[31]

In parallel, aging is associated with measurable changes in appetite-regulating hormones.[3,34,43] These include lower levels of and reduced sensitivity to ghrelin, a peptide hormone that promotes appetite by acting on the arcuate nucleus of the hypothalamus and stimulating neuropeptide Y activity.[40,44]



PYY: peptide tyrosine-tyrosine; CCK: cholecystokinin; GLP-1: glucagon-like polypeptide-1; GIP: gastric inhibitory polypeptide.

FIGURE 1. A concise representation of an appetite control center complex near the arcuate nucleus of the hypothalamus and the precise coordination of interrelated gastric and small intestinal hormones.

Conversely, older adults often have increased levels of satiety-related hormones, such as cholecystokinin[45,46] glucagon-like peptide-1, peptide YY, insulin (both in fasting and postprandial states), and fasting leptin.[2] Collectively, these hormonal shifts contribute to greater satiety and reduced hunger, reinforcing the physiological basis of AA.[15] Additionally, age-related changes in thyroid function may also influence appetite. Older adults tend to present with higher serum levels of thyroid-stimulating hormone and lower levels of free thyroid hormones, which are known to stimulate appetite, particularly among men.[31] Both hypothyroidism (≤ 5% prevalence) and hyperthyroidism (0.5 – 3%) are more common in older adults than in younger populations, and their symptoms, such as unexplained weight loss, fatigue, and depression, may overlap with other age-related conditions, potentially complicating the assessment and management of appetite disturbances in this population.[31]

Taken together, these physiological and hormonal changes help explain why many older adults experience appetite loss. The combination of digestive system and hormone level changes plus sensory decline plays a key role in the decreased desire to eat with age. These findings support the idea that appetite loss is a central biological feature of AA, rather than personal habits or social factors.

Diagnostic approach to anorexia in older patients

There is currently no consensus on the specific diagnostic criteria for AA, which can complicate both research and diagnosis. According to Aprahamian et al.,[47] this lack of standardized criteria contributes to significant variability in the identification and assessment of AA across studies. They analyzed the responses of 1,545 health care providers regarding their knowledge of AA and practice gaps in identifying and managing it. Most respondents relied on their own clinical judgment and/or frailty scores to diagnose anorexia. While a large majority (82.6%) agreed or strongly agreed that regularly using standardized tools to evaluate older patients for weight loss is crucial, less than one-third reported using a validated tool or expert-developed resource. Furthermore, 16% of respondents were unaware of any such tools or resources. Alarmingly, a high proportion of health care providers seemed to believe that anorexia is a normal part of aging, which could contribute to the failure to identify or effectively treat this condition.

In clinical and research contexts, primary and secondary anorexia (ie, resulting from chronic diseases) are often grouped under a single definition. This overlap can be problematic, since AA management requires a multifaceted approach. Moreover, although various instruments exist for screening and diagnosing primary anorexia, many were originally developed to detect malnutrition or weight loss and are not formally recommended for identifying appetite-related changes.[8] Additionally, health care professionals often focus primarily on weight loss, overlooking appetite decline, which may occur earlier and serve as a warning sign.[48] Prioritizing the diagnosis and management of appetite loss may offer a more timely and cost-effective strategy for preventing further nutritional decline in older adults.

Many current tools, such as the Comprehensive Nutritional Appetite Questionnaire,[48] the Appetite, Hunger, and Sensory Perception Questionnaire,[49] the Seniors in the Community Risk Evaluation for Eating and Nutrition,[50] and the Functional Assessment of Anorexia Cachexia Therapy,[51] are time-consuming and assess multiple interrelated nutritional domains, often treating appetite as just one of many factors.[48] Selecting an appropriate tool to identify AA requires a screening instrument that is quick, simple, and can reliably identify patients at risk.[48] In this regard, the SNAQ scale meets these requirements, providing a straightforward and efficient assessment (taking approximately 3 minutes to complete).[48] The SNAQ is the first appetite-monitoring instrument specifically validated for older adults in the United States, and it has been shown to reliably identify individuals with anorexia who are at risk of subsequent weight loss.[48] It evaluates four parameters and uses a scoring system with a maximum of 20 points, where a score of ≤ 14 indicates a 5% risk of weight loss within 6 months (sensitivity: 81.3%, specificity: 76.4%).[24] The culturally adapted Brazilian Portuguese version of the SNAQ has been validated by Zukeran et al.[52]

The search for specific biomarkers, an area still in its early stages of research, is a further challenge to identifying AA. While some studies have suggested that older adults have higher fasting and postprandial concentrations of anorexigenic hormones, such as cholecystokinin, leptin, and insulin, as well as higher postprandial concentrations of peptide YY than younger adults, the effectiveness of these biomarkers in identifying AA has not been fully validated.[53] Although these biomarkers play a role in appetite regulation, they represent only one aspect of a complex system governing feeding behavior. Other factors, such as inflammatory mediators and microorganisms associated with gut dysbiosis, may also contribute to the observed changes in appetite and energy intake.[53] Examples of these mediators include cytokines such as interleukin-1, interleukin-6, tumor necrosis factor alpha, and growth differentiation factor-15, a member of the transforming growth factor-beta family.

Although subjective tools like the SNAQ provide a practical means of identifying AA, the exploration of

biomarkers remains a crucial area for future research. Combining both approaches could enhance early detection and management of AA, although further research is necessary to confirm the effectiveness of specific biomarkers.

Treatment of anorexia of aging

Few publications have addressed AA treatment, reflecting the early stage of research in this area and the inherent challenges of modulating metabolism to stimulate appetite. A recent international survey involving researchers from Japan, Brazil, Australia, Switzerland, and Germany explored current gaps in clinical knowledge and practice regarding AA diagnosis and management, finding that the most common interventions included treating swallowing disorders (78%), pathological or dysfunctional dentition (76%), adding energy- and protein-dense foods to the diet (75%), and recommending oral nutritional supplements (74%).[47]

Based on clinical experience, 5 standard management strategies are advised for AA:

1. Assessing underlying conditions and medications that could contribute to anorexia;
2. Considering consultation with a dietitian as a fundamental component of care;
3. Optimizing the meal environment to support food intake (eg, a quiet space with pleasant lighting and a socially engaging atmosphere);
4. Accounting for personal food preferences, even in the context of dietary restrictions — especially in severe cases; and
5. Considering flavor enhancers and fortified foods to improve food intake (Figure 2).

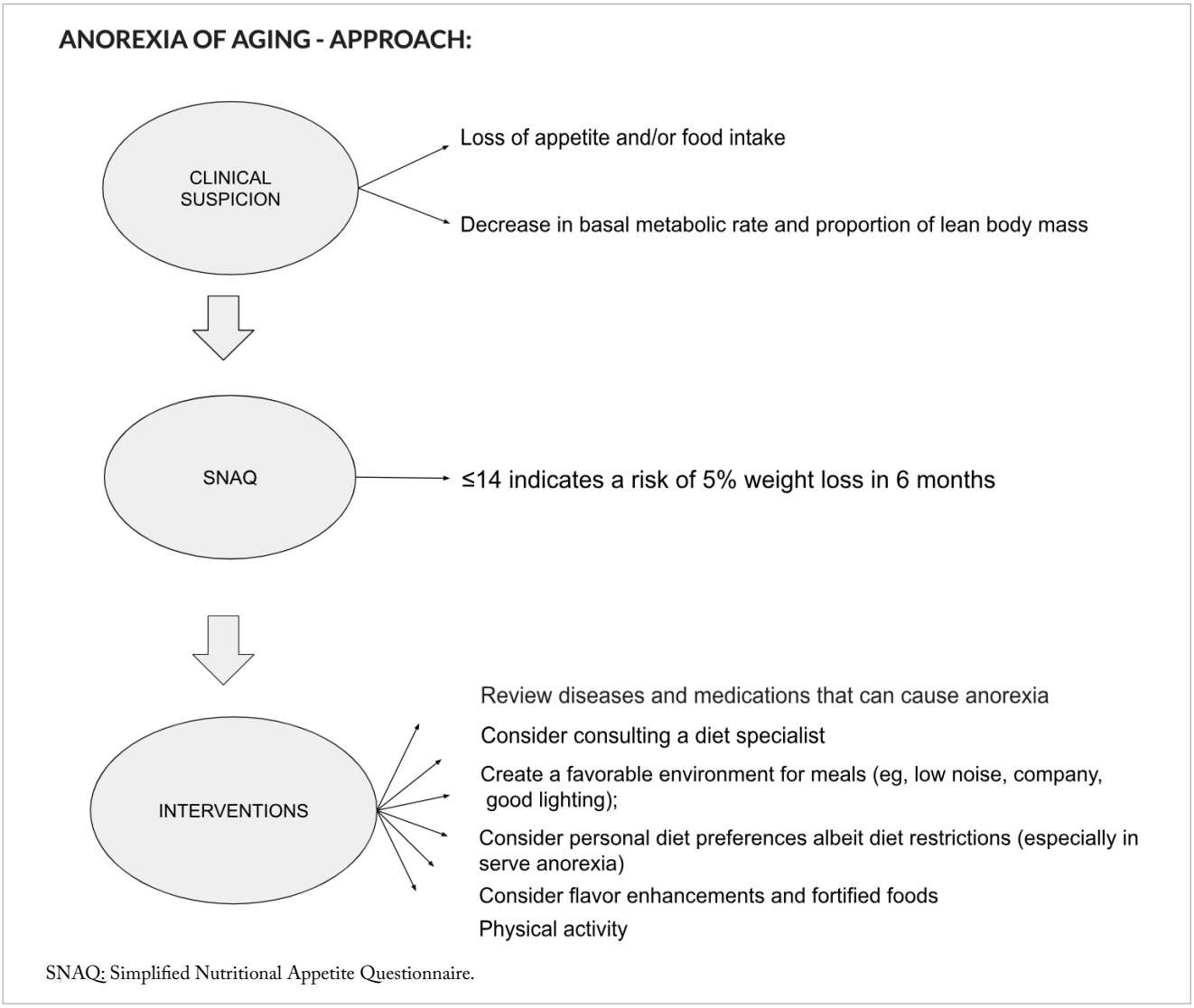


FIGURE 2. A clinical algorithm to access anorexia of aging.

A limited number of studies have examined the efficacy of nutritional interventions in managing AA. A systematic review of 18 studies reported inconclusive results, primarily due to methodological heterogeneity and inconsistent definitions of AA.[8] Interventions were classified into 9 categories, including nutritional counseling, exercise, meal adjustments (eg, flavor enhancement, variety), supplementation (eg, oral nutritional supplements, fortified foods, amino acid precursors), and pharmacological agents such as megestrol acetate. Of these, only 5 categories showed modest positive effects on appetite, particularly flavor enhancement, oral nutritional supplements, fortified foods, and megestrol acetate.[8] Flavor enhancers improved food palatability and partially mitigated the age-related decline in sensory perception. However, the quality of evidence was low, limiting clinical recommendations. While exercise did not have consistent effects on appetite,[54] methodological issues, such as poor adherence reporting, may have contributed to these findings. Considering that exercise can induce metabolic stimulation, it is still regarded as a beneficial adjunct therapy when feasible.

A previous systematic review and meta-analysis evaluated the effectiveness of oral nutritional supplements in older adults with AA, reporting beneficial effects on overall appetite, energy intake, body weight, and body mass index.[55] Based on clinical experience, however, oral nutritional supplements composed solely of protein substrates are not recommended, as protein is the most satiating macronutrient and may suppress appetite.[56] It is also advisable to administer supplements between meals, rather than as meal replacements, to avoid interfering with pre-meal appetite. The physical form of the supplement is another relevant factor; solids, such as protein-enriched cookies, may offer sensory stimulation (visual, olfactory, tactile, and gustatory) that positively influences appetite. Enhancing food presentation, including color and plating, may further contribute to improved intake.[55]

The type and form of protein supplementation also warrant attention. Evidence from 5 studies suggests that whey protein, whether incorporated into whole foods, gels, or bars, can greatly increase energy intake in older adults.[56-59] Whey, typically delivered in liquid form, appears to lower the appetite less than solids and is rich in leucine, an amino acid critical to muscle protein synthesis.[56] Conversely, certain compounds, such as polydextrose, have been shown to reduce appetite and should be avoided in individuals with AA.[55]

There is currently no established pharmacological treatment targeting specific biological pathways related to appetite in older adults. Although some experimental approaches have explored modulating neuroendocrine control (such as cholecystokinin inhibitors and ghrelin analogues, including the ghrelin-receptor agonist anamorelin) these interventions remain limited. Anamorelin, for instance, is approved in some countries for cancer cachexia but has not been specifically studied for AA.[60] Despite limited evidence, pharmacological interventions are still frequently employed in clinical practice. However, caution is recommended, given the low or very low quality of available data.[8] The efficacy of pharmacological approaches in AA remains inadequately supported and inconclusive. The most commonly prescribed agents include megestrol acetate, cannabinoids, olanzapine, mirtazapine, and cyproheptadine. Although megestrol acetate, a synthetic progestin, was previously found efficacious for anorexia and weight loss related to AIDS[61] and cancer,[62] a recent systematic review and meta-analysis did not confirm this effect.[63] The use of megestrol acetate for AA is not well supported either. A single trial involving older adults after hospitalization found no significant benefits,[64] and its use is associated with adverse effects, such as fluid retention, adrenal suppression, and increased thromboembolic risk. For these reasons, we do not recommend using megestrol acetate in this context. Dronabinol, a synthetic agonist of delta-9-tetrahydrocannabinol, has been approved for anorexia in patients with AIDS[65] and has also been used in cancer cachexia. Two small trials reported weight gain after 6-12 weeks in older adults residing in long-term care facilities and in individuals with Alzheimer's disease.[66,67] However, given the limited evidence and our clinical experience, the appetite-stimulating potential of delta-9-tetrahydrocannabinol or cannabidiol in older adults remains uncertain.

To date, no published studies have directly evaluated the effects of olanzapine, mirtazapine, or cyproheptadine specifically in AA. Olanzapine, an antipsychotic that antagonizes multiple serotonergic, dopaminergic, histaminergic, adrenergic, and cholinergic receptors, may increase appetite. Nevertheless, we suggest its use only at low doses (eg, 2.5 mg) and in severe cases of AA associated with depression or dementia, due to its adverse event profile. Similarly, mirtazapine, an antidepressant with strong antihistamine properties, particularly at lower doses (7.5 – 15 mg), may be beneficial in cases of AA accompanied by depressive symptoms.

Cyproheptadine, a weaker serotonergic and histaminergic antagonist, is occasionally prescribed at doses of 4-8 mg 3 times daily in some European countries.[52] However, it should be used with caution in older adults due to potential side effects such as dizziness, confusion, and somnolence. We consider it a last-resort option after other strategies

have failed. Anabolic agents such as nandrolone decanoate may also be considered, particularly when endocrine dysfunction is involved. Nevertheless, clinicians must weigh the benefits against risks, such as fluid retention, liver toxicity, and prostatic hypertrophy.

Another compound prescribed in clinical practice is megestrol. However, it has only been studied in 1 trial of older adults with anorexia after hospitalization, showing non-significant results.[62] Given the very low evidence, we do not recommend megestrol due to its high risk of edema, adrenal suppression, and thromboembolism.

In summary, thorough nutritional counseling, nutritional supplementation, and individualized dietary interventions remain the cornerstone of AA management, along with the potential role of physical activity. Pharmacological treatment may be considered in specific situations but it should be guided by careful clinical judgment due to the current lack of robust evidence and the risks associated with polypharmacy in older adults.[8] Narrative reviews may be subject to selection and publication bias and may omit relevant studies. The lack of quantitative synthesis precludes precise effect size estimation and formal heterogeneity assessment, while the search strategy, defined by the databases and keywords, may have excluded pertinent literature.

CONCLUSION

AA is a prevalent yet under-recognized condition associated with adverse outcomes in older adults, including malnutrition, sarcopenia, frailty, and increased mortality risk. This review provides a summary of the main data available in the literature, although we could not determine the level of evidence or strength of recommendations, making it difficult to distinguish robust findings from preliminary data.

Early identification of reduced appetite may help prevent these negative health consequences. Therefore, this review reinforces the topic's implications and relevance for clinical practice. From a clinical perspective, it is essential to actively inquire about changes in appetite among older individuals, ideally using validated tools such as the SNAQ.

Given the multifactorial nature of AA, further research is needed to refine diagnostic strategies and establish effective, evidence-based interventions. The development of standardized diagnostic criteria and the evaluation of long-term clinical outcomes should be prioritized. Randomized clinical trials are particularly needed to assess the safety and efficacy of both nutritional and pharmacological treatments. In parallel, enhancing awareness and education among health care professionals may improve early detection and management of this condition in routine care.

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Conflict of interest
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Authors' contributions
Renata Pinheiro Cavallaro de Oliveira: conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing – original draft, writing – review & editing. Marcella Nora Maia: conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing – original draft, writing – review & editing. Gabriela Cipolli: data curation, formal analysis, methodology, project administration, supervision, validation, visualization, writing – review & editing. Shirley Steffany Munoz Fernandez: data curation, formal analysis, supervision, validation, visualization, writing – review & editing. Mariana Barbosa Girotto: formal analysis, investigation, visualization. Andréia Pain: conceptualization, formal analysis, supervision, validation, visualization, writing – review & editing. Virgílio Garcia Moreira: conceptualization, formal analysis, supervision, validation, visualization, writing – review & editing. Ivan Aprahamian: conceptualization, formal analysis, methodology, project administration, supervision, validation, visualization, writing – review & editing.

Ethical approval and informed consent
Not applicable.

Data availability statement
Not applicable.

Reporting standards guidelines
None of the standard guidelines are applicable. The Manuscript Compliance Form is attached.

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