population and is not only the result of aspiration pneumonia, but also an important cause of recurrent aspiration pneumonia. Because primary and secondary sarcopenia often coexist in people with disability, rehabilitation nutrition can be used to improve their functionality (Fig. 1). Further studies on rehabilitation nutrition are important in a rapidly aging society, where the number of elderly with disability is expected to increase.

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Conflict of interest Hidetaka Wakabayashi and Kunihiro Sakuma declare that they have no conflict of interest.

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原著

摂食嚥下障害スクリーニング質問紙票EAT-10の日本語版作成と信頼性・妥当性の検証 *

keywords：EAT-10、感度、特異度

若林秀隆[1)]　Hidetaka WAKABAYASHI　栢下　淳[2)] Jun KAYASHITA

◆横浜市立大学附属市民総合医療センターリハビリテーション科[1)]
県立広島大学大学院総合学術研究科人間文化学専攻栄養科学研究分野[2)]
Department of Rehabilitation Medicine, Yokohama City University Medical Center[1)]
Culture and Science, Department of Health Sciences, Prefectural University of Hiroshima[2)]

【目的】摂食嚥下障害スクリーニング質問紙票であるEAT-10の日本語版を作成し、信頼性・妥当性を検証する。【対象及び方法】EAT-10英語版の順翻訳、逆翻訳、英語原版と逆翻訳の整合性の検討を行い、EAT-10日本語版を作成した。次に摂食嚥下障害もしくは摂食嚥下障害疑いの要介護高齢者393人を対象にEAT-10日本語版を実施した。信頼性を内的整合性であるクロンバッハのα係数で、妥当性を臨床的重症度分類とスペアマンの順位相関係数でそれぞれ検討した。【結果】EAT-10日本語版を実施できたのは237人(60%)であった。クロンバッハのα係数は0.946であった。EAT-10を実施できない場合、摂食嚥下障害と誤嚥を有意に多く認めた。EAT-10と臨床的重症度分類に有意な負の相関(r=-0.530、p<0.001)を認めた。EAT-10で3点以上の場合、誤嚥の感度0.758、特異度0.749であった。【結論】EAT-10日本語版の信頼性・妥当性が検証された。EAT-10日本語版は、摂食嚥下障害スクリーニングに有用な質問紙票である。

【目的】

栄養管理で目標とする投与ルートは、経口摂取である。経口摂取を目指す上で、摂食嚥下障害の存在は大きな問題となる。摂食嚥下障害に適切に対応しないと誤嚥性肺炎、窒息、低栄養、脱水といった生命に関わる合併症だけでなく、食べる楽しみの喪失も生じる。そのため、適切な摂食嚥下機能の評価が大切である。

摂食嚥下障害のスクリーニングには、水飲みテスト、食物テスト、反復唾液嚥下テストといったスクリーニングテストだけでなく、質問紙票がある。2002年に大熊らは、15項目の質問で構成される嚥下障害スクリーニングの質問紙を開発した[1)]。この質問紙は、肺炎の既往、栄養状態、口腔・咽頭・食道機能、声門防御機構などが反映される構造で、「A＝重い症状」、「B：軽い症状」、「C：症状なし」の3段階で回答する。「Aの回答あり」を嚥下障害ありと考えると、特異度90.1%、感度92%といずれも高く、摂食嚥下障害のスクリーニングに有用である。

一方、2008年にBelafskyらはEating Assessment Tool-10(以下、EAT-10と略)を開発した[2)]。EAT-10は10項目の質問で構成され、それぞれ5段階(0点：問題なし、4点：ひどく問題)で回答し、合計点数が3点以上であれば異常と判定する。クロンバッハのα係数は0.960と高く、信頼性および基準関連妥当性が検証された。

海外ではスペイン語への翻訳とその妥当性について報告されている[3)]。近年、国際的に摂食嚥下障害の臨床研究で使用されつつある[4)~7)]。一方、日本語版の作成、報告はされていない。本研究の目的は、EAT-10の日本語版を作成して、その信頼性と妥当性を検証することである。

Translation, reliability, and validity of the Japanese version of the 10-item Eating Assessment Tool (EAT-10) for the screening of dysphagia.

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【対象及び方法】

1.EAT-10日本語版の作成

第1段階として、著者らで協議の上、EAT-10英語版から日本語のEAT-10順翻訳版を作成して、予備テストを実施した。第2段階として、EAT-10の使用権を有するネスレ日本株式会社で専門家のチェックを受けた後、日本語のEAT-10順翻訳版を英語に逆翻訳した。第3段階として、英語原版と逆翻訳版の整合性を検討し、順翻訳版を修正した。第4段階として、予備テストを再度行い、EAT-10日本語版を完成させた。

2.信頼性・妥当性の検証

次に、完成した日本語版EAT-10(イート・テン)(以下、単にEAT-10と略)を実際の患者で実施し、その信頼性と妥当性を検証した。対象は、摂食嚥下障害もしくは摂食嚥下障害疑いの要介護高齢者とした。取り込み基準は、2012年8月から12月に摂食嚥下障害もしくは摂食嚥下障害疑いを認める65歳以上の要介護高齢者とした。除外基準は設定しなかった。信頼性は、内的整合性であるクロンバッハの α 係数で検証した。

妥当性は、臨床的重症度分類(Dysphagia Severity Scale、以下DSSと略)との比較で基準関連妥当性を検証した。DSSは、摂食嚥下障害の重症度を7段階(7:正常範囲、6:軽度問題、5:口腔問題、4:機会誤嚥、3:水分誤嚥、2:食物誤嚥、1:唾液誤嚥)で評価する重症度分類である[8]。DSSが軽度問題以下(6:軽度問題、5:口腔問題、4:機会誤嚥、3:水分誤嚥、2:食物誤嚥、1:唾液誤嚥のいずれかの場合)であれば摂食嚥下障害あり、機会誤嚥以下(4:機会誤嚥、3:水分誤嚥、2:食物誤嚥、1:唾液誤嚥のいずれかの場合)であれば誤嚥ありと判断した。臨床で摂食嚥下障害に関わり対象者を担当している医療職が、臨床場面の観察からDSSで摂食嚥下機能を評価した。医療職がDSSを評価した後に、対象者がEAT-10を実施した。つまり、EAT-10の点数を考慮せずにDSSで評価した。

EAT-10の実施の可否とDSSの関連をカイ2乗検定で、EAT-10を実施できた場合の得点とDSSの関連をスペアマンの順位相関係数でそれぞれ検討した。次にEAT-10とDSSで軽度問題以下(摂食嚥下障害の有無)および機会誤嚥以下(誤嚥の有無)のReceiver Operating Characteristic 曲線(以下、ROC曲線と略)を作成した。また、DSSのカットオフ値を軽度問題以下、機会誤嚥以下とした場合の、EAT-10の実施困難時と3点以上の感度、特異度を検討した。

すべての統計学的解析で危険率を α=0.05とした。統計ソフトはSPSS20.0を使用した。倫理的配慮として、当院倫理審査委員会の承認を取得し、被験者には文書で同意を得た。

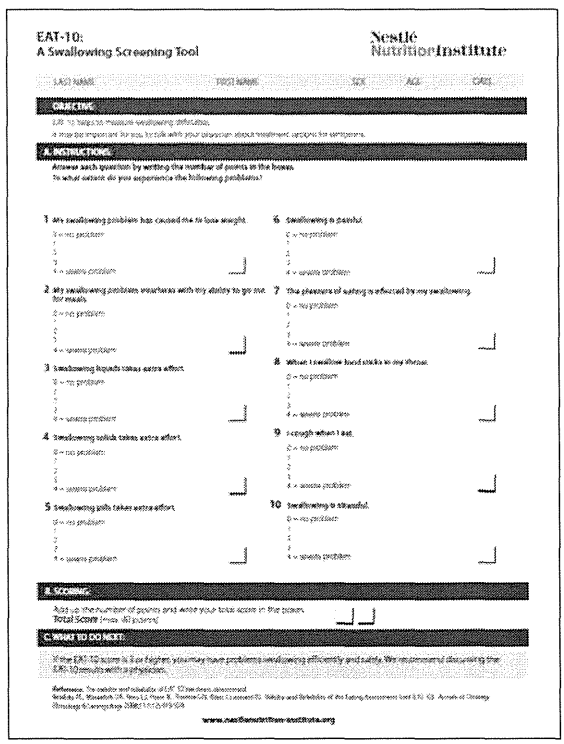
【結果】

1.EAT-10日本語版の完成

翻訳・逆翻訳の整合性の工程および予備テストを2回行い、日本語版の翻訳を完成させた。EAT-10英語版を図1に、EAT-10日本語版を図2にそれぞれ示す。

2.信頼性・妥当性

2012年8月から12月に調査を実施できた対象者は393人であった。平均年齢は83歳、男性130人、女性263人。セッティングは老人保健施設200人、急性期病院67人、


EAT-10:
A Swallowing Screening Tool

Nestlé NutritionInstitute

図1 EAT-10英語版

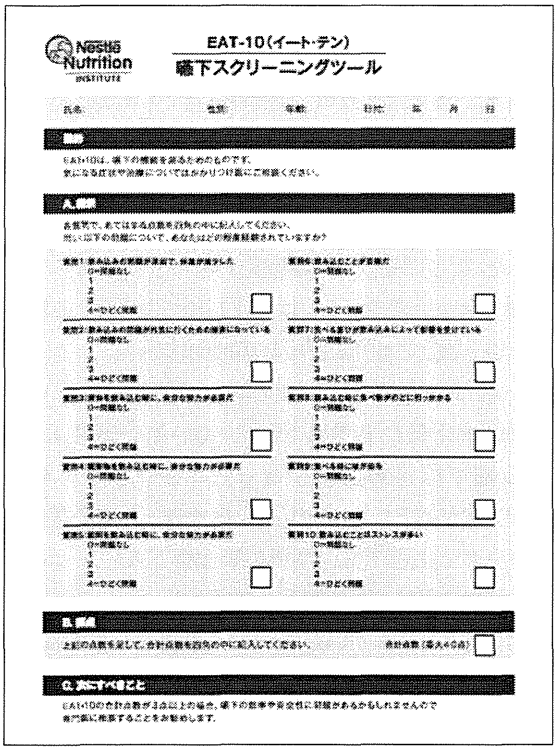

EAT-10(イート・テン)
嚥下スクリーニングツール

図2　EAT-10日本語版

在宅126人。主な疾患は脳血管障害216人、心不全68人、慢性肺疾患(慢性閉塞性肺疾患、気管支喘息、肺気腫、間質性肺炎など) 44人、パーキンソン病38人、悪性腫瘍23人であった(重複あり)。介護度は要支援1：4人、要支援2：15人、要介護1：32人、要介護2：33人、要介護3：51人、要介護4：107人、要介護5：124人、未申請27人。DSSは正常範囲82人、軽度問題86人、口腔問題53人、機会誤嚥59人、水分誤嚥50人、食物誤嚥38人、唾液誤嚥25人であった。

表1　EAT-10の実施可否とDSS軽度問題以下のクロス集計表

	DSS軽度問題以下	DSS正常範囲
EAT-10実施不可	152	4
EAT-10実施可能	159	78

カイ2乗52.5、p<0.001
感度：152÷(152+159) =0.489、特異度：78÷(4+78) =0.951

表2　EAT-10の実施可否とDSS機会誤嚥以下のクロス集計表

	DSS機会誤嚥以下	DSS口腔問題以上
EAT-10実施不可	110	46
EAT-10実施可能	62	175

カイ2乗75.2、p<0.001
感度：110÷(110+62) =0.640、特異度：175÷(46+175) =0.792

EAT-10を実施できたのは393人中237人(60%)であった。信頼性の検討では、クロンバッハの α 係数は0.946であった。妥当性の検討では、EAT-10を実施できなかった場合、軽度問題以下および機会誤嚥以下の摂食嚥下障害が有意に多かった(**表1、表2**)。EAT-10を実施できなかった場合の感度、特異度を表1、表2より計算すると、軽度問題以下で感度0.489、特異度0.951、機会誤嚥以下で感度0.640、特異度0.792であった。軽度問題以下の特異度が高く、EAT-10を実施できない場合、軽度問題以下の嚥下障害を認める可能性が高い。

次に、EAT-10を実施できた237人でDSSとの関連を検討した。平均年齢82歳、男性90人、女性147人。DSSは正常範囲78人、軽度問題64人、口腔問題33人、機会誤嚥29人、水分誤嚥26人、食物誤嚥3人、唾液誤嚥4人であった。EAT-10は、3点以上が101人、2点以下が136人で、中央値は1点(25パーセンタイル0点、75パーセンタイル9点)であった。

EAT-10とDSSに有意な負の相関(r=-0.530、p<0.001)を認めた。EAT-10とDSSで軽度問題以下および機会誤嚥以下のROC曲線を**図3、図4**に示す。機会誤嚥以下の場合、EAT-10で3点以上をカットオフ値としたときに、ROC曲線が左上隅に最も近かった。EAT-10を実施できた場合、EAT-10で3点以上の感度、特異度、ROC曲線下面積は、軽度問題以下で感度

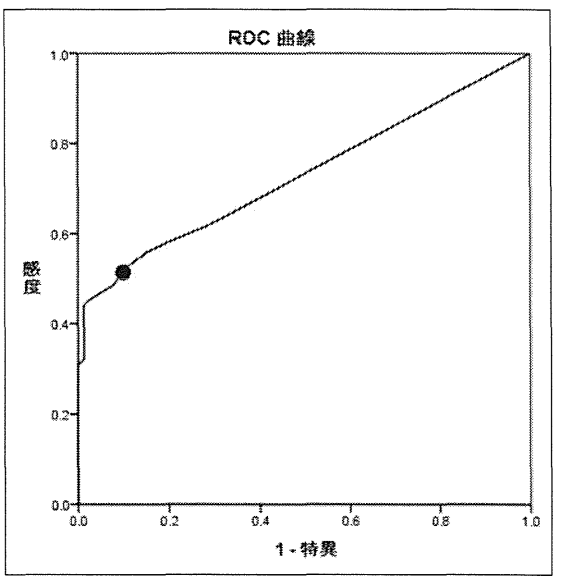


図3　EAT-10とDSS軽度問題以下のROC曲線
黒丸はEAT-10が3点以上の場合の感度・特異度

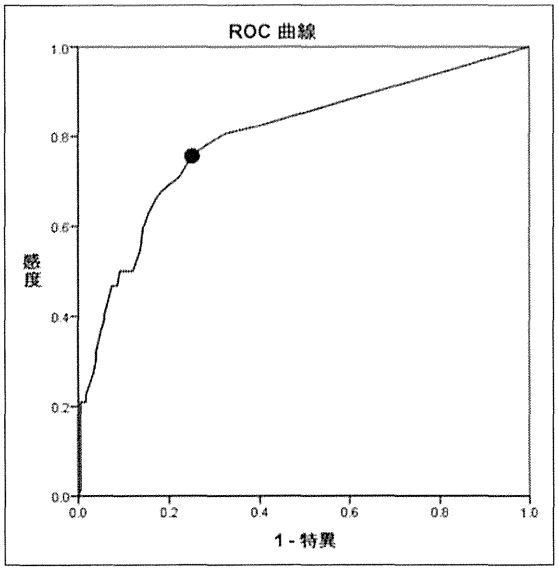


図4　EAT-10とDSS機会誤嚥以下のROC曲線
黒丸はEAT-10が3点以上の場合の感度・特異度

0.522、特異度0.897、ROC曲線下面積0.730、機会誤嚥以下で感度0.758、特異度0.749、ROC曲線下面積0.797であった。軽度問題以下の特異度が高く、EAT-10を実施できて3点以上の場合、軽度問題以下の嚥下障害を認める可能性が高い。

【考察】

海外で開発された質問紙票を日本語に翻訳する際には、順翻訳、逆翻訳、英語原版と逆翻訳の整合性の検討が必要である。この手順を踏んでEAT-10日本語版を作成した。

信頼性の検定では、クロンバッハの α 係数は0.946と、EAT-10英語版の0.960と同様に高い値を示した。クロンバッハの α 係数は0.8以上であれば内的整合性が良好とされており、内的整合性の高いことが検証された。ただし、クロンバッハの α 係数が0.9以上と高すぎる場合、同じことを尋ねている質問項目が多く、いくつかの質問項目は不必要である[9]。そのため、質問項目を少なくしたEAT-10の改訂版を作成できる可能性がある。

妥当性の検定では、EAT-10とDSSに有意な負の相関を認め、基準関連妥当性が検証された。機会誤嚥以下では、EAT-10で3点以上のときにROC曲線が左上隅に最も近くなった。つまり、3点以上が誤嚥の有無を判定するカットオフ値として適当であることが示された。

質問紙票は認知症や失語症などを認める場合、実施困難なことが少なくない。今回の研究でも実施できたのは60%のみであった。しかし、EAT-10を実施できなかった場合に摂食嚥下障害を認めることが多く、EAT-10の実施可否が摂食嚥下障害スクリーニングとなることが示された。軽度問題以下の特異度が高いため、EAT-10を実施できない場合もしくはEAT-10で3点以上の場合、摂食嚥下機能に問題を認める可能性が高い。

一方、EAT-10で2点以下の場合、軽度問題以下の感度が0.522と低く、摂食嚥下障害がないとは判断しにくい。摂食嚥下障害の認識がまったくない患者の場合、EAT-10は0点となる。そのため、摂食嚥下障害の認識がない患者では、質問紙票以外の摂食嚥下スクリーニングの実施や食事場面の観察が必要である。

本研究には限界がいくつかある。最初にEAT-10日本語版を2回実施する再テスト法で信頼性を検討していない。本研究ではEAT-10を2回実施することは困難であり、クロンバッハの α 係数で信頼性を検証した。しかし、要介護高齢者が対象者であり、再テスト法による信頼性は高くない可能性がある。今後、再テスト法による信頼性の検証が求められる。

次に摂食嚥下機能を嚥下造影検査ではなく、DSSという臨床場面の観察からの評価を用いた点である。今回の対象者は老人保健施設や在宅の要介護高齢者が多く、全員に嚥下造影検査を実施することは困難であった。摂食嚥下障害のゴールドスタンダードは嚥下造影検査であり、嚥下造影検査とEAT-10日本語版で妥当性を検証することが望ましい。しかし、臨床目的で嚥下造影検査を実施した方のみを研究対象とすると、摂食嚥下障害のない場合には当然、嚥下造影検査を実施しない。そのため、対象者のほぼ全員に摂食嚥下障害を認めることになり、妥当性の検証が難しい。一方、研究目的で摂食嚥下障害のない方に嚥下造影検査を実施することには、被曝による倫理的な問題がある。以上より、今回は臨床場面の観察によるDSSで、EAT-10日本語版の妥当性を検証した。

【結論】

EAT-10日本語版を作成し、信頼性・妥当性が検証された。EAT-10日本語版は、摂食嚥下障害スクリーニングに有用な質問紙票である。EAT-10を実施できない場合もしくはEAT-10で3点以上の場合、摂食嚥下機能に問題を認める可能性が高い。

本研究は厚生労働科学研究費(H24-長寿-一般-003：地域・在宅高齢者における摂食嚥下・栄養障害に関する研究—特にそれが及ぼす在宅療養の非継続性と地域における介入・システム構築に向けて. 研究代表者：葛谷雅文)の助成を受けた。本論文の一部は、第50回日本リハビリテーション医学会学術集会(東京、2013年6月)にて発表した。

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Translation, reliability, and validity of the Japanese version of the 10-item Eating Assessment Tool (EAT-10) for the screening of dysphagia.

Keywords : EAT-10, sensitivity, specificity

Hidetaka WAKABAYASHI[1)] Jun KAYASHITA[2)]

Objective: The 10-item Eating Assessment Tool (EAT-10) is specifically designed to address the clinical need for a rapidly self-administered and easily-scored questionnaire to assess dysphagia symptom severity. An EAT-10 score above 3 is abnormal and indicates the presence of swallowing difficulties. We translated the EAT-10 into Japanese, and studied the reliability and validity of the Japanese version of the EAT-10.

Method: Translation of EAT-10 was implemented in iterative process including forward translation, expert panel back-translation, and pre-testing. A cross-sectional study was performed in 393 elderly aged 65 years and above with dysphagia or suspected dysphagia. Severity of dysphagia was assessed by the Dysphagia Severity Scale (DSS). For assessment of reliability, we used Cronbach' s alpha coefficient. Validity was evaluated by examining the associations between the EAT-10 score and the DSS by Spearman's rank correlation coefficient. The sensitivity and specificity of the EAT-10 for dysphagia were also assessed.

Results: A total of 237 patients (60%) responded to the EAT-10. Cronbach' s alpha coefficient was 0.946. Elderly who could not respond to the EAT-10 were likely to have dysphagia. Median EAT-10 score of 237 respondents was 1 (0, 9), and 101 respondents were more than 3. There were significant correlations between the EAT-10 score and the DSS ($r=-0.530$、$p<0.001$). The sensitivity and specificity of EAT-10 with a score 3 or above for dysphagia were 0.522 and 0.897, for dysphagia with aspiration were 0.758 and 0.749, respectively.

Conclusion: The Japanese version of the EAT-10 is a useful swallowing screening tool.

Department of Rehabilitation Medicine, Yokohama City University Medical Center[1)]

Faculty of Human Culture and Science, Department of Health Sciences, Prefectural University of Hiroshima[2)]

Nutrition, Exercise, and Pharmaceutical Therapies for Sarcopenic Obesity

Hidetaka Wakabayashi[1,*] and Kunihiro Sakuma[2]

[1]*Department of Rehabilitation Medicine, Yokohama City University Medical Center, 1 4-57 Urafune-Chou, Minami ward, Yokohama City, 232-0024, Japan*

[2]*Research Center for Physical Fitness, Sports and Health, Toyohashi University of Technology, 2 1-1 Hibarigaoka, Tenpaku-Cho, Toyohashi, 441-8580, Japan*

Abstract: Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass and strength, with a risk of adverse outcomes such as physical disability, poor quality of life, and death. Sarcopenic obesity is defined as having both sarcopenia and obesity, a condition reported to be associated with a higher risk for adverse outcomes including functional disability, frailty, poor quality of life, longer hospitalization, and higher mortality rates. The definition and diagnostic criteria for sarcopenia have been described by several working groups on the disease; however, there is no standardized definition and diagnostic criteria for sarcopenic obesity. In this review, we summarize nutrition, exercise, and pharmaceutical therapies for counteracting sarcopenic obesity in humans. Although there are some pharmaceutical therapies for both sarcopenia (i.e., testosterone, growth hormone, ghrelin, and vitamin D) and obesity (orlistat, lorcaserin, phentermine-topiramate, and vitamin D), therapies combining nutrition and exercise remain the first-line choice for preventing and treating sarcopenic obesity. Resistance training combined with supplements containing amino acids are considered most effective for treating sarcopenia. Low-calorie, high-protein diets combined with aerobic exercise and resistance training are recommended for preventing and treating obesity. Therefore, nutrition therapies (low-calorie, high-protein diets, protein and amino acid supplementation) and exercise therapies (resistance training and aerobic exercise) would be expected to be the most effective option for preventing and treating sarcopenic obesity. In cases of severe sarcopenic obesity or failure to achieve muscle gain and weight loss through nutrition and exercise therapies, it is necessary to add pharmaceutical therapies to treat the condition.

Keywords: Sarcopenia, overweight, protein, low-calorie diets, resistance training.

1. INTRODUCTION

The term sarcopenia was used by Rosenberg to describe an age-related decrease in muscle mass, and originated from the Greek words sarx (flesh) and penia (loss) [1, 2]. This term was applied initially to denote loss of muscle mass. In 2010, the European Working Group on Sarcopenia in Older People described sarcopenia as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength, associated with a risk of adverse outcomes such as physical disability, poor quality of life, and death [3]. In 2011, the International Working Group on Sarcopenia defined the disease as an "age-associated loss of skeletal muscle mass and function". Sarcopenia is a complex syndrome that is associated with muscle mass loss alone or in conjunction with increased fat mass. The causes of sarcopenia are multi-factorial and can include disuse, changing endocrine function, chronic diseases, inflammation, insulin resistance, and nutritional deficiencies. While cachexia may be a component of sarcopenia, the two conditions are not the same [4]." Decreased muscle strength and physical function are now also included in the definition of sarcopenia. Developing sarcopenia treatment is very important, with nutrition and exercise therapies and several potential targets for pharmacological interventions having been identified as possible treatment options [5-7].

Sarcopenic obesity is defined as having both sarcopenia and obesity. Heber *et al.* [8] proposed a clinical definition of sarcopenic obesity as obese patients with the lowest tertile of fat-free mass estimated by bioelectrical impedance analysis. Obesity is defined as people with a body mass index (BMI) of 30 kg/m^2 or greater, while those with a BMI between 25 and 29.9 kg/m^2 were classified as overweight. The causes of sarcopenic obesity are multi-factorial and can include factors such as lifestyle (diet, physical activity, and smoking), endocrine (corticosteroids, growth factors, insulin, and catecholamines), vascular (endothelial function and coagulation), and immunology (inflammation and reactive oxygen species) [9].

The prevalence of sarcopenic obesity in elderly individuals is estimated to range between 2.75% to 19.8% [9]. The diagnostic criteria for sarcopenic obesity have varied considerably between studies. For example, sarcopenic obesity was classified as

*Address correspondence to this author at the Department of Rehabilitation Medicine, Yokohama City University Medical Center, 4-57 Urafune-chou, Minami ward, Yokohama city, 232-0024, Japan; Tel: +81-45-261-5656; Fax: +81-45-253-9955; E-mail: noventurenoglory@gmail.com

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appendicular skeletal muscle with a value lower than 2 standard deviations from that measured in the healthy population, and a fat mass greater than the 60th percentile of an age-matched population [10, 11]. Another study classified sarcopenic obesity as cases with a percentage body fat in the upper two quintiles and a relative muscle mass in the lower two quintiles [12]. Muscle mass and fat mass are assessed by several methods including BMI, mid-upper arm circumference, bioelectrical impedance analysis, dual energy X-ray absorptiometry, and computer tomography [2]. However, there is no standardized definition and diagnostic criteria for sarcopenic obesity.

Sarcopenic obesity is associated with adverse health effects such as physical disability, cardiovascular disease risk, and death [10, 11, 13, 14]. The relative risk (RR) for incident disability in obese sarcopenic subjects was reported to be 2.63 (95% confidence interval (CI), 1.19 to 5.85) after adjustment for age, sex, physical activity level, length of follow-up, and prevalent morbidity in the elderly [10]. Significantly higher odds ratios (ORs) for difficulty climbing stairs (OR, 2.45; 95% CI 0.99 to 6.04), going down stairs (OR, 3.41; 95% CI, 1.35 to 8.57), or rising from a chair or bed (OR, 2.89; 95% CI, 1.01 to 8.30) were observed more frequently in women with sarcopenic obesity than in women with sarcopenia alone [11]. Cardiovascular disease risk was also reported to be increased by 23% (95% CI, 0.99 to 1.54) in a sarcopenic-obese group in community-dwelling elderly subjects [12]. In addition, sarcopenic obesity was found to be an independent predictor of survival (hazard ratio (HR), 4.2; 95% CI, 2.4 to 7.2) in patients with solid tumors of the respiratory and gastrointestinal tracts [13]. In contrast, other studies found no association between sarcopenic obesity and functional limitations [12, 15]. Despite these inconsistent findings between studies, sarcopenic obesity is regarded as an important current and future public health issue.

Numerous interventional studies for sarcopenia and obesity treatment have been performed. However, a literature search we conducted showed there are no intervention studies for sarcopenic obesity in humans. Therefore, it is necessary to make inferences from separate intervention studies on sarcopenia and obesity. In this review, we first review nutrition, exercise and pharmaceutical therapies used to treat sarcopenia and obesity in humans, and then summarize a comprehensive approach for inhibiting sarcopenic obesity.

2. NUTRITION THERAPIES

2.1. Nutrition Therapies for Sarcopenia

Protein and amino acid supplementation can counteract sarcopenia, as low protein intake is known to be associated with declining muscle mass in older adults [16]. A Cochrane Database of Systematic Review found that protein and energy supplementation produced a small but consistent weight gain of 2.2% in older people (95% CI, 1.8 to 2.5), while mortality may be reduced in older people who are undernourished (RR, 0.79; 95% CI, 0.64 to 0.97) [11]. However, that review found no evidence of a reduction in the length of hospital stay with supplementation (-0.8 days; 95% CI, -2.8 to 1.3) [17]. A recent systematic review on the effectiveness of nutritional supplementation on muscle mass in the treatment of sarcopenia in old age also confirmed an improvement in muscle mass and muscle strength [18]. Many essential acids including large amounts of leucine are needed to effectively counteract sarcopenia [6].

Consuming sufficient energy is important, as loss of muscle mass can be a result of calorie restriction or starvation. Biolo *et al.* [19] investigated the effects of the interaction of inactivity and calorie restriction on whole-body composition and protein kinetic regulation in nine healthy volunteers. Lean body mass was measured using dual-energy X-ray absorptionometry before and at the end of 14-day periods of bed rest and controlled ambulation in subjects receiving either a hypocaloric (approximately 80% of total energy expenditure) or normal diet. During the eucaloric period, lean body mass decreased −0.1 ± 0.1 kg during ambulatory conditions and −0.3 ± 0.2 kg with bed rest. During the hypocaloric periods, lean body mass decreased −0.3 ± 0.3 kg during ambulatory conditions and −1.1 ± 0.1 kg with bed rest ($p < 0.01$ for activity effect; $p = 0.04$ for diet effect; $p = 0.03$ for interaction). These results indicate that physical inactivity under conditions of negative energy balance may lead to a rapid loss of lean body mass, and that such a catabolic effect can be prevented, at least in the short term, by a moderate level of physical activity. Evidence from other studies also suggests that maintaining protein intake during a period of disuse attenuates disuse atrophy [20], with 91% of patients with the disuse syndrome being classified as malnourished [21]. Maintaining energy and protein intake and physical activity is therefore important for preventing sarcopenia.

Because both resistance training and protein supplementation are effective treatments for sarcopenia, resistance training combined with supplements containing amino acids would be expected to be the most effective option for preventing and treating age-related muscle wasting and weakness [5-7]. Kim *et al.* [22] found that the combination of exercise and amino acid supplementation were effective for enhancing muscle strength, muscle mass, and walking speed in sarcopenic women. In a meta-analysis of protein supplementation during prolonged resistance-type exercise training, protein supplementation showed a positive effect on fat-free mass and one-repetition maximum leg press strength compared with placebo in both younger and older subjects [23]. Therefore, treatment of sarcopenia should include resistance training and protein and amino acid supplementation.

2.2. Nutrition Therapies for Obesity

Low-calorie diets can counteract obesity, as reducing caloric intake below expenditure results in weight loss. For example, a balanced diet providing an energy deficit of 500 to 750 kcal per day from daily energy requirements with approximately 1 g of high-quality protein per kilogram of body weight per day was prescribed in a 1-year, randomized, controlled trial on combined weight loss and exercise [24]. An initial weight loss goal of more than 5% was realistic and appeared to be associated with improvements in cardiovascular risk factors mainly in people with several concomitant factors [25].

There are many types of diets that produce weight loss. Balanced low-calorie diets are a standard strategy for losing body weight. Meta-analyses also showed low-carbohydrate diets were associated with significant decreases in body weight (-7.04 kg; 95% CI, -7.20 to -6.88) [26], whereas lower total fat intake was associated with a lower relative body weight (-1.6 kg; 95% CI, -2.0 to -1.2) [27]. A meta-analysis comparing low-carbohydrate and low-fat diets demonstrated that individuals assigned to low-carbohydrate diets lost more weight than individuals randomized to low-fat diets (weighted mean difference (WMD), -3.3 kg; 95% CI, -5.3 to -1.4) after 6 months [28]. However, this difference was no longer obvious after 12 months (WMD, -1.0 kg; 95% CI, -3.5 to 1.5) [28]. Another meta-analysis showed that reduction in body weight was not significantly different between low-carbohydrate and low-fat diets [29].

Meta-analysis also showed high-protein diets produced more weight loss than low-protein diets (standardized mean difference (SMD) -0.36; 95% CI, -0.56 to -0.17) [30]. Another meta-analysis showed that energy-restricted, isocaloric, high-protein and low-fat diets were better for reducing body weight (0.79 kg; 95% CI, -1.50 to -0.08) and fat mass (-0.87 kg; 95% CI, -1.26 to -0.48 kg), compared with a standard-protein, low-fat diet [31]. The Mediterranean diet was also reported to have a significant effect on weight (mean difference (MD) between -1.75 kg; 95% CI, -2.86 to -0.64) [32]. In a Cochrane Database of Systematic Review, diets with a low glycemic index or low glycemic load were shown to result in a greater decrease in body weight (WMD -1.1 kg; 95% CI -2.0 to -0.2) [33]. Very-low-calorie diets that provided less than 800 kcal/day have been used to induce rapid weight loss. Very-low-calorie diets induced significantly greater short-term weight losses (16.1 ± 1.6% vs. 9.7 ± 2.4% of initial weight, respectively; $p = 0.0001$) compared with conventional low-calorie diets that provided between 800 and 1800 kcal/day [34]. However, there were no significant long-term weight losses with the two diets (6.3 ± 3.2% vs. 5.0 ± 4.0%, respectively; $p > 0.2$) [34].

Although intervention with a low-calorie diet only was effective for reducing body weight, meta-analysis showed a pooled weight loss of 1.14 kg (95% CI, 0.21 to 2.07) was greater in the diet-plus-exercise group than the diet-only group [35]. In a 1-year, randomized, controlled trial, combination of a low-calorie diet and exercise were shown to maintain more lean body mass than either intervention alone [24]. On the basis of these results, a combination of a low-calorie diet and exercise would be recommended for obese elderly subjects.

3. EXERCISE THERAPIES

3.1. Exercise Therapies for Sarcopenia

Resistance training has been shown to be the most promising intervention for decreasing the effects of sarcopenia, as it induces skeletal muscle hypertrophy, and enhances muscle strength. A systematic review of the effects of exercise intervention for increasing muscle mass in elderly subjects identified 5 of 6 articles that concluded high-intensity resistance training resulted in significant increases in soft lean tissue and muscle mass [36]. On the other hand, the remaining three articles indicated that moderate-intensity resistance training did not affect soft lean tissue or muscle mass [36]. High-intensity resistance training of sufficient duration, frequency, repetitions, and sets is therefore effective for counteracting the loss of muscle mass associated with advancing age.

A meta-analysis of resistance exercise for muscular strength in older adults revealed that higher intensity training was associated with greater improvement in strength [37]. The increases in strength ranged from 9.8 to 31.6 kg, while the percent changes were 29 ± 2, 24 ± 2, 33 ± 3, and 25 ± 2 for leg presses, chest presses, knee extensions, and lateral pulls, respectively [37]. A Cochrane Database of Systematic Review reported progressive resistance strength training was also an effective intervention for improving physical functioning in older people as it increased muscle strength (SMD, 0.84; 95% CI, 0.67 to 1.00) and gait speed (MD, 0.08 m/s; 95% CI, 0.04 to 0.12) in older adults [38]. Careful attention should be paid when determining the amount and frequency of resistance training in the elderly, as excess intensive strength training in these people may impair effective gains in muscle strength and mass.

During disuse, skeletal muscle loss occurs at a rate of approximately 0.5% of total muscle mass per day [20]. The substantial loss of skeletal muscle mass during disuse is accompanied by a decline in strength ranging between 0.3% and 4.2% per day [20]. Physical activity and aerobic exercise are therefore important not only for increasing muscle mass, but also for maintaining muscle mass and preventing sarcopenia. Daily ambulatory activity with moderate intensity estimated by accelerometer has been shown to correlate positively with lower body muscle size and function in older adults [39]. Although there is conflicting data on the effects of short-term ambulation training, it is possible that relatively long periods of walking, jogging, or intermittent running for over half a year can increase leg muscle size in elderly adults [39].

3.2. Exercise Therapies for Obesity

Exercise and physical activity has beneficial effects, not only in causing a loss of weight but also reducing cardiovascular risk [40]. A Cochrane Database of Systematic Review reported that exercise combined with diet resulted in a greater weight reduction than diet alone (WMD -1.1 kg; 95% CI, -1.5 to -0.6), while raising exercise intensity increased the magnitude of weight loss (WMD -1.5 kg; 95% CI, -2.3 to -0.7) [41]. A meta-analysis of isolated aerobic exercise and weight loss showed that 6-month exercise programs were associated with a modest reduction in weight (WMD -1.6 kg; 95% CI, -1.64 to -1.56), while a 12-month program was also associated with a modest reduction in weight (WMD -1.7 kg; 95% CI, -2.29 to -1.11) [42]. Another meta-analysis showed that pedometer-based walking interventions were associated with weight loss (-1.27 kg; 95% CI, -1.85 to -0.70), with participants losing an average 0.05 kg per week during the intervention [43]. These results indicate that aerobic exercise alone can induce weight loss. However, a low-calorie diet should be combined with exercise as the effect of aerobic exercise on weight reduction is minimal.

Resistance training is another exercise therapy for obesity. A meta-analysis showed resistance training reduced fat mass by 2.33 kg (95% CI, -4.71 to 0.04) in patients with abnormal glucose metabolism [44]. A systematic review on the effect of exclusive resistance training on body composition and cardiovascular risk factors in overweight or obese children, showed that 4 of 6 studies reported significant changes in body composition, with an increase in fat-free mass and BMI associated with a decrease in fat mass [45].

A meta-analysis of aerobic versus resistance exercise training on reduction of visceral fat showed that there was a significant pooled effect size for the comparison between aerobic exercise and controls (-0.33; 95% CI, -0.52 to -0.14), but not for the comparison between progressive resistance training and controls (0.09; 95% CI, -0.17 to 0.36) [46]. This result suggests that aerobic exercise is a central point for exercise programs aimed at reducing visceral fat. However, recent randomized, controlled trials on the effect of 12 weeks of aerobic, resistance or combination exercise training on cardiovascular risk factors in overweight and obese subjects demonstrated there were significant improvements in body weight (-1.6%, $p = 0.044$) in the combination exercise group compared with the control and resistance groups [47]. Significant improvements in body fat percentage (-2.6%, $p = 0.008$) and abdominal fat percentage (-2.8%, $p = 0.034$) were also observed in the combination exercise group compared with controls [47]. A combination of aerobic exercise and resistance training is therefore recommended for overweight and obese adults.

4. PHARMACEUTICAL THERAPIES

4.1. Pharmaceutical Therapies for Sarcopenia

4.1.1. Testosterone

Although the mechanisms by which testosterone increases skeletal muscle are poorly understood, it has been shown to positively regulate insulin-like growth factor-1 and myostatin [5]. A meta-analysis indicated

that testosterone supplementation increased fat-free mass and muscle strength in men aged older than 45 years with low or low-normal testosterone levels [48]. Testosterone replacement was associated with a significantly greater increase in lean body mass (2.7 kg; 95% CI, 1.6 to 3.7), grip strength (3.3 kg; 95% CI, 0.7 to 5.8), and a greater reduction in fat mass (-2.0 kg; 95% CI, -3.1 to -0.8) compared with placebo [48]. Another meta-analysis of testosterone or dihydrotestosterone replacement therapy in men with a mean age of 65 years or greater revealed that the mean g-index adjusted for sample size was 0.53 (95% CI, 0.21 to 0.86) [49]. A mean g-index of 0.53 indicated that androgen treatment produced an approximately 19.3% increase in muscle strength [49].

Although testosterone treatment resulted in significant increases in fat-free mass and muscle strength, a meta-analysis of adverse effects of testosterone therapy in adult men showed it was also associated with a significant increase in hemoglobin (WMD, 0.80 g/dl; 95% CI, 0.45 to 1.14) and hematocrit (WMD, 3.18%; 95% CI, 1.35 to 5.01), and a decrease in high-density lipoprotein cholesterol (WMD, -0.49 mg/dl; 95% CI, -0.85 to -0.13) [50]. No significant effects on mortality, prostate disease, or cardiovascular outcomes were observed in that study [50]. On the other hand, a testosterone gel was shown to be associated with an increased risk of cardiovascular adverse events (total risk OR, 10.6; 95% CI, 1.3 to 84.5) in older men with limited mobility and a high prevalence of chronic disease [51]. Testosterone increases fat-free mass and muscle strength, and if no contraindications for its use are apparent it could be used as a first-line pharmaceutical therapy in sarcopenic elderly men for several months whilst monitoring side effects.

4.1.2. Growth Hormone

Growth hormone (GH) is a single-chain peptide of 191 amino acids, produced and secreted mainly by the somatotrophs of the anterior pituitary gland. GH coordinates the postnatal growth of multiple target tissues, including skeletal muscle. A systematic review of randomized, controlled trials of GH therapy in healthy, elderly subjects showed that those treated with GH therapy had a decreased overall fat mass (-2.1 kg; 95% CI, -2.8 to -1.35) and increased overall lean body mass (2.1 kg; 95% CI, 1.3 to 2.9), compared with those not receiving treatment [52]. However, subjects treated with GH were shown to be significantly more likely to experience soft tissue edema, arthralgias, carpal tunnel syndrome, and gynecomastia, and were somewhat more likely to develop diabetes mellitus and impaired fasting glucose. Therefore, GH therapy cannot be recommended as sarcopenia treatment in healthy, elderly subjects due to its adverse effects [52].

Subsequent to this systematic review, another study in healthy, elderly adults showed administration of the oral GH secretagogue, capromorelin, improved body composition and physical function (lean body mass increased with capromorelin 1.4 kg vs. placebo 0.3 kg, $p = 0.001$) [53]. Adverse events included fatigue, insomnia, and small increases in fasting glucose, glycosylated hemoglobin, and indices of insulin resistance [53]. Several randomized, controlled trials on growth hormone and/or testosterone in healthy, elderly subjects also revealed that body composition and muscle performance were improved and enhanced by GH supplementation [54-57]. For example, lean body mass increased by 2.0 ± 0.5 kg in the GH group ($p = 0.004$) and by 1.8 ± 0.5 kg in the GH and testosterone group ($p = 0.007$) compared with placebo [54]. However, GH therapy is still not recommended as a treatment for sarcopenia due to its adverse effects.

4.1.3. Ghrelin

Ghrelin is a 28-amino-acid peptide produced mainly by cells in the stomach, and is a natural ligand for the GH-secretagogue receptor [58]. Ghrelin plays a critical role in a variety of physiological processes, by stimulating GH secretion and regulating energy homeostasis by stimulating food intake and promoting adiposity *via* a GH-independent mechanism. Because of their combined anabolic effects on skeletal muscle and appetite, ghrelin and low-molecular-weight agonists of the ghrelin receptor are considered attractive candidates for treating sarcopenia.

Oral administration of the ghrelin mimetic MK-677 at a dose of 25 mg once daily for 1 year in healthy elderly adults older than 60 years was shown to cause significant increases in fat-free mass (placebo -0.5 kg; 95% CI, -1.1 to 0.2, vs. ghrelin mimetic 1.1 kg; 95% CI, 0.7 to 1.5, $p < 0.001$) [59]. However, that study did not show a significant increase in strength or function in the ghrelin-mimetic treatment group, compared with the placebo group. Patients with osteoarthritis undergoing elective total hip replacement who received intravenous injections of 2 mg/kg of ghrelin twice-daily for 3 weeks beginning 1 week before surgery, had significant increases in lean body mass ($p = 0.012$) and decreases in fat mass ($p = 0.017$) [60]. In contrast, muscle strength and walking ability did not differ significantly [60]. Although ghrelin appears to increase

lean body mass in the elderly, increased fat-free mass may not result in changes in muscle strength or physical function. Long-term, large-scale clinical trials are therefore required to recommend ghrelin as a treatment for sarcopenia.

4.1.4. Vitamin D

Vitamin D deficiency is one cause of proximal myopathy and sarcopenia which improves with vitamin D supplementation [61, 62]. Vitamin D appears to down-regulate myostatin expression and up-regulate follistatin expression, an inhibitor of myostatin. As a low vitamin D level has been shown to be associated with an increased risk of mobility limitation and disability in community-dwelling subjects [63], vitamin D supplementation appears a reasonable treatment option in sarcopenia, especially in elderly subjects with vitamin D deficiency. An association between low vitamin D and low muscle mass has been reported in several studies [64-67]. On the other hand, Marantes *et al.* [68] found the association between low vitamin D and low muscle mass occurred only in subjects younger than 65 years.

A systematic review that examined mainly community-dwelling, older women showed the association between vitamin D supplementation and physical performance remained controversial [69]. Four of the 5 studies and 2 of the 3 studies which tested the effect of vitamin D supplementation on balance and gait, respectively, showed no significant effect [69]. Four studies showed a significant effect on muscle strength, although this effect was not observed in three other studies [69]. In a recent systematic review and meta-analysis of 17 randomized, controlled trials, vitamin D supplementation was reported to have no significant effect on grip strength (SMD, -0.02; 95% CI, -0.15 to 0.11) or proximal lower limb strength (SMD, 0.1; 95% CI, -0.01 to 0.22) in adults with a baseline 25(OH)D > 25 nmol/L [70]. However, pooled data from two studies on vitamin D-deficient participants (25(OH)D < 25 nmol/L) demonstrated a large effect of vitamin D supplementation on hip muscle strength (SMD, 3.52; 95% CI, 2.18 to 4.85) [70]. Vitamin D supplementation is therefore recommended for increasing muscle strength only in elderly subjects with vitamin D deficiency.

4.2. Pharmaceutical Therapies for Obesity

4.2.1. Orlistat

Orlistat alters fat digestion by inhibiting pancreatic lipase and induces weight loss by increasing fecal fat excretion, due to the fat not being completely hydrolyzed. A Cochrane Database of Systematic Review showed obese and overweight patients treated with orlistat lost 2.7 kg of weight (95% CI, 2.3 to 3.1) compared with placebo [71]. The number of patients achieving 10% or greater weight loss was 12% higher (95% CI, 8 to 16) with orlistat therapy [71]. An updated meta-analysis of long-term pharmacotherapy for obesity and overweight revealed that orlistat reduced weight by 2.9 kg (95% CI, 2.5 to 3.2) compared with placebo [72]. A recent meta-analysis on the effects of anti-obesity drugs on cardiovascular risk factors showed that orlistat treatment was associated with a reduction of 2.39 kg in weight (95% CI, -3.34 to -1.45) , a reduction of 0.27 mmol/L in total cholesterol (95% CI, -0.36 to -0.17), a reduction of 0.21 mmol/L in low-density lipoprotein (95% CI, -0.30 to -0.12), a reduction of 0.12 mmol/L in fasting glucose (95% CI, -0.20 to -0.04), a reduction of 1.85 mmHg in systolic blood pressure (95% CI, -3.30 to -0.40), and a reduction of 1.49 mmHg in diastolic blood pressure (95% CI, -2.39 to -0.58) [73]. Orlistat is suggested as first-line pharmaceutical therapy for obesity as there is no evidence it is associated with an increased risk of cardiovascular events.

4.2.2. Lorcaserin

Lorcaserin is a selective agonist of the serotonin 2c receptor, and selectively activates central receptors and decreases food intake through the proopiomelanocortin system of neurons. In 2012, the United States Food and Drug Administration approved lorcaserin as an addition to a reduced-calorie diet and exercise regimen for obese or overweight (BMI ≥ 27 kg/m^2) patients with at least one medical comorbidity, such as type 2 diabetes, hypertension, high cholesterol, or sleep apnea. A meta-analysis of randomized, controlled trials of 1 year duration reported weight loss of 3.23 kg (95% CI, 2.70 to 3.75) and a reduction in BMI of 1.16 kg/m^2 (95% CI, 0.98 to 1.34) compared with placebo [74]. The use of lorcaserin for 8 and 12 weeks reduced weight by 1.60 kg (95% CI, 0.34 to 2.86) and 2.9 kg (95% CI, 2.2 to 3.5), respectively [74]. Headache, nausea, and dizziness were found to be significantly higher in patients receiving lorcaserin than those receiving placebo [74]. Data on long-term weight loss and safety with lorcaserin treatment are still required.

4.2.3. Phentermine-Topiramate

Phentermine is a noradrenergic sympathomimetic drug that stimulates the release of norepinephrine or

inhibits its reuptake into nerve terminals. Topiramate is an antiepileptic drug used to treat certain types of seizures in people who have epilepsy. In 2012, the United States Food and Drug Administration approved the combination of phentermine and topiramate for weight loss in obese or overweight (BMI ≥ 27 kg/m^2) patients with at least one medical comorbidity.

In the CONQUER randomized, controlled trial, changes in bodyweight after 56 weeks were -1.4 kg (least-squares mean -1.2%; 95% CI, -1.8 to -0.7), -8.1 kg (-7.8%; 95% CI, -8.5 to -7.1; p < 0.0001), and -10·2 kg (-9·8%; 95% CI, -10·4 to -9·3; p < 0.0001) in patients assigned to placebo, phentermine 7.5 mg plus topiramate 46.0 mg, or phentermine 15.0 mg plus topiramate 92.0 mg, respectively [75]. In the EQUIP randomized, controlled trial, patients in the placebo, phentermine 3.75 mg plus topiramate 23 mg, and phentermine 15 mg plus topiramate 92 mg groups lost 1.6%, 5.1%, and 10.9% of baseline body weight after 56 weeks, respectively (p < 0.0001) [76]. The SEQUEL randomized, controlled trial showed weight loss was maintained for over 2 years with 9.3% and 10.5% weight loss from baseline for phentermine 7.5 mg plus topiramate 46 mg and phentermine 15 mg plus topiramate 92 mg, respectively (p < 0.0001) [77]. Adverse reactions occurred in 5% or more of the study subjects and included parasthesia, dizziness, dysgeusia, insomnia, constipation, and a dry mouth [78]. Long-term weight loss and safety data of phentermine-topiramate treatment is necessary before its use as a first-line treatment can be recommended.

4.2.4. Vitamin D

An association between low vitamin D and obesity has been reported [79-80]. A meta-analysis indicated that there was a significant inverse weak correlation between serum 25(OH)D levels and BMI in adult population (Fisher's Z = -0.15; 95% CI, -0.19 to -0.11), except for women living in developing countries [79]. Another meta-analysis revealed that each 1 kg/m^2 higher BMI was associated with 1.15% lower 25(OH)D [80]. Low vitamin D level has been also shown to be associated with sarcopenic obesity in adult population [67, 81-83]. On the other hand, Kim *et al.* [66] found the association between low vitamin D and sarcopenia, regardless of obesity in the older population.

The effect of vitamin D supplementation on obesity remains controversial. A randomized, double blind clinical trial with 20,000 IU cholecalciferol twice a week, or 20,000 IU once a week plus placebo, or placebo twice a week for 12 months reported that there was no significant change in weight, waist-to-hip ratio or percentage body fat in any of the groups [84]. Another randomized, controlled trial showed that weight loss was not affected significantly by vitamin D supplementation (83 μg per day) or placebo (-5.7 ± 5.8 kg vs. -6.4 ± 5.6 kg; p = 0.248) [85]. Supplementation with vitamin D (25 μg per day as cholecalciferol) for 12 weeks caused a statistically significant decrease in body fat mass in the vitamin D group compared to the placebo group (-2.7 ± 2.1 kg vs. -0.47 ± 2.1 kg; p < 0.001) [86]. However, body weight and waist circumference did not change significantly in both groups. Rosenblum *et al.* [87] found that calcium and vitamin D supplemented orange juice (1050 mg calcium and 300 IU vitamin D per day) was not effective for weight change in overweight and obese adults (−2.1 ± 2.7 kg vs. −2.8 ± 3.7 kg, p = 0.3748). In contrast, the reduction of visceral adipose tissue was significantly greater in the calcium and vitamin D group than in the control group. Further clinical trials are therefore required to recommend vitamin D as a treatment for obesity.

5. COMPREHENSIVE APPROACH

Sarcopenia treatment should include resistance training and protein and amino acid supplementation. Physical activity and aerobic exercise are important for maintaining muscle mass and preventing sarcopenia. Obesity treatment should include low-calorie, high-protein diets, aerobic exercise, and resistance training. A combination of nutrition therapies (low-calorie, high-protein diets, protein and amino acid supplementation) and exercise therapies (resistance training and aerobic exercise) would therefore be expected to be the most effective option for preventing and treating sarcopenic obesity.

A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults revealed that 81% of the energy restriction groups and 39% of the energy restriction plus exercise groups lost ≥ 15% of their body weight as fat-free mass [88]. The exercise groups had modest changes in body weight and fat-free mass [88]. Another review of 18 randomized, controlled trials of exercise with or without diet components indicated that 3-18 month programs that included aerobic and strengthening exercise (2-3 days per week) with calorie restriction (typically 750 kcal deficit/day), induced the greatest change in functional performance measures compared with exercise or diet

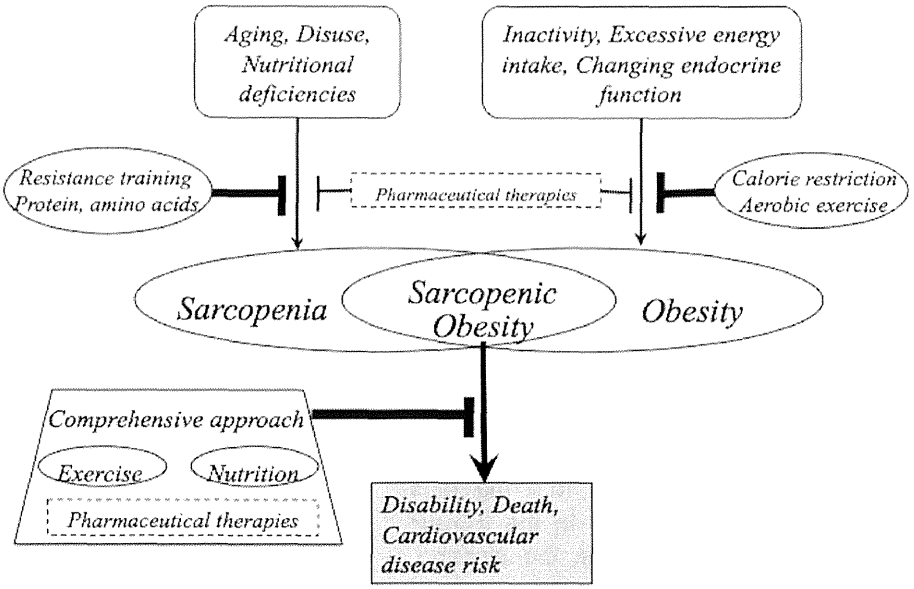

Figure 1: Comprehensive approach to sarcopenic obesity including nutrition, exercise, and pharmaceutical therapies.

alone [89]. Sakuma *et al.* [90] recommended multiple exercises including flexibility training, aerobic exercise, and resistance training, combined with nutrition therapy including caloric restriction (range of 200-750 kcal) and higher intake of protein (up to 1.5 g/kg) of high biological quality to attenuate the symptoms of sarcopenic obesity. However, there have been no intervention studies for sarcopenic obesity, with only observational studies having been reported for the condition. This is due partly to the fact that there is no standardized definition or diagnostic criteria for sarcopenic obesity. Therefore, future research for counteracting sarcopenic obesity should consider determining a standardized definition and diagnostic criteria for the condition and also undertake a multimodal intervention study for sarcopenic obesity.

In case of severe sarcopenic obesity or failure to achieve muscle gain and weight loss through nutrition and exercise therapies, pharmaceutical therapies can be added to treat the condition. In a systematic review of adding drug therapy, exercise, behavior therapy, or combinations of these interventions for obesity indicated that adding orlistat, exercise, or behavior modification to dietary advice improved long-term weight loss [91]. Weight loss program using a very-low-energy diet and orlistat induced both fat loss and fat-free mass loss (fat-free mass to fat mass loss ratio: 1 to 5.9) [92]. In contrast, testosterone replacement was associated with increasing lean body mass and reducing fat mass [48]. In the comprehensive approach for sarcopenic obesity, testosterone or orlistat can be suggested as first-line pharmaceutical therapies, depending on the severity of sarcopenia and obesity. Vitamin D supplementation is recommended in elderly subjects with vitamin D deficiency. However, careful attention should be paid to the adverse effects of testosterone, orlistat, and vitamin D supplementation.

6. CONCLUSION

Sarcopenic obesity is an important current and future public health issue. The impact of sarcopenic obesity on physical disability, cardiovascular disease risk, and death is becoming a primary concern amongst nutritionists, geriatricians, and public health officers. Although there are no intervention studies for sarcopenic obesity, nutrition therapies should include caloric restriction (range of 200-750 kcal), high protein diets (up to 1.5 g/kg), and protein and amino acid supplementation. Exercise therapies for sarcopenic obesity should include both aerobic exercise and resistance training. A combination of nutrition and exercise therapies would be expected to be the most effective option for preventing and treating sarcopenic obesity. In cases of severe sarcopenic obesity or failure to achieve muscle gain and weight loss through nutrition and exercise therapies, pharmaceutical therapies such as testosterone, orlistat, and vitamin D supplementation can be added to the treatment regimen. As shown in Figure **1**, the comprehensive approach to sarcopenic obesity includes nutrition, exercise, and pharmaceutical therapies.

CONFLICT OF INTEREST

All authors declare no conflicts of interest.

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