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厚生労働科学研究費補助金
循環器疾患・糖尿病等生活習慣病対策総合研究事業

高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索ならびに予防法の確立に資する研究

令和６年度　総括・分担研究報告書

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研究代表者 杉本　研　川崎医科大学総合老年医学 教授

研究要旨
大規模コホートや介入研究の情報を活用し、ロコモ・フレイルのスクリーニング確度の向上と効果的な予防方法の確立に資する研究に取り組んだ。質問票の妥当性検証では、J-CHS、基本チェックリスト、後期高齢者質問票のいずれも要介護リスクと関連した。総死亡とは後期高齢者質問票のみが良好な関連を示した。後期高齢者質問票と健診結果から要介護リスクを評価するためのリスクスコアを開発した。ロコモ・フレイルの発症や増悪には、身体的な因子のみならず社会的・精神的な因子も関連することを明らかにした。下肢股関節屈曲筋力がロコモティブシンドロームの増悪に関連したことから、ロコモ・フレイルの効果的な予防方法開発の手がかりを得た。

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A．研究目的

身体機能低下の各ステージに特化した評価指標が社会で利用されているが、ロコモ・フレイルの指標がどのような身体的特徴を反映するのか、また高齢期の主要アウトカムである要介護認定や総死亡とどのように関連するのか等、十分に明らかになっていない。評価指標の性能を把握した上で修正可能なリスク因子を同定すれば、発症・増悪を予防するための重要な手がかりとなる。

そこで本研究では、現有の大規模コホートや介入研究の情報を活用し、以下の課題解明を通じてロコモ・フレイルのスクリーニング確度の向上と効果的な予防方法の確立に資する。

① 評価指標（ロコモ25・J-CHS・後期高齢者質問票）の妥当性検証
② 予測モデルの開発と国民レベルでの有病者数の推計
③ 発症・増悪に関連するリスク因子の探索
④ リスク因子を修正するための予防方法の検討

機能低下のステージ	評価方法
サルコペニア	握力＋四肢骨格筋量＋ 歩行速度か５回椅子起立時間
ロコモティブ シンドローム	ロコモ 25（質問票） または ２ステップテスト ＋ 起立試験
フレイル	日本語版フレイル基準 J-CHS 後期高齢者質問票 基本チェックリスト

B．研究方法

研究代表者・分担者らが有する様々なコホートの情報を活用し、また必要に応じて追加で情報を収集することで、研究目標の達成を目指す。

（倫理面への配慮）

それぞれのコホートは、研究代表者・分担者らが所属する機関の倫理承認を得て実施している（分担研究報告書参照）。

コホート	担当	特徴
MUSCLES-DM	杉本 田原 山本	サルコペニアのリスク度が高い糖尿病患者900 名を対象としたコホート。ベースライン調査後 4 年までの追跡を終え、6 年目の追跡調査を実施している。
SONIC 研究	神出 杉本 山本	登録時 70/80/90 歳の超高齢者集団。医科学・歯科学・心理学的研究から、フレイルや認知症、老年者症候群のリスク因子の解明と予防方法の確立目指す。
ながはま コホート	田原 池添	滋賀県長浜市民 1.2 万人が対象。 5 年おきに繰り返し調査を実施し（３期調査終了）、臨床情報の経時的変化を評価できる。 2 期調査から高齢者の身体機能調査を実施。
しずおか コホート	田原 加藤	静岡県の複数の市町で実施。これまでに2,000 例を登録し、年間 1,500 例程度ずつ拡大予定。国保レセプトデータと突合し詳細な服薬・治療情報を得る。
FESTA 研究	新村	兵庫県丹波篠山圏域在住の高齢者（総参加者数 1147 名）が対象。フレイル・サルコペニアの発症リスク因子の探索を目的に、原則 2 年毎の追跡調査を実施。
RIAS コホート	丹野	東日本大震災被災地（岩手県）を対象としたコホート（約 1 万人）。生活習慣・循環器疾患リスク因子・フレイルに関する 10 年間の経時的データを蓄積
垂水 コホート	牧迫	垂水市住民（40 歳以上）が対象。年間 1,000 名程度を毎年追跡（追跡率 70％程度）。フレイル・サルコペニア、認知機能、食習慣等の情報を包括的に収集。

C. 研究結果と考察

研究①　評価指標の妥当性検証

質問表の妥当性検証に関する分担研究者の報告を一覧表に示した。要介護認定とは、J-CHS、基本チェックリスト、後期高齢者質問票のいずれも有意に関連した。J-CHSと要介護認定との関連に関しては、対象者数が限られていたため要支援以上をアウトカムとして関連を検討したが、要介護１以上をアウトカムとした場合でも同様の傾向が観察された。健康寿命のあり方に関する有識者研究会の報告書（2019年）では、要介護２以上を「日常生活動作が自立していない」と定義しているため、今後、他のコホートでの解析や文献学的な検討から、要介護２以上との関連についても検討を重ねる。

基本チェックリストに関しては、8点以上で要介護2以上と関連した。両者の関連が握力より明確であったことは、基本チェックリストでは高齢者の様々な特性を包括的に評価できることが理由として考えられた。ただし、今回の検討では東北大震災の被災者地域の調査データを用いたため、基本チェックリストのうち抑うつに関連した5項目が除外されている。今後、他のコホートでの解析や文献学的な検討から基本チェックリストの有用性について理解を深める。

	要介護			総死亡		
	集団	結果	備考	集団	結果	備考
ロコモ25（GLFS-25）				ながはま	≥70歳で有意、≥65歳以上では関連なし 低SMIの併存	1
J-CHS	SONIC	70/80/90歳。プレフレイル/フレイルは３年後の要介護認定（要支援以上）と関連。要介護とも関連する傾向				
基本チェックリスト	RIAS	64～95歳。KCL ≥8点は要介護認定（要介護２以上）と関連。要介護認定との関連は握力低下より強い	2	RIAS	全体の解析ではKCLと総死亡に関連なし 男性でKCL ≥8点が僅かに関連 要介護認定ほど関連は明確ではない。	2
後期高齢者質問票	SKDB	後期高齢者健診を受診した75～90歳 8/15項目が要介護２以上と関連。 リスクスコアを作成	3	SKDB	後期高齢者健診を受診した75～90歳 要介護に対するモデルと同じ項目＋喫煙が関連。	
身体機能	SONIC	70/80/90歳 握力と歩行速度<1m/sは３年後の要介護認定（支援＋介護）と関連				

1. Arch Gerontol Geriatr. 2025; 129:105670
2. RIAS studyでは、KCLのうち、抑うつに関連した項目（21～25の5項目）の情報はない
3. Geriatr Gerontol Int. 2025; 25:260-266

高齢者質問票については、15項目のうち8項目と属性因子（性別・年齢）、および特定健診の検査値との組み合わせで要介護2以上に対するリスク度を評価することができた。また、それらの項目の組み合わせによって算出できるリスクスコアを開発したことで、健診受診者のうちからリスク度の高い部分集団を見分けることができるようになった。

総死亡に関しては、ロコモ25は70歳以上におい

てのみ有意に関連した。ロコモ25の平均点は70歳以降に上昇する傾向を示したことから、ロコモ25はよりリスク度の高い集団においてのみ総死亡と有意な関連を示すと考えられる。基本チェックリストも男性でのみ総死亡と関連したが、両者の関連は要介護認定とのそれに比して明確ではなかった。ロコモ25や基本チェックリストは、総死亡のリスク度評価には向かないのかもしれない。

後期高齢者質問票に関しては、要介護認定より関連性は弱いものの、総死亡とも有意に関連したことから、総死亡のリスク度評価には後期高齢者質問票が最も適しているのかもしれない。

研究②　予測モデルの開発と国民レベルでの有病者数の推計

後期高齢者健診を受診した比較的健常な高齢者から、後期高齢者質問票と健診の検査値とを組み合わせることで、要介護2認定のリスク度が高い部分集団を抽出するリスクスコアを開発した。健診受診者のみに当てはめられる点で限界はあるものの、要介護リスクを簡便に見分けられるようになったことは、効率的な介入に資する知見といえる。

国民に占める身体機能が低下した者の割合を積算するためには、代表性の高い集団の情報が必要である。令和7年度から、悉皆性の高い調査データを持つ久山町研究の協力を得られることになったことから、当該研究のデータを活用してフレイルの頻度を精度よく積算する。また、各コホートの横断解析からロコモ・フレイルを推定するモデル式を開発し、それを国民健康・栄養調査の個情報（二次利用申請中）に当てはめることで、国民全体での頻度推計を試みる予定である。

後期高齢者質問票・健診結果に基づく要介護度2以上新規認定のリスクスコア

		ポイント
年齢	75–79 歳	90
	80–84 歳	96
	85–89 歳	102
性別（男性）		3
低BMI（<20 kg/m^2）		3
ベースライン時点で要支援の認定をうけている		9
尿糖（±以上）		3
尿蛋白（±以上）		4
Q01：現在の健康状態はいかがですか？（あまり良くない/良くない）		4
Q06：6カ月間で2〜3kg以上の体重減少がありましたか？（はい）		2
Q07：以前に比べて歩く速度が遅くなってきたと思いますか？（はい）		3
Q08：この1年間に転んだことがありますか？（はい）		4
Q09：ウォーキング等の運動を週に1回以上していますか？（いいえ）		3
Q10：周りの人からの物忘れがあると言われていますか？（はい）		6
Q11：今日が何月何日かわからない時がありますか？（はい）		5
Q13：週に1回以上は外出していますか？（いいえ）		4
スコアポイント		合計点 − 87

研究③　発症・増悪に関連するリスク因子の探索

横断研究・長期縦断研究から、ロコモ・フレイルの増悪に関連する因子を探索し、下表の知見を得た。垂水コホートでの検討では、増悪因子として社会的フレイルや抑うつ傾向などが抽出され、身体的な因子のみならず、社会との関わりを維持することの重要性が示唆された。一方、認知機能が保たれていることや社会的フレイルが無いことが改善要因として抽出されたことも、身体的フレイル以外の改善を目指した介入の重要性を示唆している。

ながはまコホートでの検討では、股関節屈曲筋力の低下がロコモティブシンドロームの増悪と関連した。股関節の屈曲筋力や外転筋力の低下は高齢者が困難となりやすい動作・活動（長距離歩行・速歩・階段昇降・地域活動・買い物）とも関連していた。

SONIC研究からは、フレイルのNT-proBNPがフレイルと関連することが報告された。両者が関連するメカニズムは解明されていないものの、今後、他のコホートで再現性を検討することで両者の関係性を明確にする。

	横断解析		縦断解析				
			新規発症		増悪		改善
ロコモ25	しずおか	≥40歳の1,085人。歩行速度・身体活動＋A1c・夕食（男）or熟眠感（女）			ながはま	≥65歳の433名 １年間のロコモ25点の悪化 股関節屈曲筋力が関連	
J-CHS	SONIC	76/86/96歳の593名 フレイル群でNT-proBNPが高値			垂水	≥65歳の277名を５年追跡 歩行速度の低下、起立時間の延長、情報処理の低下・活動能力指標の低下	握力が強い・遅延再生スコアが高い・社会的フレイルが無い
基本 チェックリスト					垂水	≥65歳以上の255名を５年追跡 腰痛・社会的フレイル・睡眠の質・うつ傾向	Mini-Cog・遅延再生・情報処理のスコアが高い
後期高齢者 質問票							

研究④　リスク因子を修正するための予防方法の検討

ながはまコホートでの検討から、下肢筋量のうち股関節屈曲筋力の低下がロコモティブシンドロームの増悪と関連することが明らかになった（研究③）。従来の同種の研究では大腿四頭筋に焦点が当てられており、股関節屈曲筋力に関する知見は見当たらない。今後、股関節屈曲筋力や外転筋力の強化とロコモティブシンドロームの予防とに関する知見を集積し、予防方法としての可能性を検討する。

D．結論

研究者らのコホートの情報を用いた検討から、研究①～④に関する上述の知見を得た。残された課題について引き続き検討を進め、研究目標の達成を目指す。

E．健康危険情報

該当なし

F．研究発表

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- 堀　千里, 呉代華容, 樺山　舞, 赤坂　憲, 権藤恭之，増井幸恵，新井康通，石崎達郎，山本浩一，神出　計．地域在住高齢者におけるサルコペニアスクリーニングのための下腿周囲長の変化の実態-SONIC 研究-. 第 66 回日本老年医学会学術集会. 2024 年 6 月 13 日．名古屋市.
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G．知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

外来通院糖尿病患者を対象としたサルコペニア肥満診断アルゴリズムの検証と意義
MUSCLES-DM研究

研究分担者 杉本　研　川崎医科大学総合老年医学 教授

研究要旨
MUSCLES-DM研究を対象にサルコペニア肥満診断アルゴリズム（JWGSO）を用いてサルコペニア肥満の頻度を算出するとともに関連因子との関連についてサルコペニア（AWGS2019）と比較したところ、サルコペニア肥満の頻度はサルコペニアより低いが、腎症や心疾患、転倒といったアウトカムとの関連が強かったことから、サルコペニア肥満診断の臨床的意義が明らかにされた。

A．研究目的

サルコペニアが高齢者における要介護状態や疾病発症、死亡リスクであることはこれまでの研究から明らかにされている。日本人のサルコペニアの診断にはアジアサルコペニアワーキンググループの診断アルゴリズム（AWGS2019）を用いることがサルコペニア診療ガイドライン2017において推奨されており、これまでの多くの疫学研究や臨床研究において用いられてきた。一方、食の欧米化や生活習慣病の影響で肥満高齢者が増加しているが、高齢者は若年者と異なり肥満が必ずしも心血管病や死亡リスクとならないこと（肥満パラドックス）が知られている。しかし、肥満とサルコペニアとが併存する「サルコペニア肥満」は慢性炎症を基盤とする予後不良な病態として注目され、体脂肪増加と骨格筋量低下、握力低下が併存すると最も死亡リスクが高いことが報告されているが、診断基準が統一されていないことが問題であった。2023年に日本サルコペニア・フレイル学会と日本肥満学会の合同ワーキンググループ（JWGSO）が日本のサルコペニア肥満の診断アルゴリズムを発表したことを契機に、この診断アルゴリズムの妥当性検証が進められている。そこで、我々が実施している外来通院糖尿病患者を対象としたサルコペニアに関する多施設調査（MUSCLES-DM）を用いて、JWGSOによるサルコペニア肥満診断アルゴリズムの妥当性検証を実施した。

B．研究方法

MUSCLES-DM研究は2016年に開始した外来通院糖尿病患者を対象にサルコペニアに関連する因子を調査することを目的とした多施設コホートであり、大阪大学、近畿大学、愛媛大学と２つのクリニックが参加している。現在6年目調査のデータを整理中であるが、本研究ではベースラインと１年目のデータがある847例を対象とした。

調査項目として、性、年齢、身長、体重、生活習慣や併存疾患といった基本データに加え、サルコペニア診断の要素である握力、歩行速度、下腿周囲長、体組成計（M780A、タニタ社製）を用いた四肢骨格筋指数（SMI）、サルコペニア肥満診断の要素である腹囲、四肢骨格筋量BMI補正、体組成計による体脂肪率のデータを収集・算出した。また糖尿病に関するデータとして合併症や動脈硬化性疾患の有無、血糖値、HbA1c、薬剤情報を、老年医学的要素として転倒歴やADL、フレイルの有無などを収集した。また一部の対象者（n=199）ではマルチプレックスサスペンションアレイを用いて血中液性因子濃度を測定した。

サルコペニアはAWGS2019の診断アルゴリズムに従い、SMI低下（男性7.0kg/m2未満、女性5.7kg/m2未満）に加えて握力低下（男性28kg未満、女性18kg未満）または歩行速度低下（1.0m/秒未満）のいずれかを認める場合にサルコペニアと診断した。サルコペニア肥満はJWGSOの診

断アルゴリズムに従い、四肢骨格筋量BMI補正値の低下（男性0.789kg/BMI未満、女性0.512kg/BMI未満）に加えて握力低下と歩行速度低下のいずれかを認め、かつ体脂肪率低下（男性25%以上、女性30%以上）を認める場合にサルコペニア肥満と診断した。

（倫理面への配慮）

MUSCLES-DM研究は、大阪大学医学部附属病院観察研究倫理審査委員会で承認を受けて実施している。全ての対象者から書面にて同意を確認した。

C. 研究結果

解析対象847名（男性495名、女性352名、平均年齢69.4±9.5歳）のうち、サルコペニアは61名（7.2%）、サルコペニア肥満は37名（4.4%）であった。サルコペニアの有無、サルコペニア肥満の有無で年齢、HbA1c、罹病期間、転倒、心疾患、脳血管疾患、尿Alb/Cr比を比較したところ、サルコペニア有り群は無し群に比べ有意に年齢が高く、HbA1c、尿Alb/Cr比が高値傾向、心疾患の発症が多い傾向を認めたが、一方でサルコペニア肥満有り群は無し群に比べ年齢が有意に高く、HbA1cが高値傾向で、心疾患発症は有意に多く、転倒も多い傾向を認めた（表1）。

表1 サルコペニアとサルコペニア肥満の各要因との関連

	サルコペニア肥満（JWGSO）			サルコペニア（AWGS2019）		
	なし	あり	p値	なし	あり	p値
年齢,歳	68.9±9.4	79.0±6.7	<0.001	68.9±9.6	73.8±6.8	<0.001
HbA1c,%	7.46±1.3	7.84±1.4	0.09	7.45±1.3	7.75±1.3	0.09
罹病期間,年	15.5±10.2	18.7±12.0	0.06	15.6±10.1	15.4±12.8	NS
転倒,%	17.8	32.1	0.06	18.6	17.8	NS
心疾患,%	16.5	35.1	<0.01	15.2	26.2	0.06
脳血管疾患,%	13.2	18.9	NS	13.1	18.0	NS
尿Alb/Cr,mg/gCr	114.0±371.8	238.8±658.1	0.07	121.1±398.3	94.7±220.5	NS

サルコペニア肥満診断においてBMI、体脂肪率のどちらが適しているかを検討するため、BMIまたは体脂肪率の層別によるサルコペニア頻度とともにHbA1c、すなわち血糖コントロール状態との関連を検討したところ、BMI層別では高値群（25.9kg/m2以上）ではサルコペニアは認められないが、BMIが低値になるほどサルコペニアが増加し、血糖コントロールが悪化するほど高率であった。一方、体脂肪率層別ではその高低にかかわらず一定の割合でサルコペニアを認め、血糖コントロールとの関連も認めなかった（図1）。

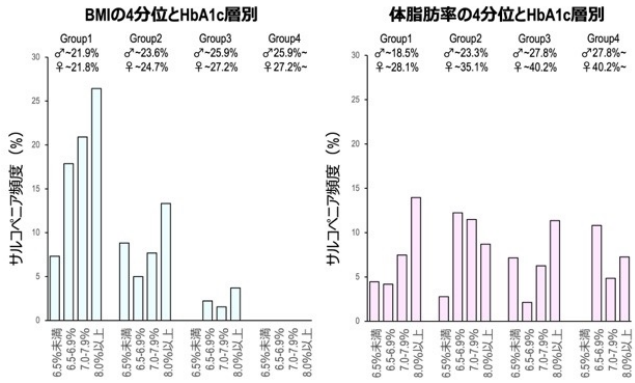

図1 BMI、体脂肪率層別によるサルコペニア頻度と血糖コントロールとの関係

さらに、血中液性因子濃度を測定し得た一部の対象者（n=199）においてサルコペニア肥満とそれらの関連を解析したところ、IL-1β、TNF-αの血中濃度がサルコペニア肥満有り群で無し群と比較し有意に高かったが、サルコペニアの有無ではその関連はみられなかった。

D. 考察

本研究により、糖尿病患者を対象とした集団においてJWGSOの診断基準によるサルコペニア肥満の頻度はサルコペニアより低率であること、またサルコペニアの有無ではみられなかった心疾患発症や糖尿病合併症の重症度、転倒との関連が認められた。糖尿病患者を対象にさまざまな方法で診断されたサルコペニア肥満の頻度を検討したメタ解析では約27%がサルコペニア肥満という結果（Clin Nutr ESPEN 58: 128-135, 2023）があることから、JWGSOの診断基準はかなり厳しい基準であると考えられる。しかし一方で、サルコペニアの有無では認められない合併症や老年症候群（転倒）の発生との関連がみられ、さらに慢性炎症のマーカーであるIL-1βやTNF-αとの関連がみられることを考慮すると、臨床的意義は高いと考えられる。ちなみに本

集団で体脂肪率高値と握力低下のみで診断したサルコペニア肥満の頻度は14.0％と多くはなるものの、合併症や転倒との関連はみられなかった。以上から、JWGSOのサルコペニア肥満診断アルゴリズムを実臨床で用いることは有用であると考えられるが、他の生活習慣病コホートや一般集団での検証が必要である。

E. 結論

糖尿病患者においてJWGSOにより診断されるサルコペニア肥満の頻度はAWGS2019により診断されるサルコペニアよりも低いものの、合併症や老年症候群との関連しているため、JWGSOは実臨床におけるサルコペニア肥満の診断法として有用であることが示唆された。

F. 健康危険情報

該当なし

G. 研究発表

1. 論文発表

該当なし

2. 学会発表

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- 杉本　研. 糖尿病患者におけるサルコペニア肥満の特定とその対策. 合同セッション「サルコペニア肥満のリハ栄養―痩せに対するだけじゃないリハ栄養」. 第14回日本リハビリテーション栄養学会学術集会. 川崎. 2025年1月25日

H. 知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

高齢者の身体機能低下に関する評価指標の検討

研究分担者 田原康玄　静岡社会健康医学大学院大学 教授

研究要旨
サルコペニア・フレイルの判定に使用されている質問票のうち、ロコモ25について総死亡との関連を検討した。地域住民を対象とした長期縦断解析から、70歳以上の高齢者において、ロコモ25は他の危険因子とは独立して総死亡と関連した。特定健診で使用されるようになった後期高齢者質問票15項目のうち、8項目が要介護認定や総死亡と関連した。当該8項目と後期高齢者健診の結果とから、要介護や死亡のリスク度を評価するリスクスコアを開発した。

A．研究目的

本研究事業の4つの到達目標（① 評価指標の妥当性検証、② 予測モデルの開発と国民レベルでの有病者数の推計、③ 発症・増悪に関連するリスク因子の探索、④ リスク因子を修正するための予防方法の検討）のうち、今年度はロコモ25の妥当性検証に取り組んだ。ロコモ25（Geriatric Locomotive Function Scale 25, GLFS-25）は、25項目の質問からロコモティブシンドロームの程度を評価するツールであり、過去の研究においてロコモティブシンドロームの新規発症や要介護認定との関連が報告されているが、生命予後との関連については知見が限られている。そこで本研究では、地域住民を対象にGLFS-25と総死亡との関連を検討することを目的とした。

B．研究方法

滋賀県長浜市民を対象とした“ながはまコホート”のデータを用いた。2012～2016年度に実施した追跡調査に参加した35歳以上80歳未満の9,850人のうち、65歳未満（6,264人）、ペースメーカー植込み（10人）、透析導入（4人）、GLFS-25の回答に欠損あり（99人）、臨床情報の欠測（16人）に該当する6,393人を除いた3,457人を解析対象とした。

ロコモ25の質問項目を表１に示した。各項目について選択肢ごとに0～4点を与え、100点満点で集計した。集計点が7点未満をグレード1、7～16点をグレード2（ロコモ度1）、16点以上をグレード3（ロコモ度2）として分類した。24点以上（路コモド3）の該当者は限られていたことから、16点以上を１つの群として統合して解析した。

表１ ロコモ25の質問項目

この１ヵ月の身体の痛みなどについてお聞きします。
1　首・肩・腕・手のどこかに痛み（しびれも含む）がありますか
2　背中・腰・お尻のどこかに痛みがありますか
3　下肢（脚のつけね、太もも、膝、ふくらはぎ、すね、足首、足）のどこかに痛み（しびれも含む）がありますか
4　ふだんの生活でからだを動かすのはどの程度つらいと感じますか

この１ヵ月のふだんの生活についてお聞きします。
5　ベッドや寝床から起きたり、横になったりするのはどの程度困難ですか
6　腰掛けから立ち上がるのはどの程度困難ですか
7　家の中を歩くのはどの程度困難ですか
8　シャツを着たり脱いだりするのはどの程度困難ですか
9　ズボンやパンツを着たり脱いだりするのはどの程度困難ですか

10　トイレで用足しをするのはどの程度困難ですか
11　お風呂で身体を洗うのはどの程度困難ですか
12　階段の昇り降りはどの程度困難ですか
13　急ぎ足で歩くのはどの程度困難ですか
14　外に出かけるとき、身だしなみを整えるのはどの程度困難ですか
15　休まずにどれくらい歩き続けることができますか
16　隣・近所に外出するのはどの程度困難ですか
17　2kg程度の買い物（1リットルの牛乳パック2個程度）をして持ち帰ることはどの程度困難ですか
18　電車やバスを利用して外出するのはどの程度困難ですか
19　家の軽い仕事（食事の準備や後始末、簡単なかたづけなど）は、どの程度困難ですか
20　家のやや重い仕事（掃除機の使用、ふとんの上げ下ろしなど）は、どの程度困難ですか
21　スポーツや踊り（ジョギング、水泳、ゲートボール、ダンスなど）は、どの程度困難ですか
22　親しい人や友人とのおつき合いを控えていますか
23　地域での活動やイベント、行事への参加を控えていますか
24　家の中で転ぶのではないかと不安ですか
25　さきゆき歩けなくなるのではないかと不安ですか

選択肢	
痛くない/少し痛い/中程度痛い/かなり痛い/ひどく痛い	Q1/Q2/Q3
つらくない/少しつらい/中程度つらい/かなりつらい/ひどくつらい	Q4
2～3km以上/１㎞程度/300m程度/100m程度/10m程度	Q15
控えていない/少し控えている/中程度控えている/かなり控えている/全く控えている	Q22/Q23
不安はない/少し不安/中程度不安/かなり不安/ひどく不安	Q24/Q25
困難でない/少し困難/中程度困難/かなり困難/ひどく困難	上記以外

総死亡は長浜市の住民基本台帳から把握した。追跡調査の参加日から2024年3月31日までを追跡期間とした。解析に投入した臨床情報のうち、骨格筋量は生体インピーダンス法で求めた四肢骨格筋指数（SMI）で評価し、男性7.0kg/m^{2}未満、女性5.7kg/m^{2}未満を低SMIとした。男女ともBMIが20kg/m^{2}未満ある場合を低BMIとした。その他の臨床情報はながはまコホートの調査データから抽出した。

（倫理面への配慮）

ながはまコホートは、京都大学医の倫理委員会ならびに長浜市事業審査委員会の承認を得て実施している。個々の対象者からは書面にて同意を確認した。

C．研究結果

解析対象者3,457人の年齢ごとのGLFS-25得点を図１に示した。GLFS-25得点は男性より女性で高く、加齢に比例して増加した。その他の臨床的特徴は表2に示した。対象者を70歳以上に限定した場合の情報も併記した。

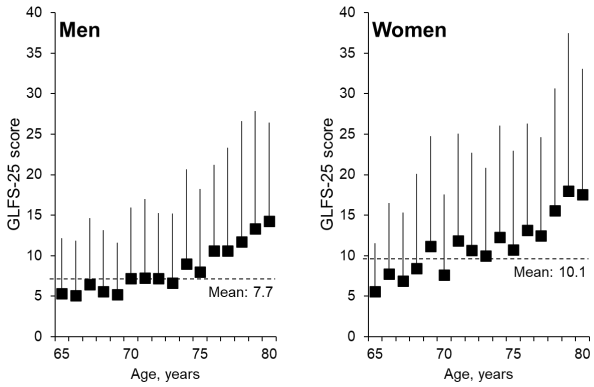


図1 性・年齢ごとのGLFS-25得点

表2 対象者の臨床的特徴

	全体	70 歳以上
	3,447	1,979
年齢, 歳	71.2 ± 4.1	74.2 ± 2.8
性別, 男性%	40.2	43.5
BMI, kg/m^2	22.5 ± 3.0	22.5 ± 3.0
低 BMI, %	20.4	20.2
SMI, kg/m^2	6.6 ± 0.9	6.6 ± 0.9
低 SMI, %	25.9	29.7
喫煙, 現在/過去/非喫煙%	68.0/25.0/7.0	67.1/27.0/5.9
飲酒量, 合/週	3.6 ± 7.2	3.7 ± 6.9
循環器疾患の既往, %	8.6	9.9
収縮期血圧, mmHg	133 ± 17	134 ± 17
拡張期血圧, mmHg	72 ± 10	72 ± 10

HbA1c, %	5.7 ± 0.5	5.7 ± 0.5
HDL コレステロール, mg/dL	65 ± 17	64 ± 17
Low コレステロール, mg/dL	117 ± 28	114 ± 27
アルブミン, g/dL	4.2 ± 0.2	4.2 ± 0.2
eGFR, ml/min/1.73m^2	70.3 ± 13.4	68.7 ± 13.5
GLFS-25 得点	9 ± 11	11 ± 13

平均追跡期間3,236日（30,566人年）の総死亡数は288人であった。70歳以上の集団での死亡数は217人であった（17,351人年）。GLFS-25のグレードごとに、総死亡に対するカプランマイヤー曲線を作成したところ（図2）、全例での解析、70歳以上での解析ともにグレードに比例して死亡率が有意に増加した。

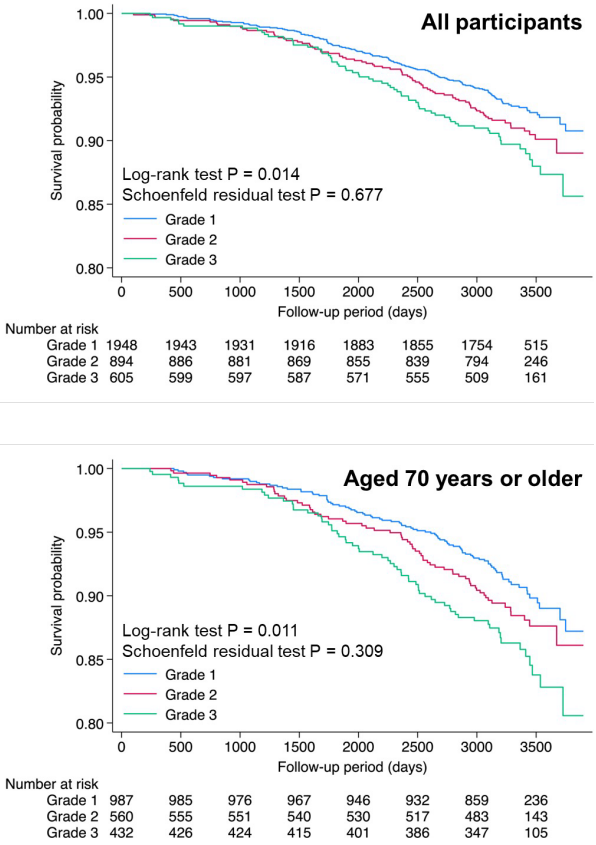


図2 総死亡に対するカプランマイヤー曲線

種々の共変量を調整したCox比例ハザード解析の結果、全例での解析では、GLFS-25は総死亡と有意に関連しなかったが（表３）、70歳以上の解析ではグレード3が総死亡と有意に関連した（表４）。この結果は、追跡開始１年間の初期死亡を除いた解析でも同様であった。

表3 総死亡に対する比例ハザード解析

	全例（n = 3,447）	
	HR (95% CI)	P
年齢, 歳	1.10 (1.07–1.14)	<0.001
性別, 男性	0.51 (0.36–0.72)	<0.001
現喫煙	1.50 (1.08–2.07)	0.015
低BMI	0.99 (0.71–1.39)	0.969
低SMI	1.61 (1.22–2.12)	0.001
GLFS-25 得点		
グレード 1	reference	
グレード 2	1.21 (0.92–1.60)	0.179
グレード 3	1.34 (0.99–1.82)	0.062

表4 総死亡に対する比例ハザード解析（70歳以上）

	70 歳以上（n = 1,979）	
	HR (95% CI)	P
年齢, 歳	1.12 (1.06–1.17)	<0.001
性別, 男性	0.54 (0.36–0.81)	0.003
現喫煙	1.69 (1.17–2.48)	0.005
低BMI	1.18 (0.81–1.71)	0.380
低SMI	1.60 (1.16–2.18)	0.004
GLFS-25 得点		
グレード 1	reference	
グレード 2	1.29 (0.93–1.78)	0.124
グレード 3	1.60 (1.14–2.22)	0.007

比例ハザードモデルで有意な関連を示した低SMIとGLFS-25グレード3の組み合わせと総死亡との関連を図３に示した。GLFS-25がグレード3であり、かつ低SMIである群においてハザード比が最も高く、GLFS-25グレード3や低SMIのみでは総死亡と関連しなかった。

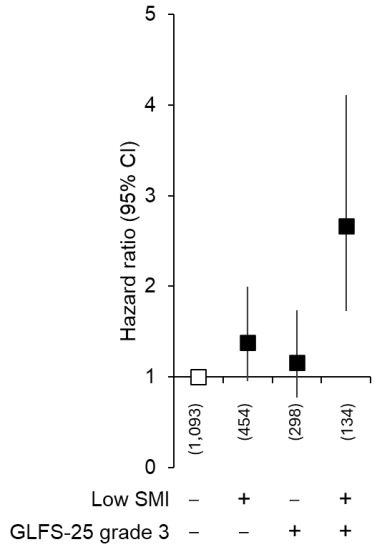


図3 GLFS-25と低SMIの組み合わせと総死亡

D. 考察

一般集団を対象とした長期縦断解析において、70歳以上の高齢者ではGLFS-25グレード3が全死因死亡と有意に関連した。この関連は、低SMIや低BMIなどの交絡因子とは無関係であった。また、早期死亡例を解析から除外しても有意であったことから、GLFS-25スコアと死亡率との関連から因果の逆転によるものではないと考えられる。

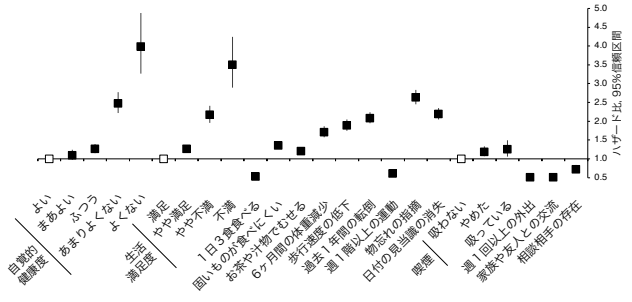
GLFS-25は、65歳以上の高齢者での使用が想定されている。我々は、GLFS-25スコアと要介護の発生率との関連については調査しなかったが、今回の結果は、地域住民のような比較的健常な集団においては、70歳以上において予後予測に優れる可能性を示している。スコアの平均点は、70歳以上の集団において年齢とともに直線的に増加しており、同様に関連は他の観察研究［Yamada K. J Orthop Sci. 2020; 25:1084-1092］でも報告されていることから、70歳以上のより高齢な集団に対してGLFS-25を適用すべきであると考えられた。

GLFS-25と総死亡との関連は、SMIとは独立していた。高齢者を対象とした以前の横断研究[Inanaga S. J Bone Miner Metab. 2023; 41:550-556.］では、GLFS-25スコアおよびGLFS-25の各構成要素（体の痛み、動作困難、普段のケア、日常生活動作、社会活動、認知）のスコアは、SMIと有意に関連しなかったと報告している。このような関連性の欠如は、様々な身体的要因とGLFS-25スコアとの関連を調査した横断研究のメタアナリシスでも報告されている[Kobayashi T. BMJ Open. 2023; 13:e068645]。これらの結果を踏まえると、GLFS-25はSMIが低いこと以外の状態を反映して、総死亡と関連している可能性がある。本研究集団の全例でGLFS-25スコアとの関連が報告されている握力や歩行速度のような身体的因子については解析していないため、GLFS-25がこれらの身体的パフォーマンス因子とは無関係に生命予後と関連するかどうかについては、さらなる調査が必要である。

総死亡のハザード比は、GLFS-25グレード3と低SMIとを組み合わせた群で最も高値であった。この結果は、GLFS-25グレード3と低SMIの組み合わせを独立変数として含めなかったCox比例ハザードモデルにおいて、両者を併存する者がGLFS-25グレード3と低SMIのハザード比を高めていたことを示している。SMIを同時に評価することは、GLFS-25グレード3の集団の中からさらにリスク度の高い部分集団を識別するために有用かもしれない。

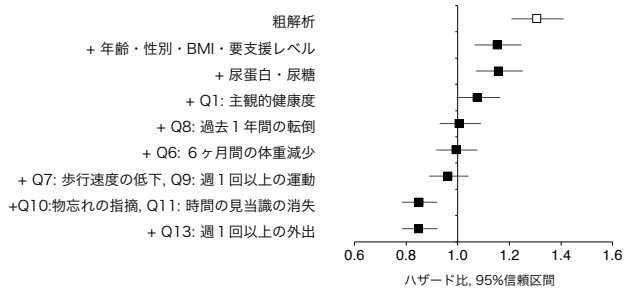
ロコモティブシンドロームの評価では、GLFS-25と2ステップテスト、立ち上がりテストとの組み合わせが提唱されている。これらの身体機能検査は対象者全例で実施していなかったため、複合スコアと予後との関連を評価することはできなかった。2ステップテストや立ち上がりテストと総死亡との関連について明確な関連は報告されていないが、複合スコアはロコモティブシンドロームの新規発症と関連することが報告されている［Yoshimura N. J Bone Miner Metab. 2022; 40:623-635］。GLFS-25スコアにこれらの身体機能検査を加えることで、GLFS-25スコアの予後予測能が改善されるかどうかについては、さらなる検討が必要である。

分担研究者らによる静岡国保データベースを用いた縦断解析［Tabara Y. Geriatr Gerontol Int. 2025; 25:260-266］では、特定健診で使用する後期高齢者質問票の妥当性について検討している。国民健康保険または後期高齢者医療制度に加入している75～90歳の静岡県民111,282人を平均1.7年（186,004人年）追跡した結果、要介護２以上の新規認定が3,501人観察され、後期高齢者質問票の15個の質問項目はいずれも要介護2以上認定と関連していた。



質問項目のうち「お茶や汁物でむせることがある」はオーラルフレイルを想定した質問であり、それ単独では要介護2以上認定と有意に関連していた。しかし、他の因子を調整することでハザード比が1.0を下回り、むせるほど要介護になりにくいことが示された。むせることは誤嚥に対する

正常な反射であるため、むせることができるほど予後が良好であると解釈すべきであろう。



要介護認定との関連が想定される主要因子（年齢・性別・低BMI・入院歴・要支援レベル・高血圧・HDLC・LDLC・HbA1c・クレアチニン・GPT・尿糖・尿蛋白）と後期高齢者質問票の各質問項目のうちお茶や汁物でむせる以外を投入したCox比例ハザードモデルにおいて、要介護2以上認定と有意な関連を示した項目は下表の通りであった。

	係数	ハザード比 (95% CI)	P
年齢（歳）	0.117	1.12 (1.11–1.13)	<0.001
性別（男性）	0.335	1.40 (1.30–1.50)	<0.001
低BMI（<20 kg/m²）	0.295	1.34 (1.25–1.45)	<0.001
ベースライン時点で要支援の認定をうけている	0.942	2.57 (2.32–2.84)	<0.001
尿糖（±以上）	0.322	1.38 (1.21–1.57)	<0.001
尿蛋白（±以上）	0.421	1.52 (1.42–1.64)	<0.001
Q01：現在の健康状態はいかがですか？（あまり良くない/良くない）	0.353	1.42 (1.31–1.55)	<0.001
Q06：6カ月間で2～3kg以上の体重減少がありましたか？（はい）	0.202	1.22 (1.12–1.34)	<0.001
Q07：以前に比べて歩く速度が遅くなってきたと思いますか？（はい）	0.258	1.29 (1.19–1.41)	<0.001
Q08：この1年間に転んだことがありますか？（はい）	0.382	1.47 (1.36–1.58)	<0.001
Q09：ウォーキング等の運動を週に1回以上していますか？（いいえ）	0.261	1.30 (1.21–1.39)	<0.001
Q10：周りの人からの物忘れがあると言われていますか？（はい）	0.598	1.82 (1.68–1.97)	<0.001
Q11：今日が何月何日かわからない時がありますか？（はい）	0.455	1.58 (1.46–1.70)	<0.001
Q13：週に1回以上は外出していますか？（いいえ）	0.376	1.46 (1.34–1.59)	<0.001

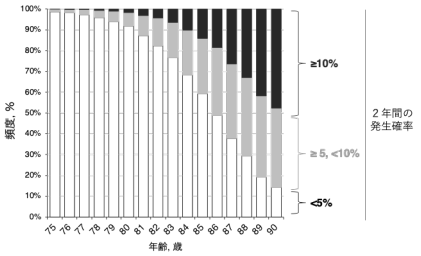
年齢・性別・低BMI・入院歴・要支援レベル・高血圧・HDLC・LDLC・HbA1c・クレアチニン・GPT・尿糖・尿蛋白・後期高齢者質問項目を投入したCox比例ハザードモデルにおいて有意な関連を示した項目。

Cox比例ハザードモデルの回帰係数から要介護度2以上認定に対するポイントを算出した。

		ポイント
年齢	75–79 歳	90
	80–84 歳	96
	85–89 歳	102
性別（男性）		3
低BMI（<20 kg/m²）		3
ベースライン時点で要支援の認定をうけている		9
尿糖（±以上）		3
尿蛋白（±以上）		4
Q01：現在の健康状態はいかがですか？（あまり良くない/良くない）		4
Q06：6カ月間で2～3kg以上の体重減少がありましたか？（はい）		2
Q07：以前に比べて歩く速度が遅くなってきたと思いますか？（はい）		3
Q08：この1年間に転んだことがありますか？（はい）		4
Q09：ウォーキング等の運動を週に1回以上していますか？（いいえ）		3
Q10：周りの人からの物忘れがあると言われていますか？（はい）		6
Q11：今日が何月何日かわからない時がありますか？（はい）		5
Q13：週に1回以上は外出していますか？（いいえ）		4
スコアポイント		合計点 – 87

対象者個人ごとに総ポイント数を求め、ベースライン年齢（75歳）のポイントを減算してスコア化した場合、スコア得点に比例して2年間の要介護2以上の発生確率が増加した。また、発生確率は加齢とともに増加した。

スコア得点	2年間の発生確率, %
<4	<1
5–9	1
10–14	1.6
15–19	2.6
20–24	4.2
25–29	6.7
30–34	10.8
35–39	17.3
≥40	≥34.1



総死亡に対して同様の解析を行った場合、後期高齢者質問票からは要介護2以上認定の場合と同じ項目が有意に関連した。加えて現喫煙、過去喫煙も総死亡と有意に関連した。

	モデル１	モデル２
年齢	1.08 (1.07–1.09)	1.08 (1.07–1.09)
性別, 男性	3.62 (3.37–3.90)	3.37 (3.11–3.66)
低BMI, <20kg/m²	1.71 (1.58–1.84)	1.70 (1.57–1.83)
ベースライン時点での介護度	1.76 (1.43–2.17)	1.76 (1.43–2.17)
	1.79 (1.49–2.15)	1.79 (1.49–2.15)
	2.07 (1.83–2.34)	2.07 (1.83–2.35)
尿糖, ≥±	1.31 (1.16–1.48)	1.30 (1.15–1.47)
尿タンパク, ≥±	1.68 (1.56–1.80)	1.67 (1.55–1.79)
FQ01 自覚的健康度, あまりよくない・よくない	1.38 (1.26–1.51)	1.39 (1.26–1.52)
FQ03 ３食の食事, いいえ	1.20 (1.05–1.36)	1.17 (1.03–1.34)
FQ06 半年間の体重減少, はい	1.39 (1.27–1.52)	1.37 (1.25–1.50)
FQ07 歩行速度の低下, はい	1.25 (1.15–1.36)	1.24 (1.14–1.35)
FQ08 １年間の転倒, ある	1.12 (1.03–1.22)	1.12 (1.03–1.22)
FQ09 定期的な運動, している	1.39 (1.29–1.49)	1.38 (1.28–1.49)
FQ10 物忘れの指摘, ある	1.13 (1.03–1.24)	1.12 (1.02–1.23)
FQ11 日の見当識の消失, ある	1.16 (1.07–1.26)	1.15 (1.06–1.25)
FQ13 定期的な外出, ない	1.27 (1.16–1.40)	1.27 (1.15–1.40)
FQ04 固い食品が食べにくい, はい		1.08 (1.00–1.16)
FQ05_汁物でむせる, はい		0.95 (0.87–1.03)
FQ12_喫煙習慣, 吸う		1.37 (1.19–1.58)
FQ12_喫煙習慣, やめた		1.17 (1.06–1.28)
FQ14_社会参加, ある		1.02 (0.89–1.16)
FQ15_社会的支援, ある		0.96 (0.83–1.12)

モデル１：要介護に対する解析で抽出された因子
モデル２：上記＋後期高齢者質問票の残りの項目

後期高齢者質問票は、後期高齢者を対象とした健診でおしなべて使用されるものであり、このスコアを当てはめることで、健診受診者における要介護2以上や総死亡のリスク度を簡便に評価できることは、社会実装の可能性の高さを裏付けている。ただし、当該スコアは健診受診者を対象に作成したものであり、より健康状態が良くない非受診者にそのまま当てはめることは困難である。

E．結論

GLFS-25は、70歳以上において総死亡の評価指標として利用可能である。後期高齢者質問票の8項目は、その他の要因と組み合わせたリスクスコアとして75歳以上の要介護2以上の新規認定や総死亡のリスク度評価に利用できる。

F．健康危険情報

該当なし

G．研究発表

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H．知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

フレイル・サルコペニア発症に寄与する要因の解析

研究分担者 新村　健　兵庫医科大学医学部 主任教授

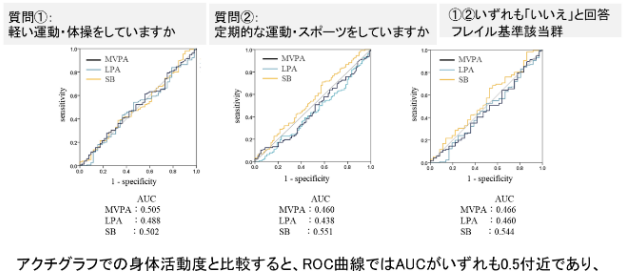
研究要旨
我々はフレイル・サルコペニアに着目して、高齢者の身体機能低下に寄与する要因を学際的な視点から明らかにすることを目的に、兵庫県丹波篠山圏域在住高齢者を対象としたコホート研究を継続している。今年度は高齢者用の簡易身体活動量質問票を開発しその妥当性を検証した。次に歯科口腔外科的視点よりフレイル・サルコペニアの発症・進展に寄与するリスク要因の解析を行った。縦断的な解析から、高齢者のフレイル・サルコペニア肥満の予防においては、口腔機能の維持が重要であることが強く示唆された。

A．研究目的

我々の研究目的は、地域在住高齢者において、フレイル・サルコペニアに着目して、身体機能低下に寄与する要因を学際的な視点から明らかにすることである。

今年度、最初に取り組んだ課題は、J-CHS基準の身体活動量質問より正確に高齢者の身体活動量を評価することができる、簡便な質問票を作成することである。その背景として我々は以前から腕時計型の身体活動量を用いて高齢者の身体活動量を評価していた。J-CHS基準の身体活動量に関する質問、①軽い運動、体操をしていますか、②定期的な運動・スポーツをしていますか、の2項目（両方ともいいえ）で高齢者の身体活動量を評価した場合、身体活動量計で計測した低強度身体活動量（LPA）、中強度身体活動量（MVPA）いずれとも弱い相関しか認められなかったからである（図1）。そこで我々は簡易高齢者身体活動質問票（BOPAQ）を開発し、その妥当性、信頼性を検討した。

図1 J-CHS基準身体活動量の質問の精度



アクチグラフでの身体活動度と比較すると、ROC曲線ではAUCがいずれも0.5付近であり、それぞれの質問の判別能は低い

Nagai K, Shinmura K 他 Geriatr Gerontol Int 2024;24(2):240-242.

次に取り組んだ課題は、口腔機能評価が将来のフレイル、サルコペニア発症に寄与しうるかを我々のコホートでの縦断的解析により明らかにすることである。我々のコホート研究では開始2年目より歯科口腔外科医師の協力のもと、口腔機能評価を全受診者に行ってきた。当初からオーラルフレイルにも着目してきたため、どのような口腔機能低下が高齢者の体組成の変化や身体機能低下に寄与するのか、オーラルフレイルは将来の身体フレイル発症に寄与しているかを明らかにすることは重要と考えた。

B．研究方法

兵庫県丹波篠山圏域在住の高齢者（総参加者数1,147名）が対象。フレイル・サルコペニアの発症リスク因子の探索を目的に、原則2年毎の追跡調査を実施している。フレイル診断はJ-CHSと基本チェックリストで、サルコペニア診断はAWGS2019で、サルコペニア肥満診断は、Japanese Working Group on Sarcopenic Obesity基準で行った。オーラルフレイル診断はOF-5により、歯科医の診察のもと口腔機能評価（残存歯数、義歯使用、咬合力、咬合バランス、咬合支持、口腔衛生、口腔湿潤、嚥下能、ディアドコキネシス、唾液分泌、舌圧）を行った。参加者は自己記載の質問表に回答し、検査に同意いただいた方には腕時計型身体活動量、アクチグラフを非利き腕に1週間、入浴以外の時間帯は継続的に装着

した。

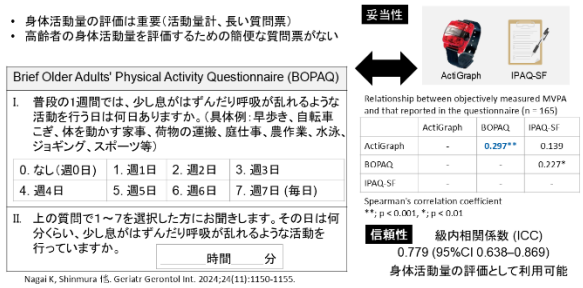
（倫理面への配慮）

研究対象者に対しては、不利益や危険性の排除などの説明後、文書による同意を得ている。本研究は、兵庫医科大学倫理審査委員会にて承認を得ている（承認番号 倫ヒ 0342）。

C. 研究結果

1. 2024年度の調査研究に参加した高齢者で、アクチグラフを5日以上装着し、BOPAQに加え、IPAQ-SFを自己記載した165名を解析対象者とした。BOPAQは、MVPAとr=0.297の相関を認めたが、IPAQ-SFとMVPAとの間には相関を認めなかった（r=0.139）（図2）。さらに級内相関係数は0.779（95%信頼区間0.638-0.869）で　高い信頼性が検証された。

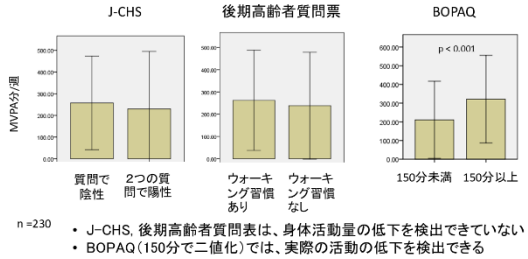
図2 地域在住高齢者に対する簡易身体活動量質問票の開発



Nagai K, Shinmura I他. Geriatr Gerontol Int. 2024;24(11):1150-1155.

BOPAQの検証目的で、2025年度の調査研究に参加した高齢者では、アクチグラフ装着、BOPAQ記載に加え、J-CHSの身体活動量質問、後期高齢者質問票に回答してもらった（n=230）。J-CHSおよび後期高齢者質問票ではMVPAで評価した場合の身体活動量の低下を検出できていなかったが、BOPAQではそれを適切に検出できることが明らかにされた（図3）。

図3 簡易な身体活動質問票における妥当性の比較



2. 解析対象者は、2回以上調査に参加した597名の高齢者。追跡時サルコペニア肥満群は10名で年齢が高く、骨格筋量が少なく身体的機能が劣っていた。さらに高血圧を合併し、残歯数が少なかった。このサルコペニア肥満群はベースラインにおいてはロバスト2名、肥満3名、サルコペニア2名、サルコペニア肥満3名であった。Cox回帰モデルでは男性、BMI、四肢筋肉量に加え、舌圧がサルコペニア肥満のリスクと有意に関連していた（オッズ比: 0.91、95%信頼区間：0.83-0.99、p= 0.028）（図4）。

図4 サルコペニア肥満、サルコペニア、肥満の発症に寄与する要因（Cox回帰分析）

	オッズ比	95%信頼区間	p値
Model 1: サルコペニア肥満の発症			
性（男性=1、女性=0）	20.191	3.151－129.366	0.002
BMI	2.118	1.554－2.886	<0.001
舌圧	0.906	0.829－0.990	0.028
四肢筋肉量	0.661	0.510－0.857	0.002
Model 2: サルコペニアの発症			
性（男性=1、女性=0）	31.231	9.660－100.974	<0.001
握力低下、椅子立ち上がり時間延長がともにない	0.188	0.065－0.543	0.002
四肢筋肉量	0.571	0.469－0.695	<0.001
Model 3: 肥満の発症			
性（男性=1、女性=0）	2.702	0.830－8.801	0.099
体脂肪量	1.192	1.095－1.297	<0.001

3. 解析対象者は、2～3年の間隔で追跡調査に参加した329名の高齢者。女性においては初回のOF-5スコアが高いほど、追跡中に身体的フレイルが進行するリスクが有意に高かった（オッズ比：1.32、95%信頼区間：1.00–1.75、P=0.049）。男性ではオーラルフレイルが存在する（OF-5 2点以上）と身体的フレイルが進行するリスクが高かった（オッズ比：3.36、95%信頼区間：1.23–9.28、P=0.018）（図5）。

4.

図5 フレイル進展に寄与する要因（多変量ロジスティック回帰分析）

	男性		女性	
男女別解析	オッズ比（95%信頼区間）	p値	オッズ比（95%信頼区間）	p値
年齢	0.98 (0.56-1.70)	0.934	1.15 (0.81-1.64)	0.436
BMI	1.53 (0.82-2.84)	0.172	1.39 (0.88-2.20)	0.156
握力	0.62 (0.34-1.13)	0.106	0.96 (0.64-1.42)	0.820
通常歩行速度	0.86 (0.53-1.42)	0.564	1.13 (0.80-1.62)	0.479
SMI	0.82 (0.39-1.71)	0.592	0.86 (0.54-1.37)	0.536
Cre/CysC	0.91 (0.53-1.58)	0.740	1.03 (0.72-1.49)	0.863
OF-5スコア（点）	1.49 (0.91-2.45)	0.107	1.32 (1.00-1.75)	0.049
男性での解析	オッズ比（95%信頼区間）	p値		
年齢	0.96 (0.55-1.69)	0.894		
BMI	1.50 (0.80-2.82)	0.209		
握力	0.61 (0.33-1.11)	0.097		
通常歩行速度	0.87 (0.52-1.44)	0.582		
SMI	0.83 (0.39-1.75)	0.622		
Cre/CysC	0.94 (0.54-1.64)	0.830		
オーラルフレイルあり（OF-5 2点以上）	3.38 (1.23-9.28)	0.018		

D. 考察

我々の開発したBOPAQはたった2問の質問で

あるが、高齢者の身体活動量低下を検出可能な質問票であることが明らかにされた。一方、BPAQは身体活動量を全体的に低めに評価し、特にMVPAの長い身体活動量の多い高齢者では不正確であることが課題として挙げられた。高齢者においては安静時間を減らし、LPAやMVPAを少しでも増やすことが有意義と考えられている。よって、BOPAQによりMVPAが少ない集団をうまく検出できるのであれば、地域在住高齢者の健康増進目的として使用することは適切ではないかと期待される。

今回、将来のフレイル・サルコペニア肥満に対するリスク要因の解析は、歯科口腔外科的視点より行った。サルコペニア肥満は、サルコペニアより予後が悪く、ハイリスク集団と考えられているが、今回の検討では男性に加え、舌圧低下がサルコペニア肥満と有意な関係を認めたことから、口腔機能の維持が高齢者のサルコペニア肥満予防において有用である可能性が示唆される。さらに身体的フレイル進行のリスクがオーラルフレイル合併で高まることが明らかにされた。つまり顕著な口腔機能低下が存在する前段階であっても、将来の身体的フレイルのリスクが高いことは、現在、医科歯科連携によるオーラルフレイル啓蒙活動の意義をより堅固にするエビデンスを言えよう。以上の結果から、高齢者のフレイル・サルコペニア予防策において、口腔機能の維持は重要な介入標的であることが示唆された。

E. 結論

高齢者の身体活動量低下を適切に検出可能で、信頼性の高い簡易質問票である、BOPAQを開発した。

高齢者のフレイル・サルコペニア予防対策として、医科歯科連携による口腔機能維持が有用である可能性が明らかにされた。

F. 健康危険情報

該当なし

G. 研究発表

1. 論文発表

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2. 学会発表

該当なし

H. 知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

日本人高齢者集団における頸動脈内膜中膜複合体厚とサルコペニアとの縦断的関連の検討 SONIC研究

研究分担者 山本浩一　大阪大学大学院医学系研究科老年・総合内科学 教授

研究要旨
SONIC研究のデータを用い、頸動脈内膜中膜厚（CIMT）とサルコペニアとの関連性を検証する横断的、縦断的解析を実施した。その結果、CIMTの増加はベースラインのサルコペニアの有無、3年後のサルコペニアの発症リスク増加と関連していることが明らかとなった。CIMTはサルコペニアの病態生理の理解やハイリスク高齢者の識別に有用な指標となる可能性がある。

A．研究目的

サルコペニアは高齢者において要介護状態や疾病発症、死亡リスクを高めることが知られており、また心血管疾患との間で相互にリスク因子となることが報告されている。頸動脈内膜中膜厚（carotid intima-media thickness; CIMT）は、超音波検査によって非侵襲的に測定できる動脈硬化の指標であり、心血管疾患発症の強い予測因子である。近年、CIMTが筋力低下や歩行速度低下、筋量減少といった指標と関連することを示す横断研究報告が散見される。しかし、縦断的研究によってCIMTの増大が将来的なサルコペニア発症と関連するかを検討した例はなく、その因果関係は十分に解明されていない。そこで本研究では、日本の地域在住高齢者を対象とした多施設共同コホート研究であるSONIC（Septuagenarians, Octogenarians, Nonagenarians Investigation with Centenarians)のデータを用い、CIMTとサルコペニアとの関連を横断および縦断的に検証することを目的とした。

B．研究方法

SONIC研究は2010年より開始された前向きコホート研究であり、参加者を70歳代・80歳代・90歳代・100歳代のグループに分け、それぞれ3年ごとに追跡調査を実施している。本解析ではそのうち70歳代コホートのデータを用い、第3波調査(Wave3)において約76歳で評価を受けた参加者群を対象とした。第3波調査では参加者757名に対し調査を行い、不備データのある者を除外後、横断解析の対象は735名となった。さらに第4波調査(Wave4; 3年後)でも追跡評価が行われた者498名を縦断解析の対象とした（図1）。

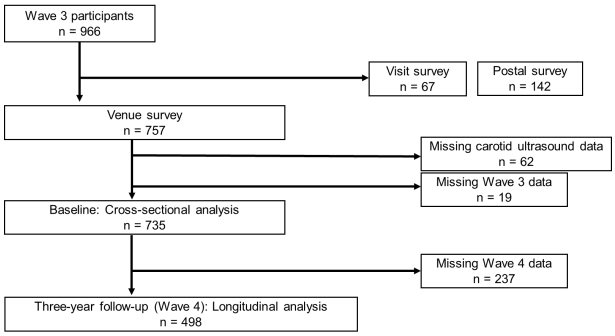

図1 フローチャート

調査項目には、生活歴・既往歴の聞き取り、身体計測、血圧測定、握力、5m通常歩行速度、SPPB（Short Physical Performance Battery）得点等を含めた。サルコペニアの診断はAWGS2019年提唱の基準に従い、筋肉量低下に加えて筋力低下または身体機能低下のいずれかを認める場合にサルコペニアと判定した。頸動脈CIMTは左右の総頸動脈(CCA)、頸動脈分岐部、および内頸動脈(ICA)の近位壁・遠位壁をBモードで走査し、動脈硬化プラークを含め観察された最大の内膜中膜厚を計測した。統計解析では、横断解析および縦断解析それぞれでサルコペニアの有無を目

的変数としたロジスティック回帰分析を行った。説明変数には最大CIMTに加え、サルコペニアに関係し得る因子として性別、BMI、収縮期血圧、CKD、喫煙歴、糖尿病、脂質異常症、心血管疾患既往を投入した。なおSONIC研究は年齢層を揃えたコホートデザインであるため、本解析では年齢を調整変数から除外した。縦断解析では上記に加え、ベースライン時（Wave3）のサルコペニア有無で調整を行い、さらにサブ解析としてWave3でサルコペニアでなかった群に限定した新規発症解析も実施した。

（倫理面への配慮）

倫理審査委員会の承認を得ており、参加者全員から書面による同意を取得した。

C．研究結果

横断解析対象735名（男性347名、女性388名、平均年齢76.0±0.9歳）のうち、130名（17.7%）がサルコペニアと判定された。サルコペニア群は非サルコペニア群に比べ、年齢、BMI、血圧、推算糸球体濾過量（eGFR）、高血圧症の割合などに有意差を認めた。多変量ロジスティック回帰分析の結果、最大CIMTはサルコペニアの独立した有意な関連因子であり、最大CIMTが1mm増加するごとにサルコペニアであるオッズ比(OR)は1.55倍（95%信頼区間1.15–2.07）となった（表1）。

表1 ベースラインの多重ロジスティック回帰分析

	OR	95% CI	p-value
Sex, male	1.23	0.68–2.24	0.50
Body mass index, kg/m^2	0.61	0.54–0.67	<0.0001
Systolic BP, mmHg	0.99	0.98–1.01	0.44
CKD	0.74	0.45–1.21	0.22
History of Smoking	1.97	1.08–3.59	0.027
Diabetes	0.78	0.36–1.70	0.53
Dyslipidemia	0.77	0.48–1.26	0.30
CVD	0.88	0.37–2.09	0.78
Maximum CIMT, mm	1.55	1.15–2.07	0.004

OR, odds ratio; CI, confidence interval; BP, blood pressure; CKD, chronic kidney disease (defined as an eGFR <60 mL/min/1.73m^2); CVD, cardiovascular disease, CIMT, carotid intima-media thickness.

縦断解析対象498名（男性247名、女性251名、ベースライン平均年齢75.9±0.9歳）のうち、ベースライン時にサルコペニアであった者は81名（16.2%）、3年後の追跡時にサルコペニアと判定された者は100名（20.1%）であった。Wave4でサルコペニアと判定された群は、非サルコペニア群と比較してベースライン時の年齢が高く、BMIが低値で、拡張期血圧が低く、脂質異常症の有病率に差が認められた。ベースライン時の最大CIMTは3年後のサルコペニア発症と有意に関連し、最大CIMTが1mm高いごとにサルコペニア発症オッズが1.63倍 (95%信頼区間1.13–2.36) に上昇した（表2）。

表2 3年後の多重ロジスティック回帰分析

	OR	95% CI	p-value
Sex, male	1.42	0.68–2.94	0.35
Body mass index, kg/m^2	0.79	0.70–0.89	<0.0001
Systolic BP, mmHg	1.00	0.98–1.02	0.96
CKD	1.32	0.73–2.37	0.36
History of Smoking	1.46	0.71–3.03	0.31
Diabetes	0.44	0.14–1.38	0.16
Dyslipidemia	0.61	0.33–1.10	0.10
CVD	1.33	0.49–3.60	0.58
Sarcopenia at baseline	9.07	4.77–17.3	<0.0001
Maximum CIMT, mm	1.63	1.13–2.36	0.010

さらにベースラインでサルコペニアでなかった群に限定した解析でも、最大CIMTの増加に伴いサルコペニア新規発症リスクが上昇し、1mmあたりのORは1.60（95%信頼区間1.04–2.47）と有意であった。

D．考察

本研究により、地域在住高齢者において頸動脈CIMTの増大がサルコペニアの有無および将来的な発症リスクとそれぞれ独立して有意に関連することが示された。これは、動脈硬化の指標であるCIMTの肥厚化がサルコペニアの病態形成に関与している可能性を示唆するものであり、頸動脈CIMTが高い高齢者はサルコペニアハイリスク者として抽出できる可能性がある。特に本研究では平均年齢76歳の同齢集団を対象としており、年齢の影響をほぼ除外した上でCIMTとサルコペニアの関連を検証した点で意義深い。今回、CIMT指標として平均値ではなく最大値を採用しているが、先行研究でも平均CIMTより最大CIMTの方が心血管疾患や認知機能低下、サルコペニアとの関連が強いことが示されている。関連する機序として筋衛星細胞と血管内皮細胞のクロストークの動脈硬化による破綻、また、慢性炎症や歯周病、低栄養、などが動脈硬化およびサルコペニア双方に影響を及ぼす可能性も挙げ

られる。但し、本研究は観察研究であり、因果関係の解釈には注意を要する。今後、機序の解明とともに、CIMTがサルコペニアのリスクマーカーとして臨床応用可能か検証する研究が望まれる。

Ｅ．結論

CIMTの増加は高齢者におけるサルコペニア発症リスクと関連しており、CIMTはサルコペニアのリスク評価および早期介入のための有用な指標となる可能性が示唆された。

F. 健康危険情報

該当なし

G. 研究発表

1. 論文発表

該当なし

2. 学会発表

該当なし

Ｈ．知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

J-CHS基準で判定したフレイルと3年後の要介護認定との関連：高齢者長期縦断(SONIC)研究からの知見

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研究要旨
高齢者長期縦断コホート研究(SONIC)に参加している地域在住高齢者において、J-CHS基準で判定したフレイル・プレフレイルは3年後の要支援1以上の要介護認定の予測因子であることが示された。これは男女で同様の結果が示され、年代別では76歳が中央値である70歳代後半の集団において最も強い関連を認めた。したがって我が国の高齢者において後期高齢者になって間もない高齢者において、J-CHS基準でフレイル・プレフレイルと判定された場合、3年後には要介護認定となるリスクが高いため、介護予防策を厳重に行うことが重要と考えられた。

A．研究目的

身体的フレイルの判定として我が国で広く使用されているJ-CHS基準(Satake S et al. 2020)は、要介護の前段階であるフレイル状態を判定し、将来の要介護状態に陥ることを避けるために介護予防の取り組みへの参加が必要な高齢者のスクリーニング方法としてその意義は確立されている。しかしながら本判定基準でフレイルと判定された高齢者がどの程度、どのくらいの期間を経て要介護認定に至るかなどを明らかにするために、将来の要介護認定をアウトカムにした縦断的な検討が行われる必要があるが、現状ではその報告は限られている。さらに要介護認定を受ける最大の影響要因は年齢であり、年齢の影響を取り除いた上で、J-CHS基準による将来の要介護認定の予測能を検討することは意義が大きい。2024年度の本厚生労働科研では、我々が2010年から行っている高齢者長期縦断コホート研究であるSONIC研究のデータを用いて、J-CHS基準によって判定されたフレイル状態が将来の要介護認定にどの程度寄与するかの検討を年代別に検討することを目的に分析を行った。

B．研究方法

SONIC研究（Kamide K. Geriatr Gerontol Int. 2025; 25:346-355）の追跡調査である第3波調査(2016年：76±1歳対象、2017年：86±1歳対象、2018年：96±1歳対象)に参加した研究対象者のうち、要介護認定情報が不明の者、すでに要介護認定がある者、J-CHS基準に関するデータに欠損があるもの、さらに3年後の第4波調査（会場/郵送）で情報収集が出来なかった者を除いた、計1126名（70歳代：610名、80歳代：330名、90歳代：186名）を対象とした。

第3波調査時点でJ-CHS基準により、ロバスト・プレフレイル・フレイルに分類した。3年後第4波調査時点での要介護認定(要支援1、要介護1,2以上)を目的変数として、説明変数はJ-CHS基準3分類、調整変数は要介護認定申請理由の疾患（認知症あるいはMCI、脳卒中、骨折、関節の痛み/変形）としてロジスティック回帰分析を行った。

（倫理面への配慮）

SONIC研究は大阪大学医学部附属病院観察研究倫理審査委員会で承認を受けている。

C．研究結果

対象者背景では年齢の中央値は、ロバスト(76歳),プレフレイル(84歳)，フレイル(86歳)と有意にフレイル・プレフレイル群で高かった。独居率、

過去1年間の転倒割合、MCI割合、骨粗鬆症罹患率、関節の痛みを有する者の割合などいずれもフレイル群で高率であった。

図１のように3年後の要介護認定率は明らかにフレイル群で高率であり、要支援から要介護5までを要介護認定として含めるとロバスト10%強に比較して、プレフレイル25%，フレイル35%程度と有意な上昇をしめした。

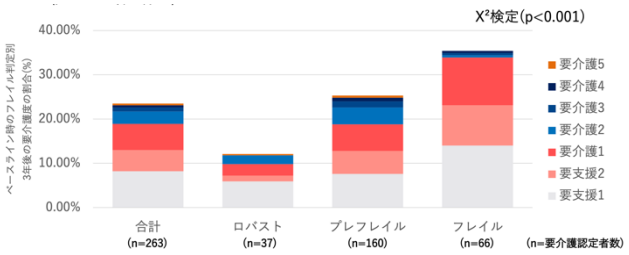

図１ J-CHS基準別３年後の要介護認定者割合

要支援から要介護5までをすべて要介護認定としたロジスティック回帰分析では、図2に示す通り、ロバストに比し、プレフレイル・フレイルはオッズ比2程度で3年後の要介護の有意なリスクとなっていた。

	Model1		Model2		Model3	
	OR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
プレフレイル	2.43 (1.65-3.59)	<0.001	1.87 (1.25-2.80)	0.002	1.88 (1.25-2.82)	0.002
フレイル	3.95 (2.51-6.24)	<0.001	2.43 (1.49-3.93)	<0.001	2.27 (1.39-3.71)	0.001

- ref: ロバスト
- Model1：ベースライン時J-CHS基準
- Model2：ベースライン時J-CHS基準＋性別＋年齢
- Model3：ベースライン時J-CHS基準＋性別＋年齢＋疾患（MCI、骨折、脳卒中、関節疾患）

疾患調整後もJ-CHS基準で判定したフレイル、プレフレイルは3年後の要介護認定に独立して関連

図２ ３年後の要介護認定との関連

この関連は要介護認定の目的変数を要支援1以上とした場合は男女別にしても確認された。また年代別にした場合、70歳代と90歳代では同様の関連が認められたが、80歳代では関連が消失した。また要介護認定の目的変数を要介護1以上とした場合は全体でプレフレイルのみでこの関連が認められ、フレイルでは有意な関連は消失した。

D．考察

J-CHS基準で判定したフレイル・プレフレイルは3年後の要支援1以上の要介護認定の予測因子であることが示された。一方、要介護1以上の判定には必ずしも有用とは言えない結果となったが、SONIC研究は会場調査で自立して会場調査に参加できる対象者を観察しており、85歳以上を多く含む対象者の割には要介護認定者が少ない、比較的元気な高齢者であったため、要介護認定者の数からこのような結果となった可能性は高い。今回は郵送調査も含まれるため、かなり情報収集はできたとは言え、3年間で185名追跡から脱落した対象者がいるため、この点は研究の限界であると言える。しかしながら全員が75歳以上の後期高齢者でJ-CHS基準による将来の要介護認定への関連を示した成果は大きな意義があると考えられる。今後脱落者を含めた分析や、より詳細な分析を加えることで高齢期におけるJ-CHS基準で判定するフレイルの意義をより精緻に明らかにする予定である。

E．結論

J-CHS基準で判定したフレイル・プレフレイルは75歳以上の地域在住高齢者における3年後の要支援1以上の要介護認定の予測因子であることが示された。これは男女で同様の結果が示され、年代別では76歳が中央値である70歳代後半の集団において最も強い関連を認めた。したがって我が国の高齢者において後期高齢者になって間もない高齢者において、J-CHS基準でフレイル・プレフレイルと判定された場合、3年後には要介護認定となるリスクが高いため、介護予防策を厳重に行うことが重要と考えられた。

F．健康危険情報

該当なし

G．研究発表

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H．知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

東日本大震災被災地域におけるフレイルと要介護認定および死亡発生の関連

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研究要旨
本研究の目的は、被災者を対象としてフレイルが高齢者の要介護認定、死亡の発生に及ぼす影響を明らかにすることである。2011年度から2020年度にかけて岩手医科大学が実施した厚生労働行政推進調査事業費補助金「岩手県における東日本大震災被災者の支援を目的とした大規模コホート研究」（RIAS Study）の調査データを分析した。本研究ではRIAS研究対象者のうち、大槌町および陸前高田市に居住する65歳以上の男女3443名を対象者とした。KCL得点区分別に総観察人年、要介護認定および死亡の発生率を求めた。また、要介護2以上の認定、および死亡の発生をアウトカムとしたCox回帰分析を行い、KCLによって測定（0-3点：robust、4-7点：pre-frail、8点+：frail）したフレイルとの関連について解析した。解析は全体および仮設住宅居住歴別に実施した。対象者全体の分析において、HRはfrail群で2.39（1.71-3.33）、pre-frail群で1.36（1.02-1.82）となり、KCL得点と要介護認定発生の間で有意な関連がみられたが、死亡発生との間では有意な関連はみられなかった。KCL得点は、震災後の被災地域において、要介護認定について一定の予測能をもっていることが示唆された。

A．研究目的

2011年に発生した東日本大震災は、東北地方沿岸部に甚大な被害を発生させた。家屋被害を受けた住民の多くは仮設住宅に入居し、そのまま長期間の生活を送ってきた。災害後の仮設住宅での生活は、被災者の健康に好ましくない影響を及ぼす可能性があることが報告されている（Takahashi, 2020）。

わが国は災害大国であり、また現在、世界で最も高齢化が進行している国となっている。本研究では、被災者を対象としてフレイルが高齢者の要介護認定、死亡の発生に及ぼす影響を明らかにすることを目的とした。

B．研究方法

2011年度から2020年度にかけて岩手医科大学が実施した厚生労働行政推進調査事業費補助金「岩手県における東日本大震災被災者の支援を目的とした大規模コホート研究」（RIAS Study）の調査データを分析した（Omama, 2020）。RIAS Studyでは、東日本大震災に被災した岩手県沿岸部に位置する山田町、大槌町、釜石市、陸前高田市を対象として、毎年、健診相乗り型の調査が実施された。対象地域の18歳以上の全住民に協力を依頼し、同意を得られた10,475人を対象者とした。調査は健診および質問紙調査により構成された。また、追跡調査により対象者の要介護認定情報および除票による死亡情報を取得している。

本研究ではRIAS Studyの調査データのうち65歳以上の男女を対象として、要介護認定情報および死亡情報を取得している大槌町および陸前高田市のデータを分析した。

要介護認定情報について、陸前高田市の情報が被災による影響で2013年4月1日以降のデータのみ利用可能であったことから、本研究では2013年4月1日～2017年10月30日の期間に発生した新規（過去に要介護2以上の認定を受けていない

者）の要介護2以上の認定、および死亡の発生をアウトカムとした。要介護認定については申請日を要介護発生日として分析した。

フレイルの測定は基本チェックリスト（KCL）により行った。KCLは25項目からなり、1-5項目は日常生活関連動作、6-10項目は運動器の機能、11、12項目は低栄養状態、13-15項目は口腔機能、16、17項目は閉じこもり、18-20項目は認知症、21-25項目はうつについて尋ねる内容となっている。東日本大震災のあった平成23年度のRIAS Study調査では、KCLの項目のうち1-20項目が実施されており、本研究では各項目を1点、計20点満点のうち4点未満をrobust、4-7点をpre-frail、8点以上をfrailとして分析した（Satake et al, 2017）。

関連要因として、RIAS Study調査の平成23年度健診調査データより握力、質問紙調査データより性別、年齢、自治体（大槌町、陸前高田市）、現在の暮らし向き（苦しい、普通）、喫煙習慣（有無）、多量飲酒、既往歴（有無）、仮設住宅居住歴について分析した。握力は改定日本版Cardiovascular Health Study基準（J-CHS基準）に基づき男性<28kg、女性<18kgを筋力低下の基準とした。多量飲酒は1日あたりの平均純アルコール摂取量換算で男性40g以上、女性20g以上を基準とした。仮設住宅居住歴については、プレハブ型仮設住宅に居住していたことのある者を居住歴ありとした。

本研究ではRIAS研究対象者のうち、2013年3月31日以前に要支援1以上の認定を受けていない、大槌町および陸前高田市に居住する65歳以上の男女3443名を対象者とした。要介護2以上の認定、および死亡の発生をアウトカムとしたCox回帰分析を行い、KCLによって測定したフレイルとの関連について解析した。また、KCL得点区分別に総観察人年、要介護認定および死亡の発生率を求めた。解析は全体および仮設住宅居住歴別に実施した。

（倫理面への配慮）

本研究は岩手医科大学医学部倫理委員会の承認を得て実施している（承認番号：MH2022-132）。

C．研究結果

表1に、対象者のうちKCL得点および要介護認定申請日に欠損値を含む259名を除外した3184名のベースライン（平成23年度健診受診）のフレイルおよび関連要因の分布・平均値（年齢）を示す。

表1　基本チェックリスト別の対象者属性

	基本チェックリスト					
	0-3点	(%)	4-7点	(%)	8点以上	(%)
対象者数	1636	100	1165	100	383	100
年齢	72.18	±4.96	73.65	±5.49	77.33	±6.24
性別（女性）	815	49.8	756	64.9	254	66.3
握力（筋力低下）	178	10.9	207	17.8	144	37.8
自治体（陸前高田市）	1201	73.4	833	71.5	258	67.4
現在の暮らし向き（苦しい）	603	37.0	564	48.5	198	52.0
現在喫煙（あり）	161	9.8	107	9.2	26	6.8
多量飲酒（あり）	136	8.5	66	5.7	12	3.2
既往歴（あり）	1256	76.8	978	83.9	339	88.5
仮設住宅居住歴（あり）	488	29.8	408	35.0	134	35.0

表2にKCL得点別の要介護認定2以上および死亡の発生率、HRを示す。要介護認定について、KCL得点が高い群ほど高い発生率を示し、HRはfrail群で2.39（1.71-3.33）、pre-frail群で1.36（1.02-1.82）と有意に高値であった。死亡について、KCL得点が高い群ほど高い発生率を示したが、HRはfrail群で1.41（0.99-2.15）、pre-frail群で0.98（0.70-1.36）と有意な関連はみられなかった。図1・2に、KCL得点別の要介護認定および死亡発生状況を表すKaplan-Meier曲線を示す。

表2　基本チェックリスト得点別の要介護認定2以上および死亡の発生率とHR（95% CI）

	対象数	観察人年	発生数	発生率	HR	95% CI
要介護認定2以上						
基本チェックリスト						
0-3	1636	7298	93	12.7	-	
4-7	1165	5089	108	21.2	1.36	1.02 - 1.82
8以上	383	1534	87	56.7	2.39	1.71 - 3.33
死亡						
基本チェックリスト						
0-3	1636	7340	89	12.1	-	
4-7	1165	5217	68	13.0	0.98	0.70 - 1.36
8以上	383	1668	39	23.4	1.41	0.93 - 2.15

調整変数：性, 年齢, 握力, 自治体, 現在の暮らし向き, 喫煙習慣, 多量飲酒, 既往歴, 仮設住宅居住歴.

図1. 基本チェックリスト得点別要介護認定発生状況の推移（全体）

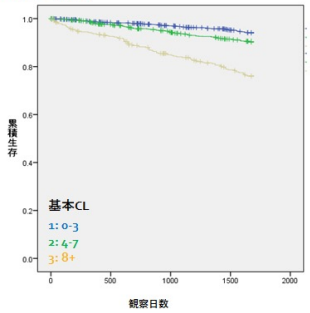


図2. 基本チェックリスト得点別死亡発生状況の推移（全体）

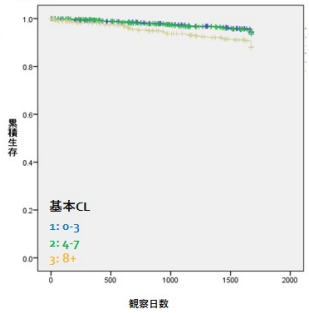


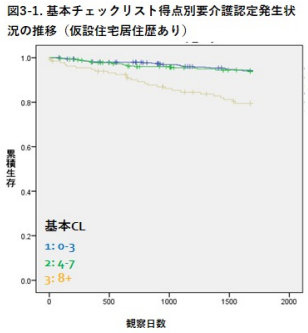
表3に、仮設住宅居住歴別にみた、KCL得点別

の要介護認定の発生率、HRを示す。仮設住宅居住歴のなかった群で、より高い要介護認定の発生率を示した。仮設住宅居住歴があった群において、HRはfrail群で1.96（1.05-3.64）と有意に高値であった。仮設住宅居住歴がなかった群において、HRはfrail群で2.59（1.74-3.85）、pre-frail群で1.70（1.22-2.38）と有意に高値であった。図3-1・3-2に、仮設住宅居住歴別にみた、KCL得点別の要介護認定の発生状況を表すKaplan-Meier曲線を示す。

表3　仮設住宅居住歴別にみた基本チェックリスト得点別の要介護認定2以上の発生率とHR（95% CI）

	対象数	観察人年	発生数	発生率	HR	95% CI
仮設住宅居住歴あり						
基本チェックリスト						
0-3	488	2172	28	12.9	-	
4-7	408	1804	24	13.3	0.77	0.43 - 1.37
8以上	134	545	26	47.7	1.96	1.05 - 3.64
仮設住宅居住歴なし						
基本チェックリスト						
0-3	1148	5126	65	12.7	-	
4-7	757	3285	84	25.6	1.70	1.22 - 2.38
8以上	249	989	61	61.7	2.59	1.74 - 3.85

調整変数：性, 年齢, 握力, 自治体, 現在の暮らし向き, 喫煙習慣, 多量飲酒, 既往歴.



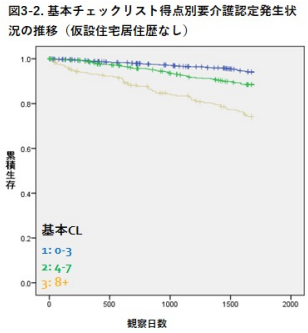
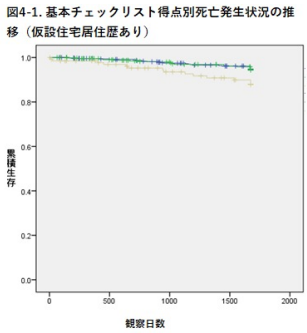


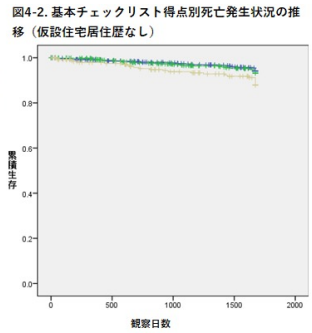
表4に、仮設住宅居住歴別にみた、KCL得点別の死亡の発生率、HRを示す。仮設住宅居住歴があった群、なかった群のいずれにおいても、HRはfrail群、pre-frail群ともに有意な関連はみられなかった。図4-1・4-2に、仮設住宅居住歴別にみた、KCL得点別の死亡の発生状況を表すKaplan-Meier曲線を示す。

表4　仮設住宅居住歴別にみた基本チェックリスト得点別の死亡の発生率とHR（95% CI）

	対象数	観察人年	発生数	発生率	HR	95% CI
仮設住宅居住歴あり						
基本チェックリスト						
0-3	488	2193	25	11.4	-	
4-7	408	1833	21	11.5	0.83	0.45 - 1.54
8以上	134	581	14	24.1	1.32	0.62 - 2.81
仮設住宅居住歴なし						
基本チェックリスト						
0-3	1148	5147	64	12.4	-	
4-7	757	3384	47	13.9	1.05	0.71 - 1.56
8以上	249	1087	25	23.0	1.48	0.89 - 2.45

調整変数：性, 年齢, 握力, 自治体, 現在の暮らし向き, 喫煙習慣, 多量飲酒, 既往歴.





D．考察

対象者全体の分析において、KCL得点と要介護認定発生の間で有意な関連がみられたが、死亡発生との間では有意な関連はみられなかった。KCL得点は、震災後の被災地域において要介護認定について一定の予測能をもっていることが示唆された。一方で、死亡については有意な関連がみられなかった。

仮設住宅居住歴別の分析において、仮設住宅居住歴がある群ではKCL（frail）、仮設住宅居住歴がない群ではKCL（pre-frail, frail）と要介護認定発生の間で有意な関連がみられた。仮設住宅の被害者には震災後から多くの支援が行われており、洪水被害の深刻な地域で脳卒中死亡率の低下がみられた（Omama, 2020）、被災者の住宅損壊と血圧低下との間に有意な関連がみられたといった研究のように、支援を受けることで健康や生活の状況が改善するケースもあることが報告されている。KCL得点と要介護認定の関連についても、仮設住宅居住者へのさまざまな支援によって、仮設住宅居住者では心身の機能低下が抑えられた可能性がある。

本研究の限界として、分析に含まれる介護・死亡データは2013年～2017年のものであり、震災直後のデータは含まれていない。また、KCLの合計得点について4点未満をrobust、4-7点をpre-frail、8点以上をfrailとする基準は、本来は25点満点で実施する際のものであるが、RIAS Studyではうつ症状に関する5点分の項目を初年度調査で実施していないため、20点満点で分析している。

E．結論

KCL得点と要介護認定発生の間で有意な関連がみられた。KCL得点は、震災後の被災地域にお

ける要介護認定の発生について、一定の予測能をもっていると考えられる。

F. 健康危険情報

該当なし

G. 研究発表

1. 論文発表

該当なし

2. 学会発表

該当なし

H. 知的財産権の出願・登録状況

該当なし

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別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

フレイルの増悪・改善に関連する因子の解明～垂水研究

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研究要旨
鹿児島県垂水市をフィールドとしたコホート研究のデータを用いて、5年間の追跡におけるフレイルの増悪および改善に関連する要因を探索した。5年間の追跡でフレイル段階が悪化した者が約20～30%、改善した者が約32～35%であった。5年後のJ-CHSによるフレイル段階の改善には握力、悪化には歩行速度、立ち座り、情報処理、JST活動能力指標が関連する要因であり、KCLによるフレイル段階の改善には認知機能、悪化には腰痛、社会的フレイル、睡眠の質、GDS-15が関連する要因として抽出された。5年後のJ-CHSおよびKCLによるフレイル段階の改善や悪化に関連する要因は、身体機能、認知機能の他、生活習慣に関連する要因も抽出された。

A．研究目的

鹿児島県垂水市をフィールドとしたコホート研究のデータを用いて、フレイルの増悪および改善に関連する要因を探索することを目的とした。とくに、本研究では改定日本語版J-CHS基準および基本チェックリスト（25項目）（KCL）をアウトカムとした5年間での変化に関連する要因を分析した。

B．研究方法

2019年に垂水研究に参加した65歳以上の高齢者687名を対象とした。そのうち、認知症および脳疾患の既往のある者、要介護認定者を除く657名から5年後の追跡調査に参加した268名を分析対象とした。さらに、アウトカムであるJ-CHSに欠損のあった9名、KCLに欠損のあった13名を除いて分析した。

（倫理面への配慮）

本研究では、「垂水市在住一般住民における前向きコホート研究」として鹿児島大学桜ヶ丘地区疫学研究等倫理委員会にて承認（170351疫-改14）が得られているデータを用いて分析した。

C．研究結果

J-CHSをアウトカムとした5年間の変化に関連する要因を検討した結果、ベースライン（2019年）でロバスト、プレフレイルであった256名（平均年齢72.0±5.0歳、女性62.5%）のうち、5年後調査（2024年）でフレイルの段階が悪化した者は50名（19.5%）であった。維持・改善群と悪化群でベースラインにおける年齢、性別、教育歴、服薬数に有意な差異は認めなかった。ベースラインの身体機能、身体組成、認知機能、生活習慣などの変数について、J-CHSの維持・改善群と悪化群で比較した結果、10m歩行時間（通常および最大）、5回椅子立ち座りテスト、情報処理速度、JST活動能力指標で有意な差異を認め、いずれも悪化群で不良な成績であった。これらの群間で差異を認めた項目について、年齢、性別、服薬数を共変量としたロジスティック解析の結果、いずれもJ-CHSによるフレイル段階の悪化と有意に関連する要因として確認された（表1）。

表 1. J-CHS によるフレイルの 5 年後の悪化に関連する要因

	Adjusted odds ratio	95% CI	p
10m 歩行時間（通常），秒	1.23	1.02—1.60	0.032
10m 歩行時間（最大），秒	1.44	1.07—1.94	0.015
5 回立ち座り，秒	1.22	1.06—1.40	0.006
情報処理，スコア	0.95	0.91—0.99	0.008
JST 活動能力指標，スコア	0.87	0.78—0.98	0.026

Covariates：年齢、性別、内服数

また、ベースラインでプレフレイル、フレイルであった126名（平均年齢73.0±5.3歳、女性

59.5%）のうち、5年後調査でフレイルの段階が改善した者は41名（32.5%）であった。改善群と維持・悪化群でベースラインにおける年齢に有意な差異は認め、維持・悪化群で年齢が高かった。J-CHSの改善群と維持・悪化群で比較した結果、握力、単語記憶（遅延再生）、社会的フレイルで有意な差異を認め、いずれも改善群で良好な成績であった。これらの群間で差異を認めた項目について、年齢、性別、服薬数を共変量としたロジスティック解析の結果、握力のみがJ-CHSによるフレイル段階の改善と有意に関連する要因であった（表2）。

表 2. J-CHS によるフレイルの 5 年後の改善に関連する要因

	Adjusted odds ratio	95% CI	p
握力，kg	1.11	1.02—1.22	0.023
単語記憶（遅延再生），スコア	1.19	0.95—1.49	0.126
社会的フレイル，あり	0.36	0.12—1.03	0.057

Covariates：年齢、性別、内服数

KCLをアウトカムとした5年間の変化に関連する要因を検討した結果、ベースラインでロバストであった131名（平均年齢71.5±4.8歳、女性67.9%）のうち、5年後調査でフレイルの段階が悪化した者は41名（31.3%）であった。維持群と悪化群でベースラインにおける年齢、性別、教育歴、服薬数に有意な差異は認めなかった。KCLの維持群と悪化群で比較した結果、腰痛、社会的フレイル、睡眠の質、GDS-15で有意な差異を認め、いずれも悪化群で不良な成績であった。これらの群間で差異を認めた項目について、年齢、性別、服薬数を共変量としたロジスティック解析の結果、いずれもKCLによるフレイル段階の悪化と有意に関連する要因として確認された（表3）。

表 3. KCL によるフレイルの 5 年後の悪化に関連する要因

	Adjusted odds ratio	95% CI	p
腰痛，あり	3.00	1.23—7.37	0.016
社会的フレイル，あり	3.61	1.18—11.03	0.024
睡眠の質，不良	4.22	1.30—13.75	0.017
GDS-15，スコア	1.43	1.12—1.83	0.004

Covariates：年齢、性別、内服数

また、ベースラインでプレフレイル、フレイルであった124名（平均年齢72.4±5.1歳、女性56.5%）のうち、5年後調査でフレイルの段階が改善した者は43名（34.7%）であった。改善群と維持・悪化群でベースラインにおける年齢、性別、教育歴、服薬数に有意な差異は認めなかった。KCLの改善群と維持・悪化群で比較した結果、Mini-Cog、単語記憶（遅延再生）、情報処理で有意な差異を認め、いずれも改善群で良好な成績であった。これらの群間で差異を認めた項目について、年齢、性別、服薬数を共変量としたロジスティック解析の結果、Mini-Cog、情報処理がKCLによるフレイル段階の改善と有意に関連する要因であった（表4）。

表 4. KCL によるフレイルの 5 年後の改善に関連する要因

	Adjusted odds ratio	95% CI	p
Mini-Cog，スコア	1.51	1.02—2.23	0.039
単語記憶（遅延再生），スコア	1.23	0.99—1.52	0.066
情報処理，スコア	1.05	1.00—1.10	0.033

Covariates：年齢、性別、内服数

これらの結果から、5年後のJ-CHSおよびKCLによるフレイル段階の改善や悪化に関連する要因は、身体機能、認知機能の他、生活習慣に関連する要因も抽出された（表5）。

表 5. 5 年後のフレイルの改善および悪化に対する関連要因

アウトカム	領域	フレイル改善の関連要因	フレイル悪化の関連要因
J-CHS	身体機能	・握力	・10m 歩行時間（通常・最大） ・5 回立ち座り
	認知機能	・単語記憶（遅延再生）※	・情報処理
	身体組成	—	—
	その他（生活習慣等）	・社会的フレイル※	・JST 活動能力指標
KCL	身体機能	—	—
	認知機能	・Mini-Cog ・単語記憶（遅延再生）※ ・情報処理	—
	身体組成	—	—
	その他（生活習慣等）	—	・腰痛 ・社会的フレイル ・睡眠の質 ・GDS-15

※単変量解析（群間比較）でのみ有意差を認めた項目

D．考察

本研究ではJ-CHSおよびKCLのそれぞれによる基準でフレイル段階を評価し、5年間の変化を調べた結果、悪化した者が約20〜30%であった一方で、改善した者が約32〜35%であり、フレイル段階は可逆性を有することが確認された。本研究のフィールドとなる垂水研究では、招聘型の健康チェックを開催しており、会場に来場した参加者のみが追跡対象となる。そのため、5年間の追跡率は約40%であり、健康状態が悪化した者もしくは悪化のリスクが高い者ほど脱落が多く、サバイバル効果の影響を考慮した解釈が必要である。

今回、J-CHSおよびKCLをアウトカムとした場合、フレイル段階の改善および改善に関連する要因はそれぞれ異なる要因が抽出された。J-CHSをアウトカムとした場合には、改善や悪化に対して身体機能や認知機能の影響が顕著であり、KCLをアウトカムした場合には、認知機能や心理機能、生活習慣など影響が示唆された。これは身体的な側面からの表現型モデルに基づく評価であるJ-CHSによるフレイル判定では、機能レベルでの状態が反映されやすいものと考えられる。一方、より多面的な要素でフレイルを包括的に判定するCKLでは、機能レベルでの指標よりも腰痛や睡眠の質など生活習慣に関与する要因がフレイル状態の変化に影響を与えやすいことが考えられた。

E．結論

地域在住高齢者の5年間の追跡では、フレイル段階が悪化した者が約20～30%、改善した者が約32～35%であった。5年後のJ-CHSによるフレイル段階の改善には握力、悪化には歩行速度、立ち座り、情報処理、JST活動能力指標が関連し、KCLによるフレイル段階の改善には認知機能、悪化には腰痛、社会的フレイル、睡眠の質、GDS-15が抽出された。

F. 健康危険情報

該当なし

G. 研究発表

1. 論文発表

該当なし

2. 学会発表

該当なし

H．知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

ロコモティブシンドロームの増悪と下肢股関節屈曲筋力との関連解明

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研究要旨
本研究は地域在住高齢者におけるロコモティブシンドローム悪化に関連する因子について検討することを目的とした。地域在住高齢者2077名を対象として、ロコモ25の質問紙によりロコモの実態調査を行った結果、ロコモ有症率は36.4%（ロコモ度1：24.4%、ロコモ度2：5.5%、ロコモ度3：6.5%）であった。また、高齢者が最も困難となりやすい動作は長距離歩行であった。さらに、1年間でのロコモ25スコアの変化量からロコモ悪化群、維持向上群の2群に分類し、ベースライン時の運動機能（握力、股関節屈曲・伸展・外転筋力、膝関節伸展筋力、足趾把持筋力、片脚立位、TUG、立ち座りテスト、筋持久力、膝関節可動域）、年齢、性別、BMIを独立変数としてロジスティック回帰分析をした結果、股関節屈曲筋力のみが有意な影響因子であった。このことから、ロコモ悪化を予防するためには運動機能の中でも特に股関節屈曲筋力に対する評価・介入が重要であることが示唆された。

A．研究目的

ロコモティブシンドローム（ロコモ）とは運動器の障害のために移動機能の低下をきたした状態のことであり、進行すると介護が必要となるリスクが高くなる。実際に厚生労働省の国民生活基礎調査によると、要支援・要介護状態となった主な原因として運動器疾患・障害は高い割合を占めており、健康寿命の延伸にはロコモの予防が極めて重要であることが指摘されている。

ロコモを早期に発見・予防するための対策を確立するためにはリスクを予測すること、すなわち将来の運動器障害による動作能力低下を予測することが重要である。ロコモ増悪による要介護状態を引き起こすリスク要因としては、筋力低下やバランス機能低下といった運動機能低下がよく知られている。ロコモと運動機能低下との関連については、横断研究によって個々の要因については調べられているものの、運動機能を多面的に評価し、ロコモの悪化にはどのような運動機能が関連しているのかについて縦断的に検討した報告はないのが現状である。

そこで、本研究においては、ロコモ悪化に関連するリスク因子として運動機能に着目し、縦断追跡調査によってロコモ増悪に関連する運動機能について明らかにすることを目的とした。

B．研究方法

1. 地域在住高齢者におけるロコモの実態調査

1）対象

対象は60歳以上の地域在住高齢者2077名（男性：730名、女性：1347名、年齢：68.3±5.4歳）とした。

2）ロコモの評価

ロコモの評価にはロコモ25の質問紙を用いた。ロコモ25は疼痛や日常生活動作（activities of daily living；ADL）の困難感、社会活動の困難感、転倒不安などに関する25項目を0～4点（0点：困難でない、1点：少し困難、2点：中程度困難、3点：かなり困難、4点：ひどく困難）で回答する質問票である。ロコモ25は点数が高いほど重症と判断され、ロコモ25のスコアが24点以上の場合はロコモ度３、16～23点の場合はロコモ度２、7～15点の場合はロコモ度１と判定される。ロコモ25におけるADL・社会活動の困難感について、基本的ADLは「ベッドや寝床から起きたり、横になったりするのはどの程度困難ですか」、「腰掛

けから立ち上がるのはどの程度困難ですか」、「家の中を歩くのはどの程度困難ですか」といった11項目、手段的ADLは「隣・近所に外出するのはどの程度困難ですか」、「2kg程度の買い物をして持ち帰ることはどの程度困難ですか」、「電車やバスを利用して外出するのはどの程度困難ですか」といった5項目、社会活動については「スポーツや踊り(ジョギング、水泳、ゲートボール、ダンスなど)は、どの程度困難ですか」、「親しい人や友人とのおつき合いを控えていますか」といった3項目で評価された。

3）分析

ロコモ25のスコアから、ロコモ度1、ロコモ度2、ロコモ度3の有症率を算出した。また、運動器の障害によって高齢者が困難となりやすい動作・活動を検討するために、ロコモ25の基本的ADL、手段的ADL、社会活動の19項目について、それぞれ平均スコアを算出した。

2. ロコモティブシンドローム増悪に関連する因子の探索

1）対象

ベースライン測定から1年後にロコモ追跡調査を実施できた地域在住高齢者433名を対象とした。なお、測定に大きな支障を及ぼすほどの重度の神経学的・整形外科的疾患や認知障害を有する者は対象から除外した。

2）ロコモの評価

ロコモの評価にはロコモ25の質問紙を用いた。

3）運動機能の評価

運動機能の評価として、握力、下肢筋力（股関節屈曲・伸展・外転筋力、膝関節伸展筋力、足趾把持筋力)、バランス能力(片脚立位保持時間)、TUG(timed up and go)、5回立ち座りテスト、筋持久力(30秒段差昇降回数)、膝関節可動域(膝屈曲・膝伸展）を測定した。下肢筋力測定は全て右下肢で行い、練習を行った後、2回計測したうちの最大値をデータ解析に用いた。また、股・膝関節筋力についてはアーム長からトルク値を求めた。片脚立位保持時間の測定は開眼で行い、60秒を上限として利き足で2回測定し、その最長時間を解析に用いた。

4）分析

ロコモ25の１年間のスコア変化量の結果から、スコア変化が2点以上の者をロコモ悪化群、スコア変化が0点以下の者をロコモ維持向上群とした。群（ロコモ悪化群、ロコモ維持向上群）を従属変数、ベースライン時の運動機能、年齢、性別、BMIを独立変数としてロジスティック回帰分析を行った。

（倫理面への配慮）

本研究は、京都大学医の倫理委員会の承認を得て実施された。対象者には事前に研究内容を説明し、書面にて研究に参加する同意を得た。

C．研究結果

1. 地域在住高齢者におけるロコモの実態調査

ロコモの有症率は36.4%（ロコモ度1：24.4%、ロコモ度2：5.5%、ロコモ度3：6.5%）であった。年代別でみたロコモ有症率は60-64歳が26.3%、65-69歳が33.4%、70-74歳が42.5%、75歳以上が52.2%と加齢によって有意にロコモ有症率が増加し、75歳以上の2人に1人がロコモに該当していた（図1）。また、70-74歳群および75歳以上群におけるロコモ度3の有症率はロコモ度2よりも有意に高値であった。

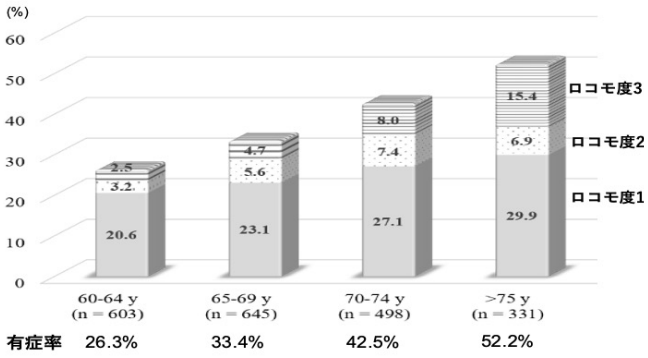

図１ 年代別ロコモ有病率

ロコモ25における基本的ADL、手段的ADL、社会活動の中で高齢者が最も困難となりやすい動作・活動は長距離歩行（ロコモ25の平均スコア：0.57点）であり、次いで速歩（平均スコア：0.42点）、階段昇降（平均スコア：0.35点）、地域での活動・イベントへの参加（平均スコア：0.26点）、買い物（平均スコア：0.16点）の順であった。

2. ロコモティブシンドローム増悪に関連する因子の探索

ベースラインでのロコモ25スコアは6.5±8.0点、1年後は8.0±9.8点であり、1年後に有意な増加を認めた。1年間でのロコモ25スコアの変化量から対象者をロコモ悪化群（スコア悪化が2点以上）、維持向上群（スコア悪化が0点以下）に分類した結果、ロコモ悪化群は169名（43.3%）、維持向上群は178名（45.6%）であった。2群間のベースライン時の運動機能を比較した結果、股関節屈曲筋力のみ2群間で有意差がみられ（表1）、さらにベースライン時の運動機能、年齢、性別、BMIを独立変数としてロジスティック回帰分析を行った結果においても、股関節屈曲筋力のみが有意（オッズ比；4.72, 95%信頼区間；1.20-18.5）であった。

表1　ロコモティブシンドローム悪化と関連する運動機能

	ロコモ悪化群	維持向上群	P-value
年齢（歳）	67.3±5.00	67.3±5.16	0.797
性別; 女性, 人数（%）	113 (65.1)	130 (66.7)	0.094
身長（cm）	157.8±8.43	156.9±8.21	0.277
体重（kg）	57.6±10.1	55.6±9.26	0.068
BMI (kg/cm^2)	23.1±3.14	22.5±2.92	0.076
握力（kg）	28.9±8.41	28.6±8.18	0.71
股関節屈曲筋力（Nm/kg）	**0.80±0.23**	**0.87±0.23***	**0.004**
股関節伸展筋力（Nm/kg）	1.51±0.89	1.55±0.86	0.742
股関節外転筋力（Nm/kg）	0.75±0.21	0.77±0.21	0.207
膝関節伸展筋力（Nm/kg）	1.97±0.68	2.10±0.74	0.069
足趾屈曲筋力（kg）	14.9±5.63	15.1±5.46	0.685
5 回立ち座りテスト（秒）	8.32±2.53	8.24±2.34	0.74
片脚立位保持時間（秒）	44.8±19.4	43.5±19.5	0.508
TUG (秒)	6.58±1.37	6.35±0.98	0.052
30 秒段差昇降回数（回）	25.4±6.56	26.3±6.93	0.172
膝関節屈曲 ROM (°)	145.2±5.92	145.1±6.70	0.87
膝関節伸展 ROM (°)	-1.55±4.40	-1.98±4.44	0.151

D．考察

ロコモ度判定基準は2020年に改訂され、従来のロコモ度1・2に加えて新たにロコモ度3が新設された。ロコモ度3は移動機能の低下が進行し、社会生活に支障をきたしている段階とされ、医療的介入の必要性が高い状態である。つまり、ロコモ度3の検出により医療へのアクセスを図り、運動器疾患・障害の早期治療を促すことが期待されている。本調査の結果、加齢によって有意にロコモ有症率が増加し、75歳以上の2人に1人がロコモに該当していた。さらに、75歳以上ではロコモ度3の有症率が高く、医療的介入を必要とする潜在的対象者が多いことが確認された。

ロコモの予防・改善対策としては、習慣的な運動、活動的な生活、適切な食生活、運動器疾患・障害の管理などが挙げられる。このうち、ロコモ対策の中心となるのは運動療法である。特に筋力低下はロコモを引き起こす主たる要因であり、筋力低下が進行すると、高齢者においては容易に日常生活動作制限を招く。そのため、筋力維持向上のための筋力トレーニングはロコモ対策として積極的に推奨される。本研究において、1年間での縦断追跡調査によりロコモ増悪に関連する運動機能について分析した結果、股関節屈曲筋力のみロコモ悪化の関連因子として抽出された。下肢筋力の中で股関節屈曲筋力のみ関連因子となった原因については、加齢による筋萎縮が最も著しい下肢筋は股関節屈曲筋（大腰筋）で

あることが影響していると考えられる。大腰筋は速歩や走行のときに大きな筋活動が必要であり、高齢者においては速歩や走行を行う機会が少なくなるため、大腰筋の廃用性筋萎縮が著しく、ロコモ悪化の危険性が高まることが推測される。このことから、高齢者のロコモ悪化予防のための運動として、股関節屈筋トレーニングを含めることが推奨される。

E．結論

ロコモ悪化に関連するリスク因子として運動機能に着目し、地域在住高齢者におけるロコモ悪化に関連する運動機能について縦断追跡調査を行った。その結果、運動機能の中で股関節屈曲筋力のみロコモ悪化の関連因子として抽出された。このことから、ロコモ対策として股関節屈曲筋に対するトレーニングも重要であることが示唆された。

F．健康危険情報

該当なし

G．研究発表

1. 論文発表

- Tabara Y, Ikezoe T, Setoh K, Kawaguchi T, Matsuda F. Association of the 25-question Geriatric Locomotive Function Scale with all-cause mortality in older adults: The Nagahama study. ***Arch Gerontol Geriatr***. 2025; 129:105670.

2. 学会発表

該当なし

H．知的財産権の出願・登録状況

該当なし

別添４

厚生労働科学研究費補助金（循環器疾患・糖尿病等生活習慣病対策総合研究事業）
分担研究報告書

ロコモティブシンドロームのリスク因子の解明と予測スコアの開発

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研究要旨
65歳以上の地域在住者を対象に、ロコモティブシンドローム（ロコモ）2度以上を特定健診の問診から予測する簡易リスクスコアを開発することを目的とした。対象は、静岡研究の賀茂および袋井コホートのベースライン調査に参加した、地域在住者2174名のうち、除外基準に適合するものを除いた1819名を対象とした。ロコモと特定健診項目は問診票で調査した。多変量ロジスティック回帰分析の結果、ロコモ２度以上の予測因子として、年齢、性別、身体活動、歩行速度、食事速度、就寝前の夕食、熟睡感が抽出された。これらの予測因子に対して重みづけを行い、予測スコアを作成した。ROC曲線の結果、予測スコアのAUCは0.771で中等度程度の判別能力であった。65歳以上の地域在住者を対象に、ロコモ2度以上を特定健診の問診から予測する簡易スコアを開発した。

A．研究目的

ロコモティブシンドローム（ロコモ）は、運動器の障害により移動能力が低下した状態を指し、要介護の主要な要因の一つである。そのため、早期発見と介入の重要性が高まっている。一方で、ロコモの評価には身体機能テストまたは25項目の問診票が必要であり、手続きが煩雑であることから、プライマリケアの現場において簡便な予測手法の整備が望まれている。特定健診における「標準的な質問票」は、中年から高齢者の心身機能を包括的に把握できることから、ロコモの予測にも有用である可能性がある。

そこで本研究では、特定健診の標準的な質問票の情報を用いて、地域在住高齢者のロコモを予測するための簡易スコアの開発を目的とした。

B．研究方法

静岡研究の賀茂および袋井コホートのベースライン調査に参加した地域在住者2174名のうち、除外基準に該当する者を除いた1819名を対象とした。ロコモの評価にはロコモ25質問票を用い、16点以上をロコモ2度以上とした。また、厚生労働省が策定した22項目からなる標準的な質問票を調査した。ロコモ2度以上に関連する因子を、単変量および多変量ロジスティック回帰分析により抽出し、得られた項目に重み付けを行ってスコアを作成した。また、ROC曲線を用いてロコモの予測精度を評価した。

（倫理面への配慮）

本研究は京都大学医学部の倫理委員会の承認を得て実施された。対象者には事前に研究内容を説明し、書面にて研究参加の同意を取得した。

C．研究結果

対象者の平均年齢は74±5歳、女性の割合は57%、BMIは22.6±3.3 kg/m²であり、255名（14%）がロコモ2度以上と判定された。単変量および多変量ロジスティック回帰分析の結果（表１）、以下の7項目がロコモ2度以上の有意な予測因子として抽出された（表1）：75歳以上（β＝0.236, P＝0.002）、女性（β＝0.248, P＝0.002）、身体活動なし（β＝0.401, P＜0.001）、歩行速度低下（β＝0.647, P＜0.001）、食事の速度が遅い（β＝0.378, P＝0.004）、就寝前の間食（β＝0.255, P＝0.015）、熟睡感がない（β＝0.401, P＜0.001）。これらの予測因子に基づき重み付けを行い、12点満点の予測スコアを作成した。

表1. 単変量解析と多変量解析の結果

項目	水準	Univariable β	Univariable P	Multivariable β	Multivariable P	weighted	Score
年齢	75歳以上	0.170	0.011	0.236	0.002	0.236/0.236=1.00	1
性別	女性	0.219	0.001	0.248	0.002	0.248/0.236=1.05	1
BMI（18.5-24.9）	<18.5	-0.090	0.582	0.003	0.984		
	>=25	0.383	0.001	0.241	0.080		
1. 降圧薬の服用	はい	0.253	<0.001	0.149	0.059		
2. 血糖降下剤の服用	はい	0.204	0.045	0.058	0.618		
3. 脂質異常症治療薬	はい	0.239	<0.001	0.154	0.059		
4. 脳卒中の既往	はい	0.267	0.065				
5. 心疾患の既往	はい	0.045	0.744				
6. 腎疾患の既往	はい	0.337	0.031	0.173	0.463		
7. 貧血の既往	はい	0.248	0.034				
8. 喫煙	はい	-0.163	0.317				
9. 成人後体重増加	はい	0.276	<0.001	-	-		
10. 運動	いいえ	0.433	<0.001	-	-		
11. 身体活動	いいえ	0.537	<0.001	0.401	<0.001	0.401/0.236=1.69	2
12. 歩行速度	いいえ	0.820	<0.001	0.647	<0.001	0.647/0.236=2.74	3
13. 咀嚼状態（何でもかめる）	かみにくいことがある	0.303	0.679				
	ほとんど噛めない	0.218	0.268				
14. 食事速度（普通）	速い	-0.141	0.185	-0.084	0.480		
	遅い	0.467	<0.001	0.378	0.004	0.378/0.236=1.60	2
15. 就寝前夕食	はい	0.253	0.005	0.255	0.015	0.255/0.236=1.08	1
16. 間食（ほとんどない）	時々	0.100	0.002	0.232	0.052		
	毎日	0.332	0.293	0.069	0.506		
17. 朝食欠食	はい	0.347	0.007	0.274			
18. 飲酒頻度（飲まない）	時々	-0.178	0.175				
	毎日	-0.167	0.246				
20. 熟眠感	いいえ	0.507	<0.001	0.401	<0.001	0.401/0.236=1.69	2

本スコアがロコモ2度以上を予測するカットオフ値は5点、感度74%、特異度66%であり、AUCは0.771（P＜0.001）であった（図1）。

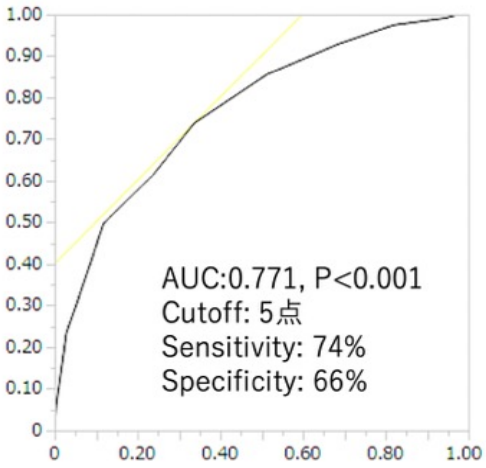

図1　ロコモティブシンドロームに対するROC曲線

D. 考察

65歳以上の地域在住者を対象に、ロコモ2度以上を予測する簡易予測スコアの開発を試みた。その結果、年齢と性別に加え、特定健診の標準的な質問票から5項目を用いることで、簡易スコアの作成が可能であった。また、本スコアは中等度の予測精度を示し、ロコモ2度以上を予測するカットオフ値は5点であった。

本研究で作成した簡易予測スコアは、地域在住後期高齢者におけるロコモ2度以上のリスクを中等度の精度で予測可能であり、特定健診で得られる既存情報を活用することで、プライマリケア現場におけるスクリーニングツールとしての活用が期待される。特に、身体機能テストを必要とせず、質問票のみで評価できる点は、現場での実用性に優れる。

さらに、本スコアに含まれる「歩行速度低下」「身体活動なし」「熟睡感がない」といった因子は、早期介入によって生活機能全体の維持および向上にもつながる可能性がある。したがって、本スコアを活用することでロコモ予備群の早期抽出が可能となり、運動指導や生活習慣の見直しなどの介入を通じて、要介護状態への進行を予防する介護予防戦略としての効果も期待される。

一方で、本研究にはいくつかの限界がある。まず、対象地域が静岡県の特定地域に限定されており、他地域への一般化には検討が必要である。また、ロコモ2度以上が発生する75歳以上の対象者に絞った感度分析や、後期高齢者の質問票を用いたさらなる検討も必要である。

Ｅ．結論

65歳以上の地域在住者を対象に、特定健診の問診票からロコモ2度以上を予測する簡易リスクスコアを開発した。本スコアは、市町が保有する既存の情報を活用することで、ロコモを簡便に予測する有用な手段となり得る。

F. 健康危険情報

該当なし

G. 研究発表

1. 論文発表

該当なし

2. 学会発表

該当なし

Ｈ．知的財産権の出願・登録状況

該当なし

別添５

研究成果の刊行に関する一覧表

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Tabara Y, Ikezoe T, Setoh K, Kawaguchi T, Matsuda F	Association of the 25-question Geriatric Locomotive Function Scale with all-cause mortality in older adults: The Nagahama study	Arch Gerontol Geriatr	129	105670	2025
Tabara Y, Shoji-Asahina A, Akasaka H, Sugimoto K, Sato Y	Prognostic significance of the Questionnaire for Medical Checkup of Old-Old for the incidence of functional disability: The Shizuoka Kokuho Database study	Geriatr Gerontol Int.	25	260-266	2025
Shirotori S, Hasegawa Y, Nagai K, Kusunoki H, Yoshimura S, Tokumoto K, Hattori H, Tamaki K, Hori K, Kishimoto H, Shinmura K	Is Oral Function Associated with the Development of Sarcopenic Obesity and Sarcopenia in Older Adults? A Prospective Cohort Study	Diseases	13	109	2025
Kusunoki H, Hasegawa Y, Nagasawa Y, Shojima K, Yamazaki H, Mori T, Tsuji S, Wada Y, Tamaki K, Nagai K, Matsuzawa R, Kishimoto H, Shimizu H, Shinmura K	Oral Frailty and Its Relationship with Physical Frailty in Older Adults: A Longitudinal Study Using the Oral Frailty Five-Item Checklist	Nutrients	17	17	2024
Kamide K, Ikebe K, Masui Y, Nakagawa T, Kabayama M, Akasaka H, Mameno T, Murotani Y, Ogawa M, Yasumoto S, Yamamoto K, Hirata K, Arai Y, Gondo Y, the SONIC study group	Multidimensional insights about healthy aging from the cohort study for community-dwelling older adults: The SONIC study	Geriatr Gerontol Int.	25	346-355	2025
Terada S, Godai K, Kabayama M, Kido M, Akagi Y, Akasaka H, Takami Y, Nakagawa T, Yasumoto S, Gondo Y, Ikebe K, Arai Y, Masui Y, Hirata T, Yamamoto K, Kamide K.	Prevalence of high N-terminal prohormone of brain natriuretic peptide levels and associated factors among community-dwelling older adults aged over 75 years: The SONIC study	BMC Res Note.		In press	2025

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Association of the 25-question Geriatric Locomotive Function Scale with all-cause mortality in older adults: The Nagahama study

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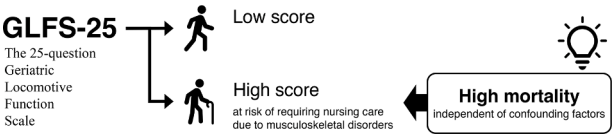
HIGHLIGHTS

- The GLFS-25 is a questionnaire to determine the severity of locomotive syndrome.
- The GLFS-25 was associated with all-cause mortality independently of sarcopenia.
- The GLFS-25 could be useful for the identification of individuals at risk.

GRAPHICAL ABSTRACT



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ABSTRACT

Backgrounds: Locomotive syndrome is a condition in which a person is at risk of requiring nursing care due to musculoskeletal disorders. The 25-question Geriatric Locomotive Function Scale (GLFS-25) was developed to determine the severity of locomotive syndrome. In this study, we aimed to determine the prognostic significance of the GLFS-25 for all-cause mortality.

Methods: The study participants consisted of 3,447 community residents aged ≥65 years. All-cause mortality was determined using residential registry records. Skeletal muscle mass assessed via bioimpedance methods was considered in the analysis as a confounding factor.

Results: During a mean follow-up period of 3,236 days (30,566 person–years), 288 cases of all-cause mortality occurred. When participants were categorized by the GLFS-25 score [grade 1: <7 points (n = 1,948); grade 2: ≥7 to <16 points (n = 894); grade 3: ≥16 points (n = 605)], their survival probability decreased linearly with increasing grade (log-rank test P = 0.014). In a Cox proportional hazards model adjusted for confounding factors, including low skeletal muscle mass, GLFS-25 grade 3 was identified as an independent risk factor for all-cause mortality (hazard ratio: 1.60; P = 0.007) in the subpopulation aged ≥70 years but not in the overall population (P = 0.062). The hazard ratio for all-cause mortality with GLFS-25 grade 3 and low skeletal muscle mass combined was 2.66 (P < 0.001).

Conclusion: The GLFS-25 is independently associated with all-cause mortality in older adults. Using this questionnaire to assess locomotive syndrome could be useful for identifying individuals at risk.

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1. Introduction

Locomotive syndrome is a concept proposed by the Japanese Orthopaedic Association to indicate a condition in which a person is at risk of requiring nursing care because of disorders of the bones, joints, muscles, and nerves (Nakamura, 2008). The 25-question Geriatric Locomotive Function Scale (GLFS-25) has generally been used as a screening tool to assess the degree of locomotive syndrome in older (≥65 years) adults (Seichi et al., 2012). Several longitudinal studies reported that the GLFS-25 score was associated with the incidence of locomotive syndrome (Yoshimura et al., 2022) and the need for long-term care (Ide et al., 2021; Niwa et al., 2021). Although one study (Niwa et al., 2021) reported a significant association with the composite outcome of care requirement and death, no study has investigated the prognostic significance of the GLFS-25 score for all-cause mortality.

Sarcopenia is a phenotype characterized by reduced skeletal muscle mass, weak muscle strength, and reduced physical activity (Chen et al., 2020), which partially overlaps with the features of locomotive syndrome. Indeed, significant correlations between locomotive syndrome and each component of sarcopenia have been noted in several observational studies (Kobayashi et al., 2023). We previously reported that a low skeletal muscle mass index (SMI) calculated from bioimpedance measures of skeletal muscles was independently associated with all-cause mortality (Tabara, Setoh, Kawaguchi & Matsuda, 2022). We also reported that a low body mass index (BMI), a representative measure of malnutrition, was associated with all-cause mortality (Tabara, Nakatani & Miyachi, 2021) through partial mediation by a low SMI (Tabara et al., 2022). Given that background, the practical use of the GLFS-25 in care prevention settings requires clarification about whether locomotive syndrome as assessed by the GLFS-25 predicts all-cause mortality independently of a low SMI and a low BMI.

In this longitudinal study in a general population, we aimed to clarify the prognostic significance of the GLFS-25 for all-cause mortality in older adults, with consideration of the possible involvement of sarcopenia in the relationship.

2. Methods

2.1. Study participants

Our analysis used data from the Nagahama study, a longitudinal cohort study of community residents living in Nagahama City, a suburban city in Shiga prefecture in central Japan (Tabara et al., 2024; Takeshita et al., 2023). The baseline survey in the Nagahama study was conducted between 2008 and 2010. Nagahama City residents aged 30–74 years who were living independently were eligible to participate. The Nagahama study design required a clinical survey to be conducted every 5 years after the baseline survey. For the present study, we analyzed data obtained at the second survey (conducted between 2012 and 2016), when locomotive syndrome was assessed using the GFLS-25. Of 9840 Nagahama study participants, 3447 were included in the analysis after the exclusion of individuals aged <65 years ($n = 6264$), having an implanted pacemaker ($n = 10$), receiving hemodialysis therapy ($n = 4$), lacking a GLFS-25 score obtained between 2013 and 2016 ($n = 99$), and lacking clinical values required for the analysis ($n = 16$).

All procedures in the Nagahama study were approved by the ethics committee of the Kyoto University Graduate School of Medicine and the Nagahama Municipal Review Board. Written informed consent was obtained from all participants before enrolment.

2.2. All-cause mortality

All-cause mortality was identified by reviewing residential registry records managed by the Nagahama City Office. Participants who had relocated out of Nagahama City were censored. The follow-up period was calculated from participation in the follow-up (second) survey to the date of relocation or death or to the study end date (March 31, 2024).

Table 1
The 25-question Geriatric Locomotive Function Scale.

1	Did you have any pain (including numbness) in your neck or upper limbs (shoulder, arm, or hand)?
2	Did you have any pain in your back, lower back, or buttocks?
3	Did you have any pain (including numbness) in your lower limbs (hip, thigh, knee, calf, shin, ankle, or foot)?
4	To what extent has it been painful to move your body in daily life?
5	To what extent has it been difficult to get up from a bed or lie down?
6	To what extent has it been difficult to stand up from a chair?
7	To what extent has it been difficult to walk inside the house?
8	To what extent bas it been difficult to wear and take off shirts?
9	To what extent has it been difficult to wear and take off trousers and pants?
10	To what extent has it been difficult to use the toilet?
11	To what extent has it been difficult to wash your body in the bath?
12	To what extent has it been difficult to go up and down stairs?
13	To what extent has it been difficult to walk briskly?
14	To what extent has it been difficult to keep yourself neat?
15	How far can you keep walking without rest?
16	To what extent has it been difficult to go out to visit neighbors?
17	To what extent has it been difficult to carry objects weighing approximately 2 kg?
18	To what extent has it been difficult to go out using public transportation?
19	To what extent have simple tasks and housework (preparing meals, cleaning up, etc.) been difficult?
20	To what extent have load-bearing tasks and housework (cleaning the yard, carrying heavy bedding, etc.) been difficult?
21	To what extent has it been difficult to perform sports activity (jogging, swimming, gate ball, dancing, etc.)?
22	Have you been restricted from meeting your friends?
23	Have you been restricted from joining social activities (meeting friends, playing sports, engaging in activities and hobbies, etc.)?
24	Have you ever felt anxious about falls in your house?
25	Have you ever felt anxious about being unable to walk in the future?

2.3. GLFS-25

The GLFS-25 is a self-administered questionnaire consisting of 25 questions relating to pain in various body parts, activities of daily living, social activities, and concerns about physical impairment (Table 1) (Seichi et al., 2012). Participants were asked to rate the 25 questions on a five-point scale from no impairment (0 points) to severe impairment (4 points). The points total was used as an index of locomotive syndrome, with higher scores indicating worsening locomotive function.

2.4. Skeletal muscle mass

Appendicular lean mass was estimated using a bioelectrical impedance analysis device (InBody 430: InBody Co. Ltd., Seoul, ROK). The device can estimate lean mass from the resistance and reactance of arms, trunk, and legs at three different frequencies (5, 50, and 250 kHz) of an alternating 250-A current. The SMI was calculated by dividing the appendicular lean mass by body height in meters squared (Chen et al., 2020). Low SMI was defined as less than 7.0 kg/m^2 in men and less than 5.7 kg/m^2 in women based on criteria published by the Asian Working Group for Sarcopenia (Chen et al., 2020).

2.5. Clinical parameters

Clinical parameters analyzed in this study were obtained at the follow-up (second) survey in the Nagahama study. Given the findings in our previous study (Tabara et al., 2021), which clarified a U-shaped association between BMI and all-cause mortality in Japanese individuals, we considered low BMI (<20 kg/m^2) to be a risk factor for all-cause mortality. Data on smoking and drinking habits, history of cardiovascular diseases including stroke and myocardial infarction, and medications were obtained using a self-reported structured questionnaire. Depressive symptom was assessed using the Center for

Table 2
Clinical characteristics of study participants.

	Overall	≥70 Years
	3447	1979
Age, years	71.2 ± 4.1	74.2 ± 2.8
Sex, men%	40.2	43.5
Body mass index, kg/m^2	22.5 ± 3.0	22.5 ± 3.0
Low body mass index, %	20.4	20.2
Skeletal muscle mass index, kg/m^2	6.6 ± 0.9	6.6 ± 0.9
Low skeletal muscle index, %	25.9	29.7
Smoking, never/past/current%	68.0/25.0/7.0	67.1/27.0/5.9
Alcohol consumption, Go/week	3.6 ± 7.2	3.7 ± 6.9
History of cardiovascular diseases, %	8.6	9.9
Systolic blood pressure, mmHg	133 ± 17	134 ± 17
Diastolic blood pressure, mmHg	72 ± 10	72 ± 10
Hemoglobin A1c, %	5.7 ± 0.5	5.7 ± 0.5
High-density lipoprotein cholesterol, mg/dL	65 ± 17	64 ± 17
Low-density lipoprotein cholesterol, mg/dL	117 ± 28	114 ± 27
Albumin, g/dL	4.2 ± 0.2	4.2 ± 0.2
Estimated glomerular filtration rate, ml/min/1.73m^2	70.3 ± 13.4	68.7 ± 13.5
CES-D score, points	13 ± 7	13 ± 7
GLFS-25 score, points	9 ± 11	11 ± 13

Values are frequencies or means with standard deviation. Low body mass index was defined as <20.0 kg/m^2. Low skeletal muscle mass index was defined <7.0 kg/m^2 in men and 5.7 kg/m^2 in women. Go is the traditional Japanese liquor unit, where 1 Go corresponds to 22 g ethanol. Cardiovascular diseases include stroke and myocardial infarction. eGFR, estimated glomerular filtration rate; CES-D, Center for Epidemiologic Studies Depression Scale; GLFS-25, 25-question Geriatric Locomotive Function Scale.

Epidemiologic Studies Depression Scale. The 25 questions of the GLFS and 20 questions of the depression scale were included in that questionnaire.

2.6. Statistical analysis

Data are presented as frequencies or means with standard deviation. The log-rank test was used to assess group differences from Kaplan–Meier curves. The proportional hazards assumption was assessed using the Schoenfeld residual test. A Cox proportional hazards model was used to identify factors associated with all-cause mortality. Statistical analyses were performed using the JMP Pro software application (version 17.2.0: SAS Institute, Cary, NC, USA) and the STATA software application (version 18.0: Stata Corp LLC, College Station, TX, USA). P Values less than 0.05 were considered indicative of statistical significance.

3. Results

Table 2 presents the clinical characteristics of the study participants. Because the mean GLFS-25 score increased after 70 years of age in both sexes (Fig. 1), an association analysis was also performed for the subpopulation aged ≥70 years (Table 2).

During the mean 3236 days of follow-up (30,566 person–years), 288 all-cause deaths occurred in the overall population, whereas 217 deaths occurred in the subpopulation 70 years of age and older (17,351 person–years). Fig. 2 presents the related Kaplan–Meier curves for all-cause mortality. When participants were categorized into groups according to GLFS-25 scores (grade 1: <7 points; grade 2: ≥7 to <16 points; grade 3: ≥16 points) (Seichi et al., 2012), a significant linear association between the grade of the GLFS-25 score and survival probability was evident. The Cox proportional hazards model analysis (Table 3) demonstrated a significant association between the highest GLFS-25 grade and all-cause mortality in the older subpopulation, but not in the overall population even after adjustment for possible confounding factors including a low SMI and a low BMI. The association in the older population remained significant even after excluding early death cases (within 1 year of follow-up) and after further adjustment of the CES-D score in the model (GLFS-25 score grade 3, hazard ratio = 1.50, $P = 0.028$).

In the Cox proportional hazards models analyzing participants aged ≥70 years, a low BMI was identified as a significant determinant when a low SMI was not included in the model (hazard ratio: 1.52; $P = 0.014$), indicating that a low SMI was an intermediate factor in the relationship between a low BMI and mortality. Even in the analysis excluding a low SMI from the model, the highest GLFS-25 grade was also significantly associated with all-cause mortality (hazard ratio: 1.64; $P = 0.004$).

Fig. 3 presents the hazard ratio for all-cause mortality based on the combination of GLFS-25 grade 3 and a low SMI, which was 2.66 ($P < 0.001$), whereas the hazard ratios for a low SMI or GLFS-25 grade 3 alone did not show a significant association with all-cause mortality.

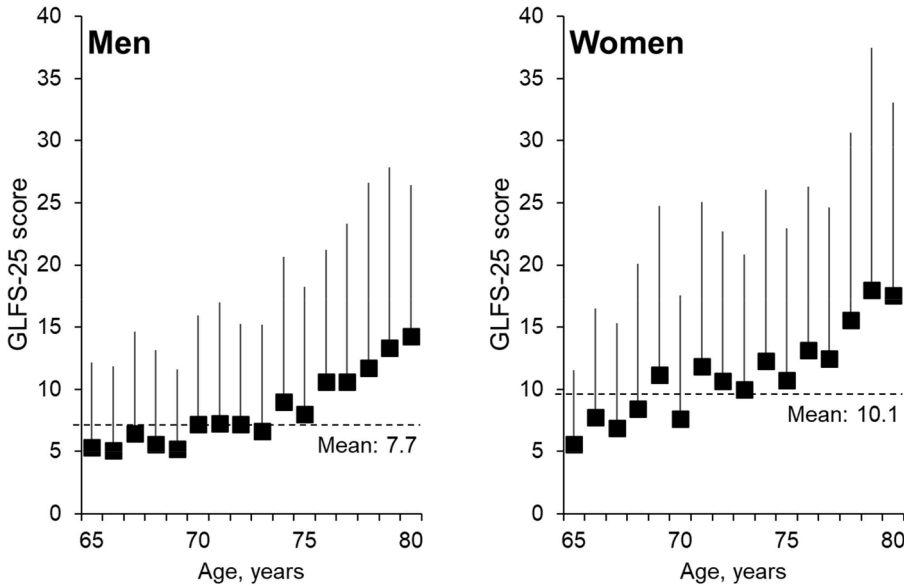

Fig. 1. Age differences for scores on the 25-question Geriatric Locomotive Function Scale.
Values are means with standard deviation. The horizontal lines indicate the mean for the study population.

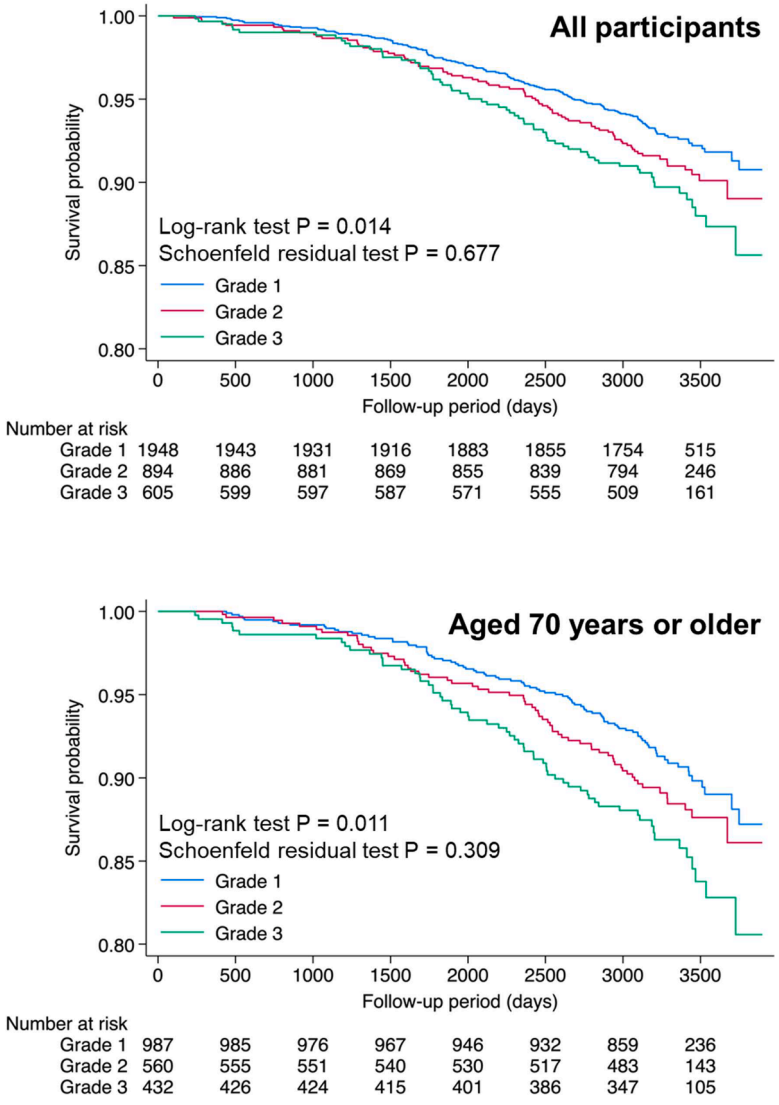

Fig. 2. Kaplan–Meier curves for all-cause mortality by score on the 25-question Geriatric Locomotive Function Scale (GLFS-25).
Participants were divided by GLFS-25 score as < 7, grade 1; ≥7–<16, grade 2; ≥16, grade 3. The proportional hazards assumption was assessed using the Schoenfeld residual test. Group differences in the Kaplan–Meier curves were assessed using the log-rank test.

Table 3
Cox proportional hazards model for all-cause mortality.

	Total participants		Participants aged ≥70 years			
					Excluding early death cases	
	HR (95 % CI)	P	HR (95 % CI)	P	HR (95 % CI)	P
Age, years	1.10 (1.07–1.14)	<0.001	1.12 (1.06–1.17)	<0.001	1.11 (1.06–1.17)	<0.001
Sex, women	0.51 (0.36–0.72)	<0.001	0.54 (0.36–0.81)	0.003	0.53 (0.36–0.80)	0.003
Smoking	1.50 (1.08–2.07)	0.015	1.69 (1.17–2.48)	0.005	1.67 (1.16–2.46)	0.006
Low body mass index	0.99 (0.71–1.39)	0.969	1.18 (0.81–1.71)	0.380	1.21 (0.83–1.75)	0.325
Low skeletal muscle mass index	1.61 (1.22–2.12)	0.001	1.60 (1.16–2.18)	0.004	1.58 (1.15–2.16)	0.006
GLFS-25 score						
Grade 1	reference		reference		reference	
Grade 2	1.21 (0.92–1.60)	0.179	1.29 (0.93–1.78)	0.124	1.30 (0.94–1.79)	0.118
Grade 3	1.34 (0.99–1.82)	0.062	1.60 (1.14–2.22)	0.007	1.56 (1.11–2.18)	0.011

Adjusted factors were history of cardiovascular diseases, systolic blood pressure, serum albumin levels, high-density lipoprotein cholesterol levels, and estimated glomerular filtration rate. Early deaths were deaths occurring within 1 year from the start of follow-up. HR, hazard ratio; CI, confidence interval; GLFS-25, 25-question Geriatric Locomotive Function Scale.

4. Discussion

In this longitudinal study of a general population, we observed that the GLFS-25 score was significantly associated with all-cause mortality in the population 70 years of age and older. That association was independent of possible confounding factors including physical factors (a

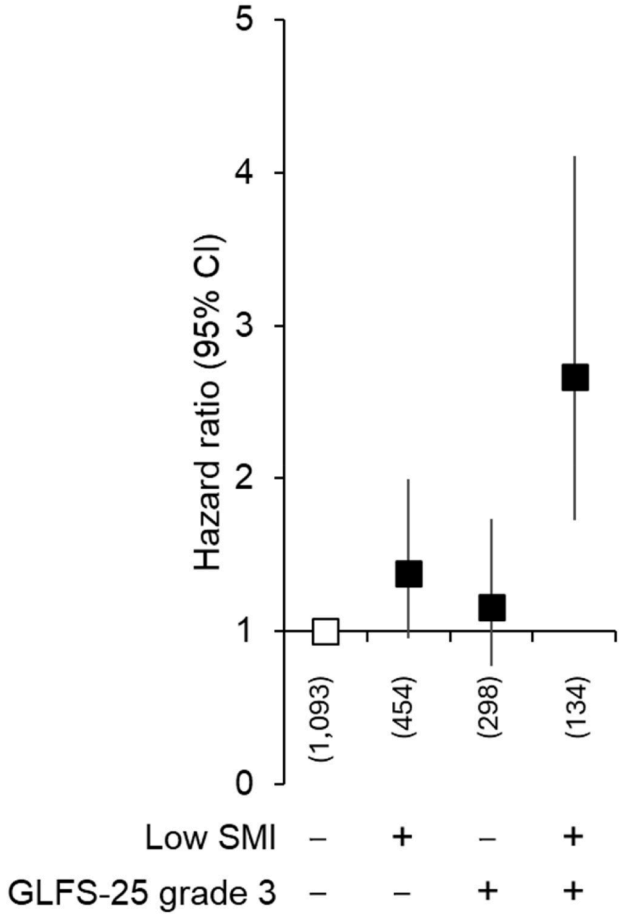

Fig. 3. Hazard ratios for all-cause mortality by the combination of a grade 3 score on the 25-question Geriatric Locomotive Function Scale (GLFS-25) and a low skeletal muscle mass index (SMI) in the population aged ≥70 years.
Hazard ratios with 95 % confidence intervals are shown. The number of participants in each group is shown in parentheses. A low SMI was defined as <7.0 kg/m^2 in men and <5.7 kg/m^2 in women. The highest GLFS-25 grade (grade 3) was defined as a score of ≥16 points. Adjustments were applied for age, sex, history of cardiovascular diseases, smoking, systolic blood pressure, serum albumin levels, high-density lipoprotein cholesterol levels, and estimated glomerular filtration rate.

low SMI and a low BMI), phycological factors (CES-D score), and history of cardiovascular diseases, which were known to be associated with mortality in older adults. Furthermore, the association remained significant even with the exclusion of early deaths from the analysis, indicating that reverse causation could be excluded from the association between the GLFS-25 score and mortality.

The GLFS-25 had been suggested for use in adults aged ≥65 years (Seichi et al., 2012). Although we did not investigate associations of the GLFS-25 score with the incidence of long-term care requirements, our findings indicated that this score might be even more appropriate for older individuals. In the present study, the GLFS-25 score demonstrated a linear increase with age in the population aged ≥70 years. Similar age-related changes were reported in another observational study (Yamada et al., 2020), supporting our suggestion regarding the age group to which the score is applicable.

The association between the GLFS-25 and all-cause mortality was independent of a low SMI. A previous cross-sectional study involving older adults (Inanaga et al., 2023) reported that the GLFS-25 score and the score of each component of the GLFS-25 (body pain, movement difficulty, usual care, activities of daily life, social activities, and cognition) were not significantly associated with the SMI. The lack of such an association was also reported in a meta-analysis of cross-sectional studies that investigated associations of various physical factors with the GLFS-25 score (Kobayashi et al., 2023). Given those results, the GLFS-25 might be associated with all-cause mortality as a reflection of conditions other than a low SMI. Unfortunately, we did not analyze physical factors such as grip strength and gait speed, which have been reported to be associated with the GLFS-25 score (Kobayashi et al., 2023) in the overall study population. Further investigation into whether the GLFS-25 is prognostic for mortality independent of those physical performance factors is warranted.

The highest hazard ratio for all-cause mortality was observed for the combination of GLFS-25 grade 3 and a low SMI, whereas the hazard ratio for either factor alone did not reach statistical significance. That observation indicates that in the Cox proportional hazards model, the participants with both GLFS-25 grade 3 and a low SMI helped increase the hazard ratio for each group when the combination of GLFS-25 and a low SMI was not included in the model as an independent variable. Measurement of the SMI might therefore be useful for discriminating individuals at higher risk from among the population with GLFS-25 grade 3.

A combination of the two-step and stand-up tests with the GLFS-25 score has been suggested as another method for assessing locomotive syndrome (Yoshimura et al., 2022). Unfortunately, data for those physical tests were not available for the entire study population; thus, we could not assess the prognostic significance of that composite score. Although no clear results have been reported concerning the association of the two-step and stand-up tests with mortality, the composite score was reported to be associated with the new onset of locomotive syndrome (Yoshimura et al., 2022). Further investigation into whether the addition of these physical tests to the GLFS-25 score improves the prognostic value of the GLFS-25 score alone is warranted.

To the best of our knowledge, this study is the first to show the prognostic significance of the GLFS-25 for all-cause mortality. Certain limitations should be noted while interpreting our findings. First, the study population consisted of physically independent community residents. Compared to the overall community residents, the study population might be health-biased. Second, because body size of East Asians including Japanese is smaller than that of European populations (Di Angelantonio & Bhupathiraju, 2016), further studies in various population is needed to extrapolate these findings in other population with different ethnic backgrounds. Third, because of a lack of data, individuals who might have had a history of fractures of the lower extremity were not excluded from the analysis. A history of fracture might have had a confounding effect on the association between the GLFS-25 score and mortality.

In conclusion, the GLFS-25 was independently associated with all-cause mortality. In addition to skeletal muscle decline, using the GLFS-25 in an assessment of locomotive syndrome could be useful for the identification of individuals at risk.

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CRediT authorship contribution statement

Yasuharu Tabara: Writing – review & editing, Writing – original draft, Funding acquisition, Formal analysis, Conceptualization. **Tome Ikezoe:** Investigation, Data curation. **Kazuya Setoh:** Investigation, Data curation. **Takahisa Kawaguchi:** Investigation, Data curation. **Fumihiko Matsuda:** Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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ORIGINAL ARTICLE

EPIDEMIOLOGY CLINICAL PRACTICE AND HEALTH

Prognostic significance of the Questionnaire for Medical Checkup of Old-Old for the incidence of functional disability: The Shizuoka Kokuho Database study

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Aim: In the Japanese health checkup system for older adults aged ≥75 years, the Questionnaire for Medical Checkup of Old-Old (QMCOO) was adopted after 2020. However, the prognostic significance of this questionnaire for the incidence of functional disability is uncertain. The current study aimed to validate the prognostic significance of the QMCOO, and to develop a simple risk score for functional disability by analyzing health insurance claims data including annual health checkup data.

Methods: This study included 111 282 older adults aged 75–90 years who did not receive long-term care services at baseline. The study period was between the earliest day of participation in the health checkup after April 2020 and September 2022. The participants who were certified as care level 2 and higher during this period were considered as incident cases of functional disability.

Results: Within a mean follow-up duration of 1.7 years (191 085 person-years), 4578 functional disability cases were identified. In addition to the basic covariates, among the 15 items in the QMCOO, nine were identified as independent determinants. The probability of developing functional disability that was calculated using the model was associated with older age, male sex, underweight and poor responses to the QMCOO items. According to the weighted score based on the model, the participants was classified as functional disability probability of <1% to >45%.

Conclusions: The nine items in the QMCOO were associated with the incidence of functional disability. The weighted scoring system could be helpful for the use of the QMCOO. **Geriatr Gerontol Int 2025; 25: 260–266**.

Keywords: functional disability, health checkup, older adults, QMCOO, screening.

Introduction

The extension of life expectancy[1] has resulted in a rapid increase in the older adult population in Japan.[2] Avoiding the need for long-term care is the most important issue among older people to maintain their independence and quality of life. It has been estimated that the total additional medical and long-term care costs generated by functional limitations were US$72.7 billion, and the long-term care costs accounted for a large part of the total costs particularly in older people aged ≥85 years,[3] showing the importance of maintaining physical independence to reduce the health burden on the individual, but also the economic burden on society.

In Japan, older adults aged ≥75 years are required to enroll in the Latter-Stage Elderly Medical Care System, a health insurance system that partially covers the medical expenditure of insured people. In addition, municipalities, the insurer of this health insurance system, are obligated to provide annual health checkups (*Kouki Koureisha Kenshin*) to insured individuals. In addition to evaluating clinical factors associated with cardiovascular diseases, this health checkup includes a questionnaire survey to assess the potential risk of health issues that cannot be assessed through clinical examination alone. Until recently, a similar structured questionnaire for individuals aged <75 years was used in the health checkup for older adults. However, the Questionnaire for Medical Checkup of Old-Old (QMCOO) was adopted after 2020 to assess health issues specific to older adults, because the main cause of disability in those aged ≥75 years is geriatric syndromes, including frailty, fall and fractures, and dementia.[4] The QMCOO consists of 15 items from the following 10 domains: health

condition, mental health, eating behavior, oral function, bodyweight loss, physical function and falls, cognitive function, smoking, social participation and social support.[4] Several cross-sectional studies have reported a close correlation between the QMCOO score and score of the Kihon Checklist,[5,6] a frailty score developed in Japan to assess for care requirement in older adults, and a frailty score of the Cardiovascular Health Study.[7] Recently, Tanaka *et al.*[8] reported that a simply summed score of 15 items on the QMCOO was independently associated with incidence of functional disability in a general population. Validating the prognostic significance of this questionnaire with further consideration of weighting of each item could provide a basis for its use in identifying individuals who are at risk. Furthermore, given the possibility of internal correlation between items, it was uncertain whether all 15 items were needed for the calculation of the total score. Considering basic clinical factors assessed in the annual health checkup together with the responses to the selected items of QMCOO might further improve the accuracy of identifying individuals at-risk.

Given these backgrounds, the present study aimed to investigate the prognostic significance of the QMCOO for functional disability by analyzing data from the Shizuoka Prefecture-wide Kokuho Database, which includes health and care insurance claims data, and the annual health checkup data for older adults, and to develop a risk score consisting of weighted scores of selected QMCOO items and basic clinical factors assessed in the annual health checkup to facilitate identification of older adults at-risk for functional disability.

Methods

Data source

This study analyzed data from the Shizuoka Kokuho Database (SKDB ver. 2024.1 with the analysis data generation system ver. 4.0),[9,10] which comprises the Shizuoka Prefecture-wide individual-level data on the medical insurance claims and health checkup of enrollees in the National Health Insurance or the Latter-Stage Elderly Medical Care System. The current version of the SKDB covers the period from April 2012 to September 2022.

The National Health Insurance partially covers the medical expenditure of insured people. This insurance system is designed for individuals aged <75 years who are not eligible to be members of any employee-based health insurance. The Latter-Stage Elderly Medical Care System is a health insurance system for individuals aged >75 years and people aged 65–74 years who are physically handicapped. Older individuals aged ≥75 years, except those who have an occupation, are required to enroll in this insurance system. Enrollees for these insurance systems have the opportunity to receive a medical checkup (*Tokuei Kenshin*, *Kouki Koureisha Kenshin*) once a year.

Furthermore, the SKDB includes data on the Long-Term Care Insurance System, a care insurance system that covers daily care expenses for older people. Insured individuals who require long-term care are eligible for in-home or facility-based services according to their certified care level. The long-term care approval board in each municipality determines the certified care level by assigning a support level (levels 1–2) or a care level (levels 1–5) based on the applicant's mental and physical condition, and the opinion of their primary doctor. The care requirement certification is designed to be applied uniformly on a nationwide basis.

Study setting

This was a longitudinal observational study comprising residents aged ≥75 years in the Shizuoka Prefecture who participated in the Latter-Stage Elderly Medical Care System. The longitudinal analysis was carried out using the earliest day of participation after 2020 in the annual health checkup as the index day, with 12 months before the index day as the baseline period (Fig. S1). The follow-up duration was calculated as the number of days from the index day to the end of the follow-up period. Withdrawal cases from the insurance were treated as a censored case.

Using the earlier version of the SKDB, re-admission cases were provided with the same insurance ID as continuous enrollees by disregarding the intermediate period during which they were unsubscribed. However, the method of calculating the follow-up period was changed to exclude the intermediate unsubscribed period by setting the baseline to fall within the consecutive insurance enrollment period.

Study population

Of the 2 654 305 residents in the Shizuoka Prefecture who were included in the current version of the SKDB, those who participated in the health checkup after April 2020 ($n = 401\,854$) were extracted. Individuals aged ≥90 years ($n = 10\,691$) and <75 years ($n = 265\,388$), those who had been certified as care levels 2–5 ($n = 3817$) at the index day, those whose data on the clinical parameters required for this study were not available or widely deviated from its distribution ($n = 8141$), and those whose responses to the QMCOO had missing value ($n = 2535$) were excluded from the study. Finally, 111 282 older adults were ultimately included in this analysis.

The ethics committee of the Shizuoka Graduate University of Public Health (SGUPH_2021_001) approved the study procedure involving the SKDB analysis. Approval from the review board of each municipality for using their insurance data in medical studies was also obtained before receiving the data. Before the receipt of the SKDB data, all personal details were anonymized by the Shizuoka Federation of National Health Insurance Organizations. To ensure that the participants can refuse the use of their data, information related to this study was disclosed on the websites of the Shizuoka Prefectural Government Office and Shizuoka Graduate University of Public Health.

Outcome definition

To meet the conditions with the criteria of healthy life expectancy, which were determined by the Ministry of Health, Labor and Welfare, the participants who were certified as care level 2 and higher were considered to have functional disability. Furthermore, the associations between the QMCOO and all-cause mortality were investigated to validate items differently associated with functional disability and all-cause mortality. All-cause mortality was identified based on the withdrawal reason described in the health insurance data.

Clinical parameters

Clinical information and responses to the QMCOO were obtained from the annual health checkup records. During the baseline period, information on the participants' latest certified care level based on the data on the Long-Term Care Insurance System was collected. The Charlson Comorbidity Index[11] was calculated using the health insurance claims requested during the baseline period and was used as an index of severe comorbidity.

Statistical analysis

Values are expressed as the mean ± standard deviation or frequency. The Cox proportional hazards model was used to investigate factors associated with functional disability and all-cause mortality. The proportional hazards assumption was verified with a Schoenfeld residual test. The Cox proportional hazards model was also used to calculate the probability of developing functional disability according to the participants' baseline characteristics. A detailed description for the calculation of the probability can be found in a previous study.[12] The score sheet for functional disability (the SKDB functional disability score) was made based on the regression coefficient obtained from the final Cox proportional hazards model.[13]

Statistical analyses were carried out using JMP version 17.2.0 (SAS Institute, Cary, NC, USA). The Schoenfeld residual test and Harrell's C-index calculation were carried out using Stata version 18.0 (StataCorp, College Station, TX, USA). *P*-values of <0.05 were considered statistically significant.

Results

Table 1 shows the clinical characteristics of the study participants. Differences in clinical characteristics between participants who developed functional disability and who did not, and between participants who died or survived, are summarized in Tables S1 and S2, respectively. During a mean follow-up duration of 1.7 years (191 085 person-years), 4578 functional disability cases were recorded. Meanwhile, there were 3195 mortality cases during this period (194 593 person-years).

Table 1 Clinical characteristics of the study participants

Age (years)	81.1 ± 4.0
Male sex (%)	25.7
Body mass index (kg/m^2)	22.5 ± 3.4
Rate of hospitalization (%)	9.7
Certified care level at baseline (%)	
Support level 1	1.4
Support level 2	1.9
Care level 1	3.3
Charlson comorbidity index	2.7 ± 2.3
Systolic blood pressure (mmHg)	135 ± 17
Diastolic blood pressure (mmHg)	73 ± 11
Hypertension (%)	35.3
HDL cholesterol (mg/dL)	64 ± 16
Low HDL cholesterol (%)	4.7
LDL cholesterol (mg/dL)	117 ± 29
High LDL cholesterol (%)	20.4
Hemoglobin A1c (%)	5.8 ± 0.6
High hemoglobin A1c (%)	61.6
Creatinine (mg/dL)	0.8 ± 0.3
High creatinine (%)	14.8
Alanine aminotransferase (U/L)	18 ± 11
High alanine aminotransferase (%)	10.3
Urinary glucose, −/±/+/≥2/≥3 (%)	95.2/1.1/1.1/0.8/1.8
Urinary protein, −/±/+/≥2/≥3 (%)	81.2/10.2/6.0/2.0/0.7

Total participants $n = 111\,282$.Values are presented as the mean ± standard deviation or frequency. History of hospitalization was obtained retrospectively from the care insurance data up to 12 months before the index date. The certification of support requirement was determined using the long-term care approval board. Hypertension: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg irrespective of antihypertensive drug use; low high-density lipoprotein (HDL) cholesterol: <40 mg/dL; high low-density lipoprotein (LDL) cholesterol: ≥140 mg/dL; high hemoglobin A1c: ≥5.6%; high creatinine: ≥1.0 mg/dL; high alanine aminotransferase: ≥42 U/L (men) or ≥ 23 U/L (women).

Table S3 summarizes the frequency of responses for each item in the QMCOO. Table S4 presents the differences in terms of responses between individuals who developed functional disability and those who did not. If the hazard ratio of each item for functional disability was calculated separately with adjustment for age, sex and body mass index, all items showed a significant association (Fig. 1). Similar results were observed in the analysis of all-cause mortality (Fig. 1).

Table S5 presents the results of the Cox proportional hazards model analysis including all items of the QMCOO for the incidence of functional disability. This analysis showed that 10 items of the QMCOO were significant determinants. Furthermore, similar results were observed in the following sensitivity analyses: further adjustment of the Charlson Comorbidity Index (Table S6), excluding incident cases of functional disability within 180 days of follow up (Table S7), age-separated analysis at 80 years-of-age (Tables S8 and S9) and sex-separated analysis (Tables S10 and S11). The factors associated with the incidence of functional disability did not change, even when all-cause mortality was considered as a competing risk factor (Table S12).

Among the 10 QMCOO items independently associated with the incidence of functional disability, Q05 (Have you choked on your tea or soup recently?) showed an opposite association in the basic factor-adjusted analysis (Fig. 1) and in the fully adjusted analysis (Table S5), even after further adjustment of the Charlson Comorbidity Index (Table S6). Figure 2 shows changes in the hazard ratio of Q05 after adding clinical markers and other items from the questionnaire into the Cox proportional hazards model. Considering the instability of the association, Q05 was ultimately excluded from the model. Similar results were obtained in the analysis for all-cause mortality (Fig. S2).

Table 2 shows the summary results of the final Cox proportional hazards model for functional disability. In this final model, given the similar hazard ratios of urinary protein ± and + or higher groups (Table S5), we included urinary protein as two groups to simplify the model. Although several factors did not meet proportional hazard assumption tested by Schoenfeld's residuals (Table S13), we did not exclude these factors from the model given the rho value. The Harrell's C-index of the final model was 0.818, whereas that of the model without the QMCOO was 0.784.

The 2-year event-free probability for the means of risk factors was approximately 0.9705. Based on these results, a score sheet for the incidence of functional disability, the SKDB functional disability score, was developed (Table 3). Furthermore, the predicted probability within 2 years was calculated (Table 3). Figure S3 shows the number of participants with a 2-year probability of ≥10% or ≥5% and <10%. The frequency of individuals with a probability of ≥5% or increased linearly with increasing age. Table S14 shows the clinical characteristics and response rates for the selected items among the subgroups divided by the probability. Participants with a higher probability were more likely to be men, underweight and certified as support level or care level at baseline. Participants with a higher probability had a greater frequency of poor responses for each item.

Discussion

The present longitudinal study that used prefecture-wide data of older adults showed that nine items in the QMCOO were

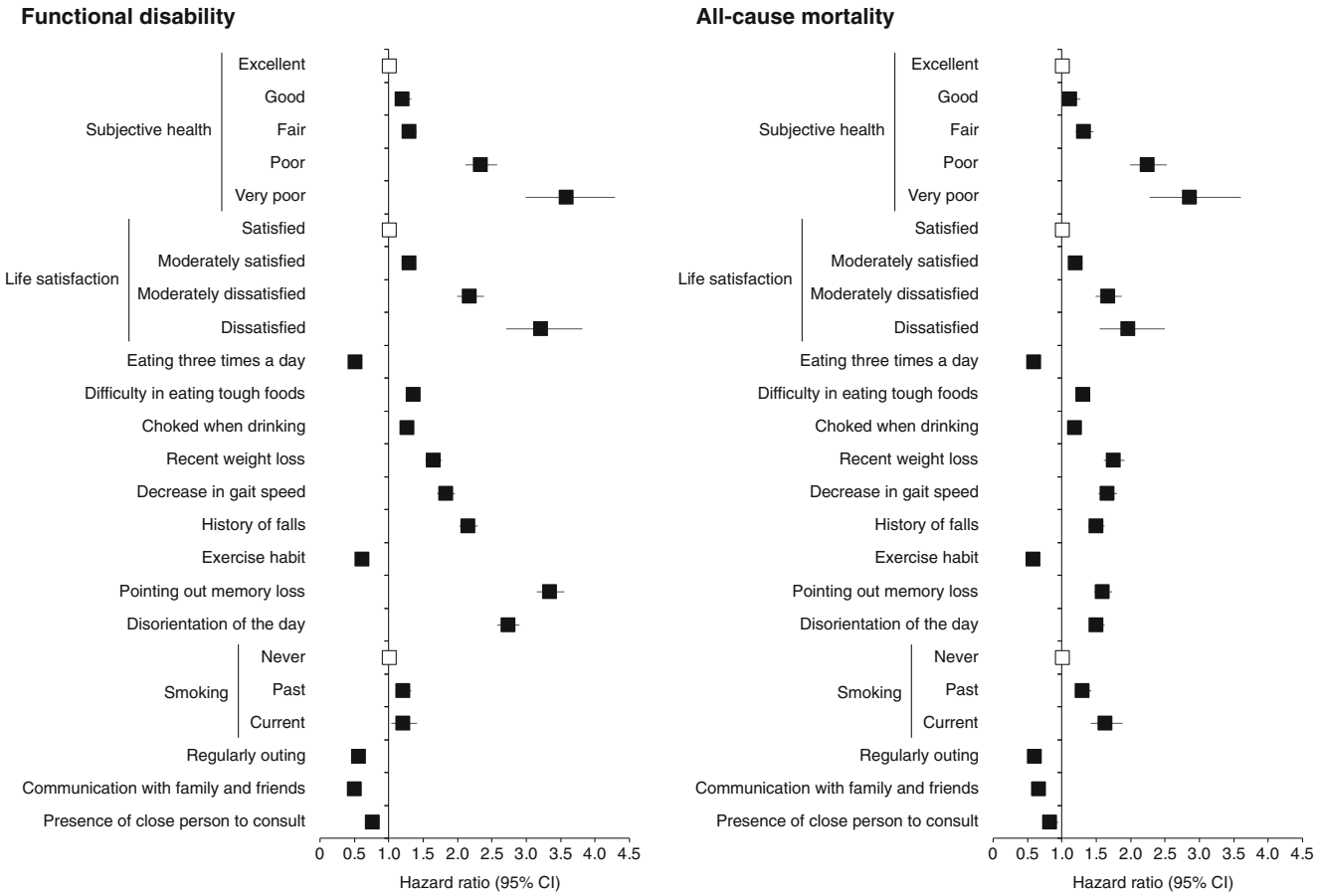

Figure 1 Hazard ratios of functional disability and all-cause mortality for each item in the Questionnaire for Medical Checkup of Old-Old. The adjusted hazard ratio and 95% confidence interval of age, sex and body mass index were calculated. The hazard ratios of each item were calculated using the Cox proportional hazards model. Open squares indicate references in the calculation of the hazard ratio.

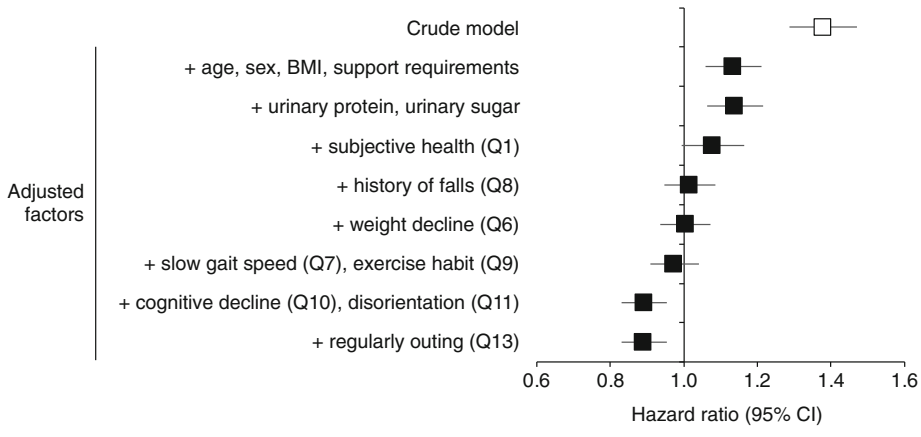

Figure 2 Changes in the hazard ratio of Q05 (choked when drinking) for functional disability through a stepwise adjustment of factors associated with functional disability. Values are presented as hazard ratio and 95% confidence interval. Body mass index (BMI; <20 kg/m^2), urinary protein level (≥±), urinary glucose level (≥±) and subjective health (Q1, poor or extremely poor) were included in the model as a dichotomized value.

independent determinants of functional disability. A simple risk score consisting of the selected QMCOO items and basic clinical factors available for identifying individuals at risk for functional disability was developed.

Japanese individuals aged ≥75 years are required to enroll in the Latter-Stage Elderly Medical Care System. Hence, the proportion of participants in this insurance system was 98.6% at 2022.[14] However, only 28.1% of all insured individuals participated in the health checkup.[15] Hence, the study results might have a healthy bias, which can be particularly strong in the older adult population with a relatively lower participation rate in health checkups.[10] Therefore, the 2-year probability of functional disability calculated in this study

Table 2 Cox proportional hazards model for functional disability including the selected factors

		Coefficient	HR (95% CI)	*P*-value
Age (years)		0.102	1.11 (1.10–1.12)	<0.001
Sex (men)		0.299	1.35 (1.27–1.44)	<0.001
Body mass index (<20 kg/m^2)		0.229	1.26 (1.18–1.34)	<0.001
Certified care level at baseline	Support level 1	0.814	2.26 (1.93–2.64)	<0.001
	Support level 2	1.137	3.12 (2.76–3.52)	<0.001
	Care level 1	1.619	5.05 (4.67–5.46)	<0.001
Urinary glucose (≥±)		0.250	1.28 (1.15–1.43)	<0.001
Urinary protein (≥±)		0.362	1.44 (1.35–1.53)	<0.001
Q01: How is your health condition? (Poor or very poor)		0.240	1.27 (1.18–1.37)	<0.001
Q03: Do you eat three times a day? (No)		0.234	1.26 (1.14–1.41)	<0.001
Q06: Have you lost 2 kg or more in the past 6 months? (Yes)		0.158	1.17 (1.08–1.26)	<0.001
Q07: Do you think you walk slower than before? (Yes)		0.248	1.28 (1.19–1.38)	<0.001
Q08: Have you experienced a fall in the past year? (Yes)		0.345	1.41 (1.32–1.51)	<0.001
Q09: Do you go for a walk for your health at least once a week? (No)		0.217	1.24 (1.17–1.32)	<0.001
Q10: Do your family or friends point out your memory loss? (Yes)		0.559	1.75 (1.63–1.87)	<0.001
Q11: Do you find yourself not knowing today's date? (Yes)		0.452	1.57 (1.47–1.68)	<0.001
Q13: Do you go out at least once a week? (No)		0.341	1.41 (1.31–1.52)	<0.001

Responses to Q03, Q09 and Q13 were flipped and then included in the regression model. CI, confidence interval; HR, hazard ratio.

Table 3 The Shizuoka Kokuho database score for functional disability

Score sheet			Predicted probability	
Items		Points	Total score	Probability (%)
Age	75–79 years	3	≤3	0.8
	80–84 years	8	4–9	1.2
	85–89 years	13	10–14	2.0
Sex (men)		3	15–19	3.2
Body mass index (<20 kg/m^2)		2	20–24	5.4
Certified care level at baseline	Support level 1	8	25–29	8.5
	Support level 2	11	30–34	13.6
	Care level 1	16	35–39	21.4
Urinary glucose (≥±)		2	≥40	≥45.6
Urinary protein (≥±)		4		
Q01: How is your health condition? (Poor or very poor)		4		
Q03: Do you eat three times a day? (No)		2		
Q06: Have you lost 2 kg or more in the past 6 months? (Yes)		2		
Q07: Do you think you walk slower than before? (Yes)		2		
Q08: Have you experienced a fall in the past year? (Yes)		3		
Q09: Do you go for a walk for your health at least once a week? (No)		2		
Q10: Do your family or friends point out your memory loss? (Yes)		6		
Q11: Do you find yourself not knowing today's date? (Yes)		5		
Q13: Do you go out at least once a week? (No)		3		

Responses to Q09 and Q13 were flipped. The points of age groups were calculated by subtracting 75 points (points for individuals aged 74 years) from the crude points of each group (75–79 years: 78 points, 80–84 years: 83 points, 85–89 years: 88 points).

might be lower than the actual value for the whole older adult population. The results of the current study should be interpretated with caution that it was useful in identifying individuals at-risk for functional disability among older individuals who participated in the annual health checkups.

Among the 15 items in the QMCOO, 10 items were significantly associated with the incidence of functional disability. Among them, nine items, except for Q05, were included in the final assessment model. After reducing the number of items, the QMCOO became easy to use as a risk assessment tool. Among the five items, which were not identified as significant determinants, "keeping communication with family and friends" (Q14) and "having close persons to consult" (Q15) had large bias (≥95%) in the frequency of responses, which could have contributed to the lack of association with the incidence of functional disability. "Satisfaction in daily life" (Q02) is a concept that represents not only physical conditions, but also socioeconomic status and other social factors.[16] Thus, it might not be suitable for the risk assessment of functional impairment.

It was challenging to consider the reason why "difficulty in eating tough foods" (Q04) was not associated with the outcomes. The conditions assessed in this question might overlap with conditions that were assessed by other questions. A previous cross-sectional study investigating the association between QMCOO

and frailty[17] also did not identify this item as a significant determinant.

Smoking is an established risk factor of cardiovascular diseases. However, there was no marked difference in the frequency of smoking habit at the baseline between a population who developed functional disability and those who did not, supporting the notion that "current smoking" (Q12) was not directly associated with the development of functional disability.

The hazard ratio of Q05 (Have you choked on your tea or soup recently?) was reduced to <1.0 after adjusting for other factors associated with the development of functional disability. This question was used in the QMCOO to assess frailty of oral function.[18] In the simple adjusted model, this question was positively associated with functional disability, probably reflecting the deterioration of oral function. The precise reason why the association was inverted in the full adjusted model was uncertain. However, a possible explanation was that laryngeal cough reflex is a normal defense response in preventing aspiration pneumonia.[19] Therefore, in the model adjusted for frailty status by other factors, it might be that those who are able to show a normal protective response to aspiration should be interpreted as being less likely to develop functional disability. It was reported that individuals with dysphagia do not always have a cough reflex.[20] A previous longitudinal study of the Japanese older population also showed a gradual decrease in the hazard ratio of this question for all-cause mortality, though the hazard ratio remained significant in the fully adjusted model.[21] Given that the previous study included a population aged ≥65 years, the prognostic significance of this question might be interpreted differently for different age groups. Another possibility was reduced reliability of responses to the questions due to cognitive decline. Because dementia was the most frequent cause of functional disability in participants aged ≥75 years,[22] it is possible that participants likely to progress to functional disability did not answer the question accurately. However, the results did not change in the analysis of participants further adjusted for severe comorbidities, including dementia. Furthermore, it was unlikely that the effects of cognitive decline would affect only Q05. The effects of cognitive decline, if any, might not be substantial to change the present findings.

The final Cox proportional hazards model included nine QMCOO items and a limited number of clinical parameters, which were consistently associated with functional disability in any conditional analysis. The final model was extremely simple and only comprised factors that could be obtained from annual health checkup data, thereby increasing the usefulness of this model in the risk assessment of older individuals in municipal health practice activities. Individuals certified as support level or care level 1 at baseline were not excluded from the analysis to ensure the availability of this risk assessment model to different individuals who participated in the annual health checkups. If individuals who are at the support level or care level 1 were excluded from the analysis, the use of this risk assessment model is limited to individuals who are physically independent. Due to the same reason, individuals who have histories of hospitalization within 12 months before the health checkup day for any reasons were not excluded from the analysis. However, hospitalization history was not consequently identified as a significant determinant. Several participants had comorbidities assessed using the Charlson Comorbidity Index. Although Tanaka *et al.*[8] reported that the hazard ratio for functional disability was higher for the combination of QMCOO and Charlson Comorbidity Index than for either alone, the baseline comorbidities were also not considered in the analysis, because information on comorbidities cannot be easily assessed during health checkups. However, further adjustment of the Charlson Comorbidity Index in the Cox proportional hazards model did not significantly change the results. Hence, disregarding comorbidities in the risk assessment did not lead to major bias.

To facilitate the use of this risk assessment model in preventing functional disability, the SKDB functional disability score was developed based on the results of the Cox proportional hazards model. Although this risk score had some errors in the calculation of the probability due to the use of an integer value than the actual regression coefficient, we believe that this score, combined with the frequency chart of high-risk populations, might help determine which individuals require intervention.

In addition to the abovementioned strengths and limitations, the present study had several limitations that should be noted. First, this study used KDB in Shizuoka Prefecture residents. The rate of care certification differs between prefectures.[23] Hence, studies using nationwide data could improve predictive performance. Second, the follow-up period was short, because the QMCOO was used after 2020. The risk assessment score developed in this study might be useful to identify individuals who will need long-term care within a few years. Third, the causes of functional disability could not be identified. The results of individual analyses based on primary diseases for functional disability, which include dementia, cerebrovascular diseases, frailty and musculoskeletal diseases, might further facilitate the classification of individuals at-risk. Fourth, although lower education attainment has been reported to be independently associated with the incidence of functional disability,[24] we did not consider socioeconomic status, because the current Japanese health checkup system for older adults is not designed to assess socioeconomic status.

In conclusion, nine items in the QMCOO were independent determinants of the incidence of functional disability. The present findings, along with the SKDB functional disability score, could help identify older individuals who require preventive interventions against functional disability.

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Disclosure statement

The authors declare no conflict of interest.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's website:

Data S1. Supporting Information.

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Is Oral Function Associated with the Development of Sarcopenic Obesity and Sarcopenia in Older Adults? A Prospective Cohort Study

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Abstract: Background: Sarcopenic obesity, defined as the concurrent loss of muscle mass and adipose tissue accumulation, is associated with reduced physical function and poor health status in older adults. Although oral function can impact the overall health of older adults, its role in the development of sarcopenic obesity remains unclear. Herein, we aimed to examine the association between oral function and the incidence of sarcopenic obesity. Methods: This longitudinal cohort study included 597 independent older adults (aged ≥65 years) from Tamba-Sasayama, a rural region of Japan, who participated in academic studies between June 2016 and December 2023. Participants underwent surveys at least twice, with a minimum two-year interval. The participants were divided into four groups (robust, obese, sarcopenic, and sarcopenic obese) according to their health condition. Sarcopenic obesity was diagnosed based on the guidelines of the Japanese Working Group on Sarcopenic Obesity. The oral function was evaluated by assessing the number of remaining teeth, tongue pressure, occlusal force, masticatory performance, and oral diadochokinesis. Cox proportional hazards regression analysis evaluated the association between oral function and the incidence of sarcopenic obesity after adjusting for relevant confounders. Results: The sarcopenic obesity group was older, had lower skeletal muscle mass, and inferior physical function. This cohort also had the highest prevalence of hypertension and significantly fewer remaining teeth. The proportion of individuals with sarcopenic obesity was 1.7% of the total population, with 2.8% in the obesity group at baseline, and 8.0% of those were diagnosed with sarcopenia progressing to sarcopenic obesity. The Cox regression model revealed that reduced tongue pressure was significantly associated with an increased risk of sarcopenic obesity, with a hazard ratio of 0.906 (95% confidence interval: 0.829–0.990; $p = 0.028$), independent of other variables related to sarcopenia and obesity. Conclusions: Our findings suggest that oral function is associated with the incidence of sarcopenic obesity but not with that of sarcopenia or obesity alone.

Keywords: sarcopenic obesity; obesity; tongue pressure; oral function; hypertension

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1. Introduction

Sarcopenia and obesity are two major health concerns impacting the older population and have substantial implications for their overall health and quality of life. Sarcopenia is characterized by the age-related loss of muscle mass, strength, and physical performance [1,2]. In older adults, obesity is associated with an elevated risk of falls, reduced functionality, diminished quality of life, and increased mortality. It also increases the risk of cardiovascular diseases, metabolic disorders, cognitive impairment, and arthritis [3,4].

The interplay between obesity and skeletal muscles in the aging population is complex, with evidence suggesting both protective and deleterious effects. Although obesity is associated with impaired physical function and resistance to anabolic stimuli, it may also lead to greater muscle mass in weight-bearing muscles than in older, lean individuals [5,6].

The coexistence of sarcopenia and obesity leads to sarcopenic obesity, a condition that has garnered increasing attention owing to its profound effects on health outcomes [6–8]. Sarcopenic obesity is characterized by muscle weakness due to sarcopenia combined with the metabolic complications of obesity. These conditions exhibit a synergistic relationship, each exacerbating the progression [8]. Sarcopenic obesity is associated with a higher risk of cardiovascular disease, diabetes, and impaired physical function than either condition alone. Sarcopenic obesity involves a vicious cycle of cross-talk between adipose and muscle tissue, and increased white adipose tissue and local muscle fat infiltration leading to inflammatory adipokine secretion, inhibiting protein synthesis and inducing catabolism. Cytokine secretion by fat mass affects muscle tissue and other organs, such as the liver and white adipose tissue, inhibiting insulin signaling and increasing the risk of insulin resistance [9,10]. Additionally, peri-muscular fat plays a critical role in different phenotypes of sarcopenic obesity, influencing inflammatory pathways and metabolic dysfunction. Furthermore, hormone-related responses vary across phenotypes, which may contribute to the secretion of inflammatory adipokines and the modulation of cytokine effects [11]. The interaction between reduced muscle quality and enhanced adiposity increases health risks, particularly in older populations [12–16].

The impact of sarcopenia and obesity on oral health is mediated via distinct pathways. A notable association exists between sarcopenia and oral function, primarily attributed to the interaction between muscle mass and masticatory abilities [17,18]. Sarcopenia typically results in reduced masticatory muscle strength, leading to compromised food intake and nutritional deficiencies. Moreover, older individuals with sarcopenia exhibit an increased susceptibility to oral health complications, including periodontal disease and dental caries, owing to difficulties in maintaining adequate oral hygiene [19].

Obesity is strongly associated with chronic systemic inflammation, exacerbating the progression of periodontal disease [20,21]. In addition, individuals with obesity have a higher propensity for recurrent and severe periodontal diseases. This phenomenon is partially attributed to decreased salivary production [22], which compromises the natural cleansing mechanisms of the oral cavity and increases the risk of dental caries [23,24].

Although the individual effects of sarcopenia and obesity on oral health have been previously studied, the combined impact of sarcopenic obesity on oral health remains elusive. Given the established associations among sarcopenia, obesity, and oral health, examining the long-term implications of sarcopenic obesity on oral health outcomes is critical. However, longitudinal studies of sarcopenic obesity, its progression over time, and its relationship with oral health are limited. Considering that both sarcopenia and obesity contribute to physical limitations and adverse health outcomes that can affect oral well-being, it is reasonable to expect that the progression of sarcopenic obesity, which combines these two conditions, is linked to oral health deterioration.

In the cohort study, we aimed to investigate the longitudinal association between sarcopenic obesity and oral health. We hypothesized that oral function is independently associated with physical condition and function, contributing to the development of sarcopenic obesity.

2. Material and Methods

This study encompassed independent older adults (aged ≥65 years) from Sasayama, rural Tamba-Sasayama City, Hyogo Prefecture, Japan, who participated in academic studies between June 2016 and December 2023. This cohort was designated the Frail Elderly in the Tamba-Sasayama Area (FESTA) study. The study was conducted in accordance with the ethical standards established by the Ethics Committees of both Hyogo Medical University (approval number: Rinhi-0342) and Niigata University (Approval number: G2021-0027).

The recruitment process was executed by placing newspaper advertisements and posters at the Sasayama Medical Center and Hyogo Medical University, resulting in the voluntary participation of study subjects. To be eligible for participation, individuals were required to meet the following criteria: they had to be independent older adults aged ≥65 years, residing in the Tamba-Sasayama region of Hyogo Prefecture, capable of traveling to the Sasayama Medical Center via public transportation or private vehicle, and without cognitive impairment (MMSE score >22). From among 1016 participants, 597 surveyed at least twice at a minimum interval of two years were included in the analysis. Individuals who could not ambulate independently (except those using a cane) were excluded. Participants were provided with comprehensive information regarding the objectives and methodology of the study, and written informed consent was obtained before their participation.

2.1. Evaluation Items

Participants were required to provide information regarding their medical and smoking histories via a questionnaire. Blood pressure was measured using a fully automatic calibrated oscillator (BP-203 RVII, Colin Co., Kyoto City, Japan).

Body composition was assessed via bioelectrical impedance analysis (BIA) using an InBody 770 device (InBody Japan, Inc., Koto Ward, Tokyo, 136-0071, Japan). Body mass index (BMI), limb skeletal muscle mass (LBM), and percent body were determined using BIA (InBody Co., Seoul, Republic of Korea).

2.2. Diagnosis of Sarcopenic Obesity

The participants were categorized into four groups based on their health status: robust, obese, sarcopenic, and sarcopenic obese. The classification method follows the flowchart depicted in Figure 1.

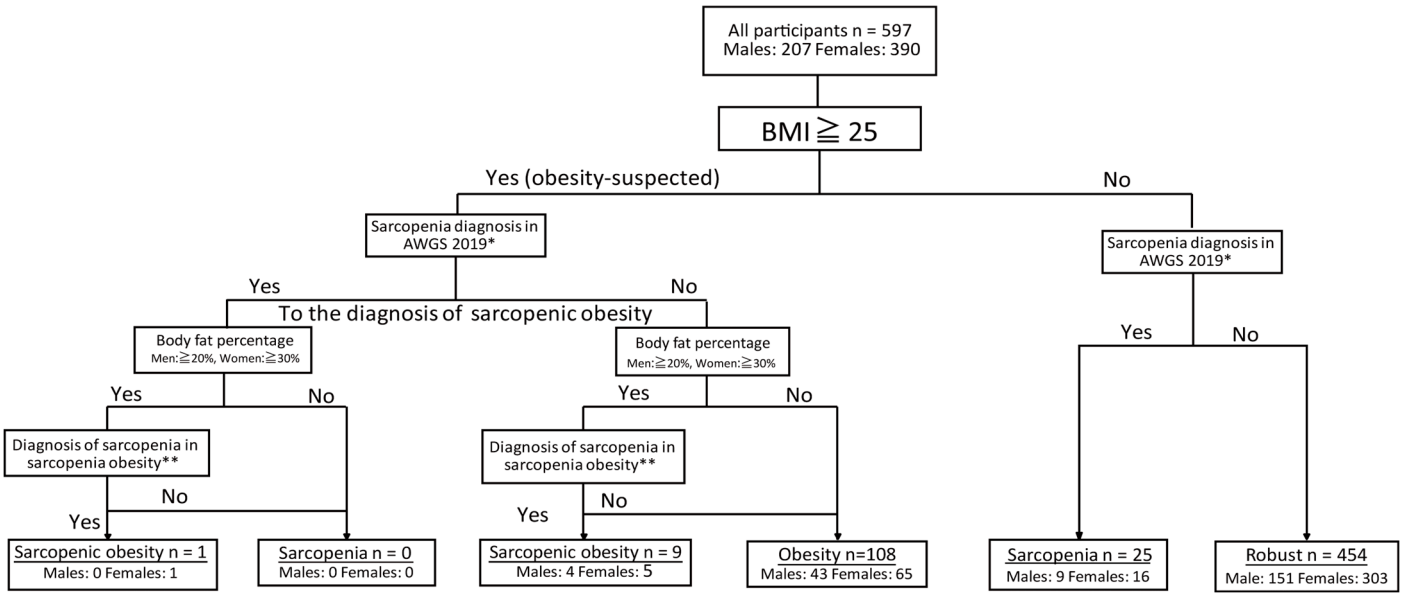

Figure 1. Classification of participants with sarcopenic obesity. *: Low skeletal muscle mass (kg/m^2) + low muscle strength or/and low physical function (diagnosis of sarcopenia [25]). **: Low skeletal muscle mass (kg/BMI) + low muscle strength or low physical function (diagnosis of sarcopenia obesity [26].

First, obesity screening was conducted according to the criteria established by the Japan Society for the Study of Obesity [26]. Individuals with a BMI of ≥25 kg/m^2 were classified as "obesity-suspected". Sarcopenic obesity was diagnosed based on the criteria established by the Japanese Society of Gerontology [26], in which obesity was determined by body fat percentage with thresholds set at >20% for males and >30% for females.

Sarcopenia was defined using the same diagnostic criteria as for sarcopenia alone, incorporating skeletal muscle mass, grip strength, and five-times-sit-to-stand-test (FTSST) performance. However, in the case of sarcopenic obesity, muscle mass was adjusted for BMI, and values of <0.789 for males and <0.512 for females were deemed to indicate low muscle mass [26]. Sarcopenic obesity was diagnosed when an individual met the criteria for both obesity and sarcopenia, as described above.

Sarcopenia was diagnosed based on the criteria set by the Asian Working Group for Sarcopenia (AWGS) [25], incorporating assessments of muscle strength (grip strength), physical function (FTSST performance), and muscle mass (height-adjusted appendicular skeletal muscle mass in kg/m^2). Sarcopenia was identified in individuals who exhibited both reduced muscle strength and physical function, as well as low muscle mass. Muscle weakness was defined as grip strength of <28 kg in males and <18 kg in females, while a decline in physical function was indicated by an FTSST completion time exceeding 12 s [25]. Muscle mass was assessed using the skeletal muscle mass index (SMI), with values below 7.0 kg/m^2 in males and 5.7 kg/m^2 in females classified as having low muscle mass [25].

Based on these criteria, individuals with low muscle mass, reduced muscle strength, and physical function were diagnosed with severe sarcopenia. Those with low muscle mass and either reduced muscle strength or reduced physical function were diagnosed with "sarcopenia". Both groups were jointly categorized as the sarcopenia group. Participants who did not meet the criteria for either obesity-suspected or sarcopenia were classified as the robust group.

In addition, sarcopenic obesity was further categorized into two distinct stages based on the disease severity. Stage I sarcopenic obesity was characterized by low muscle strength, reduced physical function, low muscle mass, and obesity. Stage II sarcopenic obesity was

defined by a further decline in muscle strength and physical function, low muscle mass, obesity, and the presence of comorbidities. Comorbidities were defined as the presence of at least one chronic disease in individuals aged ≥70 years, including metabolic disorders, liver disease, kidney disease, heart disease, respiratory disease, gastric ulcer, osteoporosis, rheumatoid arthritis, thyroid disease, collagen diseases, or stroke, which are all associated with an increased likelihood of sarcopenic obesity [7,26].

2.3. Evaluation of Oral Function

The oral function was objectively evaluated by assessing the number of remaining teeth, tongue pressure, occlusal force, masticatory performance, and oral diadochokinesis (ODK). A comprehensive oral health assessment was performed by dental professionals who had received more than two hours of training and calibration prior to the survey. The examination was conducted under optimal lighting conditions, with the subject seated in a reclining chair. Participants who routinely wore dentures were assessed while wearing the dentures.

The number of remaining teeth was defined by third molars and roots, and implants, bridges, and dentures were excluded. Tongue pressure was measured twice using a JMS Tongue Pressure Measuring Device (JMS Co., Ltd., Hiroshima, Japan), and the highest value was recorded [27]. The occlusal force was quantified using an Occlusal Force Meter (GM10, Nagano Keiki, Tokyo, Japan) [28,29]. The maximum occlusal forces on the left and right sides were measured, and their sum was used in subsequent analysis [30,31]. Masticatory performance was evaluated using a standardized masticatory performance evaluation method (scoring method) using gummy jelly [31]. The participants chewed gummy jelly (UHA Mikakuto, Osaka, Japan) 30 times, followed by a visual evaluation of the expectorated fragments using a 10-level scale ranging from 0 to 9 [32]. Tongue motor function was evaluated using ODK. The articulatory velocity of /ta/ was measured using ODK measurement equipment (KENKOU-KUN Handy; Takei Scientific Instruments Co., Ltd., Niigata, Japan) [30].

2.4. Data Analysis

Data are presented as mean ± standard error (SE) for continuous variables. Differences between the two groups were assessed using the Student's *t*-test. Comparisons among three or more groups were performed using one-way analysis of variance (ANOVA), followed by post hoc multiple comparisons. The Bonferroni correction was applied to adjust the *p*-values for multiple comparisons.

Categorical variables are presented as absolute numbers (*n*) and relative frequencies (%). Differences between categorical variables were analyzed using the chi-square or Fisher's exact test, as appropriate, based on the expected cell counts.

We conducted Cox regression analysis using the incidence of sarcopenic obesity as the event and the time from baseline to follow-up as the time variable to determine whether oral function was an independent factor contributing to the development of sarcopenic obesity. The independent variable was the onset of sarcopenic obesity, and the explanatory variables were those showing a statistically significant difference between the health status groups in the cross-sectional analysis at baseline. The adjusted variables were sex, age, and health status at baseline (divided into four groups). Those with sarcopenic obesity at baseline were excluded from the analysis. We checked for multicollinearity between the explanatory variables and selected the variable with the highest significance level in cases of overlap. The final model was determined using a stepwise method (variable reduction Wald test) and multiple imputations. The criteria for adding and deleting variables were set at $p < 0.05$ and $p < 0.10$, respectively, with a maximum of 20 iterations.

For subgroup analyses, we conducted Cox regression analyses with sarcopenia onset as the event, targeting participants assigned to the robust or obese group at baseline, and examined factors contributing to the onset of sarcopenia. We also conducted a Cox regression analysis with obesity onset as the event, targeting participants in the robust or sarcopenia groups at baseline, and examined factors contributing to the onset of obesity. The subgroup analyses excluded participants with sarcopenic obesity at baseline or follow-up. Cox regression analysis of the subgroups was based on analysis of the onset of sarcopenic obesity.

Statistical significance was defined as a *p*-value of 0.05. All the statistical analyses were performed using SPSS, version 25.0.0 (IBM Corp., Armonk, NY, USA).

3. Results

Table 1 presents the participants' characteristics.

Table 1. Baseline and follow-up characteristics of participants.

A Summary of Participant in Baseline											
		Overall (*n* = 597)			**Males (*n* = 207)**			**Females (*n* = 390)**			***p*-Value**
Age (yr) *		72.8	±	0.2	73.7	±	0.4	72.3	±	0.3	0.003
Duration (day)		947.8	±	15.2	936.3	±	26.5	954.0	±	18.5	0.579
Smoking history *		177 (29.6%)			152 (73.4%)			25 (6.4%)			<0.001
Obesity											
BMI (kg/m^2) *		22.6	±	0.1	23.2	±	0.2	22.2	±	0.1	<0.001
Body fat (%) *		27.3	±	0.3	23.1	±	0.4	29.6	±	0.3	<0.001
	High body weight	118 (19.8%)			47 (22.7%)			71 (18.2%)			0.189
	High body fat *	339 (56.8%)			149 (72.0%)			190 (48.7%)			<0.001
Sarcopenia											
Skeletal muscle mass index (kg/BMI) *		0.708	±	0.006	0.868	±	0.008	0.623	±	0.005	<0.001
Low skeletal muscle mass *		92 (15.4%)			51 (24.6%)			41 (10.5%)			<0.001
Skeletal muscle mass index (kg/m^2) *		6.45	±	0.04	7.40	±	0.05	5.98	±	0.03	<0.001
Low skeletal muscle mass		185 (31.0%)			60 (29.0%)			125 (32.1%)			0.441
Grip strength (kg) *		28.2	±	0.5	35.4	±	0.4	24.4	±	0.7	<0.001
Low muscle strength		46 (7.7%)			18 (8.7%)			28 (7.2%)			0.509
Five times sit-to-stand test (s) *		7.2	±	0.1	7.6	±	0.1	7.0	±	0.1	0.002
Low physical function		20 (3.4%)			9 (4.3%)			11 (2.8%)			0.324
Comorbidities											
Metabolic diseases											
	Diabetes mellitus *	61 (10.2%)			34 (16.4%)			27 (6.9%)			<0.001
	Hypertension *	253 (42.2%)			100 (48.3%)			152 (39.0%)			0.028
	Hyperlipemia	140 (23.5%)			40 (19.3%)			100 (25.6%)			0.083
	Cardiovascular *	40 (6.7%)			21 (10.1%)			19 (4.9%)			0.014
Asthma		14 (2.3%)			4 (1.9%)			10 (2.6%)			0.627
Tuberculosis		5 (0.8%)			2 (1.0%)			3 (0.8%)			
Pneumonia		10 (1.7%)			5 (2.4%)			5 (1.3%)			0.304
Blood pressure											
SBP (mmHg) *		139.0	±	0.7	136.7	±	1.2	140.2	±	0.8	0.013
DBP (mmHg) *		80.3	±	0.4	79.1	±	0.7	81.0	±	0.5	0.039
Diagnosis of sarcopenia obesity											
Robust		454 (76.0%)			151 (72.9%)			303 (77.7%)			0.835
Obesity		108 (18.1%)			43 (20.8%)			65 (16.7%)			
Sarcopenia											
Sarcopenia		23 (3.9%)			8 (3.9%)			15 (3.8%)			
Severe sarcopenia		2 (0.3%)			1 (0.5%)			1 (0.5%)			
Sarcopenic obesity											
Stage I		2 (0.3%)			1 (0.5%)			1 (0.3%)			
Stage II		8 (1.3%)			3 (1.4%)			5 (1.3%)			
Oral function											
	Remaining teeth	20.9	±	0.3	20.7	±	0.6	21.0	±	0.4	0.713
	Occlusal force (kg) *	59.5	±	1.4	66.4	±	2.8	55.9	±	1.6	<0.001
	Tongue pressure (kg)	33.5	±	0.3	34.0	±	0.6	33.2	±	0.4	0.295
	Oral diadochokinesis *	30.5	±	0.2	29.2	±	0.5	31.1	±	0.3	<0.001
Kihon checklist											
Masticatory function		105 (17.6%)			29 (14.0%)			76 (19.5%)			0.094
Swallowing function		146 (24.5%)			51 (24.6%)			95 (24.4%)			0.940
Dry mouth		178 (29.8%)			56 (27.1%)			122 (31.3%)			0.282

Table 1. *Cont.*

A summary of participant in follow-up											
		Overall (*n* = 597)			**Males (*n* = 207)**			**Females (*n* = 390)**			***p*-Value**
Age *		75.3	±	0.2	76.2	±	0.4	74.9	±	0.3	0.006
Smoking history *		177 (29.6%)			152 (73.4%)			25 (6.4%)			<0.001
Obesity											
BMI (kg/m^2) *		22.5	±	0.1	23.1	±	0.2	22.2	±	0.1	0.001
Body fat (%) *		27.3	±	0.3	23.2	±	0.4	29.6	±	0.4	<0.001
	High body weight	118 (19.8%)			43 (20.8%)			75 (19.2%)			0.652
	High body fat *	330 (55.3%)			143 (69.1%)			187 (47.9%)			<0.001
Sarcopenia											
Skeletal muscle mass index (kg/BMI) *		0.697	±	0.006	0.857	±	0.008	0.612	±	0.005	<0.001
	Low skeletal muscle mass *	110 (18.4%)			54 (26.1%)			56 (14.4%)			<0.001
Skeletal muscle mass index (kg/m^2) *		6.38	±	0.04	7.30	±	0.05	5.90	±	0.03	<0.001
	Low skeletal muscle mass *	113 (18.9%)			68 (32.9%)			45 (11.5%)			<0.001
Grip strength (kg) *		26.8	±	0.3	34.0	±	0.4	22.9	±	0.2	<0.001
	Low Muscle strength *	62 (10.4%)			29 (14.0%)			33 (8.5%)			0.034
Five times sit-to-stand test (s) *		7.3	±	0.1	7.6	±	0.2	7.2	±	0.1	0.038
	Low Physical function	19 (3.2%)			10 (4.8%)			9 (2.3%)			0.095
Comorbidities											
Metabolic diseases											
	Diabetes mellitus *	71 (11.9%)			35 (16.9%)			36 (9.2%)			0.006
	Hypertension *	261 (43.7%)			102 (49.3%)			159 (40.8%)			0.046
	Hyperlipemia	154 (25.8%)			46 (22.2%)			108 (27.7%)			0.146
	Cardiovascular *	52 (8.7%)			25 (12.1%)			27 (6.9%)			0.034
Asthma		14 (2.3%)			4 (1.9%)			10 (2.3%)			0.627
Tuberculosis		7 (1.2%)			2 (1.0%)			5 (1.3%)			0.733
Pneumonia		15 (2.5%)			8 (3.9%)			7 (1.8%)			0.124
Blood pressure											
SBP (mmHg) *		139.6	±	0.7	137.5	±	1.1	140.7	±	0.9	0.034
DBP (mmHg)		79.6	±	0.5	78.4	±	0.7	80.2	±	0.6	0.064
Diagnosis of sarcopenia obesity *											
Robust		440 (73.7%)			146 (70.5%)			294 (75.4%)			0.046
Obesity		108 (18.1%)			37 (17.9%)			71 (18.2%)			
Sarcopenia											
Sarcopenia		36 (6.0%)			15 (7.2%)			21 (5.4%)			
Severe sarcopenia		3 (0.5%)			3 (1.4%)			0 (0.0%)			
Sarcopenia obesity											
Stage I		0 (0.0%)			0 (0.0%)			0 (0.0%)			
Stage II		10 (1.7%)			6 (2.9%)			4 (1.0%)			
Oral function											
	Remaining teeth	20.1	±	0.3	19.9	±	0.6	20.2	±	0.4	0.619
	Occlusal force (kg)	48.9	±	1.4	51.6	±	2.6	47.4	±	1.7	0.153
	Tongue pressure (kg) *	33.0	±	0.4	34.1	±	0.6	32.3	±	0.4	0.015
	Oral diadochokinesis *	30.4	±	0.2	29.4	±	0.4	30.9	±	0.2	0.001
Kihon checklist											
Masticatory function		115 (20.5%)			44 (22.6%)			71 (19.3%)			0.368
Swallowing function		148 (26.3%)			53 (27.2%)			95 (25.9%)			0.740
Dry mouth		176 (31.4%)			52 (26.8%)			124 (33.9%)			0.086

* Data are presented as mean ± SE. $p < 0.05$, calculated using Student's *t*-test, chi-squared test, or Fisher's exact test for sex differences. Definitions: duration, number of days from baseline to follow-up. The diagnostic criteria and classification methods for sarcopenic obesity, including BMI, skeletal muscle mass index, muscle strength, and physical function, have been detailed in the 'Diagnosis of Sarcopenic Obesity' section. Participants were grouped into robust, obese sarcopenia (sarcopenia and severe sarcopenia), and sarcopenia obesity (sarcopenic obesity stages I and II) groups. Abbreviations: SBP, mean systolic blood pressure; DBP, mean diastolic blood pressure. Oral diadochokinesis: Represented tongue motor function by the "ta" sound.

This study included 597 participants (207 males and 390 females). The mean age was 72.8 ± 0.2 years, with males being slightly older (73.7 ± 0.4 years) than females (72.3 ± 0.3 years) ($p = 0.003$). Regarding obesity indicators, males had a higher mean BMI (23.2 ± 0.2 kg/m^2) than females (22.2 ± 0.1 kg/m^2) ($p < 0.001$). However, females had a higher body fat percentage (29.6 ± 0.3%) than males (23.1 ± 0.4%) ($p < 0.001$). Interestingly, a higher proportion of males (72.0%) had high body fat levels than females (48.7%) ($p < 0.001$).

Regarding sarcopenia markers, males had a higher SMI (0.868 ± 0.008 kg/BMI) than females (0.623 ± 0.005 kg/BMI) ($p < 0.001$). Males also had higher grip strength (35.4 ± 0.4 kg) than females (24.4 ± 0.7 kg) ($p < 0.001$).

At baseline, the distribution of sarcopenia and obesity categories was similar between both sexes, with 76.0% classified as robust, 18.1% as obese, 4.2% as sarcopenic, and 1.6% as sarcopenic obesity.

At follow-up, the mean age increased to 75.3 ± 0.2 years. The prevalence of sarcopenia and sarcopenic obesity showed sex-based differences ($p = 0.046$). Among male participants, 8.6% were classified as sarcopenic (including severe sarcopenia) and 2.9% as sarcopenic obese, compared with 5.4% and 1.0% among female participants, respectively. However, the differences between male and female participants were non-significant.

Table 2 shows the relationships between health conditions (robustness, obesity, sarcopenia, and sarcopenic obesity) and related factors.

Significant age differences were detected between the groups ($p < 0.001$). Participants in the sarcopenia and sarcopenic obesity groups were older than those in the robust and obese groups. The mean age increased across all groups at follow-up, with the largest increase noted in the sarcopenia group (from 76.3 to 79.6 years). There were no significant sex differences between the groups at baseline or follow-up. Body composition metrics showed consistent patterns at baseline and follow-up. BMI and body fat percentage were significantly higher in the obese and sarcopenic obesity groups than in the robust and sarcopenia groups ($p < 0.001$). The SMI (kg/BMI) was the lowest in the sarcopenic obesity group at both the baseline and follow-up. Physical function measurements revealed notable differences. Grip strength was significantly lower in the sarcopenia group at baseline ($p = 0.012$) and follow-up ($p = 0.001$). The FTSST time was significantly longer in the sarcopenia and sarcopenic obesity groups at both baseline and follow-up ($p < 0.001$), with the gap widening at follow-up. The prevalence of hypertension was highest in the sarcopenic obesity group at baseline (70.0%) and follow-up (80.0%).

Table 2. The relationship between sarcopenic obesity and associated factors.

(a): Baseline		Robust (*n* = 454)	Obesity (*n* = 108)	Sarcopenia (*n* = 25)	Sarcopenic obesity (*n* = 10)	*p*-Value	
Age *		72.5 ± 0.3	72.6 ± 0.5	76.3 ± 1.5	78.3 ± 1.2	<0.001	B, C, D, E
Sex							
Male		151 (72.9%)	43 (20.8%)	9 (4.3%)	4 (1.9%)	0.614	
Female		303 (77.7%)	65 (16.7%)	16 (4.1%)	6 (1.5%)		
Smoking history		130 (28.6%)	37 (34.3%)	7 (28.0%)	3 (30.0%)	0.715	
Obesity							
BMI (kg/m^2) *		21.6 ± 0.1	26.5 ± 0.1	20.7 ± 0.4	28.8 ± 0.8	<0.001	A, C, D, E, F
Body fat (%) *		25.5 ± 0.3	33.8 ± 0.5	27.2 ± 1.3	39.2 ± 1.2	<0.001	A, C, D, F
Sarcopenia							
	Skeletal muscle mass index (kg/BMI) *	0.726 ± 0.007	0.663 ± 0.014	0.623 ± 0.028	0.546 ± 0.040	<0.001	A, B, C
	Skeletal muscle mass index (kg/m^2) *	6.33 ± 0.04	7.09 ± 0.08	5.56 ± 0.15	6.97 ± 0.32	<0.001	A, B, D, F
Grip strength (kg) *		28.5 ± 0.7	29.5 ± 0.9	20.8 ± 1.1	22.4 ± 2.9	0.012	B, D
	Five times sit-to-stand test (s) *	7.0 ± 0.1	7.4 ± 0.2	9.3 ± 0.7	9.4 ± 1.1	<0.001	B, C, D, E
Comorbidities							
Metabolic diseases							
Diabetes mellitus		45 (9.9%)	10 (9.3%)	3 (12.0%)	3 (30.0%)	0.212	
Hypertension *		179 (39.4%)	58 (53.7%)	8 (32.0%)	7 (70.0%)	0.009	
Hyperlipemia		112 (24.7%)	23 (21.3%)	5 (20.0%)	0 (0.0%)	0.274	
Cardiovascular diseases		29 (6.4%)	9 (8.3%)	2 (8.0%)	0 (0.0%)	0.725	
Respiratory diseases							
Asthma		11 (2.4%)	3 (2.8%)	0 (0.0%)	0 (0.0%)	0.816	
Tuberculosis		4 (0.9%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0.260	
Pneumonia		8 (1.8%)	1 (0.9%)	1 (4.0%)	0 (0.0%)	0.710	
Blood pressure							
SBP (mmHg) *		137.9 ± 0.8	142.3 ± 1.5	139.3 ± 3.6	151.3 ± 5.2	0.009	
DBP (mmHg) *		79.7 ± 0.5	83.1 ± 0.9	76.6 ± 2.4	87.2 ± 2.7	0.001	A, D, F
Oral function							
	Remaining teeth *	21.3 ± 0.4	20.2 ± 0.8	20.2 ± 1.9	10.8 ± 3.2	0.001	C, E, F
	Occlusal force (kg) *	60.3 ± 1.6	60.2 ± 3.8	54.4 ± 6.7	30.0 ± 6.0	0.042	C, E
	Tongue pressure (kg) *	33.0 ± 0.4	36.8 ± 0.8	29.2 ± 1.3	32.5 ± 3.6	<0.001	A, D
	Oral diadochokinesis *	30.9 ± 0.3	30.3 ± 0.5	28.2 ± 1.1	24.6 ± 2.0	0.001	C, E
Kihon checklist							
Masticatory function		78 (17.2%)	20 (18.5%)	6 (24.0%)	1 (10.0%)	0.748	
Swallowing function *		109 (24.0%)	21 (19.4%)	11 (44.0%)	5 (50.0%)	0.017	
Dry mouth		136 (30.0%)	30 (27.8%)	10 (40.0%)	2 (20.0%)	0.590	

Table 2. *Cont.*

(b): Follow-up	Robust (n = 440)	Obesity (n = 108)	Sarcopenia (n = 39)	Sarcopenic obesity (n = 10)	p-Value	
Age *	74.9 ± 0.3	75.1 ± 0.5	79.6 ± 1.1	80.3 ± 1.5	<0.001	B, C, D, E
Sex						
Male	146 (70.5%)	37 (17.9%)	18 (8.7%)	6 (2.9%)	0.136	
Female	294 (75.4%)	71 (18.2%)	21 (5.4%)	4 (1.0%)		
Smoking history	125 (28.4%)	34 (31.5%)	15 (38.5%)	3 (30.0%)	0.583	
Obesity						
BMI (kg/m^2) *	21.6 ± 0.1	26.7 ± 0.2	20.7 ± 0.4	27.0 ± 0.5	<0.001	A, B, C, D, F
Body fat (%) *	25.5 ± 0.3	35.0 ± 0.5	24.6 ± 1.1	37.0 ± 1.5	<0.001	A, C, D, F
Sarcopenia						
Skeletal muscle mass index (kg/BMI) *	0.718 ± 0.007	0.633 ± 0.013	0.671 ± 0.024	0.585 ± 0.042	<0.001	A, C
Skeletal muscle mass index (kg/m^2) *	6.28 ± 0.04	6.97 ± 0.09	5.82 ± 0.12	6.75 ± 0.34	<0.001	A, B, D, F
Grip strength (kg) *	27.1 ± 0.3	27.9 ± 0.8	20.3 ± 0.8	24.7 ± 2.7	<0.001	B, D
Five times sit-to-stand test (s) *	7.1 ± 0.1	7.2 ± 0.2	8.9 ± 0.6	11.9 ± 1.0	<0.001	B, C, D, E, F
Comorbidities						
Metabolic diseases						
Diabetes mellitus	53 (12.0%)	12 (11.1%)	4 (10.3%)	3 (30.0%)	0.355	
Hypertension *	184 (41.8%)	63 (58.3%)	16 (41.0%)	8 (80.0%)	0.002	
Hyperlipemia	117 (26.6%)	30 (27.8%)	8 (20.5%)	2 (20.0%)	0.797	
Cardiovascular diseases	44 (10.0%)	10 (9.3%)	2 (5.1%)	0 (0.0%)	0.559	
Respiratory diseases						
Asthma	10 (2.3%)	5 (4.6%)	1 (2.6%)	0 (0.0%)	0.546	
Tuberculosis	5 (1.1%)	0 (0.0%)	2 (5.1%)	0 (0.0%)	0.083	
Pneumonia	13 (3.0%)	2 (1.9%)	2 (5.1%)	0 (0.0%)	0.698	
Blood pressure						
SBP (mmHg)	138.3 ± 0.8	142.2 ± 1.4	145.1 ± 3.3	146.0 ± 4.5	0.015	
DBP (mmHg)	79.2 ± 0.5	81.0 ± 0.9	81.4 ± 2.3	75.0 ± 1.7	0.158	
Oral function						
Remaining teeth	20.5 ± 0.4	19.4 ± 0.8	18.8 ± 1.6	17.0 ± 3.1	0.290	
Occlusal force (kg)	49.3 ± 1.6	51.7 ± 3.6	41.2 ± 4.4	25.5 ± 4.0	0.079	
Tongue pressure max (kg) *	32.4 ± 0.4	36.2 ± 0.8	31.0 ± 1.5	29.1 ± 4.1	<0.001	A, D
Diadochokinesis	30.5 ± 0.2	30.2 ± 0.5	29.7 ± 0.9	26.8 ± 2.2	0.124	
Kihon checklist						
Masticatory function	85 (20.6%)	19 (18.4%)	10 (26.3%)	1 (11.1%)	0.671	
Swallowing function *	110 (26.7%)	19 (18.4%)	15 (39.5%)	4 (44.4%)	0.041	
Dry mouth *	134 (32.7%)	21 (20.4%)	19 (50.0%)	2 (22.2%)	0.006	

Table 2a shows the baseline, and 2b shows the follow-up. Data are presented as mean ± SE. * indicates a significant difference according to one-way analysis of variance, Pearson's chi-square test, or Fisher's exact test. The p-value was calculated using the one-way analysis of variance or Pearson's chi-square test/Fisher's Exact Test, or calculated using Pearson's chi-square and Mann-Whitney U tests, with Bonferroni correction applied for multiple comparisons. The significance level was set at 5%. Significant differences between groups are denoted as follows: A, a significant difference exists between the robust and obesity groups; B, a significant difference exists between the robust and sarcopenia groups; C, a significant difference exists between the robust and sarcopenic obesity groups; D, a significant difference exists between the obesity and sarcopenia groups; E, a significant difference exists between the obesity and sarcopenic obesity groups; F, a significant difference exists between the sarcopenia and sarcopenic obesity groups. The variable descriptions are the same as in Table 1.

Participants in the sarcopenic obesity group had significantly fewer remaining teeth at baseline (p = 0.001). However, this difference was non-significant at follow-up. The obesity group exhibited the highest tongue pressure at both time points (p = 0.001).

Table 3 shows changes in health status between baseline and follow-up across four health states: robust, obesity, sarcopenia, and sarcopenic obesity.

Most participants maintained their baseline health status during follow-up, particularly those classified as "robust" (89.9%) and "obesity" (76.9%). Some participants showed improvements; 18.5% of those with obesity at baseline were reclassified as robust at follow-up, 44.0% of participants with sarcopenia improved to robust, and 60.0% of participants with sarcopenic obesity were reclassified as obese.

Conversely, the health of some participants deteriorated; 4.2% of participants classified as robust became obese, 5.5% developed sarcopenia, and 1.9% of obese participants progressed to sarcopenia. Among participants with sarcopenic obesity at baseline, 10.0% improved and became robust, while 30.0% of participants remained sarcopenic obese at follow-up.

Table 3. Changes in health status between baseline and follow-up.

		Follow-Up			
		Robust (440)	**Obesity (108)**	**Sarcopenia (39)**	**Sarcopenic Obesity (10)**
Baseline	**Robust (454)**	408 (89.9%)	19 (4.2%) A	25 (5.5%) B	2 (0.4%) †
	Obesity (108)	20 (18.5%)	83 (76.9%)	2 (1.9%) B	3 (2.8%) †
	Sarcopenia (25)	11 (44.0%)	-	12 (48.0%)	2 (8.0%) †
	Sarcopenic obesity (10)	1 (10.0%) *	6 (60.0%) *	-	3 (30.0%) *

Percentages indicate the proportion of participants within each baseline or follow-up group. A: events in the Cox regression analysis of the onset of obesity. B: events in the Cox regression analysis of the onset of sarcopenia. †: group with onset of sarcopenic obesity (events in the Cox regression analysis of sarcopenic obesity). * excluded from all Cox regression analyses.

The McNemar–Bowker test (χ^2 = 10.803, df = 6, p = 0.095) indicated no statistically significant changes in the overall distribution of health states between baseline and follow-up. During the follow-up period, most "robust" participants (408, 89.9%) maintained their health status, while 46 participants (10.1%) experienced deterioration. Among those with altered health status at baseline, 32 (22.4%) showed improved robustness.

Table 4 shows the results of examining the factors contributing to the occurrence of sarcopenic obesity based on the results of the prospective longitudinal analysis. After Cox regression analysis, four risk factors remained for the development of sarcopenic obesity. Males had a significantly higher risk of developing sarcopenic obesity than females (hazard ratio [HR] = 20.191, 95% confidence interval [CI]: 3.151–129.366, p = 0.002). As BMI increased, the risk of developing sarcopenic obesity also increased significantly (HR = 2.118, 95% CI: 1.554–2.886, $p < 0.001$). Furthermore, an increase in skeletal muscle mass significantly decreased the risk of sarcopenic obesity (HR = 0.661, 95% CI: 0.510–0.857, p = 0.002). Among oral functions, elevated tongue pressure slightly reduced the risk of sarcopenic obesity (HR = 0.906, 95% CI: 0.829–0.990, p = 0.028). The goodness of fit of the model was significant (-2 log-likelihood = 57.618, $p < 0.001$), and four significant predictors were identified from among the nine original variables.

Following the subclass analysis, three variables remained in the final model as risk factors for sarcopenia development. Males had a significantly higher risk of developing sarcopenia than females (HR = 31.231, 95% CI: 9.660–100.974, $p < 0.001$). Individuals exhibiting declining physical function (decline in grip strength or extension of the time to stand from a chair) had a significantly lower risk of developing sarcopenia (hazard ratio [HR] = 0.188, 95% CI: 0.065–0.543, p = 0.002). Furthermore, enhanced skeletal muscle mass significantly reduced the risk of developing sarcopenia (HR = 0.571, 95% CI: 0.469–0.695, $p < 0.001$). The goodness of fit of the model was significant (-2 log-likelihood = 286.929, $p < 0.001$).

The final model retained the two variables as risk factors for developing obesity. Males tended to have a higher risk of developing obesity than females, although the difference was non-significant (HR = 2.702, 95% CI: 0.830–8.801, p = 0.099). Elevated body fat percentage significantly increased the risk of developing obesity (hazard ratio [HR] = 1.192, 95% CI: 1.095–1.297, $p < 0.001$). These results were obtained using a stepwise reduction of variables (Wald test). The goodness of fit of the model was significant (-2 log-likelihood = 187.068, $p < 0.001$). Oral function variables were non-significant explanatory variables in the development of sarcopenia or obesity.

Table 4. Factors contributing to the occurrence of sarcopenic obesity, sarcopenia, and obesity.

	B	Standard Error of B	Wald	*p*-Value	Exp(B)	95.0% CI for Exp(B)	
						Lower	Upper
Model 1: Development of sarcopenic obesity							
Sex (Males = 1; Females = 0)	3.005	0.948	10.056	0.002	20.191	3.151	129.366
BMI	0.750	0.158	22.553	<0.001	2.118	1.554	2.886
Tongue pressure	−0.099	0.045	4.799	0.028	0.906	0.829	0.990
Limb skeletal muscle mass	−0.414	0.132	9.813	0.002	0.661	0.510	0.857
Model 2: Development of sarcopenia							
Sex (Males = 1; Females = 0)	3.441	0.599	33.041	<0.001	31.231	9.660	100.974
Either decreased grip strength or prolonged chair time	−1.672	0.542	9.521	0.002	0.188	0.065	0.543
Limb skeletal muscle mass	−0.561	0.100	31.275	<0.001	0.571	0.469	0.695
Model 3: Development of obesity							
Sex (Males = 1; Females = 0)	0.994	0.602	2.723	0.099	2.702	0.830	8.801
Body fat	0.176	0.043	16.546	<0.001	1.192	1.095	1.297

Cox regression analysis (stepwise variable reduction method (Wald)). The criteria for adding and removing variables were set at $p < 0.05$ and $p < 0.10$, respectively, with a maximum of 20 iterations. B: partial regression coefficient, Exp (B): hazard ratio. Events: incidence of sarcopenic obesity (model 1), sarcopenia (model 2), and obesity (model 3). Time variable: number of days from baseline to follow-up. The time from baseline to follow-up was used as a variable to determine whether oral function was an independent factor contributing to the development of sarcopenic obesity. Explanatory variables: model 1, age, sex, baseline health status (robust, obese, sarcopenic), body mass index (BMI), limb skeletal muscle mass, decreased grip strength or increased chair time, hypertension, oral diadochokinesis (ODK), and chewing performance; model 2, age, sex, baseline health status (robust, obese), BMI, limb skeletal muscle mass, loss of grip strength or prolonged chair time, hypertension, tongue pressure, and chewing performance; model 3, age, sex, baseline health status (robust or sarcopenic), BMI, limb skeletal muscle mass, body fat, hypertension, tongue pressure, and chewing performance.

4. Discussion

In the current study, we aimed to elucidate the longitudinal relationship between sarcopenic obesity and oral function in independent older adults. Sex, body composition, and muscle mass were the most consistent predictors across outcomes. Additionally, tongue pressure was associated with the risk of sarcopenic obesity but was not a significant predictor of sarcopenia or obesity.

4.1. Characteristics of Sarcopenic Obesity

We showed that individuals with sarcopenic obesity were significantly older, exhibited higher body fat, and had poorer muscle function (longer FTSST times) than their robust or obese counterparts. These findings reinforce the notion that sarcopenic obesity is a more severe phenotype resulting from the interplay between sarcopenia and obesity. Furthermore, the high prevalence of comorbid conditions in this group, such as diabetes and hypertension, aligns with previously reported findings [33,34], underscoring the systemic impact of sarcopenic obesity on metabolic and cardiovascular health.

Prospective analyses revealed that males have a substantially higher risk of developing sarcopenic obesity than females. This may be due to sex-based differences in body composition [35], hormonal changes [36], lifestyle factors [37], or oral health behaviors [37]. These findings highlight the need for sex-specific interventions to mitigate sarcopenic obesity and its associated health risks.

For gender differences in sarcopenic obesity, previous studies have shown that aging in men is associated with decreased testosterone secretion, which induces skeletal muscle loss [38]. Reduced testosterone levels are also linked to increased visceral fat accumulation, as decreased physical activity and energy imbalance result in unused energy being stored as visceral fat. Furthermore, gender differences in dietary habits may contribute to the higher risk of sarcopenic obesity in men. Visceral fat secretes inflammatory cytokines,

which may play a significant role in the development of sarcopenic obesity [6,21]. These sex-related differences may explain the higher hazard ratio observed for males in this study.

In addition, the prevalence of sarcopenic obesity revealed a slight decline over time, with some cases showing improvement or reclassification into obesity or robust categories, respectively. These trends suggest that targeted interventions focusing on weight management, physical activity, and oral health could reverse or stabilize the progression of sarcopenic obesity in older adults. Exercise interventions, such as resistance training and aerobic exercise, can effectively improve sarcopenic obesity [39]. Furthermore, while the relationship between sarcopenia, malnutrition, and oral frailty has been reported [40,41], reports have also suggested that declining masticatory function can hinder the consumption of meat and other foods high in protein, leading to a decrease in muscle mass [42]; hence, maintaining oral function may be effective in improving sarcopenic obesity.

4.2. Associations Between the Incidence of Sarcopenic Obesity and Oral Health

In this study, we confirmed the association between sarcopenic obesity and its development and oral function indices, such as tongue pressure and skeletal muscle mass. Accordingly, a decline in oral function may be associated with the development of sarcopenic obesity; however, the direction of causality remains unclear.

Inadequate nutrition could cause further muscle loss and metabolic abnormalities [43,44]. Specifically, subjects with sarcopenic obesity exhibited the lowest occlusal force and tongue pressure, which are important for chewing and overall oral health, and it was clear that occlusal force had some effect on the progression of sarcopenic obesity. Reduced tongue pressure observed in individuals with sarcopenic obesity may be attributed to several factors. Sarcopenia is associated with lower muscle quality, which can extend to the muscles involved in oral function, potentially reducing tongue pressure [45]. Chronic low-grade inflammation associated with obesity may affect muscle function, including mastication [46]. The loss of muscle mass, a well-known characteristic of sarcopenia, combined with increased fat mass in obesity, may negatively impact the strength of oral muscles [47].

The fact that tongue pressure contributes significantly to nutritional intake through its role in swallowing function and its relationship to systemic skeletal muscle strength makes it a more specific indicator than other oral function measures. Sarcopenic obesity in the elderly is characterized by the accumulation of visceral fat due to age-related loss of muscle mass and reduced physical activity. Previous cross-sectional studies have demonstrated a positive correlation between tongue pressure and total body skeletal muscle mass [48,49]. Furthermore, the tongue plays a critical role in transporting food masses during the feeding and swallowing process [50]. Considering that adequate tongue pressure supports normal nutrient intake and is positively associated with general skeletal muscle function and strength, it may be a specific factor in reducing the risk of developing sarcopenic obesity. Additionally, tongue pressure tends to be associated with sarcopenia more strongly than other oral function indicators, such as the number of teeth or swallowing ability [51]. This suggests that interventions focused solely on dental restoration or prosthetics may be insufficient. Instead, enhancing eating and swallowing functions, along with nutritional support, may be necessary to effectively prevent or manage sarcopenic obesity [52,53].

The relationship between sarcopenic obesity and reduced tongue pressure is likely bidirectional. Lower tongue pressure may lead to difficulties in eating, potentially resulting in a reduced intake of protein-rich foods and contributing to further muscle loss [45]. Conversely, the systemic effects of sarcopenic obesity may lead to reduced muscle strength in the oral system [46].

It is important to note that while our study found a significant association between tongue pressure and sarcopenic obesity, other oral function indicators, such as occlusal force

and number of remaining teeth, were not identified as significant predictors in our final model. This finding suggests that the relationship between oral function and sarcopenic obesity may be complex and multifaceted, warranting further investigation [46].

4.3. Clinical Implications

Our findings suggest that promoting a balanced nutritional intake could potentially be a useful strategy for preventing or managing sarcopenic obesity. However, our study did not include direct nutritional interventions, and this approach remains a potential avenue for future research. It may be valuable in preventing sarcopenic obesity in older adults without reducing swallowing-related oral muscles while supporting the maintenance of skeletal muscle and physical functions and managing obesity. Additionally, continuously evaluating tongue pressure and monitoring longitudinal changes may be beneficial in delaying or reversing the progression of sarcopenic obesity.

4.4. Study Limitations

This study has several limitations. A potential limitation is the relatively small number of participants diagnosed with sarcopenic obesity at baseline (n = 10), which may reduce statistical power and affect generalizability. Additionally, the small sample size may increase the risk of false positives and false negatives, making it difficult to detect significant associations. Future studies with larger sample sizes and more diverse populations are warranted to confirm our results and provide a more comprehensive understanding of the relationship between oral function and sarcopenic obesity.

Furthermore, the study cohort was derived from a specific rural region in Japan, which may limit its generalizability to other populations with different lifestyles or healthcare access. The relatively short follow-up period may also hinder the detection of long-term associations between oral function and sarcopenic obesity. However, previous studies have shown that even shorter periods (3–6 months) can detect changes in body composition related to sarcopenic obesity, suggesting that our follow-up period of over two years is sufficient for this purpose [6].

Additionally, while we attempted to adjust for some potential confounding factors, such as age, sex, and health status, in our statistical models, residual confounding factors may still be present. Factors such as nutritional intake, medication use, and exercise habits could influence both oral function and the development of sarcopenic obesity. Since this study was conducted in Japan, the findings may not be fully applicable to Western populations or other Asian countries with different dietary patterns, exercise habits, and diagnostic criteria for sarcopenic obesity. To better understand these relationships and enhance generalizability, future research should incorporate detailed dietary assessments, such as food frequency questionnaires or dietary recalls, while also focusing on larger, more diverse populations with extended follow-up periods to address potential confounders and explore causative mechanisms. Furthermore, this study did not assess comprehensive oral health, particularly periodontal status. Severe periodontitis can cause systemic inflammation and exacerbate muscle deterioration associated with sarcopenic obesity. Future studies should include periodontal assessments to clarify the role of inflammation in this relationship.

5. Conclusions

Our study showed that sarcopenic obesity was independently associated with oral function, particularly tongue pressure. Although we did not detect a direct link between sarcopenia/obesity alone and oral function, the combination of sarcopenia and obesity appeared to be strongly associated with oral health. These findings suggest that preserving and enhancing tongue muscles, which are crucial for swallowing and other oral functions,

could potentially play a role in delaying the development of sarcopenic obesity. However, further research is required to establish causality and explore the complex relationships between oral function, sarcopenia, and obesity.

Furthermore, our findings demonstrated that reduced tongue pressure was significantly associated with a decreased risk of developing sarcopenic obesity (HR = 0.906, 95% CI: 0.829–0.990, $p = 0.028$). These results suggest that tongue pressure assessment could be a valuable tool in routine geriatric evaluations, particularly for identifying individuals at risk of sarcopenic obesity. However, further research is needed to determine its validity as a definitive screening tool.

Future studies should explore intervention approaches combining nutritional guidance, resistance exercise, and tongue pressure training to improve muscle function. Additionally, developing a staging system for early sarcopenia detection and integrating oral health assessments into geriatric care may enhance diagnostic accuracy and health management.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Hyogo College of Medicine (approval no. Rinhi 0342, approval date: 23 May 2017) and Niigata University (Approval number: G2021-0027). All methods were carried out in accordance with the relevant guidelines and regulations.

Informed Consent Statement: Written informed consent has been obtained from all subjects involved in the study to publish this paper.

Data Availability Statement: Data supporting the findings of this study are available from the corresponding author upon reasonable request. However, the data are not publicly available due to privacy and ethical restrictions.

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Oral Frailty and Its Relationship with Physical Frailty in Older Adults: A Longitudinal Study Using the Oral Frailty Five-Item Checklist

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Abstract: Background/Objectives: Oral frailty, first identified in Japan in 2014, refers to a state between healthy oral function and severe decline, marked by minor issues, such as tooth loss and chewing difficulties. The oral frailty five-item checklist (OF-5) enables non-dental professionals to evaluate oral frailty using five key indicators: remaining teeth count, chewing difficulties, swallowing difficulties, dry mouth, and articulatory oral skills. Limited studies exist. Methods: This study examined the relationship between oral and physical frailties in older adults and assessed the prognosis of physical frailty using the OF-5. Participants aged ≥65 years were recruited from the frail elderly in the Sasayama–Tamba area, Hyogo, Japan, and their physical function was assessed in terms of grip strength, walking speed, and skeletal muscle mass. Blood markers, such as cystatin C, an indicator of renal function, were also analyzed. Results: A cross-sectional analysis indicated that oral frailty was correlated with reduced muscle mass, walking speed, and physical function. Women had lower hemoglobin and albumin levels and a greater prevalence of frailty than men. Longitudinal analysis revealed that initial OF-5 scores predicted increased physical frailty after 2–3 years, especially in those with higher baseline scores. The OF-5 was a significant factor for frailty progression in both sexes. Conclusions: These results suggest that early detection of oral frailty via the OF-5 may be useful in preventing the progression of overall frailty in older adults.

Keywords: oral frailty; physical frailty; oral frailty five-item checklist

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1. Introduction

Oral health is a critical component of overall health, life satisfaction, quality of life, and self-perception. Impairment of oral function is highly prevalent among older adults, and aging has been reported to interact indirectly with various domains of frailty through multiple pathways. A clear example of this relationship is age-related functional oral deterioration, characterized by poor dental hygiene, inadequate dental prostheses, and dietary deficiencies, which collectively contribute to an increased risk of nutritional frailty [1].

Oral frailty is defined as an age-related gradual decline in oral function, often accompanied by deteriorations in physical functions. This condition is associated with significant adverse health outcomes in older adults, including increased mortality, physical frailty, functional disabilities, reduced quality of life, and a higher risk of hospitalization and falls [2]. Poor oral health in the elderly is a major health concern due to its links to the pathogenesis of systemic frailty, suggesting that it is a multidimensional geriatric syndrome. As such, oral frailty may serve as a potential risk factor for systemic frailty [3]. Oral frailty was first proposed by the Japanese Geriatrics Society in 2014, and is described as an age-related decrease in oral function. Oral frailty is further defined as "the overlap of minor declines in dental or oral functions that may increase the risk of adverse health outcomes" [4,5].

This condition poses an increased risk of further decline in oral function; however, it remains reversible if early and appropriate interventions are implemented. Signs of oral frailty, including decreased tongue pressure, increased food spillage, slight chewing difficulties, and a dry mouth, are often subtle and easily overlooked. Recent studies have shown that oral frailty in older adults not only affects oral health but also has systemic implications, contributing to overall frailty and sarcopenia (age-related muscle loss) [4,6,7].

In 2023, a new diagnostic criterion for oral frailty, known as the oral frailty five-item checklist (OF-5), was proposed [4]. It comprises five items: fewer teeth, difficulty in chewing, difficulty in swallowing, dry mouth, and low articulatory oral motor skills. The OF-5 is designed to be implemented in various settings beyond dental care facilities, including non-dental healthcare facilities and community activities, and can be assessed by older individuals. The OF-5 has demonstrated robust predictive validity for physical frailty, physical impairment, and mortality among the older population in Japan [4]. Despite these advancements, the longitudinal impact of oral frailty on the progression of physical frailty, as assessed by the OF-5, remains poorly understood, particularly in rural populations.

On 1 April 2024, the Japanese Geriatrics Society, Japanese Geriatric Dentistry Society, and Japanese Society for Sarcopenia and Frailty introduced a joint statement on oral frailty diagnosed via the OF-5 [8]. The OF-5 facilitates early detection of oral frailty and promotes interdisciplinary collaboration in its management, particularly in the medical and dental fields.

In our epidemiological study conducted among community-dwelling older adults in Sasayama–Tamba, Hyogo Prefecture (the frail elderly in the Sasayama–Tamba area [FESTA] study), we focused on the relationship between oral function and physical frailty. The rural environment of Sasayama–Tamba, which is relatively close to a metropolitan area and maintains a stable population without extreme depopulation or aging, offers a unique context. It features a modern, healthy, elderly population centered on suburban agriculture, with low population turnover. This setting provides an important backdrop for studying the interaction between oral and physical frailty given its distinctive demographic and health characteristics. In our previous study, we found a significant correlation between tongue pressure and cystatin C levels, an indicator of kidney function in the FESTA study. Our findings also revealed a correlation between tongue pressure, an indicator of oral function, and physical parameters, such as grip strength, walking speed, and muscle mass [9].

The Oral Frailty Checklist/Oral Frailty Index-8 (OFI-8) was developed by the Japan Dental Association [10,11], and consists of eight items: (1) difficulties in chewing; (2) difficulties in swallowing; (3) denture use; (4) dry mouth; (5) going out less frequently; (6) feasibility of chewing hard food; (7) brushing teeth at least twice a day; and (8) regular attendance at a dental clinic. Items (1) to (3) were scored as 2, whereas the other items were scored as 1. The maximum possible score was 11: low risk, 0–2 points; moderate risk, 3 points; and high risk, >4 points. Oral frailty, as assessed using the OFI-8, was

independently associated with all-cause mortality, even after adjusting for physical and psychological frailty in older adults [12].

On the other hand, there are many reports on the associations of cystatin-C-related indices, including the creatinine-to-cystatin-C ratio (Cre/CysC ratio) and estimated glomerular filtration rate based on CysC (eGFRcys), with physical frailty and sarcopenia [13–20]. Our findings indicated that individuals at high risk for oral frailty, as assessed by the OFI-8, had lower levels of cystatin-C-related indices, grip strength, hemoglobin, and albumin, with a higher prevalence of oral frailty observed in women [21].

The OF-5 and OFI-8 share several common items, such as difficulties in chewing, difficulties in swallowing, and dry mouth. These three items are included in the Kihon checklist developed by the Japanese Ministry of Health, Labor, and Welfare, which consists of 25 questions in seven categories: physical strength, nutrition, eating, socialization, memory, mood, and lifestyle [22,23]. However, the OFI-5 differs from the OFI-8 in that it includes objective evaluations, such as the remaining teeth count and articulatory oral motor skills assessed by a dental specialist. The relationship between oral frailty and diagnosis using the OF-5, which includes objective measures based on dental examinations, grip strength, gait speed, and blood test indices, has not yet been examined. The comparative efficacy of the OF-5 in predicting physical frailty outcomes, especially in comparison to the OFI-8, has not been extensively explored, highlighting a vital area for investigation.

The longitudinal Kashiwa Study conducted by the University of Tokyo has also shown that oral frailty is a risk factor for physical frailty and is linked to life prognosis [3]. In the present study, we examined whether oral frailty, as diagnosed by the OF-5, predicts worsening physical frailty according to the Japanese Cardiovascular Health Study (J-CHS) criteria. Oral frailty, as assessed using the OF-5, has also been shown to be related to the development of physical disabilities and frailty [4].

This study aimed to assess, in a cross-sectional analysis, sex differences in physical and blood markers among individuals classified as having oral frailty by the OF-5. Additionally, using the OF-5, we aimed to investigate whether individuals classified as having suspected oral frailty (OF-5 score ≥ 2) exhibit differences in physical and biological markers, including height, weight, blood indices, and muscle strength, compared with those with lower OF-5 scores. We also explored whether these differences were associated with overall frailty. This study aimed to longitudinally assess the predictive value of the OF-5 checklist for physical frailty among older adults in Sasayama–Tamba by hypothesizing that higher OF-5 scores are significantly associated with an increased risk of physical frailty over time. Additionally, in a longitudinal analysis, we examined the association between OF-5 scores and the progression of physical frailty according to the J-CHS criteria. Finally, we evaluated the predictive value of OF-5 in comparison with other clinical markers over a follow-up period of 2–3 years.

2. Materials

2.1. Study Participants

This cross-sectional study within the FESTA study included individuals aged $\geq$65 years. Healthy community-dwelling older adults from the Sasayama–Tamba area, a rural region in Hyogo Prefecture, Japan, were recruited between 2017 and 2023. Body composition and blood sample analyses were performed as described previously [17,18]. Body composition was assessed using bioelectrical impedance analysis with an InBody 770 device (Inbody Japan Inc., Tokyo, Japan). Skeletal muscle mass index (SMI) was calculated as skeletal muscle mass divided by height squared (kg/m^2). Handgrip strength was measured according to previously established methods [17,18,24].

This cross-sectional study included 313 men and 621 women (934 in total). For the longitudinal study, 105 men and 224 women (329 in total) from the first cross-sectional survey who had no missing data in the second survey conducted 2–3 years later were included.

All procedures performed in this study, which involved human participants, adhered to the ethical standards of the institutional and/or national research committee where the studies were conducted (IRB approval number Rinhi 0342 at Hyogo Medical University) and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

2.2. Evaluation of Physical Function

To assess gait speed, the participants were instructed to walk a 12 m walkway at their usual pace, and the time taken to walk 10 m was recorded. Maximum grip strength was measured via a grip strength tester (GRIP-A; Takei Ltd., Niigata, Japan) [25]. Knee extension strength (Nm) of the dominant leg was evaluated during isometric contraction of the knee extensor in a seated position, with the knee maintained at a 60° angle using a hand-held dynamometer (Sakai Medical Co., Ltd., Tokyo, Japan) [26].

2.3. Diagnosis of Frailty

Frailty phenotypes were assessed based on the five clinical features defined in the Cardiovascular Health Study (CHS): slow gait speed, weakness, exhaustion, low physical activity, and weight loss [27]. The frailty score was calculated using a modified version of the CHS (J-CHS) [28]. The number of applicable frailty phenotypes of the five was used to determine the J-CHS score. A score of 0 was defined as robust, 1 or 2 as pre-frail, and $\geq$3 as frail.

In a longitudinal study, during the second survey conducted 2–3 years after the first survey, the participants were categorized based on changes in their J-CHS frailty scores. Seventy-four participants (27 men and 47 women) whose scores had increased were defined as "worsened", 167 (51 men, 116 women) whose scores remained unchanged were categorized as "unchanged", and 88 (27 men, 61 women) whose scores had decreased were classified as "improved". Changes in the J-CHS frailty scores were used to classify the participants as improved, unchanged, or worsened, and comparisons were made across groups in terms of physical indices, blood markers, OF-5 scores, and the number of positive subjects for each item at the time of the first survey. Logistic regression analysis, including other indices, was used to determine whether the J-CHS scores worsened during the second survey.

2.4. Diagnosis of Sarcopenia

Sarcopenia was defined according to the criteria for the Asia Working Group for Sarcopenia (AWGS) 2019 [29]. Body composition was evaluated by bioelectrical impedance analysis (BIA) using an InBody 770® (InBody Japan Inc., Tokyo, Japan). The skeletal muscle mass index (SMI) was calculated as SMM/height^2 (kg/m^2). The handgrip power, the normal and maximal gait speed, five-time chair stand test (5CS), Timed Up and Go test (TUG), and Short Physical Performance Battery (SPPB) scores were evaluated as described previously [29]. Sarcopenia was considered if the participants had a low SMI (<7.0 kg/m^2 in men; <5.7 kg/m^2 in women) and weak handgrip strength (<28 kg in men; <18 kg in women) or low physical performance (normal gait speed < 1.0 m/s, 5CS $\geq$ 12 s or SPPB $\leq$ 9).

2.5. Evaluation of Oral Function

The participants were seated in reclinable nursing chairs and underwent oral examinations. The number of remaining teeth, occlusal force, and tongue pressure were assessed. Tongue pressure was measured twice using a JMS Tongue Pressure Measuring Device

(JMS Co., Ltd., Hiroshima, Japan), and the highest value was recorded [30]. To evaluate tongue motor function (oral diadochokinesis [ODK]), we used oral function measurement equipment (KENKOU-KUN Handy; Takei Scientific Instruments Co., Ltd., Niigata, Japan) to measure the articulatory velocity of /ta/ [31].

2.6. Calculation of eGFR

We calculated creatine-based eGFR (eGFRcre) and eGFRcys using equations provided by the Japanese Society of Nephrology [32,33].

2.7. Statistical Analysis

The results are expressed as the means ± standard deviations or percentages. For intergroup comparisons, Student's *t*-test was used for data analysis. Categorical variables are presented as absolute numbers (n) and relative frequencies (%), and were analyzed using the Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to calculate the odds ratios and 95% confidence intervals. Data analysis was conducted using JMP version 17.1 software, with statistical significance set at $p < 0.05$.

3. Results

The characteristics of 313 men and 621 women (934 in total) are shown in Table 1. The prevalence of oral frailty was slightly >40% in both sexes, with no significant difference between the sexes. According to the J-CHS frailty criteria by sex, exhaustion tended to be greater in women than in men; however, there were no significant differences in the other four criteria. Muscle strength, muscle mass, and walking speed were generally greater in men than in women, although there were no sex differences in the Timed Up and Go (TUG) test or the five-time chair stand (5CS) test. Tongue pressure was greater in men, whereas ODK tended to be greater in women. However, no significant sex-related differences were observed in the number of teeth. Women also tended to be more prone to anemia, with higher total protein and albumin levels. Creatine, cystatin C, and Cre/CysC levels reflected muscle mass and tended to be higher in men than in women, whereas eGFR tended to be higher in women than in men.

Table 1. Baseline characteristics of participants according to sex.

	Total (n = 934)	**Men (n = 313)**	**Women (n = 621)**	***p***
Age (years)	74.0 ± 5.8	74.7 ± 5.9	73.6 ± 5.8	**<0.001**
Height (cm)	155.4 ± 8.3	163.9 ± 6.0	151.1 ± 5.5	**<0.001**
Body weight (kg)	55.0 ± 9.4	62.5 ± 8.8	51.2 ± 7.1	**<0.001**
Body mass index	22.7 ± 2.9	23.2 ± 2.8	22.4 ± 2.9	**<0.001**
Skeletal muscle mass (SMM) (kg)	15.7 ± 3.7	19.9 ± 2.8	13.6 ± 1.9	**<0.001**
Skeletal muscle mass index (SMI)	6.43 ± 0.93	7.37 ± 0.73	5.95 ± 0.59	**<0.001**
Body fat mass (kg)	15.3 ± 5.3	14.8 ± 5.3	15.6 ± 5.3	**0.035**
Percentage of BFM (%)	27.6 ± 7.3	23.2 ± 6.1	29.8 ± 6.9	**<0.001**
Grip power (kg)	26.7 ± 7.6	34.6 ± 6.5	22.7 ± 4.2	**<0.001**
Knee extension muscle strength (Nm)	336.5 ± 115.2	428.7 ± 114.2	290.0 ± 83.4	**<0.001**
Normal gait speed (m/s)	1.41 ± 0.24	1.38 ± 0.24	1.43 ± 0.24	**<0.001**
Maximal gait speed (m/s)	1.87 ± 0.32	1.94 ± 0.34	1.84 ± 0.30	**<0.001**
Timed Up and Go test (TUG)	6.33 ± 1.64	6.30 ± 1.93	6.35 ± 1.47	0.675
Five-time chair stand test (5CS)	7.53 ± 4.15	7.90 ± 4.77	7.34 ± 3.79	0.137

Table 1. *Cont.*

	Total (n = 934)	Men (n = 313)	Women (n = 621)	*p*
Cre (mg/dL)	0.75 ± 0.28	0.90 ± 0.19	0.68 ± 0.29	**<0.001**
CysC (mg/L)	0.95 ± 0.25	1.03 ± 0.23	0.91 ± 0.24	**<0.001**
Cre/CysC	0.80 ± 0.13	0.89 ± 0.12	0.75 ± 0.11	**<0.001**
eGFRcre (mL/min/1.73 m^2)	67.0 ± 14.1	66.2 ± 14.0	67.5 ± 14.1	**<0.001**
eGFRcys (mL/min/1.73 m^2)	73.3 ± 16.1	70.6 ± 16.5	74.7 ± 15.8	**<0.001**
eGFRcys/eGFRcre	1.10 ± 0.17	1.07 ± 0.17	1.12 ± 0.17	**<0.001**
Red blood cell (×104/μL)	439.5 ± 43.8	452.7 ± 48.5	432.9 ± 39.6	**<0.001**
Hemoglobin (g/dL)	13.5 ± 1.3	14.2 ± 1.5	13.2 ± 1.1	**<0.001**
Hematocrit (%)	40.8 ± 3.7	42.4 ± 4.0	40.1 ± 3.2	**<0.001**
Total protein (g/dL)	7.35 ± 0.47	7.33 ± 0.44	7.37 ± 0.39	**<0.001**
Albumin (g/dL)	4.32 ± 0.32	4.29 ± 0.31	4.34 ± 0.27	**<0.001**
Number of teeth, n	20.1 ± 8.8	19.6 ± 9.4	20.3 ± 8.5	0.357
Tongue pressure (kPa)	33.5 ± 8.6	34.3 ± 9.0	33.1 ± 8.3	**0.038**
Low articulatory oral motor skills (times/s)	6.05 ± 0.97	5.84 ± 1.12	6.16 ± 0.87	**<0.001**
Item of oral frailty				
Fewer teeth	316(33.8)	113(36.1)	203(32.7)	0.306
Difficulty in chewing	185(19.8)	51(16.3)	134(21.6)	0.056
Difficulty in swallowing	241(25.8)	65(20.8)	176(28.3)	**0.014**
Dry mouth	288(30.8)	73(23.2)	215(34.6)	**<0.001**
Low articulatory oral motor skills	336(36.0)	135(43.1)	201(32.4)	**0.002**
OF-5 score	1.46 ± 1.20	1.40 ± 1.11	1.50 ± 1.24	0.482
0, n(%)	227(24.3)	77(24.6)	150(24.2)	0.872
1, n(%)	296(31.7)	97(31.0)	199(32.0)	0.766
2, n(%)	234(25.0)	92(29.4)	142(22.9)	**0.031**
3, n(%)	117(12.6)	33(10.8)	84(13.5)	0.210
4, n(%)	49(5.2)	13(4.2)	36(5.8)	0.352
5, n(%)	11(1.2)	1(0.3)	10(1.6)	0.111
Oral frailty status				
Oral non-frailty, 0–1 OF-5 score, n(%)	523(56.0)	174(55.6)	349(56.2)	0.889
Oral frailty, ≥2 OF-5 score, n(%)	411(44.0)	139(44.4)	272(43.8)	
Item of frailty (J-CHS)				
Shrinking, n(%)	140(15.0)	47(15.0)	93(15.0)	1.000
Weakness (grip strength < 28 kg in men or 18 kg in women), n(%)	95(10.1)	25(8.0)	70(11.3)	0.136
Exhaustion, n(%)	223(23.9)	61(19.5)	162(26.0)	**0.028**
Slowness (gait speed < 1.0 m/s), n(%)	41(4.4)	14(4.5)	27(4.3)	1.000
Low activity, n(%)	261(27.9)	97(31.0)	164(26.4)	0.143
Frailty status (J-CHS criteria)				
Robust, n(%)	405(43.4)	138(44.1)	267(43.0)	0.780

Table 1. *Cont.*

	Total (n = 934)	Men (n = 313)	Women (n = 621)	*p*
Pre-frailty, n(%)	488(52.2)	165(52.7)	323(52.0)	0.890
Frailty, n(%)	41(4.4)	10(3.2)	31(5.0)	0.239
Sarcopenia status (AWGS criteria)				
Sarcopenia	67(7.2)	22(7.0)	45(7.2)	1.000
Non-sarcopenia	867(92.8)	291(93.0)	576(92.8)	

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist; J-CHS, Japanese Cardiovascular Health Study criteria. The *p*-value represents the significant difference between women and men.

Using the J-CHS criteria for the diagnosis of physical frailty, more than half of the participants in both men and women were categorized as prefrail, while 4.4% of the overall population were diagnosed as frail (3.2% in men and 5.0% in women). A typical phenotype of physical frailty is age-related muscle loss, known as sarcopenia. Using the AWGS2019 diagnostic criteria for Asians, the prevalence of sarcopenia was estimated to be approximately 7% in both men and women, with no significant gender differences.

A score of ≥2 on the OF-5 indicates a diagnosis of oral frailty, which is associated with older age, shorter height, lower muscle mass and strength, and reduced physical functions, such as walking speed, TUG, and the 5CS test. Tongue pressure, number of teeth, and ODK were also reduced in individuals with oral frailty. The prevalence of sarcopenia was observed to be higher in both men and women with oral frailty. However, the difference was not statistically significant in men. Overall, the findings suggest that sarcopenia exhibits a similar trend to physical frailty (Table 2).

Table 2. Comparison of physical and oral function according to oral frailty status in men and women.

	Men (n = 313)			Women (n = 621)		
	Oral Non-Frailty, 0–1 OF-5 Score (n = 174)	**Oral Frailty, ≥2 OF-5 Score (n = 139)**	***p***	**Oral Non-Frailty, 0–1 OF-5 Score (n = 349)**	**Oral Frailty, ≥2 OF-5 Score (n = 272)**	***p***
Age (years)	73.7 ± 5.4	76.0 ± 6.2	**<0.001**	72.1 ± 5.3	75.5 ± 5.9	**<0.001**
Height (cm)	164.6 ± 5.9	163.1 ± 6.2	**0.018**	151.8 ± 5.3	150.2 ± 5.6	**<0.001**
Body weight (kg)	63.2 ± 8.6	61.6 ± 9.1	0.107	51.6 ± 7.4	50.6 ± 6.7	0.103
Body mass index	23.3 ± 2.6	23.2 ± 3.1	0.715	22.4 ± 2.9	22.5 ± 3.0	0.639
Skeletal muscle mass (SMM) (kg)	20.3 ± 2.8	19.3 ± 2.7	**0.001**	13.9 ± 1.9	13.3 ± 2.0	**<0.001**
Skeletal muscle mass index (SMI)	7.48 ± 0.71	7.24 ± 0.74	**0.005**	6.00 ± 0.58	5.88 ± 0.59	**0.014**
Body fat mass (kg)	14.6 ± 4.9	15.1 ± 5.7	0.453	15.7 ± 5.5	15.6 ± 5.1	0.894
Percentage of BFM (%)	22.7 ± 5.6	23.8 ± 6.6	0.095	29.6 ± 7.0	30.1 ± 6.8	0.339
Grip power (kg)	35.7 ± 6.3	33.2 ± 6.5	**<0.001**	23.5 ± 4.2	21.7 ± 4.1	**<0.001**
Knee extension muscle strength (Nm)	446.1 ± 110.9	406.9 ± 115.3	**0.002**	304.0 ± 74.1	271.7 ± 90.6	**<0.001**
Normal gait speed (m/s)	1.42 ± 0.24	1.35 ± 0.24	**0.007**	1.47 ± 0.23	1.38 ± 0.24	**<0.001**
Maximal gait speed (m/s)	2.00 ± 0.32	1.86 ± 0.34	**<0.001**	1.90 ± 0.28	1.76 ± 0.31	**<0.001**
Timed Up and Go test (TUG)	6.02 ± 1.64	6.65 ± 2.19	**0.004**	6.03 ± 1.21	6.75 ± 1.68	**<0.001**
Five-time chair stand test (5CS)	7.25 ± 2.49	8.71 ± 6.51	**0.007**	6.90 ± 3.36	7.91 ± 4.21	**<0.001**
Cre (mg/dL)	0.91 ± 0.21	0.88 ± 0.19	0.203	0.66 ± 0.13	0.68 ± 0.14	0.931
CysC (mg/L)	1.01 ± 0.23	1.04 ± 0.25	0.134	0.89 ± 0.28	0.93 ± 0.19	0.042
Cre/CysC	0.91 ± 0.12	0.86 ± 0.13	**<0.001**	0.76 ± 0.11	0.73 ± 0.10	**0.001**
eGFRcre (mL/min/1.73 m^2)	65.8 ± 14.5	66.7 ± 13.3	0.562	68.3 ± 13.9	66.3 ± 14.2	0.085

Table 2. *Cont.*

	Men (n = 313)			Women (n = 621)		
	Oral Non-Frailty, 0–1 OF-5 Score (n = 174)	**Oral Frailty, ≥2 OF-5 Score (n = 139)**	***p***	**Oral Non-Frailty, 0–1 OF-5 Score (n = 349)**	**Oral Frailty, ≥2 OF-5 Score (n = 272)**	***p***
eGFRcys (mL/min/1.73 m^2)	72.2 ± 16.5	68.5 ± 16.3	**0.049**	77.1 ± 15.6	71.7 ± 15.4	<0.001
eGFRcys/eGFRcre	1.11 ± 0.16	1.03 ± 0.18	**<0.001**	1.14 ± 0.17	1.09 ± 0.17	<0.001
Red blood cell (×10^4/μL)	453.3 ± 47.9	452.0 ± 49.4	0.823	436.2 ± 37.2	428.7 ± 42.1	0.020
Hemoglobin (g/dL)	14.2 ± 1.4	14.2 ± 1.6	0.826	13.3 ± 1.1	13.1 ± 1.1	0.012
Hematocrit (%)	42.4 ± 3.7	42.4 ± 4.3	0.968	40.3 ± 3.1	39.8 ± 3.3	**0.041**
Total protein (g/dL)	7.28 ± 0.43	7.36 ± 0.77	**0.029**	7.39 ± 0.39	7.35 ± 0.39	0.189
Albumin (g/dL)	4.28 ± 0.31	4.29 ± 0.48	0.286	4.36 ± 0.25	4.31 ± 0.29	**0.017**
Tongue pressure (kPa)	35.3 ± 8.4	33.1 ± 9.6	**0.032**	33.7 ± 7.5	32.4 ± 9.1	0.066
Number of teeth, n	23.0 ± 7.5	15.3 ± 10.0	**<0.001**	23.4 ± 6.5	16.4 ± 9.1	**<0.001**
Fewer teeth	27(15.8)	87(62.1)		48(13.8)	155(57.0)	
Low articulatory oral motor skills (times/s)	6.21 ± 0.88	5.37 ± 1.20	**<0.001**	6.22 ± 0.74	5.82 ± 0.92	**<0.001**
Low articulatory oral motor skills	37(21.6)	99(70.7)	**<0.001**	56(16.0)	145(53.3)	**<0.001**
Item of frailty (J-CHS criteria)						
Shrinking	23(13.2)	24(17.3)	0.342	40(11.4)	53(19.4)	**0.006**
Weakness (Grip strength < 28 kg in men or 18 kg in women), n(%)	9(5.2)	16(11.5)	0.057	24(6.9)	46(16.9)	**<0.001**
Exhaustion, n(%)	19(10.9)	42(30.2)	**<0.001**	64(18.3)	98(36.0)	**<0.001**
Slowness (Gait speed < 1.0 m/s), n(%)	6(3.4)	8(5.8)	0.412	11(3.2)	16(5.9)	0.114
Low activity, n(%)	47(27.0)	50(31.0)	0.110	64(18.3)	71(26.1)	**0.024**
Frailty status (J-CHS criteria)						
Robust, n(%)	92(52.9)	46(33.1)	**<0.001**	91(33.5)	176(50.4)	**<0.001**
Pre-frailty, n(%)	79(45.4)	86(61.9)	**0.004**	159(58.5)	164(47.0)	**<0.001**
Frailty, n(%)	3(1.7)	7(5.0)	0.115	22(8.0)	9(2.6)	0.097
Sarcopenia status (AWGS criteria)						
Sarcopenia, n(%)	6(3.4)	16(11.5)	0.120	17(4.9)	28(10.3)	**0.012**
Non-sarcopenia, n(%)	94(96.6)	123(88.5)		332(95.1)	244(89.7)	

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist; J-CHS, Japanese Cardiovascular Health Study criteria.

Cystatin-C-related indices, including the Cre/CysC ratio and eGFRcys, which we have previously reported, were lower in individuals of both sexes with oral frailty [21]. Additionally, hemoglobin and albumin levels were lower in women with oral frailty. Both men and women with oral frailty were less robust and had more pre-frailty; however, owing to the small number of frail individuals, the difference was not significant in the amount of frailty.

A longitudinal study involving 329 participants (105 men and 224 women) revealed changes in oral function between the first and second follow-up surveys. Two to three years passed between the first and second follow-ups, during which no significant changes were observed in body size, grip strength, walking speed, SMI, or other parameters. However, cystatin-C-related indices (Cre/CysC, eGFRcys, and eGFRcys/eGFRcre) were significantly lower at the second follow-up in both men and women. In the second follow-up survey, albumin levels and tongue pressure did not significantly decrease in men but did show a significant decrease in women. According to the J-CHS frailty criteria, there was a tendency

for a decrease in pre-frailty among women during the second follow-up. Approximately half of the participants, both men and women, showed no changes in the relevant J-CHS items, whereas approximately a quarter showed either improvement or worsening (Table 3).

Table 3. Changes in physical and oral function from baseline to follow-up according to sex.

	Men (n = 105)			**Women (n = 224)**		
	First Survey	**Second Survey**	***p***	**First Survey**	**Second Survey**	***p***
Number of days to second survey	955.1 ± 351.7			985.5 ± 348.0		
Age (years)	73.6 ± 5.8	76.2 ± 5.9	**0.001**	72.1 ± 5.4	74.8 ± 5.4	**<0.001**
Height (cm)	164.1 ± 6.5	163.6 ± 6.6	0.566	151.4 ± 5.2	150.8 ± 5.3	0.252
Body weight (kg)	63.2 ± 8.5	62.3 ± 9.0	0.440	51.4 ± 6.6	51.1 ± 6.8	0.618
Body mass index	23.4 ± 2.6	23.2 ± 2.8	0.585	22.5 ± 2.8	22.5 ± 2.9	0.912
Skeletal muscle mass index (SMI)	7.44 ± 0.67	7.33 ± 0.70	0.242	5.93 ± 0.56	5.89 ± 0.58	0.397
Grip power (kg)	35.8 ± 7.1	34.2 ± 6.7	0.087	23.2 ± 4.2	22.8 ± 3.8	0.311
Normal gait speed (m/s)	1.39 ± 0.23	1.35 ± 0.25	0.249	1.44 ± 0.23	1.40 ± 0.23	0.117
Cre (mg/dL)	0.91 ± 0.19	0.92 ± 0.23	0.564	0.66 ± 0.14	0.69 ± 0.17	0.140
CysC (mg/L)	1.00 ± 0.22	1.09 ± 0.30	**0.017**	0.89 ± 0.17	0.95 ± 0.23	**0.001**
Cre/CysC	0.92 ± 0.13	0.86 ± 0.12	**0.001**	0.75 ± 0.10	0.72 ± 0.10	**0.005**
eGFRcre (mL/min/1.73 m^2)	65.8 ± 13.5	64.4 ± 13.5	0.453	68.6 ± 13.3	66.2 ± 13.4	0.052
eGFRcys (mL/min/1.73 m^2)	72.7 ± 15.6	66.2 ± 15.3	**0.003**	76.2 ± 14.6	70.3 ± 13.9	**<0.001**
eGFRcys/eGFRcre	1.12 ± 0.18	1.03 ± 0.16	**<0.001**	1.12 ± 0.17	1.07 ± 0.16	**0.002**
Hemoglobin (g/dL)	14.2 ± 1.4	14.0 ± 1.4	0.227	13.2 ± 1.0	13.1 ± 1.0	0.087
Albumin (g/dL)	4.3 ± 0.3	4.2 ± 0.3	0.128	4.4 ± 0.3	4.3 ± 0.3	**<0.001**
Number of teeth, n	20.7 ± 8.8	19.6 ± 8.8	0.380	21.1 ± 8.2	20.2 ± 8.3	0.271
Tongue pressure (kPa)	34.8 ± 8.8	34.4 ± 9.2	0.734	33.4 ± 8.5	31.8 ± 8.5	**0.040**
Low articulatory oral motor skills (times/s)	5.83 ± 1.12	5.98 ± 1.08	0.329	6.18 ± 0.80	6.13 ± 0.94	0.575
Item of oral frailty						
Fewer teeth, n(%)	36(34.3)	40(38.1)	0.667	67(29.9)	74(33.0)	0.542
Difficulty in chewing, n(%)	18(17.1)	26(24.8)	0.235	42(18.8)	47(21.0)	0.542
Difficulty in swallowing, n(%)	24(22.9)	29(27.6)	0.525	63(28.1)	61(27.2)	0.636
Dry mouth, n(%)	25(23.8)	30(28.6)	0.530	70(31.3)	73(32.7)	0.916
Low articulatory oral motor skills, n(%)	47(44.8)	35(33.3)	0.120	74(33.0)	76(33.9)	0.762
OF-5 score	1.43 ± 1.03	1.52 ± 1.13	0.523	1.41 ± 1.22	1.48 ± 1.20	0.559
0, n(%)	21(20.0)	21(20.0)	1.000	62(27.7)	50(22.3)	0.230
1, n(%)	36(34.3)	33(31.4)	0.663	69(30.8)	79(35.3)	0.318
2, n(%)	33(31.4)	32(30.5)	1.000	47(21.0)	50(22.3)	0.819
3, n(%)	12(11.4)	14(13.3)	0.835	33(14.7)	32(14.3)	1.000
4, n(%)	3(2.9)	4(3.8)	1.000	11(4.9)	9(4.0)	0.820
5, n(%)	0	1(1.0)	1.000	2(0.9)	4(1.8)	0.685
Oral frailty states						
Oral non-frailty, 0–1 OF-5 score, n(%)	57(54.9)	54(51.4)	0.782	131(58.7)	129(57.8)	0.849
Oral frailty, ≥2 OF-5 score, n(%)	48(45.7)	51(48.5)		92(41.3)	94(42.2)	
Item of frailty (J-CHS criteria)						
Shrinking	17(16.2)	17(16.2)	1.000	35(15.6)	33(14.7)	0.895
Weakness (grip strength < 28 kg in men or 18 kg in women)	7(6.7)	15(14.3)	0.113	16(7.2)	20(8.9)	0.603

Table 3. *Cont.*

	Men (n = 105)			Women (n = 224)		
	First Survey	**Second Survey**	***p***	**First Survey**	**Second Survey**	***p***
Exhaustion	18(17.1)	22(21.0)	0.598	49(21.9)	56(25.0)	0.504
Slowness (gait speed < 1.0 m/s)	4(3.8)	8(7.6)	0.373	6(2.7)	11(4.9)	0.323
Low activity	36(34.3)	23(21.9)	0.065	74(33.0)	41(18.3)	**<0.001**
J-CHS frailty status						
Robust, n(%)	43(41.0)	45(42.9)	0.889	92(41.1)	111(49.6)	0.088
Pre-frailty, n(%)	60(57.1)	58(55.2)	0.889	125(55.8)	99(44.2)	**0.014**
Frailty, n(%)	2(1.9)	2(1.9)	1.000	7(3.1)	14(6.2)	0.179
J-CHS change category						
Improved, n(%)	27(25.7)			61(27.2)		
Unchanged, n(%)	51(48.6)			116(51.8)		
Worsened, n(%)	27(25.7)			47(21.0)		

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist; J-CHS, Japanese Cardiovascular Health Study criteria.

We also analyzed the baseline characteristics of the groups classified as improved/unchanged and worsened. In men, lower grip strength and fewer teeth at baseline were associated with disease worsening. In those who worsened, an OF-5 score of $\geq$2 at baseline was common, and many patients were assessed as having oral frailty at the first time point. Among women, swallowing and chewing problems were more frequently reported at baseline in the worsened group, although the only significant sex difference was observed in the total OF-5 scores. In summary, individuals with higher baseline OF-5 scores were more likely to experience worsening J-CHS scores at the second time point (Table 4).

Table 4. Baseline characteristics and oral frailty according to frailty progression status in men and women.

Results of First Survey	Men (n = 105)			Women (n = 224)		
	Improved or Unchanged (n = 78)	**Worsened (n = 27)**	***p***	**Improved or Unchanged (n = 177)**	**Worsened (n = 47)**	***p***
Age (years)	73.1 ± 5.7	75.1 ± 5.9	0.108	71.9 ± 5.4	73.2 ± 5.1	0.125
Height (cm)	164.3 ± 6.6	163.4 ± 6.2	0.544	151.5 ± 5.1	150.8 ± 5.6	0.426
Body weight (kg)	63.1 ± 8.3	63.6 ± 9.1	0.788	51.2 ± 6.5	52.4 ± 6.8	0.250
Body mass index	23.3 ± 2.5	23.8 ± 3.0	0.452	22.3 ± 2.8	23.0 ± 2.8	0.106
Skeletal muscle mass index (SMI)	7.48 ± 0.65	7.32 ± 0.70	0.276	5.93 ± 0.54	5.95 ± 0.67	0.784
Grip power (kg)	36.7 ± 7.4	33.2 ± 5.6	**0.027**	1.45 ± 0.22	1.44 ± 0.24	0.810
Normal gait speed (m/s)	1.41 ± 0.23	1.34 ± 0.22	0.215	23.3 ± 4.3	22.5 ± 3.6	0.239
Cre (mg/dL)	0.91 ± 0.19	0.91 ± 0.17	0.930	0.66 ± 0.13	0.67 ± 0.17	0.818
CysC (mg/L)	0.99 ± 0.22	1.04 ± 0.20	0.276	0.89 ± 0.16	0.91 ± 0.21	0.418
Cre/CysC	0.93 ± 0.13	0.88 ± 0.14	0.162	0.75 ± 0.10	0.74 ± 0.11	0.426
eGFRcre (mL/min/1.73 m^2)	66.2 ± 14.0	64.6 ± 12.0	0.613	68.5 ± 12.9	69.1 ± 14.9	0.765
eGFRcys (mL/min/1.73 m^2)	74.1 ± 15.9	62.4 ± 14.3	0.111	76.5 ± 14.0	75.2 ± 16.8	0.615
eGFRcys/eGFRcre	1.13 ± 0.18	1.07 ± 0.19	0.158	1.13 ± 0.17	1.10 ± 0.17	0.273
Hemoglobin (g/dL)	14.3 ± 1.5	14.0 ± 1.1	0.282	13.2 ± 1.0	13.2 ± 1.1	0.715
Albumin (g/dL)	4.3 ± 0.3	4.2 ± 0.3	0.289	4.4 ± 0.2	4.3 ± 0.3	0.807
Number of teeth, n	21.2 ± 8.7	19.2 ± 9.0	0.304	21.4 ± 8.2	19.9 ± 8.3	0.247
Tongue pressure (kPa)	35.6 ± 9.2	32.6 ± 7.4	0.141	33.3 ± 8.3	34.0 ± 9.3	0.635

Table 4. *Cont.*

Results of First Survey	Men (n = 105)			Women (n = 224)		
	Improved or Unchanged (n = 78)	**Worsened (n = 27)**	***p***	**Improved or Unchanged (n = 177)**	**Worsened (n = 47)**	***p***
Low articulatory oral motor skills (times/s)	5.86 ± 1.11	5.75 ± 1.13	0.658	6.22 ± 0.82	6.02 ± 0.74	0.127
Item of oral frailty						
Fewer teeth, n(%)	22(28.2)	14(51.9)	**0.035**	51(28.8)	16(34.0)	0.480
Difficulty in chewing, n(%)	12(15.4)	6(22.2)	0.554	28(15.8)	14(29.8)	**0.036**
Difficulty in swallowing, n(%)	16(20.5)	8(29.6)	0.425	43(24.3)	20(43.6)	**0.018**
Dry mouth, n(%)	17(21.8)	8(29.6)	0.438	52(29.4)	18(38.3)	0.076
Low articulatory oral motor skills, n(%)	34(43.6)	13(48.1)	0.823	58(32.8)	16(34.0)	0.863
OF-5 score	**1.29 ± 1.01**	**1.81 ± 1.00**	**0.023**	**1.31 ± 1.17**	**1.79 ± 1.37**	**0.017**
0, n(%)	17(21.8)	4(14.8)	0.580	53(29.9)	9(19.1)	0.199
1, n(%)	32(41.0)	4(14.8)	**0.018**	54(30.5)	15(31.9)	0.860
2, n(%)	21(26.9)	12(44.4)	0.099	40(22.6)	7(14.9)	0.315
3, n(%)	5(6.4)	7(25.9)	**0.011**	24(13.6)	9(19.1)	0.357
4, n(%)	3(3.8)	0(0.0)	0.568	4(2.3)	7(14.9)	**0.002**
5, n(%)	0(0.0)	0(0.0)	1.000	2(1.1)	0(0.0)	1.000
Oral frailty states						
Oral non-frailty, 0–1 OF-5 score, n(%)	49(62.8)	8(29.6)	**0.004**	107(60.5)	24(51.0)	0.250
Oral frailty, ≥2 OF-5 score, n(%)	29(37.2)	19(70.4)		70(39.5)	23(49.0)	

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist.

Univariate logistic regression analysis was conducted to calculate the odds ratios for each indicator at baseline in the worsening group in the second survey. For men, significant associations were found between reduced grip strength and tooth loss, whereas an OF-5 score of ≥2 and a diagnosis of oral frailty at the first visit were also significant worsening risk factors. Significant associations were observed between decreased chewing ability and swallowing function in the women. The OF-5 score was a significant worsening risk factor in both men and women; however, in women, there was no significant difference in those with an OF-5 score ≥2 (Table 5A).

Table 5. Regression analysis.

Variables	Men		Women	
	OR (95%CI)	***p* Value**	**OR (95%CI)**	***p* Value**
A. Univariate logistic regression analysis for baseline factors predicting worsening frailty according to sex				
Age (per 1SD)	1.43(0.92–2.22)	0.108	1.28(0.93–1.75)	0.129
Body mass index (per 1SD)	1.18(0.77–1.82)	0.450	1.30(0.94–1.78)	0.108
Skeletal muscle mass index (SMI) (per 1SD)	0.78(0.49–1.22)	0.268	1.05(0.76–1.44)	0.783
Grip power (per 1SD)	**0.57(0.34–0.95)**	**0.022**	0.82(0.58–1.14)	0.232
Normal gait speed (per 1SD)	0.76(0.49–1.18)	0.213	0.97(0.70–1.33)	0.837
Cre/CysC (per 1SD)	0.71(0.44–1.15)	0.149	0.87(0.63–1.22)	0.420
eGFRcys/eGFRcre (per 1SD)	0.71(0.44–1.15)	0.145	0.83(0.59–1.16)	0.265
Hemoglobin (per 1SD)	0.79(0.52–1.21)	0.285	0.94(0.68–1.30)	0.714
Albumin (per 1SD)	0.79(0.51–1.22)	0.287	0.96(0.70–1.33)	0.806
Number of teeth (per 1SD)	0.80(0.53–1.22)	0.307	0.84(0.62–1.13)	0.255

Table 5. *Cont.*

Variables	Men		Women	
	OR (95%CI)	***p* Value**	**OR (95%CI)**	***p* Value**
Tongue pressure (per 1SD)	0.72(0.46–1.12)	0.139	1.08(0.78–1.50)	0.632
Low articulatory oral motor skills (per 1SD)	0.91(0.59–1.40)	0.657	0.78(0.57–1.07)	0.128
Item of oral frailty				
Fewer teeth (absence = 0, presence = 1)	**2.74(1.11–6.75)**	**0.028**	1.28(0.64–2.53)	0.487
Difficulty in chewing (absence = 0, presence = 1)	1.57(0.53–4.70)	0.427	**2.26(1.07–4.75)**	**0.037**
Difficulty in swallowing (absence = 0, presence = 1)	1.63(0.60–4.40)	0.340	**2.31(1.18–4.52)**	**0.015**
Dry mouth (absence = 0, presence = 1)	1.51(0.56–4.05)	0.418	1.49(0.76–2.92)	0.297
Low articulatory oral motor skills (absence = 0, presence = 1)	1.20(0.50–2.89)	0.682	1.06(0.54–2.09)	0.869
OF-5 score (per 1 point)	**1.65(1.06–2.57)**	**0.023**	**1.36(1.05–1.76)**	**0.019**
Oral frailty states				
Oral frailty, ≥2 OF-5 score (absence = 0, presence = 1)	**4.01(1.56–10.33)**	**0.004**	1.46(0.77–2.80)	0.248
B. Multivariate logistic regression analysis for baseline factors associated with worsening of frailty according to sex				
Age (per 1SD)	0.98(0.56–1.70)	0.934	1.15(0.81–1.64)	0.436
Body mass index (per 1SD)	1.53(0.82–2.84)	0.172	1.39(0.88–2.20)	0.156
Grip power (per 1SD)	0.62(0.34–1.13)	0.106	0.96(0.64–1.42)	0.820
Normal gait speed (per 1SD)	0.86(0.53–1.42)	0.564	1.13(0.80–1.62)	0.479
Skeletal muscle mass index (SMI) (per 1SD)	0.82(0.39–1.71)	0.592	0.86(0.54–1.37)	0.536
Cre/CysC (per 1SD)	0.91(0.53–1.58)	0.740	1.03(0.72–1.49)	0.863
OF-5 score (per 1 point)	1.49(0.91–2.45)	0.107	**1.32(1.00–1.75)**	**0.049**
C. Multivariate logistic regression analysis for baseline factors associated with worsening of frailty in men				
Age (per 1SD)	0.96(0.55–1.69)	0.894		
Body mass index (per 1SD)	1.50(0.80–2.82)	0.209		
Grip power (per 1SD)	0.61(0.33–1.11)	0.097		
Normal gait speed (per 1SD)	0.87(0.52–1.44)	0.582		
Skeletal muscle mass index (SMI) (per 1SD)	0.83(0.39–1.75)	0.622		
Cre/CysC (per 1SD)	0.94(0.54–1.64)	0.830		
Oral frailty states				
Oral frailty, ≥2 OF-5 score (absence = 0, presence = 1)	**3.38(1.23–9.28)**	**0.018**		

OR, odds ratio; CI, confidence interval; SD, standard deviation; Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist.

A multivariate logistic regression analysis was performed using age, BMI, grip strength, gait speed, SMI, Cre/CysC ratio, and OF-5 score, which are associated with frailty and sarcopenia, as explanatory variables. In men, grip strength was identified as a significant risk factor in univariate analysis; consequently, OF-5 score did not remain a significant risk factor in multivariate analysis. However, in women, the OF-5 score remained a significant risk factor (Table 5B).

The same multivariate logistic regression analysis was repeated for men by adjusting the OF-5 score to ≥2, and a significant difference remained (Table 5C).

4. Discussion

This study offers a comprehensive examination of sex-specific differences in oral frailty and related factors in a cohort of older adults, highlighting the important aspects of oral and physical function. Oral dysfunction is regarded as a significant contributor to systemic decline. Oral frailty is defined as a mild decline in oral functions during the early and

reversible stages of frailty. Many community-dwelling older people have reduced oral function or oral hypofunction, which is significantly associated with frailty and aging. Appropriate evaluation of oral function and effective intervention to suppress oral function deterioration may be effective in extending the healthy life expectancy of older people [34].

Frailty, in contrast, is considered a state of increased vulnerability to disease onset and physical dysfunction due to a decline in several functions associated with aging. Sarcopenia, a state of reduced muscle mass, is a typical physical frailty phenotype. The prevalence of oral frailty is similar between men and women, affecting >40% of the population. The 40% prevalence of oral frailty was in agreement with several previous reports [4,35,36].

Women tended to report more fatigue and anemia, whereas men reported greater muscle strength, muscle mass, and tongue pressure. These findings underscore the need to consider sex-based physiological differences when evaluating frailty and sarcopenia, particularly oral-health-related parameters.

One of the key results of this study was the significant association between oral frailty and reduced physical functions, such as walking speed, muscle mass, and tongue pressure, confirming an intricate link between systemic frailty and oral health. In both sexes, a higher OF-5 score of $\geq$2, which indicates a diagnosis of oral frailty, was correlated with diminished physical and oral functions, including grip strength and the number of teeth. These findings suggest that oral frailty can serve as a valuable early marker of declining physical capacity and could help identify individuals at risk of sarcopenia or broader systemic frailty.

The longitudinal component of this study provides further insights into the progression of oral frailty. Over a follow-up period of 2–3 years, significant declines in cystatin-C-related indices (Cre/CysC and eGFRcys) and oral functions, including tongue pressure and albumin levels, were observed, particularly in women. These changes were not accompanied by significant alterations in muscle strength, walking speed, or other systemic parameters, indicating that oral frailty may progress rapidly or independently of systemic physical decline. This underlines the importance of targeted interventions focusing on oral health to mitigate the progression of frailty.

Importantly, the logistic regression analysis identified distinct risk factors for the worsening of oral frailty. In men, reduced grip strength and tooth loss were significant predictors, consistent with previous studies linking oral health to systemic physical capacity. In contrast, impaired chewing and swallowing functions were more prominent risk factors in women, underscoring the role of oral function in overall health deterioration in older women. Notably, although the OF-5 score was a significant risk factor for worsening frailty in both sexes, its effect was more pronounced in women, suggesting a potential sex difference in the relationship between oral health and progression of systemic frailty.

Approximately one-fourth of the participants demonstrated improvements in J-CHS scores for both men and women during the second survey. Neither pharmacological nor exercise interventions specifically targeting frailty were implemented. Therefore, the observed improvement in J-CHS scores may be attributed to increased activity levels among older adults following the lifting of COVID-19-related restrictions in Japan, such as the state of emergency declarations.

This interpretation is supported by the findings in Table 3, which show a decrease in the number of participants categorized under 'Low Activity' during the second survey for both men and women. During the first survey, many older adults had limited outdoor activities due to self-imposed restrictions stemming from the pandemic. In contrast, by the second survey, a substantial number of these older adults had resumed their regular activities, potentially explaining the observed changes.

Despite these significant findings, it is important to acknowledge the limitations of this study. The sample size of frail individuals was relatively small, limiting the ability

to detect subtle differences between sexes or within subgroups. Additionally, although longitudinal data were collected, the follow-up period may not have been sufficiently long to fully capture the trajectory of oral frailty in this population. Future studies with larger, more diverse cohorts and extended follow-up periods are needed to clarify the dynamics between oral and systemic frailty, and to identify effective interventions that target both domains. Moreover, the inclusion of healthy volunteers may have influenced the representativeness of the study population. Previous reports indicated that the prevalence of frailty, according to the J-CHS criteria, is approximately 10% among older adults in the Japanese populations [37–39]. However, in this study, the prevalence of frailty was considerably lower at 3.2% for men and 5.0% for women.

During the 2–3-year observation period, no significant decline in grip strength, gait speed, or muscle mass was observed. However, even with a limited number of participants and short observation period, a diagnosis of oral frailty using the OF-5 was associated with an increase in J-CHS scores, suggesting that the OF-5 score is significantly linked to the worsening of long-term physical frailty. Oral frailty, as assessed using the OF-5, was also significantly associated with higher J-CHS scores after adjusting for age, BMI, grip strength, gait speed, SMI, and other frailty-related factors. These findings indicate that the OF-5 is a promising predictor of frailty onset. The novelty of this study lies in the significant relationship between OF-5 score and other frailty indices.

In the original article that introduced the OF-5 in 2023, difficulty in chewing, difficulty swallowing, and dry mouth were evaluated using subjective questionnaires, whereas objective data from dental examinations were used to assess the number of teeth and articulatory oral motor skills. Similarly, the present study evaluated articulatory oral-motor skills via ODK, and a dentist assessed the number of teeth, to objectively evaluate these aspects.

The results of the objective evaluation of ODK and subjective evaluation via questionnaires were in good agreement [39]. In April 2024, a joint consensus statement on "Oral Frailty" in Japan suggested that the objective assessment of ODK is no longer necessary and can be replaced with the following question: "Have you had difficulty with clear pronunciation recently?". This statement also allows for a self-reported assessment of whether respondents had >20 teeth. Future studies should investigate whether oral frailty, as assessed by the OF-5 subjective questionnaire, is associated with lower muscle mass, slower gait speed, and reduced physical function in cross-sectional studies, and whether it significantly correlates with the progression of physical frailty in longitudinal studies.

5. Conclusions

In conclusion, this study provides valuable evidence on the relationships between oral frailty, systemic frailty, and risk factors in older adults. These findings emphasize the importance of integrating oral health assessments into frailty screening protocols, particularly for older women in whom oral dysfunction may serve as an early marker of systemic health decline. These insights have implications for the development of interventions aimed at preventing or mitigating frailty and its associated adverse outcomes in aging populations.

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REVIEW ARTICLE

Multidimensional insights about healthy aging from the cohort study for community-dwelling older adults: The SONIC study

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The Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study was established considering population trends and targeting the oldest-old population. This study is unique in its narrow age range, consisting of individuals aged in their 70s, 80s and 90s, and is carried out as a longitudinal cohort study with follow ups every 3 years in urban and rural areas of eastern and western Japan. The aims of the SONIC study are primarily to clarify aging-related changes in multiple domains of human functioning, explore the dynamics of interactions among these domains and identify factors influencing healthy longevity, including psychological well-being. Investigations spanning medical, dental, nutritional, psychological and sociological fields were carried out by specialists, yielding important results. Findings from the SONIC study in Japan, a super-aged society, will provide valuable information for addressing the global aging trend. This review introduces the results from the SONIC study, and explains factors contributing to healthy longevity and happy aging. **Geriatr Gerontol Int 2025; 25: 346–355**.

Keywords: healthy longevity, longitudinal cohort, multidimensional aspects, oldest-old population, SONIC study.

Introduction

Recent epidemiological studies on aging have identified factors related to health outcomes and longevity. In Japan, life expectancy has increased to 81.1 years for men and 87.1 years for women in 2024. The number of centenarians has surpassed 95 000, and is expected to quintuple by 2060. The most rapidly growing age group over the next decade will be the oldest-old (≥85 or ≥90 years). The Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study was established with this trend in mind, targeting the oldest-old population (Fig. 1).[1]

The SONIC study has two primary objectives: first, to clarify aging-related changes across various domains of human functioning and the interactions between these domains, and second, to identify factors that influence healthy longevity, including psychological well-being. The SONIC study's framework includes several unique characteristics. The first feature is its interdisciplinary nature, involving researchers from diverse fields, including medicine, biology, dentistry, nutrition, psychology and sociology.

The second characteristic is the participant diversity. The study spans four urban and non-urban areas in Kanto (Itabashi Ward and Nishitama area: Hinohara Village, Hinode Town, Okutama Town,

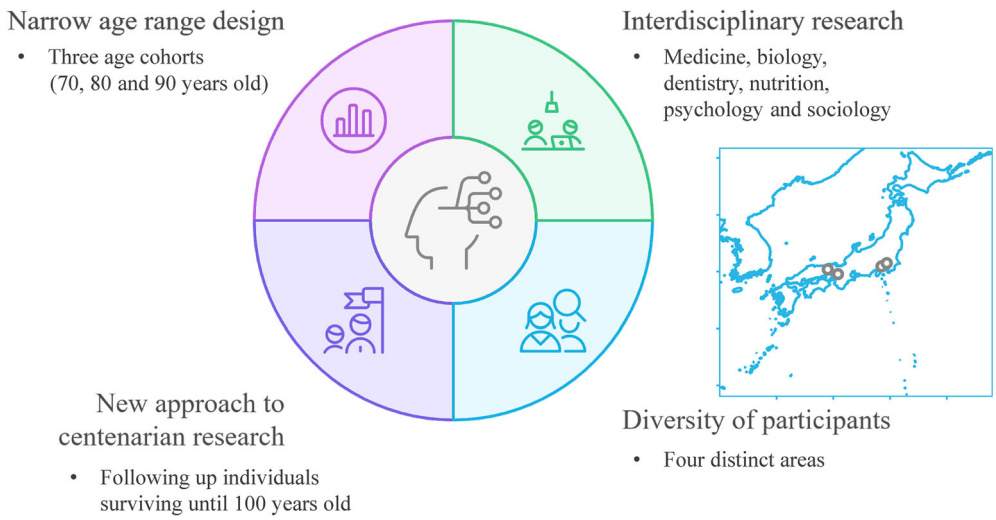

Figure 1 The features of the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study.

and part of Ome City) and Kansai (Itami City and Asago City), each with distinct demographic and regional attributes. Participants represent varied sociodemographic backgrounds, including education, work experience, family structure and residential environment.

A third unique feature is the study's narrow age range design, which sets up three age cohorts (70, 80 and 90 years), each with a 3-year age span rather than a broader range. Follow-up surveys are carried out every 3 years for each cohort. By maintaining a narrow age range, the results can reflect individual differences without needing age as an adjustment variable.

A fourth feature positions the SONIC study as a novel approach to centenarian research, as indicated by its acronym. The study includes a large cohort with the potential to reach 100 years. For example, of the oldest cohort (90th) venue survey participants recruited in 2012 for the first time ($n = 325$, 140 men, 185 women), >47 survived until 100 years-of-age, and two could participate in the invitation-type study over the age of 100 years.

Participants completed various examinations in a random order at survey venues: verifying pre-filled questionnaires, answering additional psychosocial questions in interviews, undergoing cognitive tests, physical function tests, medical tests (including blood samples, blood pressure, breathing capacities, carotid ultrasonography) and dental assessments. (including natural teeth count, occlusal force, taste sensitivity and masticatory performance).

Data collection varied by cohort due to participant volume. The first wave began in 2010 for the 70s cohort, 2011 for the 80s cohort and 2012 for the 90s cohort. The second wave started in 2013 in the same sequence. For the 90s cohort, due to lower participation, additional recruitment occurred in 2015 and 2018.

All participants were recruited through residential registries, providing their name, sex, birth date and address within specific birth date ranges. These ranges differed slightly across the four study regions due to local government database schedules, time allocations for data transcription and regional recruitment start dates.

The SONIC study uses an invitation-based survey method, inviting participants to nearby survey venues, primarily local community centers owned by local governments. Invitations explained the study's purposes and methods. Participants confirmed their participation by returning an agreement letter specifying their preferred date and time. Additionally, invitees received a questionnaire booklet covering socioeconomic status, psychosocial variables, medical and dental conditions, and food intake to complete in advance. Participants who could not fill out the booklet themselves or with help from family completed it at the survey venue.

Tables 1 and 2 show participant totals and follow-up study participation by age cohort and sex.

Medical aspects

The main aim of the SONIC study is to investigate factors associated with healthy longevity, focusing on the decline of physical and cognitive function, diseases that influence the definition of healthy longevity, and related biomarkers, which are crucial for health promotion in Japan's super-aging society.[2]

Genetic factors in longevity

In the SONIC study, we explored genetic factors, focusing on genes associated with longevity and cardiovascular diseases (CVD). The Forkhead box transcription factor 3A (*FOXO3A*) gene is a strong candidate gene for longevity.[3,4] It has been reported that the single-nucleotide polymorphism, rs2802292, in *FOXO3A* is associated with both longevity[3] and protection against CVD[5] in Japanese Americans. We investigated the association of rs2802292 in *FOXO3A* with heart diseases in participants aged 70 and 80 years in the SONIC study, finding a newly clarified sex difference in this association.[6] Additionally, rs2802292 in *FOXO3A* was associated with hypertension in older women in the SONIC study.[7] The tumor suppressor genes, *CDKN2A/CDKN2B*, and the long non-coding RNA, ANRIL, at chromosome region 9p21 are known susceptibility loci for CVD.[8] We examined the association of several single-nucleotide polymorphisms in this region with CVD and longevity among the SONIC study participants and centenarians/supercentenarians, finding a positive association with CVD, but not with longevity.[9] We also explored mechanisms involving the expression of ANRIL and *CDKN2A/CDKN2B* in SONIC participants with carotid atherosclerosis.[10]

Factors related to cognitive decline and dementia

Dementia is a major threat to healthy longevity in Japan. In the SONIC study, we examined factors related to cognitive decline and dementia, particularly lifestyle-related diseases, such as hypertension, dyslipidemia and diabetes mellitus, which are prevalent in older adults and are potential risk factors for cognitive decline.[11]

Table 1 Invitation type participants of the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study by data collection waves and years

		Sampled			Total			1st Wave			2nd Wave			3rd Wave			4th Wave			5th Wave		
Survey years							70	2010			2013	2014		2016	2017		2019	2020		2022	2023	
							80	2011			2014	2015		2017	2018		2020	2021		2023	2024	
							90	2012	2015	2018	2015	2018	2021	2018	21/22	23/24	2021	23/24	2027	23/24	2027	2030
		M	F	Total	M	F	Total	M	F	total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
70	*n*	2247	2451	4698	576	653	1229	478	521	999	426	484	910	380	442	822	272	278	550	198	221	419
	%				25.6	26.6	26.2	83.0	79.8	81.3	74.0	74.1	74.0	66.0	67.7	66.9	47.2	42.6	44.8	34.4	33.8	34.1
80	*n*	2406	3451	5857	582	631	1213	460	513	973	487	497	984	272	268	540	85	83	168	60	59	119
	%				24.2	18.3	20.7	79.0	81.3	80.2	83.7	78.8	81.1	46.7	42.5	44.5	14.6	13.2	13.8	10.3	9.4	9.8
90	*n*	8441	15 566	24 007	422	461	883	393	414	807	151	189	340	57	51	108						
	%				5.0	3.0	3.7	93.1	89.8	91.4	35.8	41.0	38.5	13.5	11.1	12.2						

(1) Sampled indicates total number of people invited to the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study.

(2)Total indicates the total number of participants in the SONIC study.

(3) We performed the 70s and 80s cohorts' first wave survey in 2010 and 2011. About the 90s cohort's, we recruited 90 years participants and performed first wave survey in 2012. In addition, we also recruited new 90 years participants and performed first wave survey both in 2015 and 2018.

(4) During the second wave of survey recruitment, we recruited the new 70s and 80s participants to compensate for the dropouts by sending an invitation letter.

(5) To increase participation, we recruited participants for two consecutive years from the second wave.

(6) We could not perform the invitation-type survey in 2020, because of the COVID-19 pandemic.

(7) In the 90s cohort, we will collect fifth wave data for participants recruted in 2015 future in 2027 and 2030, and we will collect fourth wave data for participants recruted in 2018 fourth wave data in 2030.

F, female; M, male.

Table 2 Number of mail survey participants during the COVID-19 pandemic

		2020				2021			
		Summer		Winter		Summer		Winter	
		M	F	M	F	M	F	M	F
70		366	456	298	353	339	410	300	358
80		269	306			178	227		
90	2012	24	42			10	23		
	2015	63	71			39	46		
	2018	106	94			70	71		

Mail surveys were performed four times for participants aged in their 70s, and twice for participants aged in their 80s and 90s.
F, female; M, male.

Blood pressure (BP) level is associated with cognitive decline, showing age-related differences.[12,13] Daily BP variability, measured at home, is also a factor associated with cognitive decline in individuals age >85 years.[14] Additionally, white coat and masked hypertension showed distinct characteristics across age groups.[15] Comorbid hypertension and diabetes mellitus[16] or dyslipidemia[17] were strong predictors of future cognitive decline. Silent strokes, commonly seen in older adults with hypertension, were also identified as a risk factor for cognitive decline.[18] Conversely, cognitive decline might lead to anemia in older adults.[19] Biomarkers for cognitive decline identified in the SONIC study include inflammation indicators, such as serum A/G ratio,[20] high-sensitivity C-reactive protein,[21] respiratory function[22] and a novel N-glycopeptide.[23] Daily alcohol intake might increase cognitive decline risk, whereas wine consumption might offer protective benefits.[24]

Factors related to physical frailty/sarcopenia and long-term care

The SONIC study also explored factors contributing to physical frailty and sarcopenia. Advanced age and musculoskeletal diseases are strongly associated with physical frailty.[25] However, we identified factors associated with future physical frailty that were stratified by the presence of musculoskeletal diseases.[26] Heart disease was a significant risk factor for future frailty in community-dwelling older adults.[27] Age differences were also evident in the associations between sleep status and frailty,[28] and the relationship of frailty with heart disease and social factors.[29] Low BP control among participants with hypertension at age 80 years was found to increase frailty risk.[13] Furthermore, no association was observed between daily salt intake and systolic BP in participants with physical frailty. In contrast, robust participants showed a positive association between systolic BP and salt intake.[30] Thus, salt intake restriction might be careful in older adults with frailty. Novel biomarkers related to frailty and sarcopenia included plasma adiponectin,[31] serum vitamin D[32] and the serum creatinine/cystatin C ratio.[33] Bodyweight loss was a strong predictor of frailty/sarcopenia, and we examined age-specific factors associated with weight loss in the 70s, 80s and 90s cohorts.[34] For long-term care certifications, diseases, such as stroke, musculoskeletal diseases and cancer, were linked to social subgroups.[35] Slow walking speed was a predictor of future long-term care certifications.[36] During the COVID-19 pandemic, we observed declines in daily activities and identified related factors in the SONIC study.[37]

Characteristics of diseases and geriatric syndrome in older adults

In the SONIC study, we investigated disease characteristics in older adults. Anemia is common among older adults and is a major factor in geriatric syndromes, potentially linked to low self-rated health in community-dwelling older adults.[38] Depressive symptoms, another common geriatric syndrome, might correlate with IADL decline, with differences across age groups.[39] Strict diabetes management might negatively impact mental health in older adults.[40] For atherosclerosis risk, we found that elevated uric acid levels were associated with carotid atherosclerosis in women at age 70 years, suggesting uric acid as a risk factor limited to certain age groups.[41] Additionally, adequate protein intake might not only slow chronic kidney disease progression in older adults, but also protect against frailty.[42]

Polypharmacy in older populations

Polypharmacy is a significant health concern in older adults, leading to frailty and increased healthcare costs in Japan. The SONIC study found that higher neuroticism in men and lower extraversion in women were associated with polypharmacy.[43] Taking ≥10 medications was linked to reduced grip strength and walking speed, whereas taking one to four medications was associated with increased walking speed.[44] Polypharmacy was also linked to a higher risk of falls.[45] Effective health management for older adults should emphasize minimizing unnecessary medication to improve health outcomes.

Validation of the health assessment questionnaire in older adults

To prevent lifestyle-related diseases and frailty, the Japanese government has implemented a screening program for older adults, especially those aged ≥75 years. This program includes a 15-item health assessment questionnaire focusing on frailty (12 items), general health (2 items) and smoking habits (1 item). Confirmatory factor analysis showed that a model with a higher-order factor of "frailty" with five subfactors (physical function, nutritional status, oral function, cognitive function and social aspects) was a good fit.[46] The 12 frailty-related items showed high predictive power for frailty prevalence based on the Japanese Cardiovascular Health Study criteria, with cut-off points of 3 and 4, yielding 55.9% sensitivity and 85.8% specificity, respectively.[47] These results suggest the questionnaire is effective for screening frailty in community-dwelling older adults.

Dental and nutritional aspects

Tooth loss and oral function

Tooth loss is one of the most prevalent oral health issues associated with aging. Our studies have shown that a reduction in posterior occlusal support is linked to an increased risk of tooth loss.[48,49] Hatta *et al.* reported that dental implants placed in free-end edentulous spaces might help extend the longevity of adjacent teeth.[50] The mechanism linking reduced occlusal support to tooth loss likely involves increased occlusal load or trauma to the remaining teeth. Tooth loss has a profound impact on masticatory function. Higashi *et al.* found that reduced occlusal support was associated with decreased masticatory performance.[51] Seto *et al.* showed that the number of teeth, occlusal force and depression can influence subjective evaluations of chewing difficulty.[52] Additionally, Hatta *et al.* showed that although tongue pressure decreased significantly over time, occlusal force did not, suggesting that tongue muscles might be more susceptible to aging than masticatory muscles.[53]

Impact of periodontal disease

Miki *et al.* identified that the periodontal inflamed surface area, which measures the severity and extent of periodontitis, was associated with high-sensitivity C-reactive protein, a marker of systemic inflammation.[54] Kitamura *et al.* suggested that maintaining good periodontal health might be important for preventing atherosclerosis development and progression.[55] Furthermore, periodontal probing depth correlated significantly with occlusal force and self-rated food acceptability, even among individuals with complete posterior occlusal contacts and no tooth mobility.[56]

Oral health-related quality of life

Takeshita *et al.* reported that personality traits are associated with oral health-related quality of life, independently of objective oral health measures.[57] Mihara *et al.* suggested that oral health-related quality of life correlates significantly with the degree of gerotranscendence, independent of objective oral health status.[58]

Association with nutritional intake

Inomata *et al.* examined the relationship between occlusal force, number of teeth and nutritional intake using a self-administered diet quality questionnaire.[59,60] The results showed that lower occlusal force was significantly associated with lower intake of vegetables and antioxidant vitamins. In the 70s age group, the number of teeth was associated with intake of calcium and zinc, whereas no significant associations were observed in the 80s group, suggesting that nutrient intake might be more closely related to occlusal force than to the number of teeth. Inomata *et al.* also reported that removable partial denture wearers consumed more vegetables, n-3 fatty acids, calcium, vitamin A and dietary fiber than non-wearers.[61] Mameno *et al.* found that occlusal force and occlusal contact area were significantly associated with dietary hardness.[62] These findings underscore the importance of prosthetic rehabilitation for maintaining adequate nutritional intake. Additionally, Fukutake *et al.* found that oral stereognostic ability was significantly associated with green and yellow vegetable intake in older complete denture wearers.[63] Tada *et al.* suggested that reduced posterior occlusion was associated with an increased prevalence of atherosclerosis due to declines in key dietary intakes, such as fish, shellfish, vitamin B6 and n-3 fatty acids.[64]

Association with physical function

Fukutake *et al.* assessed the impact of occlusal force and the number of teeth on body mass index reduction in older adults over a 3- to 6-year follow-up period.[65] The analysis showed that although the number of teeth was not significantly associated with body mass index reduction, lower occlusal force correlated with a decline in body mass index, suggesting that reduced occlusal force might contribute to weight loss. Okada *et al.* found that slow walking speed (<0.8 m/s) was significantly linked to occlusal force, with lower protein intake mediating this association.[66] Hatta *et al.* concluded that a lack of posterior occlusal support at baseline predicted reduced walking speed over 3 years.[67] These findings suggest that dental treatments to preserve occlusal support might help prevent a decline in walking speed. Our studies also identified that occlusal force, masticatory performance and tongue pressure were significantly associated with grip strength.[68,69] Murotani *et al.* found that tongue–lip motor and swallowing functions were good indicators of walking speed.[69] These measures could serve as proxies for physical decline in older adults, and may be valuable for screening physical frailty.

Association with cognitive function

In our study, the relationship between cognitive function and oral status was examined from multiple perspectives.[70–76] Ikebe *et al.* comprehensively explored this relationship, concluding that occlusal force correlated with cognitive function.[73] Path analysis showed both direct and indirect associations through dietary intake, even after controlling for potential confounding factors. Okubo *et al.* reported that a diet rich in vegetables, soy products, fruits, fish, and foods with dietary hardness might benefit cognitive function in older adults.[71,74] These findings suggest that decreased oral function might coincide with early cognitive decline. Longitudinal studies also support the role of maintaining occlusal force in preventing cognitive decline. Hatta *et al.* found that the number of teeth and occlusal force were associated with cognitive function at follow up, even after adjusting for other risk factors.[75] Mameno *et al.* observed that the intake of green and yellow vegetables, and meat, influenced by the number of teeth, was associated with cognitive function in a 9-year study.[76] These findings imply that preserving teeth and occlusal force might protect against cognitive decline.

Conversely, the impact of cognitive function on taste and dietary habits has also been studied. Uota *et al.*[77] and Ogawa *et al.*[78] evaluated taste sensitivity for sweetness, bitterness, saltiness and sourness. They found that individuals with lower cognitive function had reduced sensitivity to saltiness.[77,78] Additionally, sex was identified as a major factor affecting taste sensitivity, with sensitivity to sweetness being less affected by aging.[77–79] Fukutake *et al.* reported that cognitive decline was associated with reduced oral perception, which is crucial for effective mastication, appetite and food enjoyment.[80]

Association with psychological status

Akema *et al.* assessed the relationship between occlusal force and psychological frailty, defined as a World Health Organization-5 Well-Being Index score of <13 and a Montreal Cognitive Assessment in Japanese score of <23.[81] After controlling for potential confounding factors, occlusal force was associated with a reduced

prevalence of psychological frailty. Mameno *et al*. found a significant association between oral function and mental health status, mediated by fruit and vegetable intake, and social interactions.[82]

Summary

Tooth loss and reduced occlusal force are linked to dietary changes, weight loss and declines in walking speed, suggesting that maintaining oral function is crucial for physical health in community-dwelling older adults. The findings also underscore the relationship between oral function and cognitive and psychological health. Maintaining oral health is essential for promoting the overall well-being of older adults.

Psychosocial aspects

The psychosocial study in the SONIC study has two main aims. The first is to develop appropriate scales and confirm the applicability of pre-existing tools for evaluating long-term aging-related changes. The second aim is to clarify the influence of psychosocial factors on physical and cognitive function, and psychological well-being, covering a wide age range in the older population. Both qualitative and quantitative approaches were applied.

Regarding psychological well-being, we reported on elements that constitute the well-being of centenarians and the process of achieving this state, based on interviews with centenarians.[83,84] These unique findings helped develop a core framework to uncover the structure and longitudinal change of well-being, especially in the oldest-old population. One example is the development of the Japanese version of the Valuation of Life scale.[85] The Valuation of Life scale includes a positive evaluation of the future, and positive emotions that compensate for the loss of physical and social resources. We found that the Valuation of Life scale is related to mental health and individual differences in the desired remaining years of life. We also developed and confirmed the applicability of the Gerotranscendence Scale. The Gerotranscendence Scale describes a shift in behavior from active engagement in life to innate disengagement, with a change in thinking from a realistic view to a more abstract and cosmic view. We found that the construct of gerotranscendence differs for Japanese older people compared with Western populations, leading us to develop a Japanese-specific scale.[86,87] In relation to psychological well-being, a higher Gerotranscendence Scale score is associated with better subsequent mental health[6] and with greater well-being in individuals who experience a decline in physical functioning.[88] Longitudinal data over 9 years from four collection points showed that the Gerotranscendence Scale score increases in the 70s, and remains stable in the 80s and 90s, showing positive psychological development through the oldest years.[88]

Using the SONIC study's wide age coverage, we reported age-related physical and psychosocial characteristics among participants aged in their 70s, 80s and 90s. In physical functioning, using the Short Physical Performance Battery tool, we found only slight differences between the 70s and 80s, whereas differences were larger between the 80s and 90s.[89] Regarding social activities, we reported fewer leisure activities in the older age groups.[90] These studies highlight the importance of personal and internal resources for the daily activities of older adults. We also confirmed that the Montreal Cognitive Assessment is a highly reliable tool for evaluating cognitive function across a wide age range in a normal population, showing both construct validity and reliability.[91] An analysis of factors influencing well-being in participants aged in their 90s showed that living with family, economic conditions and a sense of being useful to others are important for men and women, respectively.[92]

We showed the importance of lifestyle and environmental factors on health outcomes. Variables, such as educational background, work style in middle age and leisure activities in older age, were examined. Regarding current lifestyle, we reported a simple relationship between leisure activity involvement and cognitive function.[93] Further complex analysis showed a direct influence of leisure activities on physical and cognitive function, and mental health, which are components of successful aging.[94] Additionally, a reciprocal relationship between cognitive and physical function was confirmed. In interviews about lifelong job experience, the complexity of the longest-held job was related to higher memory, reasoning test scores[95] and global cognition.[96] Combined analysis of job complexity and current leisure activities showed that both variables are important for global cognition.[96] Regarding social participation and subjective well-being, associations varied depending on the type of social participation.[97] A detailed analysis showed that participation in regional organizations had the highest association with well-being compared with participation in nonprofit organizations, volunteer groups, sports clubs or hobby groups.[97] However, these findings are limited by the use of retrospective and single-cohort data; we are planning to confirm these results using longitudinal data.

In addition to the aforementioned studies, we introduced new methods in the SONIC study data collection. We confirmed that body analogy assists in carrying out cognitive tasks (mental rotation), even in participants aged in their late 90s,[98] suggesting that pre-existing cognitive frameworks can help compensate for cognitive decline throughout life. To better assess emotional states in older people, we applied short-interval sampling methods in a small sample of SONIC study participants.[99] Using a daily diary method, we found that emotional stability was higher in older adults compared with younger counterparts. This method was also used to analyze the relationship between pre-night sleep and daytime fatigue.[100] To expand this approach, a smartphone app for microscopic data sampling is in development. We also found associations between salivary testosterone levels and cognitive function in 70-year-olds.[101] Testing new methodologies in the SONIC study is essential for developing a gerontology-based biopsychosocial model of successful aging.

Study under the COVID-19 pandemic

As aforementioned, the COVID-19 pandemic affected longitudinal data collection in the SONIC study. During the restricted period, we carried out a mail survey for all participants, regardless of the pre-planned invitation schedule. The mail survey enabled us to analyze longitudinal changes in participants' behavior and adaptation processes. In the early phase, participants restricted their activities, influenced by COVID-19 anxiety.[37] Women with lower COVID-19 anxiety had more direct interactions, whereas those with higher anxiety tended toward indirect interactions.[102] Additionally, younger individuals and those living in cities restricted their activities more than others.[37] Pre-COVID walking speed was also associated with a decrease in activity.[37] In contrast, we observed that 80-year-old participants increased the frequency of exercise and

social interactions in the later phase of the pandemic, with exercise frequency especially increasing among those living alone.[103] Details of preventive behaviors were reported based on face-to-face interviews with participants.[104] These studies provide new insights into older adults, highlighting a shift from viewing them as "weak and frail" to recognizing their adaptability and resilience.

Conclusion

The SONIC study was established considering population trends and specifically targeting the oldest-old population. This study is characterized by its unique narrow-age range of participants in their 70s, 80s and 90s, and by a longitudinal cohort design with 3-year intervals, conducted in both urban and rural areas of eastern and western Japan. The main aims of the SONIC study are to clarify aging-related changes across multiple domains of human functioning, to explore the dynamics of interaction among these domains and to identify factors influencing healthy longevity, including psychological well-being. Investigations in the SONIC study are carried out through a multidimensional approach encompassing medical, dental, nutritional, psychological and sociological perspectives contributed by professionals from each field. The greatest advantage of the SONIC study is its integration of various multidimensional studies to examine factors contributing to healthy longevity. Nowadays, not everyone wants to live a long life, so it is hoped that the factors that lead to happy aging and well-being will be clarified.

As detailed above, many important findings have been obtained so far, and these results are already being referenced in medical and dental care for older adults, as well as in guidelines for elderly care in Japan.

Overall, based on the study's characteristics, it can be said that old age spans a long period from age 65 years to >100 years, and physical and mental changes occur throughout this period, indicating correlations between various factors depending on age. Furthermore, it is important to consider differences between men and women, as well as regional differences. Figure 2 provides a summary of the achievements from the SONIC study. We are confident that the results obtained from the SONIC study in Japan's super-aged society will provide significant and valuable information for addressing the global aging trend.

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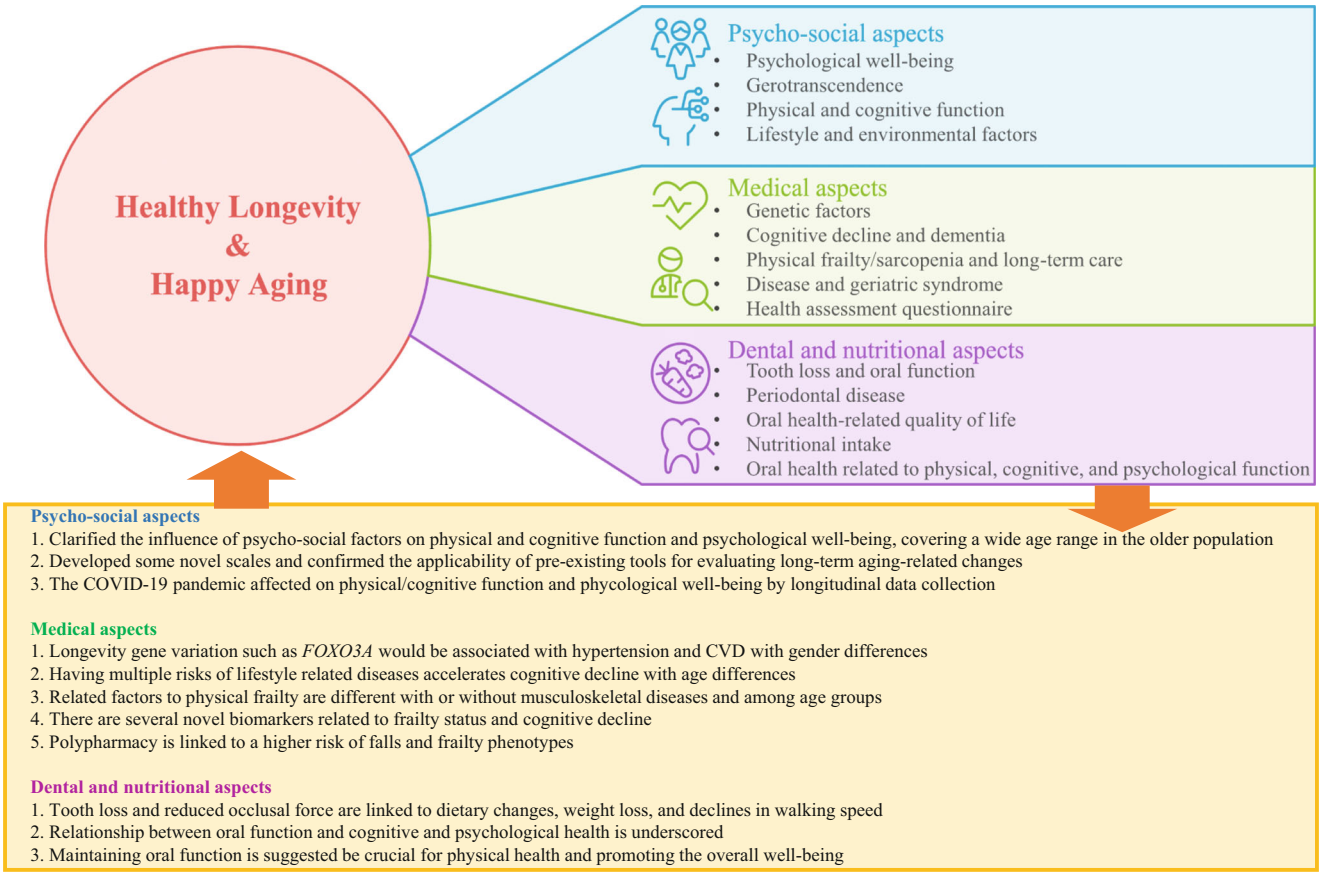

Figure 2 The overview of findings from the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study. CVD, cardiovascular disease.

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Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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別添6　　2025 年 3 月 31 日

厚生労働大臣 殿

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所属研究機関長　職　名　学長

氏　名　砂田 芳秀

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

１．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

２．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

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４．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	□　■	□		□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

その他（特記事項）

(※2) 未審査に場合は、その理由を記載すること。
(※3) 廃止前の「疫学研究に関する倫理指針」、「臨床研究に関する倫理指針」、「ヒトゲノム・遺伝子解析研究に関する倫理指針」、「人を対象とする医学系研究に関する倫理指針」に準拠する場合は、当該項目に記入すること。

５．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　　未受講 □

６．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 5 月 7 日

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氏　名　宮地 良樹

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

1．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

2．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

3．研究者名　（所属部署・職名）社会健康医学研究科・教授

（氏名・フリガナ）田原 康玄・タバラ ヤスハル

4．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	■　□	■	京都大学	□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

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5．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　未受講 □

6．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 4 月 3 日

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次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

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４．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
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遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
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当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 2 月 14 日

厚生労働大臣 殿

機関名　国立大学法人大阪大学

所属研究機関長　職　名　大学院医学系研究科長

氏　名　熊ノ郷 淳

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

1．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

2．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

3．研究者名　（所属部署・職名）大学院医学系研究科・教授

（氏名・フリガナ）山本 浩一・ヤマモト コウイチ

4．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	■　□	■	大阪大学	□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

その他（特記事項）

(※2) 未審査に場合は、その理由を記載すること。
(※3) 廃止前の「疫学研究に関する倫理指針」、「臨床研究に関する倫理指針」、「ヒトゲノム・遺伝子解析研究に関する倫理指針」、「人を対象とする医学系研究に関する倫理指針」に準拠する場合は、当該項目に記入すること。

5．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　未受講 □

6．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 5 月 1 日

厚生労働大臣 殿

機関名　国立大学法人大阪大学

所属研究機関長　職　名　大学院医学系研究科長

氏　名　石井　優

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

1．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

2．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

3．研究者名　（所属部署・職名）大学院医学系研究科保健学専攻・教授

（氏名・フリガナ）神出　計・カミデ ケイ

4．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	■　□	■	大阪大学	□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

その他（特記事項）

(※2) 未審査に場合は、その理由を記載すること。
(※3) 廃止前の「疫学研究に関する倫理指針」、「臨床研究に関する倫理指針」、「ヒトゲノム・遺伝子解析研究に関する倫理指針」、「人を対象とする医学系研究に関する倫理指針」に準拠する場合は、当該項目に記入すること。

5．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　未受講 □

6．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 3 月 26 日

厚生労働大臣 殿

機関名　岩手医科大学

所属研究機関長　職　名　学長

氏　名　小笠原 邦昭

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

1．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

2．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

3．研究者名　（所属部署・職名）衛生学公衆衛生学講座・教授

（氏名・フリガナ）丹野 高三・タンノ コウゾウ

4．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	■　□	■	岩手医科大学	□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

その他（特記事項）

(※2) 未審査に場合は、その理由を記載すること。
(※3) 廃止前の「疫学研究に関する倫理指針」、「臨床研究に関する倫理指針」、「ヒトゲノム・遺伝子解析研究に関する倫理指針」、「人を対象とする医学系研究に関する倫理指針」に準拠する場合は、当該項目に記入すること。

5．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　未受講 □

6．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 5 月 7 日

厚生労働大臣 殿

機関名　鹿児島大学

所属研究機関長　職　名　学長

氏　名　井戸 章雄

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

1．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

2．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

3．研究者名　（所属部署・職名）学術研究院医歯学域・教授

（氏名・フリガナ）牧迫 飛雄馬・マキザコ ヒュウマ

4．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	■　□	■	鹿児島大学	□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

その他（特記事項）

(※2) 未審査に場合は、その理由を記載すること。
(※3) 廃止前の「疫学研究に関する倫理指針」、「臨床研究に関する倫理指針」、「ヒトゲノム・遺伝子解析研究に関する倫理指針」、「人を対象とする医学系研究に関する倫理指針」に準拠する場合は、当該項目に記入すること。

5．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　未受講 □

6．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 4 月 14 日

厚生労働大臣 殿

機関名　関西医科大学

所属研究機関長　職　名　学長

氏　名　木梨 達雄

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

１．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

２．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

３．研究者名　（所属部署・職名）リハビリテーション学部・教授

（氏名・フリガナ）池添 冬芽・イケゾエ トメ

４．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	■　□	■	京都大学	□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

その他（特記事項）

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(※3) 廃止前の「疫学研究に関する倫理指針」、「臨床研究に関する倫理指針」、「ヒトゲノム・遺伝子解析研究に関する倫理指針」、「人を対象とする医学系研究に関する倫理指針」に準拠する場合は、当該項目に記入すること。

５．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　未受講 □

６．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
・分担研究者の所属する機関の長も作成すること。

2025 年 4 月 7 日

厚生労働大臣 殿

機関名　常葉大学

所属研究機関長　職　名　学長

氏　名　安武 伸朗

次の職員の令和 6 年度厚生労働科学研究費の調査研究における、倫理審査状況及び利益相反等の管理については以下のとおりです。

１．研究事業名　循環器疾患・糖尿病等生活習慣病対策総合研究事業

２．研究課題名　高齢者の身体機能低下に関する評価指標の検討、リスク要因の探索、ならびに予防法の確立に資する研究（24FA1005）

３．研究者名　（所属部署・職名）健康科学部・教授

（氏名・フリガナ）加藤 倫卓・カトウ ミチタカ

４．倫理審査の状況

	該当性の有無	左記で該当がある場合のみ記入 (※1)		
	有　無	審査済み	審査した機関	未審査 (※2)
人を対象とする生命科学・医学系研究に関する倫理指針 (※3)	■　□	■	京都大学	□
遺伝子治療等臨床研究に関する指針	□　■	□		□
厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針	□　■	□		□
その他、該当する倫理指針があれば記入すること（指針の名称：　　）	□　■	□		□

(※1) 当該研究者が当該研究を実施するに当たり遵守すべき倫理指針に関する倫理委員会の審査が済んでいる場合は、「審査済み」にチェックし一部若しくは全部の審査が完了していない場合は、「未審査」にチェックすること。

その他（特記事項）

(※2) 未審査に場合は、その理由を記載すること。
(※3) 廃止前の「疫学研究に関する倫理指針」、「臨床研究に関する倫理指針」、「ヒトゲノム・遺伝子解析研究に関する倫理指針」、「人を対象とする医学系研究に関する倫理指針」に準拠する場合は、当該項目に記入すること。

５．厚生労働分野の研究活動における不正行為への対応について

研究倫理教育の受講状況	受講 ■　未受講 □

６．利益相反の管理

当研究機関におけるＣＯＩの管理に関する規定の策定	有 ■　無 □（無の場合はその理由：　　）
当研究機関におけるＣＯＩ委員会設置の有無	有 ■　無 □（無の場合は委託先機関：　　）
当研究に係るＣＯＩについての報告・審査の有無	有 ■　無 □（無の場合はその理由：　　）
当研究に係るＣＯＩについての指導・管理の有無	有 □　無 ■（有の場合はその内容：　　）

（留意事項）　・該当する□にチェックを入れること。
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