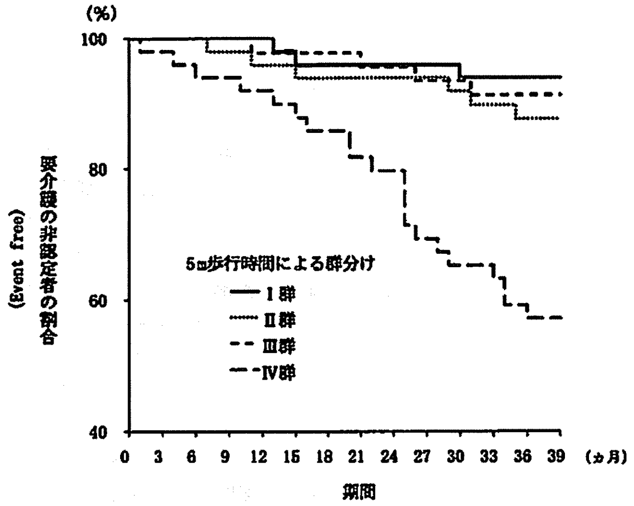

Ⅰ群：男性 3.7 秒以下，女性 4.2 秒以下
Ⅱ群：男性 3.8 ～ 4.2 秒，女性 4.3 ～ 4.8 秒
Ⅲ群：男性 4.3 ～ 5.1 秒，女性 4.9 ～ 5.7 秒
Ⅳ群：男性 5.2 秒以上，女性 5.8 秒以上

図1 Kaplan-Meier 法による新規要介護認定の発生率曲線

表3 Cox 比例ハザード回帰分析による新規要介護認定の発生に対するハザード比

	偏回帰係数	ハザード比	95% 信頼区間	p 値
Body Mass Index (kg ／ m^2)	-0.13	0.88	0.78-0.99	0.03
5 m 歩行時間（秒）	0.50	1.65	1.37-1.98	＜ 0.01

比）による Cox 比例ハザード回帰分析の結果，モデル χ^2 検定は有意となり（p ＜ 0.01），新規要介護の発生と有意な関連を認めた変数は，BMI と 5 m 歩行時間であった。それぞれの要介護認定の新規発生に対するハザード比は，5 m 歩行時間（秒）が 1.65（95%信頼区間 1.37 － 1.98，p ＜ 0.01），BMI（kg ／ m^2）が 0.88（95%信頼区間 0.78 － 0.99，p ＝ 0.03）であった（表3）。

考　察

本研究では，介護予防事業として自治体が実施した健診に参加した地域在住後期高齢者を対象として，将来の要介護認定の新規発生に対する歩行速度の影響を検証した。その結果，5 m 歩行時間が遅い高齢者では将来の要介護発生のリスクが有意に高く，後期高齢者の歩行能力は将来の要介護発生に影響を与える重要な要因のひとつであることが示された。

我が国の平成 20 年度末現在での約 453 万人の要介護認定者数のうち 80%以上が 75 歳以上の後期高齢者であり[1]，高齢であるほど要介護状態に陥る危険は高い。また，地域在住高齢者を対象とした大規模な縦断調査では，新規の要介護認定発生率は 4.5 ～ 8.3%（追跡期間 12 ～ 40 ヵ月）と報告されている[19-21]。本研究では 75 歳以上の後期高齢者を対象とした 39 ヵ月間の追跡で 17.9%と高い要介護発生率を認めた。これまでの先行研究においても，高年齢は要介護発生の予測要因のひとつであり[19)20)]，高齢になるほど要介護認定のリスクが高くなることが示されている。本研究では，5 m 歩行時間を測定して男女別に 4 分位により 4 群に分類して比較すると，遅いⅣ群ではさらに高い要介護発生率を認め，Ⅳ群 49 名のうち 40%以上にあたる 21 名で新規に要介護認定の発生を認めた。また，追跡期間中の 39 ヵ月間におけるそれぞれの群による要介護発生率曲線の差を比較すると 5 m 歩行時間が遅いⅣ群ではその他の 3 群と比べて有意に高い要介護認定発生率を認めた。さらに，年齢および BMI のほか，脳血管疾患や心疾患などの循環器疾患のリスクを増大させる因子である LDL コレステロール値[22] や高血圧の有無[23]，全身栄養状態を反映する血清アルブミン値[24] を共変量とした Cox 比例ハザード回帰分析の結果では，5 m 歩行時間が新規の要介護発生と有意に関連する変数であり，新規の要介護発生に対する 5 m 歩行時間（秒）のハザード比は 1.65 で統計学的に有意であった。このことは，後期高齢者において 5 m 歩行時間が遅い者では，39 ヵ月以内に要介護を発生する危険が高いことを示しており，歩行能力は将来

の要介護発生に影響を与える重要な要因のひとつであるといえる。さらに，この結果は要介護認定の発生の危険因子であるとされる年齢やベースラインにおける栄養状態，循環器疾患の発症リスクと関連がある生化学検査値で調整した上で示された結果であり，後期高齢者における歩行能力の低下は新規要介護認定発生の独立した危険因子であることが示唆された。

歩行速度は60歳を超えたあたりから加速的に低下し，高齢になるほどにその低下率は大きくなる[25)]。高齢期における歩行速度の低下は歩幅が減少することによる影響が大きく[13)]，その背景にある下肢筋力や立位バランスの維持も重要な要素であると考えられる。それらを代表する運動機能として歩行速度は非常に重要な指標であり[26)]，特に高齢期においては様々な将来の機能状態を予測する上で歩行評価は有益である。Cesariら[14)]による歩行速度と生命予後に関する報告では，通常歩行速度が男性で約1.15 m／秒以下，女性で約0.98 m／秒以下の歩行速度が低下した高齢者における5年生存率は65～80%程度とされている。本研究の対象者における5 m歩行時間の4分位による群分けを用いた検討では，もっとも遅い群である男性で約0.96 m／秒以下（5 m歩行時間が5.2秒以上），女性で約0.86 m／秒以下（5 m歩行時間が5.8秒以上）の者が，それ以上の歩行速度であった群よりも要介護の新規発生のリスクが高かった。生存率と歩行速度との関連を示したCesariら[14)]の先行研究では75歳未満の前期高齢者も含めた検討であるため，75歳以上のみを対象とした本研究の結果と比べて，歩行速度が速い群においても追跡調査での生存率に差異が示されているものと考えられる。一方，日本人の大規模集団を対象とした6年間の追跡調査により歩行速度とADL低下の関係を検討した報告では，75歳以上の後期高齢者を分析した結果，通常歩行速度が男性で1.02 m／秒，女性で0.87 m／秒を下回ると将来のADL低下のリスクが高まることが示されている[11)]。これは，本研究により検討した将来の新規要介護発生のリスク増大と歩行速度との関係を支持する結果であり，要介護状態を引き起こす背景にあるADL低下と歩行能力の関係についての重要性が示された結果であるものと推察され，これらの先行研究と比較して本研究で用いた群分けによる5 m歩行時間は妥当な結果であると考えられる。しかしながら，これらの先行研究では，歩行速度のみならず，筋力および片脚立位時間といった運動機能や筋量などの身体組成を考慮した結果であり，より包括的な指標による要介護発生のリスクに関する検討は今後の課題であると考える。また，3年4ヵ月間の縦断調査により在宅自立高齢者の要介護認定に関連する身体的および心理的要因を検証した研究では，男女ともに共通して要介護発生の予知因子として1 km以上の連続歩行ができない，もしくは難儀するといった歩行能力の低下を示唆する項目が有意に抽出されており，身体的な要因として歩行能力の重要性が示されている[19)]。今回の我々の結果も踏まえて，日常生活における歩行による動作制限の有無に加えて，実測による歩行速度の低下も含めた高齢者の歩行能力低下が将来の要介護認定の新規発生には強く関連する要因であると考えられた。また，Cox比例ハザード回帰分析の結果，歩行速度の低下と同様にBMIの低下が将来の要介護認定の新規発生と関連する因子として抽出された。地域在住高齢者におけるBMIの低下は，生命予後やADLの低下と関連することが報告されている[27)]。しかしながら，本研究の対象者におけるBMIの平均値は男性が23.2 ± 3.0 kg／m^2，女性が24.2 ± 3.3 kg／m^2であり，BMI18.5 kg／m^2以下に該当する割合は男性3.5%，女性3.8%と極めて少数であり，多くの対象者は標準的な範囲内の体型であることが推測され，これらの報告を直接的に支持するのは困難であると考える。一方で，高齢期における肥満も生命予後や身体機能の低下と関連する要因とされており[28)29)]，BMIと新規要介護認定の発生との関連を検証するにはさらに大規模集団での分析が必要であり，今回の結果からこれらの関連についての結論を導き出すには至らないが，少なくとも後期高齢期においては年齢を考慮した上でも体型の要素が将来の要介護認定の発生と関連する要因のひとつとなり得ると考えられた。

本研究にはいくつかの限界が含まれ，今回の結果を一般化するには注意すべき点がある。まずは，本研究の対象者は自治体主催の介護予防健診に自発的に参加した高齢者であり，かつ要介護認定の新規発生の有無が追跡可能であった者に限られた解析である点を認識しておかなければならない。また，生存分析において，本研究で用いた新規要介護認定の発生が事象発生として成立するかを慎重に論ずる必要がある。要介護認定を事象発生として捉える場合，対象者によって申請からの認定までの期間が異なる，認定申請が自らまたは家族の申告によって開始されるなど，事象を決定する上では様々な要因が影響を与える恐れがある。また，要介護認定を新規に発生した原因については言及できていない。そのため，要介護を引き起こす原因となった疾患や機能低下の背景にある要因については明らかとするに至っていない。さらに，本研究では要介護認定の新規発生への影響が考えられる心理的もしくは社会的要因については加味されていない。たとえば，社会支援状況や家族との接触頻度，もの忘れの有無，糖尿病の有無などといった社会，心理，医学的な要因が要介護の発生と関連することが指摘されている[20)21)]。本研究では，社会，心理，医学的な要因については検証がなされていないため，今後はこれらの多面的な要素を加味した包括的な解析が必要となると考

える。現状の介護予防事業では十分な医学的な情報を取得することが困難であるものの，要介護の発生に対する身体機能の影響を明示するためには，要介護発生の原因となることが予測される疾病の背景にある基礎疾患のほか，心理・社会的要因によって調整した分析により要介護認定の新規発生に対する身体機能の影響がさらに明確になるものと考えられる。以上のような限界は含むものの，今回の結果より地域在住の後期高齢者における歩行速度の低下は将来の要介護発生に影響を与える重要な要因のひとつであることが確認された。また，歩行速度の評価は簡便に実施することができ，地域で実施される介護予防事業や保健福祉活動においては積極的に評価することが推奨され，これらの評価結果を地域で展開する予防を重視した理学療法領域で要介護発生リスクの早期発見，早期対処の方策や効果検証の一部としてさらに活用されることが期待できる。

結　論

地域在住の後期高齢者における5 m歩行時間は，将来の要介護発生と関連することが示された。特に5 m歩行時間が男性5.2秒以上，女性5.8秒以上の後期高齢者では，それ以上の歩行能力を有する者に比べて39ヵ月以内に要介護を発生する危険が高いことが示された。地域在住の後期高齢者における歩行速度は，将来の要介護発生に影響を与える重要な要因のひとつであることが確認された。

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〈Abstract〉

Relationship between 5-m Walking Time and the Need for Long-term Care Among Community-dwelling Adults Aged Above 75 Years: A 39-month Longitudinal Study

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Purpose: The aim of this study was to determine the relationship between 5-m walking time and the need for long-term care among community-dwelling adults aged above 75 years.
Methods: A total of 190 older individuals living aged $\geq$ 75 years (mean age, 80.1 [SD 4.2] years) and living at home participated in this study. Inpatients and current recipients of long-term care were excluded. In the baseline survey, participants performed the 5-m walking test and were followed-up for 39 months.
Results: During the 39-month follow-up, 34 participants (17.9%) were certified for long-term care need. The log-rank test of survival curves indicated that the number of subjects certified for long-term care during the follow-up period was significantly higher in the slower walking speed group than in the faster walking speed group ($p < 0.001$). Cox's proportional hazard model revealed that the 5-m walking speed and body mass index were significantly associated with the need for long-term care during the 39 months follow-up period, and the hazard ratio of 5-m walking speed was 1.65 ($p < 0.01$).
Discussion and Conclusion: These results suggested that the slow usual walking speed could relate to the future need for long-term care in community-dwelling older adults.

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■原 著

ステップエルゴメーターのアイソキネティック運動におけるピークパワーと身体機能との関連

The Relationship between Peak Power of Isokinetic Exercise on a Step Ergometer and Physical Function of Community-dwelling Elderly

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ABSTRACT: [Purpose] The aim of this study was to examine the relationships between peak power in the lower extremities during isokinetic movement using a step ergometer and physical performance of community-dwelling elderly. [Methods] Twelve elderly women (mean age 78.3 years) completed physical performance tests which included lower limb muscle power using a step ergometer (60 and 90 steps/minute), the timed up-and-go (TUG) test, and isometric muscle strength of knee extension and flexion. Pearson's correlation coefficients and a stepwise multiple regression model were used to examine the relationships among measurements. [Results] The muscle power at 60 and 90 steps/min showed significant correlations with the TUG test and isometric muscle strength in knee extension, and the TUG test and isometric muscle strength in knee extension and flexion, respectively. In multiple regression analysis, the muscle power of 90 steps/min was only significantly associated with the TUG. [Conclusion] The measurement of the isokinetic power using a step ergometer is valid and useful for evaluating muscle performance of the elderly.
Key words: muscle power, elderly people, Timed Up-and-Go Test

要旨：〔目的〕ステップエルゴメーター（Biostep）を用いて，地域在住高齢者におけるアイソキネティック運動時のピークパワーと身体機能評価との関連を検討することを目的とした。〔対象〕高齢女性12名（平均年齢78.3歳）とした。〔方法〕ステップエルゴメーターによる筋パワーの測定（60および90 steps/min），Timed Up and Go Test（TUG），等尺性膝伸展，屈曲筋力を測定した。分析は測定値間の関係を検討するためPearsonの相関係数を算出し，TUGを従属変数としたステップワイズ重回帰分析を行った。〔結果〕60 steps/minパワーはTUG，膝伸展トルクに有意な相関を認めた。90 steps/minパワーはTUG，膝伸展，膝屈曲トルクに有意な相関を認めた。重回帰分析では，90 steps/min パワーのみが抽出された。〔結語〕ステップエルゴメーターを使用した筋パワーの測定は，筋力や歩行機能を反映した指標であり，高齢者の身体機能を評価する指標として妥当であると考えられた。
キーワード：筋パワー（筋仕事率），高齢者，Timed Up and Go Test

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I. はじめに

高齢者において筋力低下は日常生活活動（activity of daily living: ADL）能力の低下を引き起こす要因である。とくに下肢の筋力低下は，立ち上がりや歩行，階段昇降など起居，移動を中心としたADL動作の困難さが生じる大きな原因となる[1,2]。

加齢に伴う筋量の減少はサルコペニアといわれているが，サルコペニアの臨床定義や診断基準を作成するEuropean Working Group on Sarcopenia in Older Peopleの報告では，サルコペニアを筋量の低下と筋機能（筋力やパフォーマンス）の低下により定義しており，高齢期における筋機能の重要性が改めて注目されている[3]。加齢に伴う筋萎縮は，遅筋線維に比べ速筋線維の萎縮が著しく，特にType II a線維が選択的に萎縮することが報告されている[4,5]。また，加齢によって筋量の減少や筋線維の萎縮のみならず，等尺性運動時の筋力および等速性（アイソキネティック）運動時の筋パワーの低下が生じることが明らかにされている[6]。筋力は力の発揮能力であり，筋パワーは筋力をいかに速く発揮できる能力（力×速さ）と定義されている[7]。加齢により最大筋力だけではなく筋パワーも著明に低下し，とりわけ速筋線維に関連した高速度でのアイソキネティック運動時の筋パワーの低下が著しいといわれている[8,9]。筋パワーの低下は，筋力に比較してよりADL能力の遂行に重要であることが指摘されており[10,11]，加齢によるADL能力低下を予測，予防するためには，等速性運動機器による筋パワーの測定が必要であると考えられる。疾病後の運動機能低下に対し運動療法を行う病院ではアイソキネティック運動時の筋パワー測定を行うことが多いが介護予防事業や老人保健施設，特別養護老人ホームなどでは等速性運動機器を用いての計測は一般的になされていない現状にある。

近年病院以外の施設や事業において，アイソキネティック運動の行えるステップエルゴメーターが運動機能向上を目的として広く用いられている。本研究では，アイソキネティック運動時の計測も行えるステップエルゴメーターを用いて地域在住高齢者におけるピークパワーを測定し，運動機能評価として頻繁に実施される歩行機能および等尺性最大筋力との関連について調べ，その妥当性を検討することを目的とした。

II. 対象と方法

1. 対象

東京都板橋区に在住する下肢疾患の既往のない，歩行および手段的ADLが自立している地域在住高齢者女性12名（平均年齢78.3±2.6歳，平均身長145.6±3.3 cm，平均体重51.3±4.9 kg）を対象とした。対象者には本研究の主旨と目的，方法を口頭，書面にて十分に説明し，本人の同意を得た。なお本研究は，東京都健康長寿医療センターの倫理審査委員会で承認されたものである。

2. 方法

パワーの測定はアイソキネティック運動が可能な運動機器であるステップエルゴメーター（BIODEX Biostep，酒井医療株式会社，日本）を用いて実施し，目標ステップ数はアイソキネティックモードの60 steps/min（60 step），90 steps/min（90 step）と設定した。成人を対象にした予備調査により，ピークパワーまでの時間は10秒以内であったことから，15秒間に駆動時間を設定した。シート位置はステップエルゴメーター駆動時の最大伸展時での膝関節屈曲角度が20度になるように調節し，上肢はシート横のハンドグリップを把持した。測定前に目標ステップ数に達するように十分な練習を行ったが，60 stepについては漕ぎはじめは重く感じるが，それに負けないように速く漕ぐようにと説明した。測定開始時には「全力で漕いで，それを15秒間保つように」と教示し，測定中は目標ステップ数が維持できるように「そのまま維持するように」と声掛けを行った。測定回数はそれぞれ1回とし，施行間は3分以上の休憩を挟み，疲労感がないことを確認した。60 step，90 stepの施行順はコイントスにてランダムに設定した。駆動時のパワー（仕事率；W）は，解析ソフト（SpErgo2，酒井医療株式会社，日本）を用い，駆動開始からサンプリング周波数60 Hzにて測定した。目標ステップ数に達した後の最大値をピークパワーとして解析に用いた。

身体機能評価として，膝関節屈曲および伸展の等尺性最大筋力，Timed Up and Go Test（TUG）の測定を行い，ステップエルゴメーターを用いた測定とは別の日に実施した。

等尺性最大筋力はハンドヘルドダイナモメーター（μ-Tas F1，アニマ，日本）を用い，膝関節屈曲90度の椅子座位で，等尺性収縮による最大膝伸展筋力，最大膝屈曲筋力（N）を測定した。測定肢は利き足とし，2回の測定のうち最大値を採用した。測定値に対し，膝関節裂隙から測定部位までの長さ（m）を乗じ，体重（kg）で除した1 kgあたりの膝屈曲，膝伸展トルク（Nm/kg）を解析値とした。

TUGはPodsiadloら[12]の原法に基づき，所要時間（秒）をストップウォッチにて計測した。計測は最大歩行速度で2回測定した後，所要時間の短い測定値を採用した。TUGは虚弱高齢者の移動機能を評価する目的で開発された指標であり，下肢筋力[13,14]，動的バランス[15]，ADL[12,15]と関連することが知られており，高齢者における転倒のスクリーニングとしても活用されている[16,17]。また日本

理学療法士会が作成したElderly Status Assessment Set（E-SAS）の歩行機能評価においても採用されており，高齢者の機能評価場面では頻繁に利用されている[18]。

解析は，ピークパワーおよび身体機能評価で得られた各測定値について，Shapiro-Wilk検定にて正規性を確認した上で，60 step，90 step時のピークパワーと，各身体機能評価との関係性を検討するためにPearsonの相関係数を算出した。従属変数をTUG所要時間，独立変数を年齢，BMI，60 step時のピークパワー，90 step時のピークパワー，膝伸展トルク，膝屈曲トルクとしたステップワイズ重回帰分析をTUGに対する説明力の強さを検討するために実施した。統計処理は統計解析用ソフトSPSS11.0J（SPSS inc.）を用い，統計学的有意水準は危険率を5%未満とした。

III. 結　果

各step数でのピークパワー，身体機能評価の各測定値の平均値を表1に示した。なお，全ての測定値において正規性を認めた。

ステップエルゴメーターの各step数でのピークパワーと身体機能評価との相関関係（表2）は，60 stepのピークパワーとTUG所要時間（r＝−0.672, p<0.05），膝伸展トルク（r＝0.893, p<0.01）で有意となり，90 stepのピークパワーとTUG所要時間（r＝−0.890, p<0.01），膝伸展トルク（r＝0.716, p<0.01），膝屈曲トルク（r＝0.638, p<0.05）でそれぞれ有意な相関を認めた。また，TUG所要時間はピークパワーに加え，膝伸展トルク（r=−0.729, p<0.01），膝屈曲トルク（r＝−0.639, p<0.05）との有意な相関関係を認めた。

TUG所要時間を従属変数とし，年齢，BMI，60 step，90 stepのピークパワー，膝伸展トルク，膝屈曲トルクを独立変数としたステップワイズ重回帰分析では，TUG所要時間に関連する項目として90 stepのピークパワーのみが抽出され，高い調整済み重決定係数（R^2＝0.771（p<0.05））を示した。

表1　各測定値の平均値

		平均値	標準偏差
60stepピークパワー	(W)	305.75	49.9
90stepピークパワー	(W)	253.50	58.17
TUG	(s)	6.22	0.72
膝伸展トルク	(Nm/kg)	1.21	0.27
膝屈曲トルク	(Nm/kg)	0.49	0.11

表2　パワーと身体機能評価との相関係数

	TUG 所要時間	膝伸展 トルク	膝屈曲 トルク
60 stepピークパワー	−.672*	.893**	.482
90 stepピークパワー	−.890**	.716**	.638*
TUG所要時間		−.729**	−.639*

r：Pearson の相関係数，*p<0.05，**p<0.01

IV. 考　察

本研究で使用したBiostepは，リカンベント式のステップエルゴメーターであり，背もたれで身体を支えることが可能なため，高齢者においても安全に駆動を行うことが可能であった。アイソキネティック運動のパワーの測定は，全力で駆動することでより大きいパワーが得られる。さらにステップエルゴメーターでは下肢筋全体の筋活動が認められるため[19]，下肢筋全体の最大パワーの測定が可能であると考えられる。本研究では，20～30歳代の健常成人を対象にした予備調査から，測定時間を15秒と設定し駆動を行った。短時間の測定であるために対象者の疲労感の訴えはほとんど聞かれず，また，膝痛や転倒などの有害事象の発生も認めなかった。

アイソキネティック運動時のピークパワーの値と各身体機能評価との関係において，60 stepのピークパワーとTUG所要時間，膝伸展トルク，90 stepのピークパワーとTUG所要時間，膝伸展トルク，膝屈曲トルクとの間に，いずれも中程度以上の相関を認めた。先行研究では運動が高速になるにつれ，筋電図および筋音図による筋活動の増加が認められている[20-23]。これらアイソキネティック運動機器（Cybex およびSpark System dynamometer）で設定される回転数と，本研究で使用したステップエルゴメーターによるステップ数は同様の条件ではないため，一様に比較することは困難であるが，本研究でもステップ数の増加に伴い，下肢筋の筋活動が増加していた可能性がある。したがって，ステップエルゴメーター駆動は下肢筋全体の運動であるため，ピークパワーが膝伸展筋や膝屈曲筋トルクと相関を示したものと考えられ，特に，高速運動でありより大きな筋活動が予想される90 stepの駆動が膝伸展筋，屈曲筋トルク両方と関連性を示したことが考えられた。この結果は，ステップエルゴメーターを用いたピークパワーの測定が，対象者の筋力を反映した指標として用いることができることを示唆している。

さらに，本研究ではステップエルゴメーターを用いたアイソキネティック駆動時のパワー値が，高齢者の身体機能評価としての妥当性を有しているかを検討するために，TUGとの関連性を検証した。TUGは下肢筋力や動的バランス，ADL，歩行と関連し[6,24]，地域在住高齢者の転倒予測として有効であるとされている[17]。TUG所要時間を従属変数とした重回帰分析では，90 step

のパワーが適合度として有意な回帰が認められた。これはTUG所要時間が，膝伸展トルクや膝屈曲トルクのような単一の筋の静的な活動よりも，ステップエルゴメーターの駆動のように下肢全体の動的な運動と関係が強いことを示していると考えられた。また，高速の運動になるにつれ筋活動が増加することが明らかになっており，より筋活動を要するとされる90 stepの方がTUGの説明因子として適合度が高かったと考えられた。先行研究でも筋パワーとTUG所要時間との関連性が示されており[6]，ステップエルゴメーター駆動によるパワーの測定が，高齢者の身体機能評価としての妥当性を有していると考えられる。加えて，TUGのような複合的な運動を速く遂行することが求められる課題には，高速域での筋出力を高めることが重要であることが示唆された。

膝伸展筋力やTUG所要時間は，地域在住高齢者における身体機能評価として頻繁に用いられている。特に，TUGと高い関連が認められたステップエルゴメーターを用いた筋パワーによる機能評価法は，高齢者の身体機能を説明する指標として妥当であると考えられ，今後の運動処方の検討や予測指標としての活用が期待できると考えられた。

本研究における限界は，対象とした高齢者の人数が12名と少ないことが挙げられる。また，ステップエルゴメーターによる筋パワー評価の信頼性の検証を行っていない点，さらに駆動時間や設定ステップ数など本実験プロトコールの妥当性についても未検証であるため今後の検討課題といえる。

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A Significant Relationship between Plasma Vitamin C Concentration and Physical Performance among Japanese Elderly Women

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Background. Maintenance of physical performance could improve the quality of life in old age. Recent studies suggested a beneficial relationship between antioxidant vitamin (eg, vitamin C) intake and physical performance in elderly people. The purpose of this study was to examine the relationship between plasma vitamin C concentration and physical performance among Japanese community-dwelling elderly women.

Methods. This is a cross-sectional study involving elderly females residing in an urban area in Tokyo, Japan, in October 2006. We examined anthropometric measurements, physical performance, lifestyles, and plasma vitamin C concentration of participants.

Results. A total of 655 subjects who did not take supplements were analyzed. The mean age (±standard deviation) of participants was 75.7 ± 4.1 years in this study. The geometric mean (geometric standard deviation) of plasma vitamin C concentration was 8.9 (1.5) μg/mL. The plasma vitamin C concentration was positively correlated with handgrip strength, length of time standing on one leg with eyes open and walking speed, and inversely correlated with body mass index. After adjusting for the confounding factors, the quartile plasma vitamin C level was significantly correlated with the subject's handgrip strength (p for trend = .0004) and ability to stand on one leg with eyes open (p for trend = .049).

Conclusions. In community-dwelling elderly women, the concentration of plasma vitamin C related well to their muscle strength and physical performance.

Key Words: Plasma vitamin C—Physical performance—Elderly women—Japanese.

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PHYSICAL performance and physical ability are the most important indicators of health status in elderly people and are also closely related to the quality of life. Declines in physical performance and physical activity, whether from specific disease, fall, fracture, poor nutrition, or aging itself, are associated with future disability, morbidity, and death (1,2).

In recent years, many studies have examined the roles of diet, protein, and vitamins in physical performance and physical activity(3–5). Several studies have associated low serum albumin concentration with deteriorated muscle strength and function (6,7). Some other studies have examined the relationship between serum vitamin D level and physical performance such as muscle mass, muscle strength, handgrip, walking speed, and functional capacity (8,9). Cesari et al. (3) examined the relationship between antioxidant vitamin intake (vitamin C, vitamin E, β-carotene, and retinol) and physical performance in elderly people and showed significant positive correlations between most antioxidants, especially vitamin C, and higher skeletal muscular strength in this group of people.

There are a number of mechanistic hypotheses about the potential beneficial effects of antioxidant vitamins(10–12). Vitamin C, vitamin E, β-carotene, and retinol are important antioxidants that are not synthesized by humans and, therefore, are mainly supplied via dietary intake. Vitamin C (ascorbic acid) is a water-soluble antioxidant present in the cytosol and extracellular fluid and can directly react with free radicals such as superoxide ($O_2\cdot^-$) and hydroxyl radicals (·OH) (13,14). Each one of these oxygen-derived intermediates is considered highly reactive because of their unstable electron configurations, which could attract electrons from other molecules, resulting in another free radical that is capable of reacting with yet another molecule. This chain reaction is thought to contribute to lipid peroxidation, DNA damage, and protein degradation during oxidative stress. Oxidative damage is thought to play an important role in the age-related decline of functional activity in human skeletal muscle (15). Concentration of plasma vitamin C, which has potent antioxidant activity, is known to increase after exercise (4).

An increase in the amount of blood vitamin C content has been used as an indicator of increased oxidative reaction (11). Previous studies have examined the effects of vitamin C supplementation on physical performance and exercise (4,11). Although findings from some of the previous studies do not support any beneficial effect of increased antioxidant intake on physical performance, other studies have shown improved recovery from exercise with antioxidant intake and have also shown a preventive role of antioxidant supplementation against oxidative damage. These studies were carried out on athletes after heavy exercise. So far, however, there has been no study examining the relationship between physical performance and blood levels of vitamin C, which may be a more direct marker of the antioxidative ability of the human body.

The present study, to the best of our knowledge, is the first report that examines the relationship between plasma vitamin C concentration and physical performance in Japanese community-dwelling elderly women.

SUBJECTS AND METHODS

Study Subjects

The present cross-sectional study was carried out as part of a project involving mass health examination of community-dwelling people ("Otasha-kenshin" in Japanese) aged 70 years and older living in Itabashi-ku, Tokyo. "Otasha-kenshin," which literally means "health examination for successful aging," is a comprehensive health examination program for community-dwelling older adults aimed at preventing geriatric syndromes including falls and fractures, incontinence, mild cognitive impairment, depression, and undernutrition (16).

The eligible subjects were all female residents, aged between 70 and 84 years, living in the Itabashi area, an urban part of Itabashi-ku, Tokyo, Japan in October 2006. The population of women belonging to this age range and residing in the Itabashi area was 5937, and they were recruited by invitation through postal mail. Of them, 1,112 women applied for admission and 957 women ultimately participated in this study. The participants who were taking vitamin C supplements (n = 238) were excluded from the primary analyses for examination of the relationship between plasma vitamin C and physical performance because intake of supplements could strongly influence the plasma vitamin C level. Thus, data from 655 subjects were ultimately used for the primary analysis. However, data from the 238 supplement users were also used for subanalysis to determine whether any relationship exists between vitamin C supplementation and physical performance.

All participants were examined at the Tokyo Metropolitan Institute of Gerontology's hall. Physical performance, blood examinations, lifestyle assessments, and anthropometric measurements were performed as described below (9).

The present study was approved by the ethics review committee of the Tokyo Metropolitan Institute of Gerontology. All subjects gave written informed consent.

Anthropometric Measurements

Height and weight of each participant were measured, and body mass index was defined as weight/height^2 (kg/m^2). Body composition measurements (percent body fat) were obtained by segmental bioelectrical impedance using eight tactile electrodes according to the manufacturer's instructions (In Body 3.0; Biospace, Seoul, Korea). Measurements for the triceps surae muscles were taken between the knee and the ankle, at the level of maximum circumference of the medial and anterior calf of the left leg of each participant at sitting position.

Physical Performance

Physical performance was assessed by muscle strength (handgrip strength), balance capability, and usual and maximal walking speeds, without prior practice before the actual measurements. These assessments are routinely conducted for the elderly community as described previously (9). Handgrip strength (kg) was measured once for the dominant hand with the subjects in a standing position using a Smedley's Hand Dynamometer (Yagami, Tokyo, Japan). Grip devices were calibrated with known weights. Subjects held the dynamometer at thigh level and were encouraged to exert the strongest possible force. Balance capability was measured in terms of the length of time standing on one leg, that is, we asked the subjects to look straight ahead at a dot 1 m in front of them and to stand on the preferred leg with their eyes open and hands down alongside the trunk. The time until balance was lost (or maximum 60 seconds) was recorded. We used the better of two trials in the analysis. To determine the walking speed, participants were asked to walk on a flat surface at their "usual and maximum walking speeds." Two marks were used to delineate the start and end of a 5-m path. The start mark was preceded by a 3-m approach to ensure that the participants achieved their pace of usual or maximum before entering the test path. The participants were also instructed to continue walking past the end of the 5-m path for a further 3 m to ensure that their walking pace was maintained throughout the test path. The time taken to complete the 5-m walk was measured by an investigator and used for analysis. Walking test at maximum speed was repeated twice, and the faster speed was recorded for the test.

All physical performance tests were performed between 9 AM and 4 PM during the day. We have no data on the reproducibility of the measurements. To reduce interexaminer variation, each test was conducted by the same staff member specifically trained for this study.

Blood Examinations

Blood samples (nonfasting) were collected from the subjects between 9 am and 4 pm during the day. There was no difference in mean plasma vitamin C concentration with regard to the time of collection (data not shown). Venous blood samples were drawn into Ethylene diamine tetraacetic acid tubes. Plasma was then obtained by centrifugation at 3,000 rpm for 15 min at 4°C and subsequently used for biochemical assays. Plasma was treated with Ethylene diamine tetraacetic acid to prevent the spontaneous vitamin C degradation. Next, 100 μl of the plasma was dispensed into storage tubes, to which 450 μl of 3% metaphosphoric acid solution was added, and the mixture was stored at −80°C until further use. Vitamin C concentration was determined by an High performance liquid chromatography-electrochemical detection–based method (17). The analysis was carried out centrally in our laboratory. Serum albumin concentration was measured by the Bromocresol Green method (Special Reference Laboratories Inc., Tokyo, Japan). The coefficient of variation for serum albumin found using this method was less than 1% (9).

Lifestyle Assessment

Information regarding the participants' general health (such as medical history, smoking habits, alcohol drinking habits, regular exercise habits, vegetable intake, fruit intake and use of vitamin C supplement) was collected by interview, and history of medical conditions including hypertension, stroke, heart attack, diabetes mellitus, and hyperlipidemia was self-reported.

Alcohol drinking habits of the subjects were classified as nondrinker, current drinker, or ex-drinker. Smoking habits of the subjects were classified using three categories: never smokers, current smokers, and ex-smokers. The frequency of vegetable and fruit intake was asked using four categories: almost every day, once every two days, once or twice per week, and almost never. Subsequently, for analysis, the categories were summarized as almost every day and others.

Statistical Analysis

Data were summarized as mean and standard deviation or percentage values. The data of plasma vitamin C concentration was logarithmically transformed to approximate a normal distribution and was summarized as the geometric mean and geometric standard deviation.

Table 1. Characteristics of Study Subjects (N = 655)

Characteristic	Mean (*SD*)
Age (y)	75.7 (4.1)
Height (cm)	149.1 (5.7)
Weight (kg)	51.0 (8.3)
Body mass index (kg/m^2)	22.9 (3.4)
Triceps surae muscle (cm)	33.1 (2.8)
Plasma vitamin C (μg/ml)*	8.9 (1.5)
Serum albumin (mg/dL)	4.3 (0.2)
Body composition	
Percent body fat (%)	32.2 (7.0)
Physical performance tests	
Handgrip strength (kg)	18.7 (4.4)
One leg standing with eyes open (s)	35.2 (23.5)
Usual walking speed (m/s)	1.2 (0.3)
Maximal walking speed (m/s)	1.8 (0.4)
	%
Medical history	
Hypertension	50.7
Stroke	6.6
Heart attack	21.2
Diabetes mellitus	9.0
Hyperlipidemia	34.7
Alcohol drinking habit	
Current	25.3
Former	5.0
Never	69.6
Smoking habit	
Current	3.7
Former	5.7
Never	90.7
Regular exercise habit	
Yes	69.2
No	30.8
Vegetable intake	
Everyday	84.2
Others†	15.8
Fruit intake	
Everyday	81.8
Others†	18.2

Notes: Data of vitamin C supplement users were excluded.
*The geometric mean and geometric *SD*.
†Including participants taking vegetables/fruits not everyday or almost never.

The age-adjusted Pearson's correlation coefficient between the plasma vitamin C concentration and other factors were calculated. The least square means and SEs adjusted for potential confounders were calculated and compared between categories by analysis of covariance. To examine the relationship between plasma vitamin C concentration and physical performance, statistical adjustment was done by analysis of covariance for variables (except for other physical performance variables) that were correlated to plasma vitamin C concentration with $p < .20$. The same analyses were repeated for the 238 users of vitamin C supplement. All statistical analyses were performed using the SAS (version 9.0; SAS Institute Inc., NC).

Results

Table 1 summarizes the basic characteristics of the subjects. As shown, the mean age (±standard deviation) of the

Table 2. Correlation between Plasma Vitamin C Concentration and Selected Factors ($N = 655$)

Factor	Correlation* r	p
Age	−0.004	.91
Height	0.04	.27
Weight	−0.05	.19
Body mass index	−0.08	.054
Triceps surae muscle	0.001	.98
Serum albumin	−0.04	.33
Percent body fat	−0.12	.002
Handgrip strength	0.16	<.001
One leg standing with eyes open	0.15	<.001
Usual walking speed	0.14	<.001
Maximal walking speed	0.09	.036

Notes: Number of subjects is slightly different for the selected factors because of missing values.

*Age-adjusted Pearson's correlation coefficient between logarithm of vitamin C concentration and each factor.

subjects was 75.7 ± 4.1 years. The geometric mean (geometric standard deviation) of plasma vitamin C concentration was 8.9 (1.5) μg/mL. The prevalence of women eating vegetables everyday was 84.2% and those eating fruits everyday was 81.8%.

The age-adjusted geometric mean of plasma vitamin C concentration was significantly lower in subjects who had a medical history of hypertension (8.53 vs 9.22, $p = .0015$) and diabetes mellitus (7.59 vs 9.00, $p = .002$) as compared with those who did not. A history of stroke, heart attack, or hyperlipidemia was not associated with plasma vitamin C concentration. Subjects who took fruits every day had a significantly higher concentration of vitamin C than those who did not (9.14 vs 7.78, $p < .0001$). Vegetable intake, alcohol drinking habit and smoking habit were not related to plasma vitamin C concentration (not shown in table).

Table 2 shows the age-adjusted correlations between the plasma vitamin C concentration and selected factors. As shown, the plasma vitamin C concentration was positively but modestly correlated with handgrip strength, length of time standing on one leg with eyes open, as well as usual walking speed and maximal walking speed, and modestly inversely correlated with body mass index and percent body fat of the subjects.

Table 3 shows the relationship between plasma vitamin C concentration and each physical performance after adjusting for confounding factors. Results obtained after the adjustment for potential confounders confirmed that the plasma vitamin C concentration was correlated with the handgrip strength independently from the other factors (eg, p for trend = .0004 after adjusting for age, body mass index, percent body fat, hypertension, diabetes mellitus, and fruit intake; Table 3). There was also a significant relationship between the plasma vitamin C level and the subject's length of time standing on one leg with eyes open after adjustments for age, body mass index, percent body fat, hypertension, diabetes mellitus, and fruit intake (Table 3; p for trend = .049). We did not observe any significant association between the plasma vitamin C level and the usual or the maximal walking speed of the subjects.

A subanalysis using data from the 238 vitamin C supplement users showed almost null relationship between handgrip strength and plasma vitamin C concentration (data not shown).

Discussion

A previous study has shown an association between higher daily dietary intake of vitamin C and skeletal muscle strength in elderly people (3). Results described in the present study indicated that plasma vitamin C concentration was positively related with muscle and physical performance in community-dwelling elderly women. To the best of our knowledge, this is the first study showing a significant

Table 3. Relationship between Plasma Vitamin C Concentration and Physical Performance Adjusted for Potential Confounder

Physical performance	Quartile of plasma vitamin C level: Q1 Mean ± *SE*	Q2 Mean ± *SE*	Q3 Mean ± *SE*	Q4 Mean ± *SE*	p for trend
Handgrip strength (kg), *N*	154	159	154	152	
Age adjusted	17.70 ± 0.34	18.75 ± 0.33	18.75 ± 0.34	19.60 ± 0.34	.0001
Multivariate adjusted*	17.83 ± 0.34	18.83 ± 0.32	18.89 ± 0.33	19.60 ± 0.33	.0004
One leg standing with eyes open† (s), *N*	162	163	164	161	
Age adjusted	31.44 ± 1.71	33.98 ± 1.70	37.70 ± 1.70	37.83 ± 1.71	.003
Multivariate adjusted*	33.39 ± 1.74	34.08 ± 1.67	37.63 ± 1.67	37.50 ± 1.70	.049
Usual walking speed (m/s), *N*	146	154	145	147	
Age adjusted	1.13 ± 0.02	1.19 ± 0.02	1.23 ± 0.02	1.21 ± 0.02	.008
Multivariate adjusted*	1.18 ± 0.02	1.19 ± 0.02	1.22 ± 0.02	1.21 ± 0.02	.23
Maximal walking speed (m/s), *N*	146	154	154	147	
Age adjusted	1.70 ± 0.03	1.76 ± 0.03	1.82 ± 0.03	1.76 ± 0.03	.15
Multivariate adjusted*	1.76 ± 0.03	1.77 ± 0.03	1.80 ± 0.03	1.75 ± 0.03	.94

Notes: Values are least squares mean and *SE* adjusted for the factors by analysis of covariance. Q1–Q4: first to fourth quartile groups of plasma vitamin C concentration, respectively.

*Adjusted for age, body mass index, percent body fat, hypertension, diabetes mellitus and **fruit intake**.

†Length of time standing on one leg with eyes open.

correlation between plasma vitamin C concentration and handgrip strength and ability to stand on one leg with eyes open. We, however, were unable to find any relationship between skeletal muscle mass and plasma vitamin C concentration. Handgrip strength has been found to correlate well with the strength of other muscle groups and is thus a good indicator of overall strength (18). Consistent with this idea, handgrip strength was found to be a strong and consistent predictor of all-cause mortality and morbidity of Activities of Daily Living in middle-aged people (19). The handgrip test is considered an easy and inexpensive screening tool to identify elderly people at risk of disability. Handgrip strength, an indicator of overall muscle strength, is thought to predict mortality through mechanisms other than underlying disease that could cause muscle impairment (18,19). The one leg standing test is one of the balance tests (20). The test is a clinical tool to assess postural steadiness in a static position by quantitative measurement. Many studies have shown that the decreased one leg standing time is associated with declines in Activities of Daily Living and increases in other morbidities including osteoporosis and fall (20).

Our findings suggest that vitamin C may play an important role in maintaining physical performance and thereby may help to improve healthy life expectancy in the elderly. However, the usual and maximal walking speeds did not relate to plasma vitamin C concentration. Walking speed test may be an efficient tool in screening older persons with higher risk of mortality and may easily identify high-risk groups in the community (21). Walking is a rhythmic, dynamic, and aerobic activity of the large skeletal muscles that confers multifarious benefits with minimal adverse effects. Muscles of the legs, limbs, and lower trunk are strengthened, and the flexibility of their joints are preserved (22). One of the reasons why walking speed was not related to vitamin C concentration may be because walking requires coordinated movements of arms, legs, and many parts of the body rather than a simple muscle and balance function. Previous reports showed that walking balance function did not correlate with standing balance function (23). Although we did not find any clear association between walking and plasma vitamin C concentration in this study, vitamin C may still have effects on relatively simple strength and balance functions.

One of the possible explanations for the observed relationship between vitamin C and physical performance, especially handgrip strength and the ability to stand on one leg with eyes open, may be the potential protective effects of the antioxidant vitamins against muscle damage (4,11). Vitamin C is a six-carbon lactone that is synthesized from glucose in the liver of most mammalian species, but not in humans (12). Vitamin C is an antioxidant because, by donating its electrons, it prevents other compounds from being oxidized (12). Thus, vitamin C readily scavenges reactive oxygen and nitrogen species, thereby effectively protects other substrates from oxidative damage (10,24). Although habitual exercise reduces systemic inflammation and oxidative stress as the production of endogenous antioxidants are enhanced, acute exercise increases the generation of oxygen-free radicals and lipid peroxidation (4,25). Strenuous physical performance can increase oxygen consumption by 10- to 15-folds over the resting state to meet the energy demands and results in muscle injury (26). Prolonged submaximal exercise was shown to increase the amount of both whole-body and skeletal muscle lipid peroxidation by-products; in the case of the former, the increase was indicated by greater exhalation of pentane but not of ethane (4,27,28). Supplementation with vitamin C was shown to decrease the exercise-induced increase in the rate of lipid peroxidation (27,28). Several studies suggested that oxidative damage may play a crucial role in the decline of functional activity in human skeletal muscle with normal aging (15). Consistent with this idea, several studies showed significantly lower plasma vitamin C level in the elderly population than in the younger adult population (29–31). Because the plasma vitamin C levels in these apparently healthy elderly persons rose markedly after an oral dose of vitamin C, their initially low plasma levels can be attributed to the low intake rather than to an age-related physiological defect.

In fact, the relationship between handgrip strength and plasma vitamin C concentration was significantly different between supplement users and nonusers, that is, an almost null relationship in the former and a positive relationship in the latter (data not shown). This finding suggested that vitamin C supplementation did not have any beneficial effect on the physical performance and muscle strength despite the increased plasma level of vitamin C. A number of studies reported that vitamin C supplement users had significantly higher blood vitamin C concentration than non-users (29, 32, 33). Several studies have examined the effects of exercise on changes in the serum vitamin C concentration (34–36). Some other experimental studies have shown that vitamin C supplementation can reduce symptoms or indicators of exercise-induced oxidative stress (37–40). However, the results regarding vitamin C supplementation are equivocal, and most well-controlled intervention studies report no beneficial effect of vitamin C supplementation on either endurance or strength performance (41,42). Likewise, vitamin C restriction studies showed that a marginal vitamin C deficiency did not affect the physical performance (43). Although evidence from a number of studies show that vitamin C is a powerful antioxidant in biological systems in vitro, its antioxidant role in humans has not been supported by currently available clinical studies.

Vitamin C is especially plentiful in fresh fruits and vegetables. Plasma vitamin C concentration may be merely a marker for intake of other nutrients that are abundant in fruits and vegetables. However, the statistical adjustment for fruit intake did not attenuate the relationship between plasma vitamin C and physical performance (Table 3), suggesting that vitamin C did have some beneficial effects independently of other nutrients. A number of biochemical, clinical, and observational epidemiologic studies have indicated that diets rich in fruits, vegetables, and vitamin C may be of benefit for the prevention of chronic diseases such as cardiovascular disease and cancer (44,45). Several cohort studies have examined associations between plasma vitamin C concentration and mortality from stroke or coronary heart disease (30,46,47). The effects of vitamin C supplementation are, however, still unclear. A pooled study suggested reduced incidences of coronary heart disease events with higher intake of vitamin C supplement (48), while another study showed that a high intake of vitamin C supplement is associated with an increased risk of mortality due to cardiovascular diseases in postmenopausal women with diabetes (49). A randomized placebo controlled 5-year trial, however, did not show any significant reduction in the mortality from, or incidence of, any type of vascular disease or cancer (50). These studies, in fact, have failed to demonstrate any benefit from such supplementation.

There are a number of potential weaknesses in our study that should be mentioned here. The subjects used in this study were not selected randomly from the study population, and they may be relatively healthy elderly women who were able to come to the health examination hall from their homes. A previous study assessed the correlation of antioxidants with physical performance and muscular strength (3) and demonstrated that a higher daily intake of vitamin C and carotene associated with skeletal muscle strength. However, we have no data regarding the presence of other dietary antioxidants in blood such as vitamin E, retinol, and carotene. In our questionnaire, participants were asked to respond "Yes" or "No" to whether they took supplements, and not about the frequency and quantity of intake of the supplements. Thus, we were unable to examine the reason why plasma vitamin C was not related to the handgrip strength in the supplement users by considering the dose of vitamin C they took.

This study was a cross-sectional study and, therefore, does not provide cause/effect relationships, although we demonstrated a significant correlation between physical performance and concentration of plasma vitamin C. Therefore, longitudinal follow-up studies and controlled clinical trials are necessary to confirm the role of plasma vitamin C and physical performance of the elderly women. These limitations should be considered in future studies.

In conclusion, we found a strong correlation of a higher plasma vitamin C concentration with handgrip strength and one leg standing time in community-dwelling elderly women. Although the elderly are prone to vitamin C deficiency, and they appear to have a higher dietary requirement for vitamin C, the beneficial effects of vitamin C supplementation to maintain physical performance in elderly people are equivocal and thus, need further in-depth studies.

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Effects of Exercise and Amino Acid Supplementation on Body Composition and Physical Function in Community-Dwelling Elderly Japanese Sarcopenic Women: A Randomized Controlled Trial

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OBJECTIVES: To evaluate the effectiveness of exercise and amino acid supplementation in enhancing muscle mass and strength in community-dwelling elderly sarcopenic women.

DESIGN: Randomized controlled trial.

SETTING: Urban community in Tokyo, Japan.

PARTICIPANTS: One hundred fifty-five women aged 75 and older were defined as sarcopenic and randomly assigned to one of four groups: exercise and amino acid supplementation (exercise + AAS; n = 38), exercise (n = 39), amino acid supplementation (AAS; n = 39), or health education (HE; n = 39).

INTERVENTION: The exercise group attended a 60-minute comprehensive training program twice a week, and the AAS group ingested 3 g of a leucine-rich essential amino acid mixture twice a day for 3 months.

MEASUREMENTS: Body composition was determined using bioelectrical impedance analysis. Data from interviews and functional fitness parameters such as muscle strength and walking ability were collected at baseline and after the 3-month intervention.

RESULTS: A significant group × time interaction was seen in leg muscle mass ($P = .007$), usual walking speed ($P = .007$), and knee extension strength ($P = .017$). The within-group analysis showed that walking speed significantly increased in all three intervention groups, leg muscle mass in the exercise + AAS and exercise groups, and knee extension strength only in the exercise + AAS group (9.3% increase, $P = .01$). The odds ratio for leg muscle mass and knee extension strength improvement was more than four times as great in the exercise + AAS group (odds ratio = 4.89, 95% confidence interval = 1.89–11.27) as in the HE group.

CONCLUSION: The data suggest that exercise and AAS together may be effective in enhancing not only muscle strength, but also combined variables of muscle mass and walking speed and of muscle mass and strength in sarcopenic women. J Am Geriatr Soc 60:16–23, 2012.

Key words: sarcopenic women; exercise; amino acid supplementation; muscle mass; muscle strength

Sarcopenia, defined as age-related involuntary loss of skeletal muscle mass and strength,[1,2] has been associated with physical disability, functional decline, falls, impaired mobility, and mortality in elderly people.[3,4] Therefore, treating or reversing sarcopenia is important in the maintenance of health and life expectancy in the elderly population. Although many factors, such as chronic disease, physical inactivity, and decreased muscle protein synthesis, may contribute to loss of muscle mass,[5–7] it has been suggested that only skeletal muscle disuse and undernutrition are potentially preventable or reversible with targeted interventions.[8]

Many studies have shown a strong relationship between resistance exercise and strength improvement, through which the efficacy of resistance exercise for the prevention and treatment of sarcopenia has been confirmed.[9] The previous studies have also shown that ingestion of essential amino acids can induce muscle protein anabolism in elderly adults.[10,11] One study showed that the combination of resistance exercise and essential amino acid supplementation (AAS) augmented muscle protein

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synthesis, suggesting it as a strategy to reverse sarcopenia[12] but in a small sample size. There are few randomized controlled trials (RCTs) on the effects of exercise and AAS on body composition and functional capacity.

The purpose of this study was to investigate the effects of exercise and AAS on muscle mass, strength, and walking ability in sarcopenic women.

METHODS

Subjects

A letter outlining the comprehensive geriatric health examination survey, describing its objective and the way that the personal data would be used, was mailed to the women randomly selected from the Basic Resident Register of 5,932 people aged 75 and older residing in the Itabashi ward of metropolitan Tokyo inviting them to participate in the study. Two thousand eighteen people responded to the mailed letters of invitation to participate in the study, with 1,670 people agreeing and 348 people declining to participate. The baseline assessment was conducted at the Tokyo Metropolitan Institute of Gerontology (TMIG) from October 12 to November 3, 2008. One thousand three hundred eighty-three women aged 75 and older were screened; 287 who originally agreed to participation were absent. Written informed consent was obtained for baseline screening; six people did not sign the informed consent form and were not included in this study.

Three hundred four of 1,377 women (22.1%) were operationally defined as sarcopenic (Figure 1), with selection based on categorization into one or more of the following inclusion criteria groups: appendicular skeletal muscle mass/height^2 less than 6.42 kg/m^2 and knee extension strength less than 1.01 Nm/kg[13,14] (n = 68), appendicular skeletal muscle mass/height^2 less than 6.42 kg/m^2 and usual walking speed less than 1.22 m/s (n = 65),[14] body mass index (BMI) less than 22.0 kg/m^2[14] and knee

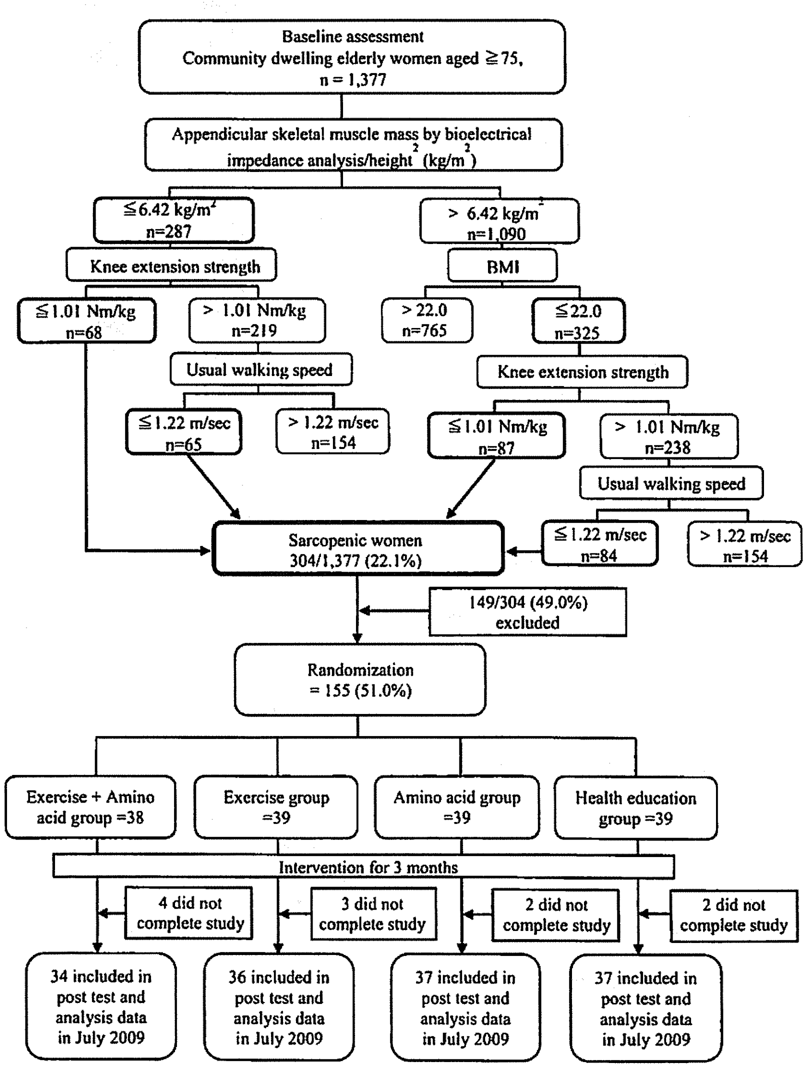

Figure 1. Algorithm for the selection of women who were operationally defined as sarcopenic and flowchart of participants in the randomized controlled trial of exercise and amino acid supplementation.

extension strength less than 1.01 Nm/kg (n = 87), and BMI less than 22.0 kg/m^2 and usual walking speed less than 1.22 m/s (n = 84). Exclusion criteria were severe knee or back pain; severely impaired mobility; impaired cognition (Mini-Mental State Examination (MMSE) score < 24);[16] missing baseline data; and unstable cardiac conditions such as ventricular dysrhythmias, pulmonary edema, or other musculoskeletal conditions. One hundred forty-nine (49.0%) of the potential sarcopenic participants were excluded because they were classified into one or more of the exclusion criteria or declined participation. The Clinical Research Ethics Committee of TMIG approved the study protocol. The intervention procedures were fully explained to all participants, and written informed consent was obtained (Figure 1).

Randomization

Randomization was performed after the baseline assessment; any variable that identified personal information was not included in the randomization process. Computer-generated random numbers were assigned to 155 participants who were then sorted and divided into four equal groups. The groups were randomly assigned to one of the four interventions groups: exercise + AAS (n = 38), exercise (n = 39), AAS (n = 39), or health education (HE; n = 39). All participants agreed to the group allocations that were mailed to them. There was no attempt to equalize the size of the groups based on their characteristics or to recruit subjects with specific characteristics. The co-investigators were blind to the randomization procedure and group allocations, separate physical therapy staff members who were also blind to the allocation of treatments collected data.

Outcome Measures

Outcome measures were evaluated according to data collected from interviews, body composition assessments using bioelectrical impedance analysis (BIA), and physical fitness tests at baseline and after the 3-month intervention.

Interview Survey

Face-to-face interviews were conducted to assess the individual's history of fractures and falls over the previous year, number of falls, cause of falls, urinary incontinence, exercise habits, smoking status, and MMSE score.

Body Composition Assessment

Measurements of height and weight were used to calculate BMI (kg/m^2). Body composition was measured using a segmental multifrequency BIA instrument that operated at frequencies of 5, 50, 250, and 550 kHz (Well-Scan 500, Elk Corp., Tokyo, Japan). Participants removed their socks, stood on two metallic electrodes on the floor scale barefoot, and held metallic grip electrodes placed in the palm of the hand with the fingers wrapped around the handrails. Using segmental body composition and muscle mass values of both legs, both arms, and the trunk, appendicular skeletal muscle mass and leg muscle mass values were obtained and used for analysis by summing the appropriate segmental muscle mass values.[13,17,18] Reliability of body composition measurements in all 155 participants in this study was not analyzed, although for the AAS group (n = 39), measurements were taken for a second time 1 week after baseline testing, and reliability was examined; the intraclass correlation coefficients (ICC) were: 0.98 for the right arm, 0.97 for the left arm, 0.97 for the right leg, 0.96 for the left leg, and 0.93 for the trunk.

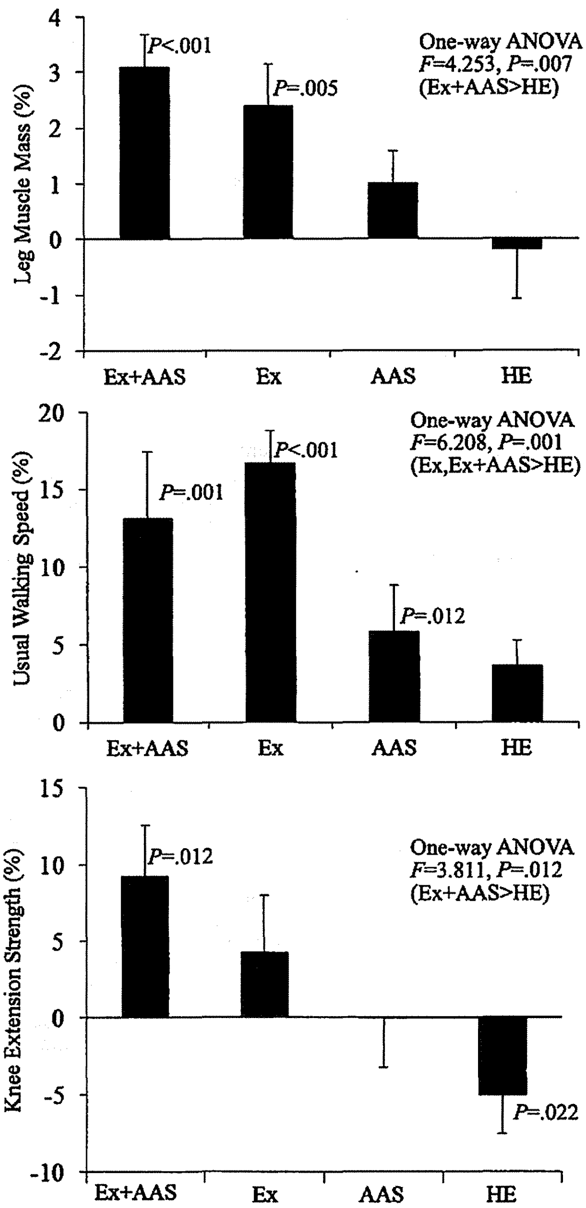

Figure 2. Mean percentage changes (standard errors) in leg muscle mass, usual walking speed, and knee extension strength after exercise (Ex), amino acid supplementation (AAS), both (Ex + AAS), or health education (HE). Bars indicate average changes from baseline to after the 3-month intervention. ANOVA = analysis of variance.

Functional Fitness Test

Calf girth and functional fitness variables including usual and maximum walking speeds and knee extension strength were measured. In measures of walking speed, participants were allowed to use assistive walking devices only if they expressed strong concerns about walking without a device or if there was any danger of falling. The knee extension strength measurement was taken twice, and the higher value divided by body weight (Nm/kg) were analyzed. The procedures for the functional fitness tests have been described in detail in previous reports.[19,20]

Intervention

Exercise

A comprehensive physical fitness and muscle mass enhancement training program of moderate intensity was provided for the participants in the exercise groups. The exercise intervention consisted of 60-minute exercise sessions held at the TMIG twice per week for 3 months. Each exercise intervention group was divided into two subgroups, with participants exercising together within their assigned group in one of four exercise sessions offered per day.

Each exercise session consisted of a 5-minute warm-up, 30 minutes of strengthening exercise, 20 minutes of balance and gait training, and 5 minutes of cool down. The strengthening exercises were performed in a progressive sequence from seated to standing positions. For each type of exercise, participants were instructed to complete up to eight repetitions of the movements. When the exercises were properly executed without significant fatigue or loss of proper execution, the resistance was increased. The progressive resistance was provided through the use of resistance bands or ankle weights. Intensity was maintained at approximately 12 to 14 on the Borg Rate of Perceived Exertion scale.[21] The principal investigator, along with the exercise instructor and assistant trainers, assessed each individual's ability to increase intensity.

Chair exercise: The chair-seated exercises were used in the early stages of the program because the participants were frail older adults and it provided a secure and stable position. Repetitions of toe raises, heel raises, knee lifts, knee extensions, and others were performed while seated on a chair. Hip flexions, lateral leg raises, and repetitions of other exercises were performed standing upright behind the chair and holding the back of the chair for stability.

Ankle-weight exercise: To strengthen lower extremities, a fixed weight was placed on the ankle while participants performed strengthening exercises. Weights of 0.50, 0.75, 1.00, and 1.50 kg were prepared and used in accordance with each participant's strength level as the resistance progressively increased. The exercises performed using these ankle weights included seated knee flexion and extension and standing knee flexion and extensions.

Exercises using a resistance band: Resistance bands were used to strengthen the upper and lower body. Lower body exercises included leg extension and hip flexion. Upper body exercises included double-arm pull downs and biceps curls.

Balance and gait training: The balance training was focused on improvement of static, dynamic, and lateral balancing ability. Exercises included standing on one leg, multidirectional weight shifts, tandem stand, and tandem walk. Participants practiced proper gait mechanics that focused on the maintenance of stability during walking and increasing stride length, toe elevation of the forward limb, heel elevation of the rear limb, frequency of stepping, and heel–floor angle. Exercises included raising the toes (dorsiflexion) during the forward swing of the leg, kicking off the floor with the ball of the foot, walking with directional changes, and gait pattern variations.

Amino Acid Supplementation

Essential AAS was provided for the participants in the AAS groups every 2 weeks. Packets of powdered amino acid supplements (42.0% leucine, 14.0% lysine, 10.5% valine, 10.5% isoleucine, 10.5% threonine, 7.0% phenylalanine, and 5.5% other) were provided for the participants to be taken with water or milk, and they were instructed to take the 3-g supplement two times a day (6 g daily) every day for 3 months.[22] To monitor their amino acid intake accurately, participants were given record sheets that were collected every 2 weeks on which they recorded what time of day they took the supplement and the amount of amino acid taken every day.

Health Education

Participants in the HE group took a class once a month for 3 months, a total of three times. The classes focused on cognitive function, osteoporosis, and oral hygiene. Participants were asked to continue their regular lifestyle habits, and no specific instructions on diet or physical activity were given.

Data Analysis

Sample size calculations using univariate one-factor repeated-measures analysis of variance (ANOVA) to examine significant differences in means at baseline and after the 3-month intervention ($\alpha = 0.05$, power = 0.80) with an effect size of 0.15 required a sample size of 28 participants. Esimating a potential attrition rate of 25%, 38 subjects per group were required.[23] One-way ANOVA was used to test any differences in baseline measures and percentage changes between groups, and chi-square tests were performed on categorical variables. Percentage changes in muscle mass and functional fitness after the intervention were calculated using the following formula: % change = ((postintervention value–baseline value)/(baseline value) × 100). Two-way repeated-measures ANOVA was used to evaluate the differences in the effect of the intervention on the outcome measures between groups, and a post hoc test was done on variables showing significant differences to determine which groups were different. Multiple logistic regressions were performed to compare the effects of the four intervention groups on each outcome variable after 3 months of intervention. All analyses were performed using SPSS version 15.0 of Windows (SPSS, Inc., Tokyo, Japan).

RESULTS

The baseline demographic, fitness, and interview variables of the participants in the four groups are summarized in Table 1. All of the baseline characteristics were similar between the groups.

The mean attendance rates during the 3-month intervention were 70.3% in the exercise + AAS group, 80.5% in the exercise group, 72.2% in the AAS group, and 71.8% in the HE group. Eleven participants (exercise + AAS = 4, exercise = 3, AAS = 2, HE = 2) were unable to complete the study after randomization because of spouse care (n = 3), admission to nursing home (n = 2), lack of motivation (n = 2), severe knee or back pain (n = 1), death (n = 1), falls and hip fracture (n = 1), and hospitalization (n = 1; Figure 2).

In comparing the pre- and postintervention changes in body composition and functional fitness of the groups (Table 2), there was a significant group × time interaction for leg muscle mass ($F = 4.253$, $P < .007$; exercise + AAS > HE), usual and maximum walking speeds (exercise and exercise + AAS > HE), and knee extension strength ($F = 3.558$, $P = .02$; exercise + AAS > HE).

The within-group analysis showed significant changes in leg muscle mass in the exercise + AAS ($P < .001$) and exercise ($P = .005$) groups and changes in usual walking speed in the exercise + AAS ($P = .001$), exercise ($P < .001$), and AAS groups ($P = .01$). Knee extension strength improved significantly only in the exercise + AAS group ($P = .01$), no improvement was seen in exercise or AAS, and a statistically significant decrease was observed in the HE group ($P = .02$; Figure 1).

Table 3 shows the effects of the type of intervention on changes in combined variables of muscle mass and physical function. Significant increases in leg muscle mass and knee extension strength (odds ratio (OR) = 4.89, 95% confidence interval (CI) = 1.89–11.27) and leg muscle mass and usual walking speed (OR = 4.11, 95% CI = 1.33–13.68) were observed in only the exercise + AAS group.

DISCUSSION

Although many definitions of sarcopenia have been reported,[1 3,24] there has recently been a focus not only on the loss of appendicular skeletal muscle mass, but also on functional decline.[25] In this study, sarcopenic women were operationally defined based on declines in muscle strength or walking ability that accompany the loss of skeletal muscle mass or low BMI. Because defining sarcopenia was beyond the scope of this study, the focus of the discussion will be on the effects of the intervention. To evaluate the intervention effects, the changes observed in the single variables as well as the combined variables will be discussed.

Many studies have focused on exercise or nutrition as interventions to reverse sarcopenia, but the results of these studies have not always been consistent.[8,9,12,26]

This study demonstrated that appendicular muscle mass and walking speed increased with the combination of exercise and essential amino acid ingestion, as well as with the separate exercise and amino acid interventions, but muscle strength improved only with the combination of exercise and amino acid ingestion.

A recently published meta-analysis[9] and a Cochrane review article also confirmed that resistance training two to three times a week can improve physical function and functional limitations and can reduce disability and muscle weakness in older people.[27] Previous studies have demonstrated that resistance training in elderly people produces

Table 1. Selected Variable Characteristics of Participants at Baseline According to Study Group

Characteristic	Exercise + AAS (n = 38)	Exercise (n = 39)	AAS (n = 39)	Health Education (n = 39)	F-Value*	P-Value*
Age, mean ± SD	79.5 ± 2.9	79.0 ± 2.9	79.2 ± 2.8	78.7 ± 2.8	0.577	.63
Height, cm, mean ± SD	147.1 ± 6.7	147.7 ± 4.4	145.8 ± 4.5	146.5 ± 4.9	0.960	.41
Body weight, kg, mean ± SD	39.5 ± 5.5	41.1 ± 4.7	40.1 ± 3.2	40.4 ± 3.9	0.874	.46
Body mass index, kg/m^2, mean ± SD	18.3 ± 2.5	18.9 ± 2.0	18.9 ± 1.6	18.8 ± 1.7	0.745	.53
Calf girth, cm, mean ± SD	18.3 ± 2.5	18.9 ± 2.0	18.9 ± 1.6	18.8 ± 1.7	0.745	.53
Lean body mass, kg, mean ± SD	29.1 ± 3.4	30.0 ± 2.6	28.8 ± 2.0	29.3 ± 2.4	1.505	.22
Muscle mass, kg, mean ± SD	26.9 ± 3.1	27.7 ± 2.3	26.5 ± 1.8	27.0 ± 2.2	1.538	.21
Appendicular muscle mass, kg, mean ± SD	13.3 ± 1.6	13.7 ± 1.3	13.1 ± 1.0	13.3 ± 1.2	1.502	.22
Legs muscle mass, kg, mean ± SD	9.8 ± 1.2	10.1 ± 1.0	9.7 ± 0.7	9.9 ± 0.9	1.570	.20
Usual walking speed, m/s, mean ± SD	1.26 ± 0.27	1.29 ± 0.28	1.29 ± 0.20	1.18 ± 0.22	1.701	.17
Maximal walking speed, m/s, mean ± SD	1.62 ± 0.37	1.67 ± 0.31	1.67 ± 0.27	1.55 ± 0.32	1.150	.33
Knee extension strength, Nm, mean ± SD	45.9 ± 11.3	46.6 ± 11.1	46.7 ± 7.8	47.4 ± 10.5	0.139	.94
Falls, %	21.1	17.9	15.4	20.5	0.519	.91
Exercise habit, %	26.3	25.6	38.5	33.3	2.029	.57
Urinary incontinence, %	44.7	38.5	41.0	25.6	3.414	.33
Osteoporosis history, %	36.8	43.6	48.7	30.8	2.987	.39
Heart disease history, %	10.5	15.4	12.8	17.9	0.977	.81
Diabetes mellitus history, %	7.9	5.1	5.1	12.8	2.156	.54

* One-way analysis of variance for continuous variables and chi-square test for categorical variables.
AAS = amino acid supplementation; SD = standard deviation.