労災疾病臨床研究事業費補助金

介護・看護職の腰痛予防をシームレスに実施する新しい運動器検診システム開発に関する研究

平成 27 年度　総括研究報告書

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Ⅰ．総括研究報告

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総括研究年度終了報告書

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研究要旨：本研究は、新しい運動器検診を開発し、それをシームレスに実施するために、対象となる看護師を取り巻く事業者、管理者などのステークホルダーが情報を共有するシステム構築することを目的とする。平成 27 年度には、はじめに質問紙により、腰痛の実態、腰痛関連因子の抽出、腰痛による労働生産性への影響、安全性と関連した看護動作に関する調査を実施した。この結果から、腰痛関連動作の抽出された。このことから前後屈、ひねり＋前後屈動作が腰痛と関連する可能性が示唆され、運動器検診項目抽出、バイオメカニクス解析において検証を行い、有効性が期待される結果が得られた。急性腰痛、慢性腰痛共に労働生産性の低下と関連しており、教育、環境調整、業務調整を行う際のモチベーションとなる資料として有効であった。今後はこれらの分析を完遂し、その結果を多くのステークホルダーに発信することで社会還元する予定である。

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Ａ．研究目的

「職場における腰痛予防対策指針」（平成２５年６月改訂）によると、介護・看護職を含む労働者の腰痛予防は、「作業管理」「作業環境管理」「健康管理」「労働衛生教育」の 3 管理 1 教育を主軸に行われている。これらの項目のうちで「健康管理」については産業医が健康診断、定期健康診断を行う事としている。現状の運用においては産業医の診断に負うことが大きいことから、産業医の負担が大きく、他職種や対象者本人との健康情報のシェアにつながりにくい.

述べるまでもなく、腰痛の発症のリスクは変動するものであり、点評価では十分ではない。また介護・看護職の労働災害は腰痛だけではなく、肩こりや膝痛など多岐に渡るが、現存の腰痛に特化した健康診断はそ

れら全てをスクリーニングすることはできない。そこで本研究においては、新しい運動器アセスメントと組織アセスメントを開発し、それを段階的シームレスに実施するシステム構築を行うことを目的とする。

B．研究方法

平成２７年度は以下の項目について研究分担を行い、実施した。

● 質問紙によるに関する腰痛関連動作のスクリーニング

〈対象〉京都市内の大規模急性期病院に勤務する看護職(看護師または看護助手1100名）を対象に行った。

〈方法〉調査項目は、基本属性（性別、年齢、勤務体制、夜勤の有無等）、病棟属性（残業時間、所属部署等）、腰痛予防動作（運動習慣、移動・移乗介助時の行動と意識等）、症状（腰痛の有無、抑うつ傾向）、労働生産性（WLQ）とした。

（倫理面での配慮）本研究は京都大学大学院医学研究科・医学部及び医学部附属病院 医の倫理委員会の承認（R0131)を得て行った。質問紙調査は15分位の時間を要し、精神的、肉体的な苦痛は少ないと考えられるが、体調の悪化などに配慮して無記名、任意参加とした。

● 運動器検診項目抽出に関する研究

〈対象〉質問紙によるスクリーニングの結果から看護度の高い部署と低い部署を選出し、運動器測定、腰痛部位の特定、インタビュー調査（87名）を行った。

（倫理面での配慮）本研究は京都大学大学院医学研究科・医学部及び医学部附属病院 医の倫理委員会の承認（R0386)を得て行った。

● ノーリフト教育に関する研究

〈方法〉2015年5月より2016年3月の期間に、安全な患者の移動介助（ノーリフト）のための職員教育プログラムの作成、プログラムの実施、及びニーズ調査に基づく移動介助器具の配置を行った。

● 看護業務中の動作分析デバイスの開発に関する研究

〈対象者〉健常成人 12 名（男性 6 名，女性 6 名）。平均年齢 20.9 ± 0.8 歳、身長 164.0 ± 7.6 cm、体重 57.1 ± 10.1 kg であった。

〈方法〉加速度計と角速度計は 8 チャンネル小型無線モーションレコーダ mini（MVP-RF8-GC, MicroStone 株式会社）を用い、頸部（C7）と腰部（L3）に貼付し、1,000Hz でデータサンプリングを行った。角度は動作角度計測ソフトウェア（MVP-DA2-S, MicroStone 株式会社）を使用し、モーションレコーダから得られたデータを積分し、センサー両者の差分で表した。

三次元動作解析（MA-8000, アニマ株式会社）は、両側の肩峰、C7、L7、腸骨稜，上前腸骨棘にマーカーを貼付し、250Hz でデータサンプリングを行った。

被験者には直立してもらい、１．両手で両膝を触る。２．体幹を側屈して右手で右膝を触る。３．右手で左膝を触る。という 3 つの課題を課した。その時の矢状面、前額面、水平面角度を 3 次元動作解析装置から得られた角度と比較した。この時、三次元動作解析装置から得られ

た角度を正解値とした。

統計解析にはSPSS Ver.22を用い、試行間信頼性の検討には級内相関係数を、モーションレコーダから得られた体幹角度と三次元動作解析装置から得られた角度との関連性検討にはピアソンの相関係数を用いた。有意水準は5%未満とした。

（倫理面への配慮）

本研究は畿央大学研究倫理委員会の承認（H25-35）を得て実施し、被験者への書面と口頭での説明を行った後、文書での同意を得られた被験者のデータのみを使用した。

- **看護業務中の医療事故と勤務内容の分析に関する研究**

〈対象〉病院勤務の看護師

〈方法〉看護中に発生した有害事象、アクシデント、インシデントの報告書から発生原因、勤務体制、勤務内容を分析する。またヒアリング、質問紙等にて安全性や使用感などを調査する。

C．研究結果

- **質問紙によるに関する腰痛関連動作のスクリーニング**

回答は915例であり、そのうち同意が得られた807例を解析対象とした。

1年以内に発生した腰痛の割合は64.3%（518/805）であり、そのうち3ヶ月以上継続した腰痛は25.9%（134/518）であった。とりわけ看護必要度の高い部署では、夜勤回数の多寡にかかわらず、3ヶ月以上継続した腰痛は14.3%（51/356）と低かったが、一方で3ヶ月未満の腰痛は52.8%（188/356）と高い傾向がみられた。

基本属性の各項目と１年以内の腰痛の有無との関連についてχ^2検定を行った結果、年齢が高いほど腰痛の発生割合も高くなり、統計的に有意な関連が認められた（p=0.0014）。キャリア年数についても同様の結果であった。また、勤務体制でも有意差が認められ（p=0.0131）、準夜と16時間2交代制で腰痛の発生割合が78.8%（26/33）と最も高く、夜勤のある3交代制では46.2%（24/52）と最も低かった。

移乗介助器具について、普段よく使用する器具として最も腰痛の発生割合が低かったのは、イージーモーションの60.4%（32/53）であった。また、使用者が最も多かったのはスライディングボードで、その腰痛発生割合は65.0%（371/571）であった。

看護業務と過去1年の腰痛の有無の関連について、キャリア年数で調整したオッズ比を求めた。その結果、過去1年の腰痛の有無と有意な関連を示した業務は、「体位変換」（オッズ比：1.57, 95%CI：1.15-2.14）、「ベッドから車いす等への移乗介助」（オッズ比：1.65, 95%CI：1.20-2.30）、「仰臥位から座位への介助」（オッズ比：1.79, 95%CI：1.28-2.53）、「座位から立位への介助」（オッズ比：1.61, 95%CI：1.15-2.28）であった。

介助器具の使用については、スライディングボードが部署にあるのを知っている者は696人（86.5）%と高い認知度を示し、そのうち571人（82.0%）が使用していると回答した。

一方で、スライディングシートでは、部署にあるのを知っている者は480人（59.6）%・そのうち使用は203人（42.3%）、

アームが外れる車いすは部署にあるのを知っている者は399人（49.6%）・そのうち使用は156人（39.1%）、イージーモーションでは部署にあるのを知っている者は247人（30.7%）・そのうち使用は53人（21.5%）であった。

● 腰痛の労働生産性に対する影響

労働生産性についての評価については労働生産性総合評価は急性腰痛で90.1%、慢性腰痛では91.6%と低下していた。細目では急性腰痛において時間管理(86.9%)、身体活動（74.9%）、集中力（80.8%）、仕事の結果（79.6%）であり、慢性腰痛において時間管理（85.5%）、身体活動（69.4%）、集中力（79.1%）、仕事の結果（78.4%）と慢性腰痛において低下が著しい事が明らかになった。これから損失金額を算定すると京大病院の場合、腰痛により年間29,278,080円の損失がある事がわかった。

● 運動器検診項目抽出に関する研究

対象にした87名の参加者のうち非特異的腰痛と診断された46名を対象とした。決定木分析を行い、前後屈による腰痛誘発による層別化が可能である結果が示唆された。現在はNが少ないため、決定的な結果は得られていないが今後Nを増やして確定する予定である。

● ノーリフト教育に関する研究

1．安全な患者の移動介助（ノーリフト）のための看護師教育プログラムの作成

本院看護部の協力を得て、安全な患者の移動介助のための職員教育プログラム（ノーリフト認定プログラム）レベルⅠ～Ⅲを作成した。各プログラム内容は以下の通りである。

1) レベルⅠ

患者の移動介助における、Safety Patient Handling を理解し、移動介助器具を使用した安全な患者の移動技術の習得を目的に、筋骨格系の解剖生理と腰痛機序、ノーリフトの概念及び労働安全衛生についての講義およびペーパー試験を行う。さらに移動介助器具を用いた患者の援助方法についての実技試験を行う。

2) レベルⅡ

レベルⅠを習得した者において、移動介助におけるポジショニング及び端坐位への介助技術の演習を行い、実技試験を行う。

3) レベルⅢ

レベルⅡを習得した者において、患者姿勢のアセスメントに基づくスリングの選定及びリフトを使用したベッドから車椅子への移動技術の実技演習及び実技試験を行う。

2．ノーリフト認定プログラムの実施

各プログラムについて5月・6月・8月に講習会を開催し、講義及び試験を実施し、それぞれの合格者は68名・3名・8名であった。

3．移動介助器具のニーズ調査に基づく配置

移動介助器具のニーズ調査として、6月に

「重症度、医療・看護必要度評価」を用いて、移動介助を必要とする患者を抽出するとともに、看護部署を対象としたアンケート調査を行い、移動介助器具の必要数を算出した。

算出数をもとに、リフト、特殊車椅子、移動用シート及びボード等の移動介助器具を購入し部署に配置した。

- 看護業務中の動作分析デバイスの開発に関する研究

モーションレコーダから得られた体幹角度の試行間ICC(1.1)は、0.890, p＜0.01であり、ICC(1.3)は、0.919, p ＜ 0.01であった。

センサーから得られた角度と三次元動作解析装置から得られた体幹屈伸角度はr＝0.89, p＝0.01 、側屈角度はr＝0.70, 0.028、回旋角度はr ＝ 0.72, p ＝ 0.019であった。動作中の相関係数はタスク1が最もICCが高く、タスク2、タスク3の順で下がっていった。

- 看護業務中の医療事故と勤務内容の分析に関する研究

質問紙によるスクリーニングの結果、医療事故と勤務内容に関する明確な結果は得る事はできなかった。

D．考察

質問紙によるスクリーニング調査の結果、看護動作において「体位変換」「ベッドから車いす等への移乗介助」「仰臥位から座位への介助」「座位から立位への介助」が腰痛の発症に関与する事が明らかになった。これらの動作に基づく分析を運動器検診の観点からと、バイオメカニクスの視点から解析を行った。運動器検診の結果からは前後屈に伴う疼痛誘発テストが腰痛と関連することが明らかになった。加速度センサーを用いたバイオメカニクス解析の結果からはこれらの看護動作を可視化するデバイスの開発の可能性が示され、今後精度を高くすることで腰痛関連動作の定量化が可能になる可能性がある。

腰痛による労働生産性に対する影響を検証した結果からは急性腰痛、慢性腰痛共に労働生産性の低下を惹起し、下位項目においてもさまざまな低下項目が認められた。

これらの結果をもとに、ノーリフト教育の充実、環境調整、業務内容調整を行っていく予定である。ノーリフト教育の検証作業結果から一定の成果をあげているものの、受講率の低さについては今後の検討項目である。また介助器具の適正配置に関しては今後検証を行う事で、インフラ整備の妥当性について調査を行う事は意義が深い。

看護業務と安全性に関する調査は平成27 年度も有意な結果は得られていないが、重要な項目であることから、平成28 年度も継続的に取り組んでいく予定である。

E．結論

平成２７年度には質問紙によるスクリーニング調査の結果から運動器検診抽出、バイオメカニクス研究を行う際の指標抽出に効果を認めることができた。またこの結果は教育、環境、業務調整の際の基

礎資料として有効であった。

Ｆ．健康危険情報

なし

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H．知的財産権の出願・登録状況
（予定を含む。）

1. 特許取得
該当なし

2. 実用新案登録
該当なし

3. その他
該当なし

Ⅱ．分担研究報告

労災疾病臨床研究事業費補助金
分担研究報告書

介護・看護職の腰痛予防をシームレスに実施する
新しい運動器検診システム開発に関する研究

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研究要旨：本研究は、新しい運動器検診を開発し、それをシームレスに実施するために、対象となる看護師を取り巻く事業者、管理者などのステークホルダーが情報を共有するシステム構築することを目的とする。研究同意を得られた 807 名を対象に質問紙による 1st screening を行った。1 年以内に発生した腰痛の割合は 64.3% (518/805) であった。看護必要度の高い部署では、急性腰痛は 52.8% (188/356) と高いのに対して、慢性腰痛は 14.3% (51/356) と低い傾向がみられた。逆に看護必要度の低い部署では急性腰痛は 38.0% (73/192)、慢性腰痛は 21.4% (41/192) と看護必要度の高い部署と反対の傾向を認めた。これらの結果から腰痛発生の原因は当初想定されていたものを異なる可能性が示唆されたため、腰痛発生の多い部署と少ない部署で 87 名を対象に運動器検診並びにインタビュー調査を行った。現時点では結論する事は不十分であるが、運動器検診における確度の高い項目が抽出される可能性が示された。

労働生産性は労働生産性総合評価は急性腰痛で 90.1%、慢性腰痛では 91.6%と低下していた。これにより腰痛のため年間 29,278,080 円の損失がある事が明らかになったこれらをどのようにステークホルダー間で共有するかについては今後の開発が必要である。

A．研究目的

職業性腰痛に対しては、国内外において様々な研究や取り組みがなされてきた。これまでは主にアンケートによる実態調査や産業医が有訴者の診察を行うなどであり、腰痛の原因の一つである運動機能の不全に着目した運動器健診は実施されてこなかった。

そこで本研究では、新しい運動器検診を開発し、それをシームレスに実施するシステム構築を行うため、妥当な運動器セルフアセスメント項目の抽出及び対象者を取り巻く事業者、管理者などのステークホルダーが腰痛予防の共有を行うためにアブセンティイズム、プレゼンティイズムなどの労働生産性を算定し、腰痛防止の重要性を再認識することを目的に研究を行った。

B．研究方法

運動器の検診項目については二段階の調査で調査対象を絞って行った。はじめに京都大学医学部附属病院で勤務する看護師または看護助手の1100名を対象に、腰痛に関する質問紙調査を実施した。

この調査の結果から、腰痛発生の多い病

棟と少ない病棟を抽出し、それぞれにおいて運動器測定、腰痛部位の特定、インタビュー調査を行った。

労働生産性については同質問紙調査においてWLQを用いて調査し、アブセンティイズム、プレゼンティイズムの算定を行った。

（倫理面への配慮）

本研究は京都大学大学院医学研究科・医学部及び医学部附属病院 医の倫理委員会の承認（R0131)を得て行った。質問紙調査は15分位の時間を要し、精神的、肉体的な苦痛は少ないと考えられるが、体調の悪化などに配慮して無記名、任意参加とした。

C．研究結果

平成27年度における腰痛に関する質問紙調査の参加対象者は、京都大学医学部附属病院の32部署で勤務する看護師または看護助手の 915 例であり、そのうち同意が得られた対象者は807例であった。

1年以内に発生した腰痛の割合は64.3%(518/805）であった。そのうち 3 ヶ月未満の腰痛(急性腰痛)は 52.8%（188/356）の発症頻度であった。これに対して 3 ヶ月以上継続した腰痛(慢性腰痛と定義）は25.9%（134/518）であった。病棟別に急性腰痛と慢性腰痛の発症と看護必要度（B算定)の関係を調査すると

看護必要度の高い部署では、急性腰痛は52.8%（188/356)と高いのに対して、慢性腰痛は 14.3%（51/356）と低い傾向がみられた。逆に看護必要度の低い部署では急性腰痛は 38.0%（73/192)、慢性腰痛は21.4%（41/192）と看護必要度の高い部署と反対の傾向を認めた。

これらの結果から看護度の高い部署と低い部署を選出し、運動器測定、腰痛部位の特定、インタビュー調査（87 名）を行った。この結果から決定木分析にて腰痛原因を特定できるアセスメント項目が抽出できる可能性が示唆された。現在はNが少ないため、決定的な結果は得られていないが今後 N を増やして確定する予定である。

労働生産性についての評価については労働生産性総合評価は急性腰痛で 90.1%、慢性腰痛では91.6%と低下していた。細目では急性腰痛において時間管理(86.9%)、身体活動（74.9%）、集中力（80.8%）、仕事の結果（79.6%）であり、慢性腰痛において時間管理（85.5%）、身体活動（69.4%）、集中力（79.1%）、仕事の結果（78.4%）と慢性腰痛において低下が著しい事が明らかになった。これから損失金額を算定すると京大病院の場合、腰痛により年間29,278,080円の損失がある事がわかった。

D．考察

今回の調査で明らかになった結果は看護必要度によって発症する腰痛のタイプが異なることである。すなわち看護必要度が低い部署では慢性腰痛が多く、看護必要度が高い部署では急性腰痛が多いという事実である。これは発症原因となるバイオメカニクスが異なる可能性があり、当初想定されていた発症原因と異なる可能性が示唆された。これらのことから発症原因の見直しと共に構造的な問題点も考えられることから、腰痛の発生率の高

い部署と低い部署において運動器検診を行い、インタビュー調査から再調査を行う事は必要な観点である。

　また労働生産性については低い結果が示されたが、これらの数字をステークホルダーが意識して行動変容するためには工夫が必要なことから、これらの手法についても今後開発する必要がある。

Ｅ．結論

　調査の結果、当初想定された看護動作だけが腰痛発症原因ではない可能性が示唆された。この事は従来考えられていたバイオメカニクスに基づく運動器評価だけでは不十分である可能性を有する事から、運動器評価システムを再構築する必要がある。

　腰痛により労働生産性が低下する事が示されたが、今後はその結果を如何にステークホルダーが認識し、行動変容するための方法を開発する必要がある。

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H．知的財産権の出願・登録状況（予定を含む。）

1. 特許取得

該当なし

2. 実用新案登録

該当なし

3. その他

該当なし

労災疾病臨床研究事業費補助金
分担研究年度終了報告書

介護・看護職の腰痛予防をシームレスに実施する 新しい運動器検診システム開発に関する研究

研究分担者 任　和子　京都大学大学院医学研究科人間健康科学系専攻　教授

研究要旨：新しい運動器検診を開発し、それをシームレスに実施するシステム構築を行うことを目的として、ノーリフト教育を行っている大学病院の看護職員を対象にアンケート調査を行った。805人のデータを解析した結果、1年以内の腰痛は64.3%に発生しており、年齢が高く、キャリア年数が多く、業務頻度が多いほど腰痛発生率が高かった。スライディングボードを除いては、介助器具の使用割合は低かった。運動器検診の開発と並行して、介助器具使用の障害となっている要因を明らかにしていく必要がある。

A．研究目的

腰痛対策としての安全な患者の移動・移送については、「ノーリフト」として日本の病院や介護施設に導入されている。「ノーリフト」は1996年頃からオーストラリア看護連盟が看護師の腰痛予防のために提言したもので、危険や苦痛の伴う、人力のみの移乗・移動を禁止し、患者さんの自立度を考慮した適切な器具や用具を使用することを義務付けているものである。

日本では法的規制はないものの、「ノーリフト」の概念は広がりを見せており、ノーリフトポリシーを作成し、器具等を整備している病院や施設が増えてきている。

そこで本研究では、新しい運動器検診を開発し、それをシームレスに実施するシステム構築を行うために、器具を整備しノーリフト教育を全職員に行っている大学病院における、看護業務と腰痛の関連について調査を行った。

B．研究方法

本研究では、京都市内の大規模急性期病院（看護師約1100人勤務）に勤務する看護職（看護師または看護助手）を対象に、腰痛に関するアンケート調査を実施した。

調査項目は、看護職情報（性別、年齢、キャリア年数、所属病棟）、1年以内の腰痛の有無、急性・慢性腰痛の有無、病院の受診の有無、移乗介助業務の頻度、移乗介助器具の使用の有無とした。

C．研究結果

平成27年度における腰痛に関するアンケート調査の参加対象者は、看護師または看護助手の915人であり、解析対象は805人であった。1年以内の腰痛は518人(64.3%)が経験しており、続いて急性腰痛 378人(47.0%)、慢性腰痛 134人

(16.6%)であった。また年齢が高いほど腰痛の発生割合が高かった（p=0.0014)。キャリア年数についても同様の結果であった(p<0.0001)。

看護業務と過去 1 年の腰痛の有無の関連について、キャリア年数で調整したオッズ比を求めた。その結果、過去 1 年の腰痛の有無と有意な関連を示した業務は、「体位変換」(オッズ比：1.57, 95%CI：1.15-2.14)、「ベッドから車いす等への移乗介助」（オッズ比：1.65, 95％CI：1.20-2.30)、「仰臥位から座位への介助」（オッズ比：1.79, 95%CI：1.28-2.53)、「座位から立位への介助」(オッズ比：1.61, 95%CI：1.15-2.28）であった。

介助器具の使用については、スライディングボードが部署にあるのを知っている者は 696 人（86.5%）と高い認知度を示し、そのうち 571 人（82.0%）が使用していると回答した。

一方で、スライディングシートでは、部署にあるのを知っている者は 480 人（59.6%）・そのうち使用している者は 203 人（42.3%)、アームが外れる車いすでは部署にあるのを知っている者は 399 人（49.6%)、そのうち使用している者は 156 人（39.1%)、イージーモーションでは部署にあるのを知っている者は 247 人（30.7%)、そのうち使用している者は 53 人（21.5%）であった。

D．考察

今回の対象はノーリフト教育を実施している大学病院であったが、看護師の腰痛有訴率は、これまでの報告 [1] と同程度であった。１年以内の腰痛の発生との関連を検討した結果、年齢、キャリア年数、業務頻度に有意な関連が認められた。

業務による身体的負担を軽減するためには、介助器具の使用が求められる。そこで介助器具と認知度・使用の有無について検討した。スライディングボードでは認知度も使用度も高かったものの、スライディングシート・アームが外れる車いす・イージーモーションでは、部署に装備されていても認知度は低く、あることを知っていても使用している割合は低かった。これら認知度が低く使用されていない介助器具については、利点や使用方法について研修を行うなど、何らかの対策が求められる。

E．結論

ノーリフト教育を実施している大学病院であっても看護職員の腰痛は制御できていなかった。腰痛は看護業務の頻度に関連しており、業務中の腰痛予防に使用されるべき器具の使用は不十分であった。

今後は、介助器具の使用を障害している要因を明らかにしていくことが、運動器検診の開発と、それをシームレスに実施するシステム構築を行うために重要である。

F．研究発表

1.　論文発表

該当なし

2.　学会発表

該当なし

G．知的財産権の出願・登録状況
（予定を含む。）

1. 特許取得

該当なし

2. 実用新案登録

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労災疾病臨床研究事業費補助金
分担研究報告書

介護・看護職の腰痛予防をシームレスに実施する 新しい運動器検診システムに関する研究

研究分担者 山中　寛惠 京都大学医学部附属病院看護部　副看護部長

研究要旨：本研究は、京都大学医学部附属病院において看護師の腰痛を予防するとともに患者にとっての安全な移動介助技術を推進するために、本院おけるノーリフト認定プログラムの構築及び教育の実施と、患者および看護師のニーズに基づく移動介助器具の配置を行った結果、人力のみの移動介助から患者及び職員にとって安全で安楽な移動介助のケアシステムの構築が進んだ。今後は、看護師に対する教育機会の保障、患者のニーズに対応するさらなる移動介助器具の配置及び管理などの継続的な教育と環境の整備、業務プロセスの見直し及びアウトカムの明確化が必要である。

A．研究目的

我が国では 1994 年に厚生労働省が発表した「腰痛の予防対策指針」が 2013 年に 19 年ぶりに改訂され、「福祉・医療分野等における介護・看護作業」について対策を充実させているにもかかわらず、看護・介護者の約 8 割に腰痛があるとされている。

看護・介護者の腰痛の要因として、人力のみによる患者の移動介助動作があげられており、腰痛対策における移動介助器具の導入は有効な方策である。

一方で、人力のみによる移動時の摩擦によって患者の皮膚損傷や転倒事故、移動介助を受ける際の患者の緊張、疼痛や苦痛が引き起こされることも明らかとなっている。

本研究では、京都大学医学部附属病院においてこれらのリスクを予防し、患者のアセスメントによる適切な器具を用いた安全で安楽な患者のケアシステムの構築について検討した。

B．研究方法

2015年5月より2016年3月の期間に、安全な患者の移動介助（ノーリフト）のための職員教育プログラムの作成、プログラムの実施、及びニーズ調査に基づく移動介助器具の配置を行う。

C．研究結果

1．安全な患者の移動介助（ノーリフト）のための看護師教育プログラムの作成

本院看護部の協力を得て、安全な患者の移動介助のための職員教育プログラム（ノーリフト認定プログラム）レベルⅠ～Ⅲを作成した。各プログラム内容は以下の通りである。

1） レベルⅠ

患者の移動介助における、Safety Patient Handling を理解し、移動介助器具を使用した安全な患者の移動技術の習得を目的に、筋骨格系の解剖生理と腰痛機序、ノーリフトの概念及び労働安全衛生についての講義およびペーパー試験を行う。さらに移動介助器具を用いた患者の援助

方法についての実技試験を行う。

2）　レベルⅡ

　レベルⅠを習得した者において、移動介助におけるポジショニング及び端坐位への介助技術の演習を行い、実技試験を行う。

3）　レベルⅢ

　レベルⅡを習得した者において、患者姿勢のアセスメントに基づくスリングの選定及びリフトを使用したベッドから車椅子への移動技術の実技演習及び実技試験を行う。

２．ノーリフト認定プログラムの実施

　各プログラムについて5月・6月・8月に講習会を開催し、講義及び試験を実施し、それぞれの合格者は68名・3名・8名であった。

３．移動介助器具のニーズ調査に基づく配置

　移動介助器具のニーズ調査として、6月に「重症度、医療・看護必要度評価」を用いて、移動介助を必要とする患者を抽出するとともに、看護部署を対象としたアンケート調査を行い、移動介助器具の必要数を算出した。

　算出数をもとに、リフト、特殊車椅子、移動用シート及びボード等の移動介助器具を購入し部署に配置した。

D．考察

　今年度の活動により、本院の看護師におけるノーリフト認定者は79名（7.1%）となった。また、ニーズに基づく移動介助器具の配置によって、人力のみの移動介助から患者及び看護師にとって安全で安楽な移動介助のケアシステムが構築されつつある。しかし、移動介助器具の配置については未だ不十分であり、器具の不足が使用を阻む要因の一つである。

　今後の課題として、ノーリフト認定者を増やすための教育機会の保障、患者のニーズに対応する移動介助器具の適正配置及び管理、業務プロセスの見直しおよびアウトカムの明確化が必要である。

E．結論

　看護師の腰痛予防対策として、移乗介助器具の使用は重要であるが、同時にそれは患者の安全や安楽を守る行為でもある。

　ノーリフトを推進するためには、継続的な教育と環境の整備が不可欠である。

F．研究発表

1．論文発表

　該当なし

2．学会発表

　該当なし

G．知的財産権の出願・登録状況　（予定を含む。）

1．特許取得

　該当なし

2．実用新案登録

　該当なし

3．その他

　該当なし

労災疾病臨床研究事業費補助金
分担研究報告書

介護・看護職の腰痛予防をシームレスに実施する新しい運動器検診システム開発に関する研究

研究分担者　手良向　聡　京都府立医科大学 大学院医学研究科生物統計学 教授
研究協力者　横田　勲　京都府立医科大学 大学院医学研究科生物統計学 助教
研究協力者　坂林　智美　京都府立医科大学 研究開発・質管理向上統合センター
生物統計・データマネージメント部門 特別研究補助員

研究要旨：本研究は、社会的課題となっている看護職員の腰痛に関連する業務形態・作業内容を明らかにすることを目的とする。平成 27 年度に実施した腰痛に関する質問紙調査では、病院に勤務する 807 例の看護職員を対象として集計を行った。その結果、１年以内に発生した腰痛の割合は 64.3%であり、年齢、キャリア年数、および勤務体制と有意な関連が認められた。そのうち３ヶ月以上継続した腰痛は 25.9%であった。とりわけ看護必要度の高い部署では、夜勤の回数の多寡にかかわらず、3 ヶ月以上継続した腰痛は少なかったが、一方で 3 ヶ月未満の腰痛は多い傾向がみられた。今後は、腰痛予防に対する効果や腰痛発生に対するリスクの大きさを縦断的に検証し、評価することが重要である。

A．研究目的

医療分野において、腰痛の発生に関与する要因は、患者の状態、活用できる福祉用具の状況、介助人数など多岐にわたることから、腰痛で悩む看護職員は多い。腰痛有訴者の70％近くが、「体位変換」「中腰姿勢」「移乗介助」時に腰痛を感じており、腰痛対策として、看護職員個々人で実施できる姿勢・動作の見直しだけでなく、組織としての作業管理が早急に求められている。

そこで、本研究の目的は社会的課題となっている看護職員（助手含む）の腰痛に関連する業務形態・作業内容を明らかにすることである。

B．研究方法

本研究では、京都大学医学部附属病院で勤務する看護師または看護助手の1100名を対象に、腰痛に関する質問紙調査を実施した。

調査項目は、基本属性（性別、年齢、勤務体制、夜勤の有無等）、病棟属性（残業時間、所属部署等）、腰痛予防動作（運動習慣、移動・移乗介助時の行動と意識等）、症状（腰痛の有無、抑うつ傾向）、労働生産性（WLQ）とした。

（倫理面への配慮）

本研究で使用する質問紙は大きな負担を生じるものではないが、万が一、体調の悪化等が生じたりした際には、直ちに質問紙記入を中止する。計測時間は最大

で約１５分であり、精神的・肉体的な拘束時間はわずかである。

C．研究結果

平成27年度における腰痛に関する質問紙調査の参加対象者は、京都大学医学部附属病院の32部署で勤務する看護師または看護助手の 915 例であり、そのうち同意が得られた対象者は807例であった。

1年以内に発生した腰痛の割合は64.3%（518/805）であり、そのうち 3 ヶ月以上継続した腰痛は 25.9%（134/518）であった。とりわけ看護必要度の高い部署では、夜勤回数の多寡にかかわらず、3ヶ月以上継続した腰痛は 14.3%（51/356）と低かったが、一方で3ヶ月未満の腰痛は52.8%（188/356）と高い傾向がみられた。

基本属性の各項目と１年以内の腰痛の有無との関連について χ^2 検定を行った結果、年齢が高いほど腰痛の発生割合も高くなり、統計的に有意な関連が認められた（p=0.0014）。キャリア年数についても同様の結果であった。また、勤務体制でも有意差が認められ（p=0.0131）、準夜と 16 時間 2 交代制で腰痛の発生割合が78.8%（26/33）と最も高く、夜勤のある3交代制では 46.2%（24/52）と最も低かった。

移乗介助器具について、普段よく使用する器具として最も腰痛の発生割合が低かったのは、イージーモーションの60.4%（32/53）であった。また、使用者が最も多かったのはスライディングボードで、その腰痛発生割合は 65.0%（371/571）であった。

D．考察

看護者の基本属性と１年以内の腰痛の発生との関連を検討した結果、年齢、キャリア年数、および勤務体制に有意な関連が認められた。

しかしながら腰痛の要因には、勤務形態や作業内容等の「業務システム」、不良姿勢頻度や装具制動評価等の「作業形態」、ノーリフト理解度やボディコントロール知識等の「個人要因」と様々なものが存在する。

そこで今後は、腰痛予防に対する効果や腰痛発生に対するリスクの大きさを縦断的に検証し、評価することが重要と考える。

E．結論

平成27年度の看護師または看護助手を対象とした腰痛調査において、同意が得られた 807 例のうち、１年以内の腰痛の発生割合は64.3%であった。腰痛の発生には年齢、キャリア年数、および勤務体制に有意な関連が認められた。所属部署との関連は認められなかったものの、とりわけ看護必要度の高い部署では、夜勤回数の多寡にかかわらず、3ヶ月未満の腰痛が多く、3ヶ月以上継続する腰痛は少ない傾向がみられた。

今後は、腰痛予防に対する効果や腰痛発生に対するリスクの大きさを縦断的に検証し、評価することが重要と考える。

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
（予定を含む。）
1．特許取得
該当なし
2．実用新案登録
該当なし
3．その他
該当なし

労災疾病臨床研究事業費補助金
分担研究報告書

介護・看護職の腰痛予防をシームレスに実施する
新しい運動器検診システム開発に関する研究

研究分担者　長尾　能雅　名古屋大学医学部附属病院医療の質・安全管理部　教授

研究要旨：本研究においては看護師の腰痛予防のためのアセスメントシステム（運動器、セルフ、組織）の安全性、有害事象に関する検証、倫理的問題点について検証することを目的とする。今年度行われたアセスメントシステムについてはまだ開発途上であり判定は不可能である。しかしながらそれぞれの研究については各施設の倫理委員会の審査をクリアしており、現段階では特に問題は認めない。

A．研究目的

職場での腰痛予防に関して本研究で導入される新しい運動器アセスメントおよび組織アセスメントの安全性、有害事象等について評価を行う。

B．研究方法

介入中に医療従事者に発生する有害事象、アクシデント、インシデントの報告書を作成し、医療者からの提出を求め、発生原因を分析する。また、ヒアリング、アンケート等にて安全性や使用感などを調査する。

C．研究結果

今年度は開発途上のため、調査は十分ではないことから結果は次年度以降調査予定である。使用している介助機器については特に大きな問題はない。

各研究においては倫理委員会の承認を得て実施されており、研究として実施、継続する分には問題点は認めない。

D．考察

現時点では検証材料に乏しいため、考察は困難である。しかしながら研究として実施する手法には問題はなく、継続性に問題はない。

E．結論

今年度は判定材料が乏しいため、安全性については判定困難であるが、次年度以降にシステム構築された際に判定を行う。

F．健康危険情報

該当なし

G．研究発表

1．論文発表

① 堺常雄、木村壮介、長尾能雅監修：『院内事故調査の手引き　第１版』．日本病院会学会.2015年

② 永田眞三郎編、長尾能雅：医療事故調査制度が有効に機能するための課

題.『動き出す医療事故調査制度』. 株式会社SCICUS. 2015年. 61-62ページ.

③ 長尾能雅：～緊急提言～　保険適用外診療行為・禁忌薬使用など、安全性の確認されていない医療行為を行う際の倫理的手続きのあり方.『化学療法の領域』. 第31巻8号. 2015年. 86-90ページ.

④ 長尾能雅、北野文将：医療事故調査制度の施行を迎えて.『医療の質・安全学会誌』. 第10巻4号. 2015年. 447-455ページ.

２．学会発表

① 長尾能雅：大学病院における医療事故調査の取り組みと新しい事故調査制度について. 第29回　日本医学会総会　特別企画３． 2015年4月.

② 長尾能雅：医療事故後の対応と医療事故調査制度. 第67回　日本産科婦人科学会学術講演会　指導医講習会. 2015年4月.

③ 長尾能雅：患者安全～最近の動向～. 第104回　日本病理学会総会　医療安全講習会. 2015年5月.

④ 長尾能雅：東京女子医科大学病院、千葉県がんセンター・群馬大学病院の医療事故調査を経験して. 第10回　医療の質・安全学会　シンポジウム１－１． 2015年11月.

⑤ 長尾能雅：医療事故調査制度　現場からの意見. 第28回　日本内視鏡外科学科総会　シンポジウム１． 2015年12月.

⑥ 長尾能雅：医療安全の国家長期ビジョン～医療事故死ゼロ世界へ向けて～. 第2回　日本医療安全学会シンポジウム４. 2016年3月.

H．知的財産権の出願・登録状況
（予定を含む。）

1. 特許取得
該当なし
2. 実用新案登録
該当なし
3. その他
該当なし

労災疾病臨床研究事業費補助金
分担研究年度終了報告書

介護・看護職の腰痛予防をシームレスに実施する新しい運動器検診システム開発に関する研究

研究分担者 福本貴彦 畿央大学 健康科学部理学療法学科 准教授

研究要旨
目的：廉価で場所の制約を受けない加速度計を、動作分析ツールとして運動器検診システムに採用するための妥当性評価を行うこと。
方法：加速度計を頸部（C7）と腰部（L3）に貼付して三種類の動作中の加速度と角速度を計測する。それと同時に、三次元動作解析装置による動作解析を行い、それぞれの相関を観察した。
結果：センサーから得られた角度と三次元動作解析装置から得られた体幹屈伸角度はｒ = 0.89, ｐ = 0.01 、側屈角度はｒ = 0.70, 0.028、回旋角度はｒ = 0.72, ｐ = 0.019であった。動作中の相関係数はタスク1が最も高く、タスク2、タスク3の順で低下した
考察：角速度センサーを用いて角度を計測するには積分を行う。この際には積分定数分の誤差が生じることになる。変位角度が大きくなると、この誤差は無視できるが、変位角度が小さい回旋などを捉える場合は誤差が大きくなる傾向を示した。

A．研究目的

腰痛予防のための運動器検診システム開発のためには、動作分析ツールが必要不可欠である。

主な動作分析は、客観性を持たせるために、研究室内で床反力計を同期した三次元動作解析装置を用いるが、これらは場所の制約を受け、非常に高価であるという難点がある。そこで、近年、場所の制約を受けず、廉価である加速度計が注目されている。しかし、加速度計による歩行分析も、貼付位置や歩行速度による誤差などにより、客観性のある動作（歩行）分析ツールとしての問題点が報告されている。

そこで、今回は、頸部と腰部に貼付した加速度計・角速度計によるデータと、三次元動作解析装置による動作分析との関係を観察することにより、『介護・看護職の腰痛予防をシームレスに実施する新しい運動器検診システム』の動作分析ツールとして加速度計・角速度計の使用の妥当性について、検証を行った。

B．研究方法

対象者は、健常成人12名（男性6名，女性6名）。平均年齢20.9 ± 0.8歳、身長164.0 ± 7.6 cm、体重57.1 ± 10.1 kg であった。

加速度計と角速度計は 8 チャンネル小

型無線モーションレコーダ mini（MVP-RF8-GC, MicroStone 株式会社）を用い、頸部（C7）と腰部（L3）に貼付し、1,000Hz でデータサンプリングを行った。角度は動作角度計測ソフトウェア（MVP-DA2-S, MicroStone 株式会社）を使用し、モーションレコーダから得られたデータを積分し、センサー両者の差分で表した。

三次元動作解析（MA-8000, アニマ株式会社）は、両側の肩峰、C7、L7、腸骨稜，上前腸骨棘にマーカーを貼付し、250Hz でデータサンプリングを行った。

被験者には直立指示し、１．両手で両膝を触る。２．体幹を側屈して右手で右膝を触る。３．右手で左膝を触る。という3つの課題を課した。その時の矢状面、前額面、水平面角度を3次元動作解析装置から得られた角度と比較した。この時、三次元動作解析装置から得られた角度を正解値とした。

統計解析には SPSS Ver.22 を用い、試行間信頼性の検討には級内相関係数を、モーションレコーダから得られた体幹角度と三次元動作解析装置から得られた角度との関連性検討にはピアソンの相関係数を用いた。有意水準は 5%未満とした。

（倫理面への配慮）

本研究は事前に畿央大学研究倫理委員会の承認（H25-35）を得て実施し、被験者への書面と口頭での説明を行った後、文書での同意を得られた被験者のデータのみを使用した。

Ｃ．研究結果

モーションレコーダから得られた体幹角度の試行間 ICC(1.1)は、0.890, $p < 0.01$ であり、ICC(1.3)は、0.919, $p < 0.01$ であった。

センサーから得られた角度と三次元動作解析装置から得られた体幹屈伸角度は $r = 0.89$, $p = 0.01$ 、側屈角度は $r = 0.70$, 0.028、回旋角度は $r = 0.72$, $p = 0.019$ であった。動作中の相関係数はタスク 1 が最も ICC が高く、タスク 2、タスク 3 の順で低下した。

Ｄ．健康危険情報

Ｅ．研究発表

1. 論文発表
   該当なし
2. 学会発表
   該当なし

Ｆ．知的財産権の出願・登録状況

1. 特許取得
   該当なし
2. 実用新案登録
   該当なし
3. その他
   該当なし

Ⅲ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

1．学会等における口頭・ポスター発表

発表した成果（発表題目、口頭・ポスター発表）	発表者	発表した場所（学会名等）	発表した時期	国内・外の別
医療事故後の対応と医療事故調査制度	長尾能雅	第 67 回 日本産科婦人科学会学術講演会　指導医講習会，横浜市	2015 年 4 月 9 日～ 12 日	国内
大学病院における医療事故調査の取り組みと新しい事故調査制度について	長尾能雅	第 29 回 日本医学会総会　特別企画 3，京都市	2015 年 4 月 11 日～ 13 日	国内
The influence of re-mobilization on altered cartilage induced by joint immobilization - pathological process of the cyst formation	Nagai M,Ito A, Tajino J,Zhang X,Yamaguchi S,Iijima H,Kiyan W, Aoyama T,Kuroki H.	2015 World Congress on Osteoarthritis, Seattle, WA.	2015 年 4 月 30 日～ 5 月 3 日	国外
患者安全～最近の動向～	長尾能雅	第 104 回 日本病理学会総会医療安全講習会，名古屋市	2015 年 4 月 30 日～ 5 月 2 日	国内
The effect of low intensity pulsed ultrasound treatment combined with mesenchymal stromal cell injection for cartilage regeneration in a knee osteochondral defect model of rats	Yamaguchi S, Aoyama T,Ito A,Nagai M,Iijima H,Tajino J,Zhang X, Kiyan W,Kuroki H.	2015 World Congress on Osteoarthritis, Seattle, WA.	2015 年 4 月 30 日～ 5 月 3 日	国外
Effect of initiation timing of gentle treadmill exercise on cartilage and subchondral bone in a model of destabilization of medial meniscus of rats	Iijima H,Aoyama T, Ito A,Yamaguchi S, Nagai M,Tajino J,Zhang X, Kiyan W,Kuroki H.	2015 World Congress on Osteoarthritis, Seattle, WA.	2015 年 4 月 30 日～ 5 月 3 日	国外
大学生野球選手における腰痛と自主練習内容との関連性の実態調査	田坂精志朗、廣野哲也、西口周、福谷直人、田代雄斗、堀田孝之、森野佐芳梨、城岡秀彦、野崎佑馬、平田日向子、山口萌、青山朋樹	第 50 回日本理学療法学術集会，東京都	2015 年 6 月 5 日～ 7 日	国内
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妊娠期の腰椎骨盤痛に対する骨盤アライメントおよび歩行動作の関連性	森野佐芳梨、高橋正樹、西口周、福谷直人、田代雄斗、堀田孝之、城岡秀彦、野崎佑馬、平田日向子、山口萌、赤尾静香、谷川あゆみ、松本大輔、青山朋樹	第 50 回日本理学療法学術集会 , 東京都	2015 年 6 月 5 日～ 7 日	国内
産後女性における骨盤痛と骨盤アライメントの関連性	赤尾静香、森野佐芳梨、山口萌、平田日向子、岸田智行、山口剛司、枡井健吾、松本大輔、青山朋樹、朴玲奈、梅田綾	第 50 回日本理学療法学術集会 , 東京都	2015 年 6 月 5 日～ 7 日	国内
8 週間の関節不動後の自由飼育が関節軟骨に与える影響～嚢胞様軟骨変性像の形成過程に関する報告～	長井桃子、伊藤明良、太治野純一、山口将希、飯島弘貴、張項凱、喜屋武弥、青山朋樹、黒木裕士	第 50 回日本理学療法学術集会 , 東京都	2015 年 6 月 5 日～ 7 日	国内
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変形性膝関節症患者における外側スラストの出現は安静時痛，動作時痛，日常生活動作の困難さに影響する	福谷直人、飯島弘貴、青山朋樹、山本裕子、平岡正和、宮信和幸、陳之内将志、金田瑛司、坪山直生、松田秀一	第 50 回日本理学療法学術集会 , 東京都	2015 年 6 月 5 日～ 7 日	国内
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2．学会誌・雑誌等における論文掲載

掲載した論文（発表題目）	発表者名	発表した場所（学会誌・雑誌等名）	発表した時期	国内・外の別
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長尾能雅		堺常雄，木村壮介，長尾能雅 監修	院内事故調査の手引き　第１版	日本病院会	東京都	2015 年	
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Ⅳ．研究成果の刊行物・別冊

Factors associating with shuttle walking test results in community-dwelling elderly people

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ORIGINAL ARTICLE

Factors associating with shuttle walking test results in community-dwelling elderly people

Daiki Adachi · Shu Nishiguchi · Naoto Fukutani · Hiroki Kayama · Takanori Tanigawa · Taiki Yukutake · Takayuki Hotta · Yuto Tashiro · Saori Morino · Minoru Yamada · Tomoki Aoyama

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Abstract
Background The shuttle walking test (SWT) is a simple, widely used method for assessing endurance performance in the elderly. Despite widespread community use, its associated factors are unclear.
Aims We aim to identify previously undefined SWT association factors in community-dwelling elderly people.
Methods Herein, 149 healthy elderly Japanese subjects performed the SWT, and were assessed for height, weight, smoking history, 10-m walk time, Timed Up and Go (TUG) scores, handgrip strength, skeletal mass index (SMI), forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), cardio-ankle vascular index, and ankle brachial index. We divided men and women into higher and lower SWT score groups, compared between-group parameters, and performed stepwise multivariate logistic regression analysis to identify factors independently associated with SWT scores.
Results Age, BMI, 10-m walk time, TUG score, SMI, FVC (L; %-predicted), and FEV_1 (L; %-predicted) were significantly different between SWT score groups for men, while in women, significant differences were observed in age, TUG score, handgrip strength, FVC (L; %-predicted), and FEV_1 (L; %-predicted) ($p < 0.05$). In the multivariate logistic regression model, 10-m walk time, and FEV_1 showed significant associations with SWT results in men; among women, age was the only significantly associated factor ($p < 0.05$).
Conclusions Results indicate that better lung function and shorter walk time independently associate with SWT results in community-dwelling men; in women, age is the only association. Our findings may offer insight when considering the focus of community exercise programs among the elderly.

Keywords Shuttle walking test · Endurance function · Community-dwelling elderly people · Lung function

Introduction

In our currently aging society, it has been shown that preserving higher endurance in elderly populations increases their level of physical activity [1] and prevents frailty [2], cardiovascular disease [3], and even mortality [4]. The accepted standard for endurance evaluation is the measuring of maximum oxygen consumption (VO_2 max) via treadmill. However, this requires technical equipment and the expertise of a tester, and is instituted only in laboratory or hospital settings. Thus, to preserve endurance among the community-dwelling elderly, a more straightforward and acceptable endurance assessment is required.

The incremental shuttle walking test (SWT) was developed by Singh [5] to assess the endurance of patients with chronic obstructive pulmonary disease (COPD) [5] or chronic heart failure [6, 7]. The SWT required subjects to walk back and forth along a 10-m flat course, with progressive increases in pace imposed by audio signals, until the subject was no longer able to maintain the pace [5]. The SWT can yield a physiological response similar to a treadmill test [8]. Therefore, use of the SWT is pervasive as

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a reliable endurance assessment test. The SWT can be administered in the local community; some previous studies have demonstrated its usefulness for evaluating endurance in community-dwelling people [9–11]. Moreover, to evaluate large numbers of people in varied non-laboratory settings, the SWT is a simpler and low-cost method than the treadmill test, which is regarded as the most precise endurance test for community-dwelling elderly.

In recent years, SWT results have been shown to associate with various factors such as age [10, 11], sex [11], body composition [10], gait parameter [7, 10, 12], lung function [13] and cardiovascular function [14]. However, the enrolled study subjects were of varied age, and presented with an array of health conditions ranging from healthy subjects to patients suffering from COPD or heart failure. For the community-dwelling elderly, investigating the determinants of SWT data may reveal what function physicians should focus on to increase endurance performance of this demographic. However, relatively few studies exist that aim to investigate SWT results in such an age group. Therefore, the aim of the present study was to determine the factors associated with SWT results in community-dwelling elderly people.

Materials and methods

Subjects

Elderly community-dwelling subjects were recruited through local press advertising from November 11–12, 2012. A total of 149 subjects (73 men and 76 women aged 74 ± 4 years) were enrolled upon having met the inclusion criteria (age ≥65 years, able to walk independently). Exclusion criteria were using walking aids such as a cane or walker, having a medical history (or post-operative history) of severe cardiac, musculoskeletal, or pulmonary disease, and having significant hearing impairment. Demographic data including age, body mass index (BMI), and smoking history were obtained. To assess smoking history, the pack-years index [15] was calculated for each subject by multiplying the number of cigarette packs smoked per day by the number of smoking years.

Written informed consent was obtained from each subject in accordance with the guidelines of the Kyoto University Graduate School of Medicine and the 1995 Declaration of Helsinki. This study protocol was approved by the ethics committee of the Kyoto University Graduate School of Medicine.

SWT

The SWT required subjects to walk back and forth along a 10-m flat course, with progressive increases in pace imposed by audio signals, until the subject was no longer able to maintain the pace. Up to 50 successions of the SWT were performed (500 m total walking). We divided subjects into two groups based on SWT scores: ≤40 or >41 [16].

Motor function tests

All subjects were assessed using the 10-m walk test, Timed Up and Go (TUG) test, and handgrip strength test. In the 10-m walk test, subjects walk along 10-m flat pathways at a comfortable speed [17]. In the TUG test, participants were instructed to stand up from a standard chair with a seat height of 40 cm, walk a distance of 3 m at their fastest pace, turn, walk back to the chair, and sit down. The time elapsing from the verbal command to begin the task until completion was recorded with a stopwatch [18]. The 10-m walk time and TUG scores were defined as the mean time in seconds recorded at the subjects' second trials. In the handgrip strength test, participants used a hand-held dynamometer with the arm kept to the side of the body. Participants squeezed the dynamometer with maximum isometric effort. No other body movement was allowed [19]. The handgrip test score was defined as the better performance of two trials.

Skeletal muscle mass index (SMI)

A bioelectrical impedance data acquisition system (Inbody 430; Biospace Co., Ltd., Seoul, Korea) was used to determine body composition [20]. Participants were asked to stand on two metallic electrodes and hold metallic grip electrodes while the system applied a constant current of 800 mA at 50 kHz through the body. The data acquisition system calculated the resistance value and muscle mass of the respective body parts (right arm, left arm, right leg, left leg, and trunk). Appendicular skeletal muscle mass was determined using segmental body composition and muscle mass excluding the trunk; a value for the appendicular skeletal muscle mass was determined and used for the current analysis. SMI was obtained by dividing the appendicular skeletal muscle mass by the square of height (kg/m^2). This index has been used and well documented in several epidemiological studies [21].

Lung function

All subjects underwent spirometric evaluation. Forced vital capacity (FVC), and forced expiratory volume in 1 s (FEV_1) were measured by a spirometer (Spiro Sift SP-370; Fukuda Denshi Co., Ltd., Tokyo, Japan). Next, we calculated percent predicted FVC and FEV_1, corrected for height and age. Pulmonary function tests were carried out

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according to the guidelines of the Japanese Respiratory Society [22]. The formulae for calculating percent predicted FVC and FEV_1 were derived from Japanese criteria [23]. The FEV_1/FVC ratio was also calculated.

Cardiovascular function

All subjects underwent cardio-ankle vascular index (CAVI) evaluation and ankle brachial index (ABI) evaluation, which were determined using the VaSera-1500 (Fukuda Denshi Co., Ltd., Tokyo, Japan) as previously reported [24, 25].

CAVI is a novel method for measuring arterial stiffness. Until recently, pulse wave velocity (PWV) was the most popular measure; however, PWV was dependent on blood pressure at the time of measurement. CAVI was calculated based on parameter β, independent of blood pressure [26]. Scores $\leq$9.00 were considered normal while scores >9.00 were considered indicative of suspected arteriosclerosis [27]. The ABI described the arterial occlusion with a ratio of the ankle to brachial systolic blood pressure [28]. Normal values $0.91 \leq \text{ABI} \leq 1.30$ and values $\leq$0.90 indicated suspected peripheral artery disease (PAD) [29].

When measuring CAVI and ABI, subjects were supine and had blood pressure cuffs on both of the brachia and ankles. Measurements were taken once per subject, and mean values of the right and left CAVI and ABI scores were calculated. Using these index values, we calculated the population (%) with suspected arteriosclerosis and PAD.

Statistical analyses

We analyzed the difference in each variable between men and women, and between subjects with higher and lower SWT results. We performed a Chi-squared (χ^2) test to analyze the population with suspected arteriosclerosis and PAD. Moreover, statistical tests such as *t* tests were also conducted to assess the influence of other variables.

Next, we examined factors associated with the SWT results using a stepwise multivariate logistic regression model. We assigned the high SWT results group as a dependent variable and age, BMI, SMI, 10-m walk time, handgrip strength, FVC (L), FEV_1 (L), FEV_1/FVC ratio, and suspected arteriosclerosis population as explanatory variables.

All statistical analyses were performed with SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). A $p < 0.05$ was considered statistically significant for all analyses.

Results

Measurements of the 149 subjects are summarized in Table 1. There were significant differences between men and women in the pack-years index, TUG score, handgrip strength, SMI, FVC (L), FEV_1 (L), FEV_1 (%-predicted), and suspected arteriosclerosis population ($p < 0.05$).

Forty-two men and 26 women were classified into the higher SWT results group and 31 men and 50 women were classified into the lower SWT results group. Among men, there were significant differences between higher and lower SWT results groups in age, BMI, 10-m walk time, TUG score, SMI, FVC (L), FVC (%-predicted), FEV_1 (L), and FEV_1 (%-predicted) ($p < 0.05$). In women, there were significant differences between higher and lower SWT results groups in age, TUG score, handgrip strength, FVC (L), FVC (%-predicted), FEV_1 (L), and FEV_1 (%-predicted) ($p < 0.05$).

In the multivariate logistic regression analysis, variables that remained in the final step of the regression model were considered to be significantly correlated with a higher SWT result. In men, these were 10-m walk time ($p = 0.001$), and FEV_1 ($p < 0.001$), whereas in women, age ($p < 0.001$) was the only significantly correlated variable (Table 2).

Discussion

We analyzed the association between SWT results and age, body composition, motor function, lung function, and cardiovascular function in community-dwelling elderly people. We found that younger age, higher FEV_1, and shorter 10-m walk time were associated with higher SWT results in men, and that younger age associated with higher SWT results in women. To date, there are few studies of the relationship between lung function and SWT results in community-dwelling elderly people. The results of the present study suggest that maintaining better lung function and walk speed is the key to preserving endurance in community-dwelling elderly men.

It has been previously shown that a decrease in FEV_1 increases dyspnea during exercise and results in decreased walk speed and endurance in patients with airflow limitation [13, 30, 31]. We considered that in community-dwelling elderly populations, a lower capacity for lung function would increase subjects' dyspnea during the SWT test, resulting in decreased walk speed and SWT results. According to the American College of Chest Physicians guidelines [32], it is still unclear which lung function is improved by pulmonary rehabilitation in airflow limitation patients. Moreover, there are only a few studies that report that pulmonary rehabilitation improves lung function among community-dwelling elderly people. Therefore, we consider that pulmonary exercises, such as improving thorax and respiratory muscle mobility, and employing breathing techniques, may sustain better lung function and preserve endurance performance in this demographic.

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Table 1 Comparison of demographic characteristics and measurements

	Men				Women				p value**
	All (n = 73)	Higher level SWT (n = 42)	Lower level SWT (n = 31)	p value*	All (n = 76)	Higher level SWT (n = 26)	Lower level SWT (n = 50)	p value*	
General characteristics									
Age, years (SD)†	73.7 (4.6)	72.3 (4.1)	75.6 (4.7)	0.002	73.4 (4.3)	70.2 (3.5)	75.1 (3.7)	<0.001	0.71
BMI, kg/m^2 (SD)†	23.4 (3.1)	24.1 (3.0)	22.6 (3.1)	0.048	23.3 (2.7)	22.6 (2.3)	23.7 (2.8)	0.09	0.81
Smoking-pack-years index (SD)†	29.0 (30.0)	27.2 (33.7)	29.9 (24.6)	0.81	0 (0)	0 (0)	0 (0)	–	<0.001
Motor function									
10-m walk time, s (SD)†	7.3 (1.0)	6.9 (0.7)	7.8 (1.1)	<0.001	7.3 (1.3)	6.9 (0.8)	7.5 (1.5)	0.06	0.81
TUG, s (SD)†	6.4 (1.1)	6.1 (0.9)	7.0 (1.0)	<0.001	6.9 (1.1)	6.4 (0.8)	7.2 (1.1)	0.004	0.008
Handgrip strength, kg (SD)†	33.4 (5.9)	34.4 (5.8)	32.4 (5.9)	0.09	23.0 (3.8)	24.3 (3.1)	22.3 (3.9)	0.02	<0.001
Body composition									
SMI, kg/m^2 (SD)†	7.3 (0.7)	7.5 (0.7)	7.0 (0.6)	0.01	5.8 (0.6)	6.0 (0.6)	5.7 (0.5)	0.02	<0.001
Lung function									
FVC, L (SD)†	3.2 (0.6)	3.4 (0.5)	3.0 (0.4)	<0.001	2.2 (0.5)	2.5 (0.4)	2.1 (0.5)	<0.001	<0.001
FVC, %-predicted (SD)†	96.2 (13.8)	99.1 (12.7)	92.2 (14.3)	0.03	97.6 (16.0)	104.5 (15.6)	94.0 (15.1)	0.01	0.56
FEV_1, L (SD)†	2.3 (0.6)	2.5 (0.5)	2.0 (0.5)	<0.001	1.6 (0.5)	1.9 (0.4)	1.5 (0.4)	<0.001	<0.001
FEV_1, %-predicted (SD)†	88.1 (18.4)	92.5 (17.3)	82.1 (18.4)	0.02	96.9 (21.1)	105.5 (20.2)	92.4 (20.3)	0.01	0.007
FEV_1/FVC, % (SD)†	71.0 (10.5)	72.7 (8.9)	68.8 (12.1)	0.11	72.6 (11.2)	75.5 (11.9)	71.1 (10.6)	0.10	0.39
Cardiovascular function									
Suspected arteriosclerosis, %††	72.6	71.4	74.2	0.79	48.6	34.6	56.0	0.08	0.003
Suspected PAD, %††	5.5	0	0	–	1.3	0	2.0	0.47	0.56

BMI body mass index, *TUG* Timed Up and Go, *SMI* skeletal mass index, *FVC* forced vital capacity, *FEV_1* forced expiratory volume in 1 s, *PAD* peripheral artery disease

† t test

†† χ^2 test

* Comparison between higher and lower level of SWT

** Comparison between men and women

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Table 2 Multivariate logistic regression model with stepwise selection to determine the association with shuttle walking test level

	Odds ratio	95 % CI	*p* value
Men			
10-m walk time (s)	0.24	0.11–0.54	0.001*
FEV_1 (L)	12.80	3.05–53.70	0.001*
Women			
Age	0.69	0.57–0.82	<0.001**

CI confidence interval, FEV_1 forced expiratory volume in 1 s

* $p < 0.05$

** $p < 0.001$

Further investigation, such as measuring dyspnea following the SWT, is needed to prove this hypothesis. In addition, we demonstrated an association between lung function and endurance exclusively among men. This may be attributed to the difference in smoking history between men and women in our study. As shown in Table 1, compared to women, men had a significantly higher pack-years index and significantly lower FEV_1. Smoking is one of the strongest risk factors for respiratory disease [33]. Our results in community-dwelling elderly men indicate that smoking may decrease lung function, resulting in lower SWT results. To better understand the association between lung function and endurance in community-dwelling elderly women, further research should be conducted in another population that includes women with a history of smoking.

We have shown that age associates with SWT results in women. Reports indicate that age can adversely affect a person's cardiovascular function and endurance level [34, 35]. Moreover, it is possible to separate factors that affect endurance according to utilization theory and presentation theory [36]. Utilization theory acts on the premise that endurance is determined by the oxygen (O_2)-consuming parties, while presentation theory states that it is determined by the O_2-supplying party. Saltin et al. [36] showed that endurance is more markedly affected by O_2 presentation than by utilization. In the present study, lung function, considered to be a presentation theory component, affected endurance performance more so than SMI, cardiovascular function, and motor function, which are components of the utilization theory. We also considered that our findings, with regard to age, may be associated with low cardiac function, which could potentially yield decreased SWT results. It would have been beneficial to additionally measure cardiovascular function parameters, such as stroke volume and pulse.

There are several limitations to the scope of our research. First, because this is a cross-sectional study, the causal relationship between endurance and lung function, walk speed, or age is uncertain. Moreover, the study sample did not include women with a history of smoking. As smoking history has great impact on lung function, this may be a source of sampling bias; therefore, the scope of our investigation should be extended to subjects in other communities. Another source of study limitation is that we were unable to assess other SWT-affecting factors, although these may indeed affect SWT results. In addition to cardiovascular function and dyspnea factors, previous studies have shown that step length can affect SWT or 6-min walk test results [7, 37]. Thus, further analysis should be undertaken to identify additional factors that may be of importance to endurance performance.

Conclusion

We found a significant association between lung function, walk speed, and SWT results in community-dwelling elderly men, and between age and SWT results in women. In this society, prevention for bedridden and taking care is an important issue in terms of medical economics. Elderly men with a high level of expiratory function display high endurance performance. Although this is a cross-sectional study, our results may help advise physicians of ways in which they can promote endurance performance among the elderly, through focusing and adapting community exercise programs. However, further investigation is required to assess the impact of cardiovascular function on SWT results in community-dwelling elderly populations.

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Conflict of interest None.

Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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ORIGINAL ARTICLE

The physiological characteristics of community-dwelling elderly Japanese with airflow limitation: a cross-sectional study

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Abstract
Background and aims The aim of this study was to investigate the physiological characteristics of community-dwelling elderly subjects, aged ≥65 years, with airflow limitation in the Japanese community.
Methods Subjects were recruited through local press advertisement, and 180 individuals were enrolled. Data on age, body mass index (BMI), gender, smoking history, and past medical history were obtained, as were pulmonary function parameters, skeletal muscle mass index, and physical activity.
Results The final study population comprised 161 participants from whom we obtained valid spirometry results. The mean age of this population was 73.4 ± 4.4 years, and 78 participants (48.4 %) were men. The prevalence of airflow limitation was 29.2 % ($n = 47$). Subjects with airflow limitation were significantly older ($P = 0.01$) and had poorer pulmonary function ($P < 0.01$), lower BMI ($P < 0.01$), and lower skeletal muscle mass index ($P = 0.03$) than healthy elderly subjects. Furthermore, skeletal muscle mass index was significantly correlated with the percentage of predicted forced vital capacity ($r = 0.45$, $P < 0.05$) and forced expiratory volume in 1 s ($r = 0.50$, $P < 0.05$) only in men with airflow limitation.
Conclusions We found that the skeletal muscle mass index was significantly reduced in community-dwelling elderly with airflow limitation, and the skeletal muscle mass index was correlated with pulmonary function only in men with airflow limitation.

Keywords Airflow limitation · Pulmonary function · Skeletal muscle mass index · Community-dwelling elderly · Japanese

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation [1] that is usually progressive and irreversible [2]. Today, COPD is a global health problem and is predicted to become the fifth most common cause of disability in the world by 2020 [3] and the third largest cause of death by 2030 [4]. The prognosis of COPD is strongly influenced by the severity level of the airflow limitation [5]. The Nippon COPD Epidemiology (NICE) Study reported that Japan has an estimated 5.3 million subjects with airflow limitation [6]. Of them, 5 million (95 %) remain undiagnosed within the community, and only some patients received treatment in the hospital. Therefore, early detection of subjects with airflow limitation in the community is very important.

Early detection of cases has the potential to reduce the future burden of COPD for both morbidity and mortality [7]. However, COPD is frequently diagnosed at a relatively late stage of the disease, probably because early symptoms of the disease are subtle and unrecognized due to individual perception and interpretation. Early symptoms of the

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disease may not be evident, even though spirometry reveals airflow limitation. Therefore, even if there are no subjective clinical symptoms, early detection of community-dwelling elderly subjects with airflow limitation using spirometry is a major social issue that should be tackled immediately.

To date, many previous studies focused on physiological characteristics have investigated COPD patients. It is known that COPD has a negative influence not only on respiratory function but also on the whole body, being associated with systemic inflammation, cardiovascular disease, osteoporosis, and changes in body composition such as weight loss [8]. Although many studies report on the association between body composition and exercise function in COPD patients [9, 10], skeletal muscle wasting is of particular interest in that because it directly influences exercise performance [11] and is associated with poor health-related quality of life [12]. Ju and Chen [13] demonstrated that total-body skeletal muscle mass was significantly decreased in COPD patients compared with controls. In addition, Ischaki et al. [14] demonstrated that lean total skeletal muscle mass is associated with pulmonary function. Although these effects have been well described in COPD patients, no studies have been published on such physiological characteristics related to an adverse prognosis in community-dwelling elderly Japanese, aged ≥65 years, with airflow limitation.

Therefore, the purpose of this study was to investigate physiological characteristics of community-dwelling elderly Japanese with airflow limitation aged ≥65 years.

Materials and methods

Participants

Elderly community-dwelling subjects aged ≥65 years were recruited through local press advertisement, and 180 participants were enrolled. The inclusion criteria were age ≥65 years, living in the community, and the ability to walk independently (or with a cane). The exclusion criteria were cognitive impairment, severe cardiac or musculoskeletal disorders, previously diagnosed pulmonary disease, and hearing impairment. Written informed consent was obtained from each participant in accordance with the guidelines of the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1995. This study protocol was approved by the ethical committee of the Kyoto University Graduate School of Medicine.

Measurements

Demographic data

Data on age, body mass index (BMI), gender, smoking history, and past medical history (hypertension, hyperlipidemia, diabetes mellitus, cardiovascular disease, and osteoporosis) were obtained. All subjects completed a self-reported questionnaire on smoking history and past medical history. All data were collected at study onset. Furthermore, the pack-year index was calculated for each subject by multiplying the number of cigarette packs smoked per day by the number of smoking years [15].

Pulmonary function tests

All subjects underwent spirometric evaluation. Pulmonary function tests were carried out according to the guidelines of the Japanese Respiratory Society [16]. In the recent global initiative for chronic obstructive lung disease (GOLD) guideline, all values for forced expiratory volume in 1 s (FEV_1) refer to post-bronchodilator FEV_1, but our values were obtained without a bronchodilator. Forced vital capacity (FVC), FEV_1, and peak flow were measured by spirometry (Spiro Sift SP-370; Fukuda Denshi Co., Ltd, Tokyo, Japan). After that, we calculated FVC % predicted and FEV_1 % predicted, corrected by height and age. The formulae for calculating FVC % predicted and FEV_1 % predicted were derived from the Japanese criteria [17]. Airflow limitation was defined as a ratio of FEV_1/FVC of <70 % [18]. The severity of airflow limitation was based on FEV_1 % predicted, in accordance with the GOLD criteria ($FEV_1 \geq 80$ % predicted, mild; FEV_1 50–79 % predicted, moderate; FEV_1 30–49 % predicted, severe; $FEV_1 < 30$ % predicted, very severe) [19].

Skeletal muscle mass index (SMI)

A bioelectrical impedance data acquisition system (Inbody 430; Biospace Co., Ltd, Seoul, Korea) was used to determine bioelectrical impedance. This system applies a constant current of 800 mA at 50 kHz through the body. Participants stood on 2 metallic electrodes and held metallic grip electrodes. Appendicular skeletal muscle mass was determined using segmental body composition and muscle mass, and the value for the appendicular skeletal muscle mass was determined and used for the present analysis. SMI was obtained by dividing the appendicular skeletal muscle mass by the square of height (kg/m^2) [20].

Table 1 Distribution according to the severity of airflow limitation

	Mild ($FEV_1 \geq 80$ % predicted)	Moderate ($50 \% \leq FEV_1 < 80$ % predicted)	Severe ($30 \% \leq FEV_1 < 50$ % predicted)	Very severe ($FEV_1 < 30$ % predicted)	Total
Gender					
Overall	15 (31.9)	29 (61.7)	3 (6.4)	0 (0.0)	47
Male	3 (12.0)	20 (80.0)	2 (8.0)	0 (0.0)	25
Female	12 (54.5)	9 (40.9)	1 (4.6)	0 (0.0)	22

Values are shown as *n* (%); *FEV_1* forced expiratory volume in 1 s

Physical activity

We distributed pedometers and note paper to participants for recording physical activity. Participants were asked to wear the pedometer in the pocket of their dominant leg for 14 consecutive days except when bathing, sleeping, and performing water-based activities. The pedometers had 30-day data storage capacity. The reproducibility and validity of the pedometers in counting walking steps have been previously established in healthy people [21]. The pedometers and note papers were sent to our laboratory by mail after 2 weeks. We calculated averages of daily step counts for 2 weeks.

Statistical analyses

The participants were divided into two groups: those with airflow limitation and those who were healthy. We statistically analyzed the differences between the 2 groups using the unpaired *t* test for age, pulmonary function, body composition, and physical activity, and the χ^2 test for gender, smoking history, and past medical history. The correlation between SMI and pulmonary function was analyzed using Pearson's correlation analysis. Additionally, partial correlation analysis controlling for the variable of age was carried out subsequently to assess the influence of age on SMI and pulmonary function. All statistical analyses were performed with SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at $P < 0.05$ for all analyses.

Results

Prevalence of airflow limitation

Of 180 initially selected community-dwelling elderly Japanese aged ≥65 years, 19 were excluded owing to invalid spirometry results. Thus, the study population comprised 161 community-dwelling elderly. The mean age of this population was 73.4 ± 4.4 years, and 78 (48.4 %) participants were men. Undiagnosed Airflow limitation existed in 29.2 % ($n = 47$) of the study population. According to the GOLD stage classification, 31.9 % ($n = 15$) of participants were classified as mild, 61.7 % ($n = 29$) as moderate, and 6.4 % ($n = 3$) as severe; no participants were classified as very severe (Table 1). Regarding smoking history, the smoking rate was 39.8 % ($n = 64$) in the entire population and 34.0 % ($n = 16$) in airflow limitation subjects.

Comparison of characteristics between airflow limitation subjects and healthy older subjects

Demographic characteristics for the airflow limitation subjects and healthy elderly subjects are shown in Table 2. Subjects with airflow limitation were older ($P = 0.01$) and had poorer pulmonary function (FVC % predicted, $P = 0.03$; FEV_1, FEV_1 % predicted, FEV_1/FVC, and peak flow, $P < 0.01$) and lower BMI ($P < 0.01$) than healthy elderly subjects. In addition, the SMI of those with airflow limitation was 6.3 ± 0.9 kg/m^2, whereas that of healthy elderly subjects was 6.6 ± 1.0 kg/m^2; this difference was statistically significant (Fig. 1, $P = 0.03$). Furthermore, physical activity of those with airflow limitation was 6,601 ± 2,650 steps/day, whereas that of healthy elderly subjects was 7,553 ± 3,237 steps/day; although the difference in physical activity was not significant, it tended to be lower in those with airflow limitation.

Correlation between SMI and pulmonary function

SMI was significantly positively correlated with FVC % predicted ($r = 0.45$, $P < 0.05$) and FEV_1 % predicted ($r = 0.50$, $P < 0.05$) in men with airflow limitation, but no correlation was found in women with airflow limitation. This significant correlation in men with airflow limitation was apparent after controlling for age using partial correlation analysis (FVC % predicted, $r = 0.48$; FEV_1 % predicted, $r = 0.48$). By contrast, there was no correlation between SMI and pulmonary function in healthy elderly subjects, as shown in Table 3.

Discussion

This cross-sectional study provides two new findings. First, compared with healthy elderly subjects, SMI was

Table 2 Comparison of demographic characteristics and measurements between airflow limitation subjects and healthy elderly subjects

	Airflow limitation subjects ($n = 47$)	Healthy elderly subjects ($n = 114$)	P value
Age (year)	74.8 ± 4.3	72.9 ± 4.3	0.01[b]
Gender[a]			0.45
Male	25 (53.2 %)	53 (46.5 %)	
Female	22 (46.8 %)	61 (53.5 %)	
Pack-year index[a]			0.87
0–24	35 (74.5 %)	83 (72.8 %)	
25–49	7 (14.9 %)	16 (14.0 %)	
50+	5 (10.6 %)	15 (13.2 %)	
Pulmonary function			
FVC(L)	2.6 ± 0.7	2.8 ± 0.7	0.82
FVC % predicted	97.4 ± 20.2	104.5 ± 17.7	0.03[b]
FEV_1 (L)	1.5 ± 0.4	2.2 ± 0.5	<0.01[c]
FEV_1 % predicted	71.4 ± 17.1	103.1 ± 18.9	<0.01[c]
FEV_1/FVC (%)	57.9 ± 10.2	77.9 ± 5.0	<0.01[c]
Peak flow (L)	2.3 ± 1.5	4.6 ± 2.0	<0.01[c]
Body composition			
BMI (kg/m^2)	21.8 ± 2.9	23.7 ± 2.8	<0.01[c]
SMI (kg/m^2)	6.3 ± 0.9	6.6 ± 1.0	0.03[b]
Physical activity			
Steps/day	6601 ± 2650	7553 ± 3237	0.08
Complication[a]			
Hypertension	15 (31.9 %)	47 (42.0 %)	0.16
Hyperlipidemia	4 (8.5 %)	19 (17.0 %)	0.13
Diabetes	6 (12.8 %)	13 (11.6 %)	0.91
Cardiac disorder	5 (10.6 %)	9 (8.0 %)	0.76
Osteoporosis	8 (17.0 %)	6 (5.4 %)	0.03[b]

Data are shown as n (%) or mean ± standard deviation; Pack-year index was calculated for each subject by multiplying the number of cigarette packs smoked per day by the number of smoking years

BMI body mass index, *FEV_1* forced expiratory volume in 1 s, *FEV_1 % predicted* FEV_1 as percentage of predicted, *FVC* forced vital capacity, *FVC % predicted* FVC as percentage of predicted, *SMI* skeletal muscle mass index

[a] χ^2 test

[b] $P < 0.05$

[c] $P < 0.01$

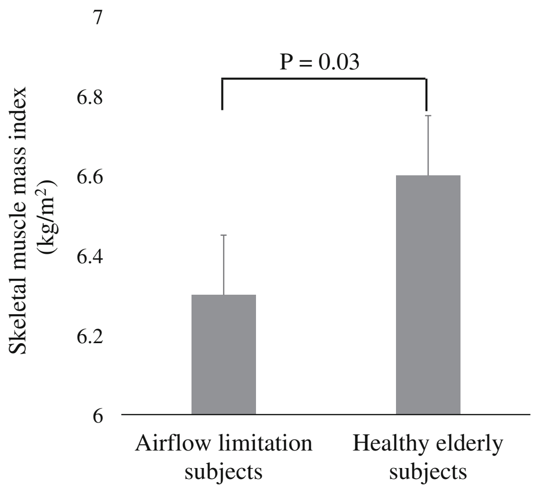

Fig. 1 The difference [mean ± standard error (SE)] in skeletal muscle mass index between airflow limitation subjects and healthy elderly subjects. Airflow limitation was defined as a ratio of forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) of <70 %

Table 3 Single and partial correlation between skeletal muscle mass index and pulmonary function

	Skeletal muscle mass index		Skeletal muscle mass index (controlling for age)	
	Men	Women	Men	Women
Airflow limitation subjects				
FVC % predicted	0.45[a]	−0.25	0.48[a]	−0.31
FEV_1 % predicted	0.50[a]	−0.11	0.48[a]	−0.19
Healthy elderly subjects				
FVC % predicted	0.16	0.10	0.16	−0.05
FEV_1 % predicted	0.23	0.15	0.23	0.05

FVC % predicted forced vital capacity as percentage of predicted, *FEV_1% predicted*, forced expiratory volume in 1 s as percentage of predicted

[a] Correlation is significant at the 0.05 level

significantly decreased in those with airflow limitation. Second, SMI was significantly correlated with pulmonary function in men with airflow limitation.

Airflow limitation was found in 29.2 % of our participants. Previous epidemiological studies for 40 years or more in Japan have reported the prevalence of airflow limitation to be approximately 10 % [6, 22]. However, Akamatsu et al. [23] reported that the prevalence of airflow limitation exceeded 15 % in elderly subjects aged 60–69 years and 28 % in those aged >70 years. The difference in prevalence means that the prevalence of airflow limitation increases with aging, and the association between aging and prevalence of airflow limitation has been reported by a previous study [24]. Therefore, our results for subjects aged ≥65 years (mean age was 73.4 ± 4.4 years) are in accordance with the results of a previous study [23], and we believe that our study did not overestimate or underestimate the spirometry measurements. However, a limitation of the process is that the participants might not yield the real picture of airflow limitation, because we excluded subjects with cognitive impairment. Previous study reported that cognitive impairment has been associated with poor pulmonary function [25]. However, we excluded patients with cognitive impairment as they were unable to perform accurately a spirometry measurement because a previous study reported that reproducibility of spirometric measurements was definitely poor in subjects with cognitive impairment [26].

To the best of our knowledge, this is the first study to indicate a reduction in skeletal muscle mass in community-dwelling subjects with airflow limitation. The mechanisms of skeletal muscle wasting are not precisely understood; however, inactivity [27] and systemic inflammation [28] are considered to be major factors in skeletal muscle wasting. We found that the difference in physical activity was not significant compared with healthy elderly subjects, but it tended to be lower in subjects with airflow limitation. Pitta et al. [29] reported that daily physical activity values in COPD patients were significantly lower than those in healthy controls. This previous study targeted patients with mild to very severe COPD, but because we targeted airflow limitation subjects with few symptoms and no consultation history in the community, the possibility that there are no significant differences in physical activity in comparison with healthy older subjects is high. However, the trend of reduced physical activity in subjects with airflow limitation is consistent with the results of a previous study in COPD patients [29]. Therefore, there is a possibility that the decrease in physical activity is associated with skeletal muscle wasting. On the other hand, pulmonary function disorders are often associated with a systemic inflammatory state [30]. Although age [31], gender [32], and smoking history [33] have been reported to accelerate systemic inflammation, we found a significant difference only for age between airflow limitation subjects and healthy elderly subjects. Therefore, the reduction in SMI in subjects with airflow limitation may be dependent on systemic inflammation related to older age.

The present study found a significant correlation between SMI and pulmonary function in men with airflow limitation after controlling for age using partial correlation analysis. This relationship might be a consequence of the high resting energy expenditure due to the increased work of breathing [34], inadequate dietary intake, physical inactivity [35], and excessive apoptosis of skeletal muscle due to increased systemic inflammation [36]. However, with the exception of physical activity, our data do not support these hypotheses. To our knowledge, we believe that the recognized gender differences are a reflection of systemic inflammation. Previous studies reported in cross-sectional and longitudinal analyses that systemic inflammation is negatively correlated with both FEV_1 and FVC in men but not in women [32, 37, 38]. That is, it is possible that systemic inflammation contributed to both skeletal muscle wasting and poor pulmonary function in men with airflow limitation. Because the prognosis for elderly people with decreased skeletal muscle mass and pulmonary function is generally adverse, it is important to detect airflow limitation at an early stage in the community.

There are several limitations that warrant mention in this study. First, because the participants were recruited through local press advertisements, there may be a selection bias. The participants may have been highly health conscious; on the other hand, the subjects with health problems might not participate in this study. Second, self-reported questionnaires may not always provide precise data due to recall bias. Third, because we performed only a simple pulmonary function test to detect airflow limitation in the community-dwelling elderly in our study, we were not able to examine pulmonary function in detail. Fourth, because this study was cross-sectional, a cause–effect relationship between SMI and pulmonary function remains unknown. Further investigations, including prospective studies, are required to confirm our discussion.

Conclusions

To the best of our knowledge, this is the first study to investigate the physiological characteristics of community-dwelling elderly Japanese with airflow limitation aged $\geq$65 years. We found a significant reduction in SMI in subjects with airflow limitation compared with healthy elderly subjects. Furthermore, we found a significant correlation between SMI and pulmonary function in men with airflow limitation, but not in women. Additional studies are needed for the early detection of subjects with airflow limitation and to determine the characteristics of community-dwelling elderly Japanese, aged $\geq$65 years, with airflow limitation.

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Conflict of interest None of the authors have conflicts of interest or financial disclosures.

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ORIGINAL ARTICLE

Rehabilitation Program After Mesenchymal Stromal Cell Transplantation Augmented by Vascularized Bone Grafts for Idiopathic Osteonecrosis of the Femoral Head: A Preliminary Study

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Abstract

Objective: To determine the feasibility and safety of implementing a 12-week rehabilitation program after mesenchymal stromal cell (MSC) transplantation augmented by vascularized bone grafting for idiopathic osteonecrosis (ION) of the femoral head.

Design: A prospective case series.

Setting: University clinical research laboratory.

Participants: Participants (N=10) with ION who received MSC transplantation augmented by vascularized bone grafting.

Intervention: A 12-week exercise program, which included range-of-motion (ROM) exercises, muscle-strengthening exercises, and aerobic training.

Main Outcome Measures: Measures of ROM, muscle strength, Timed Up and Go test, and Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) were collected before surgery and again at 6 and 12 months after surgery.

Results: All participants completed the 12-week program. External rotation ROM as well as extensor and abductor muscle strength significantly improved 6 months after treatment compared with that before treatment ($P<.05$). Significant improvements were also seen in physical function, role physical, and bodily pain subgroup scores of the SF-36 ($P<.05$). No serious adverse events occurred.

Conclusions: This study demonstrates the feasibility and safety of a multiplex rehabilitation program after MSC transplantation and provides support for further study on the benefits of rehabilitation programs in regenerative medicine.

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Idiopathic osteonecrosis (ION) of the femoral head is a painful disorder that progresses to femoral head collapse and osteoarthritis of the hip joint.[1,2] This disease mainly affects individuals aged 30 to 40 years.[3] The exact pathologic mechanism of ION remains unknown; however, obstruction of blood flow to the femoral head, which causes death of bone-forming cells, is a hallmark of this condition. Without bone-forming cells, bone tissue gradually loses

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its mechanical properties and eventually collapses, causing articular surface deformities.[1-3]

Recently, surgical treatment has become more common than nonsurgical treatment for ION in the United States.[4] Conservative treatment to offload forces by limiting weight-bearing, activity modification, and physical therapy is thought to have limited success in preventing disease progression.[3,4] If the disease progresses, the patient eventually requires total hip arthroplasty (THA).[1-3] Although the survival rate of THA has improved markedly, individuals with ION are typically young, and THA durability is limited; therefore, joint-preserving treatment is preferred. However, recent data indicate that joint-preserving procedures are performed less often than THA.[3]

Regenerative medicine using cell transplantation is a promising treatment for patients with refractory disease. Mesenchymal stromal cell (MSC) transplantation, for example, is a promising new treatment for joint preservation in ION. MSCs can differentiate into cells of osteogenic, chondrogenic, and adipogenic lineages in vitro.[5-7] During early-stage ION, treatment with MSCs in combination with core decompression surgery has resulted in significant delay and even prevention of femoral head collapse.[8-12] However, in more advanced stages, the result of this procedure has not been satisfactory.[12-14] Because bone marrow pressure is elevated in the early stage of ION,[15] core decompression to reduce the pressure is required. However, in advanced-stage disease, when subchondral bone fractures occur, initial strengthening, instead of decompression, is needed to prevent collapse.[16]

We designed a protocol using a combination of MSCs and vascularized bone grafts for treating advanced stages of ION.[17] Because ION is caused by loss of blood supply and bone-forming cells as well as mechanical vulnerability, vascularized bone grafting is, theoretically, a reasonable treatment for this condition.[16,17] Although MSC transplantation is a promising therapeutic strategy, rehabilitation interventions after surgery may have a significant effect on the ultimate treatment result. However, detailed information about rehabilitation programs after cell transplantation has not yet been reported.[8-14] Moreover, the effect of rehabilitation alone on ION is controversial.[18,19] This study aimed to determine the feasibility and safety of a rehabilitation program that was performed in a clinical trial of MSC transplantation augmented by vascularized bone grafting for ION.

Methods

The current study was a prospective case series of subjects enrolled in a clinical trial. Details of this prospective, open-labeled, proof-of-concept clinical trial, conducted at Kyoto University Hospital, have been previously reported.[17] The study protocol was approved by the Ethics Committee of Kyoto University Graduate School and Faculty of Medicine and was conducted according to the Declaration of Helsinki. For this clinical trial, participants were recruited via the website page of Kyoto University Hospital and the University Hospital Medical Information Network (UMIN) Clinical Trials Registry.

List of abbreviations:

ION	**idiopathic osteonecrosis**
MSC	**mesenchymal stromal cell**
RM	**repetition maximum**
ROM	**range of motion**
SDIC	**Specific Disease Investigation Committee**
SF-36	**Medical Outcomes Study 36-Item Short-Form Health Survey**
THA	**total hip arthroplasty**

Assessment of necrotic lesion and radiographic stage

Necrotic lesion type and size were assessed using the radiographic classification proposed by the Specific Disease Investigation Committee (SDIC) in Japan (appendix 1).[20] Staging of ION proposed by the SDIC in Japan is a modified version of the system proposed by the Association Research Circulation Osseous Committee.[20]

Inclusion criteria

Patients aged 20 to 50 years with radiographic stage 3A or 3B, according to SDIC staging,[20] were eligible for enrollment. Written informed consent was obtained from all participants in the clinical trial.

Exclusion criteria

Exclusion criteria were a history of transplantation on the affected part of the hip, heavy smoking (Brinkman index >600), current use of warfarin, diabetes mellitus (defined as hemoglobin A1c >9.0%), arteriosclerosis obliterans, pregnancy, malignant disease, myocardial infarction, brain infarction, rheumatoid arthritis, dialysis use, hematologic disease (leukemia, myeloproliferative disorder, myelodysplastic disorder), limited life expectancy, hepatitis B, hepatitis C, human immunodeficiency virus infection, syphilis, hypotension (systolic blood pressure <90mmHg), low body weight (<40kg), loss of marrow function (neutrophil count <1500/mm^3, hemoglobin level <11.0g/dL [men] or <10.0g/dL [women], platelet count <100,000/mm^3), change in medication (bisphosphonates or steroids) within 3 months of the study, and ineligibility determined by a doctor.

MSC transplantation augmented by vascularized bone grafting

Under general anesthesia, 100mL of bone marrow was obtained from the posterior iliac crest. Mononuclear cells containing MSCs were cultured for approximately 2 weeks under 20% partial pressure of oxygen (PO_2) and 5% partial pressure of carbon dioxide (PCO_2) conditions at 37°C.

MSC transplantation was augmented by vascularized bone grafting. Briefly, participants were placed on the table in the supine position. A curved skin incision (modified Smith-Peterson approach) was made from the iliac crest to the anterior aspect of the proximal thigh.[17] The rectus femoris was released, and the anterior aspect of the femoral neck was explored. Then, a cortical window (1.5×4cm) was prepared, through which a bony trough connecting the necrotic area was created under both fluoroscopic and endoscopic guidance. MSCs ($0.5-1.5\times10^8$) premixed with β-tricalcium phosphate granules (Osferion[a]) were transplanted into the cavity created by curettage. Tricortical iliac crest bone was harvested with a vascular pedicle and grafted into the bone trough.[16] Then, the joint capsule and rectus femoris were sutured.

Rehabilitation program

Rehabilitation was performed at a hospital for 12 weeks. During the initial 4 weeks, rehabilitation was performed at an acute care hospital (table 1). Participants continued rehabilitation at a special rehabilitation hospital for 8 additional weeks. During the first 4 weeks,

Table 1 Rehabilitation program

Time Course After Treatment	Side	Day 1	Day 3	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 8	Week 10	Week 12	Discharge
Rest level		Bed rest		Wheelchair	Walk on crutch	→					→	Walk on T-cane	
Weight-bearing		NWB	→					→	1/3 WB	1/2 WB	2/3 WB	FWB	
ROM exercise	Transplant				Passive F, E →								→
						Passive Ab →							→
									Passive R →				→
												Active F, E, Ab, R	
	Nontransplant		Passive & active F, E, Ab, R →										→
Muscle strength exercise	Transplant								Isotonic (Straight leg raising, no weight) →				→
											Isotonic (Straight leg raising, 2-kg weight)		
									Isokinetic F, E →				→
										Isokinetic Ad →			→
											Isokinetic R →		→
												Isokinetic Ab Squat & heel raise	
	Nontransplant		Isometric F, E, Ab, R		→								→
												Isokinetic F, E, Ab, R	
									Squat & heel raise	→			→
				Muscle strength exercise of upper limb →									→
Aerobic training											Aerobike →		→

Abbreviations: Ab, abduction; Ad, adduction; E, extension; F, flexion; FWB, full weight-bearing; NWB, non—weight-bearing; R, rotation; WB, weight-bearing.

physical therapy was performed for 40 minutes at a time, once a day, 5 days a week. After the initial 4 weeks, it was performed for 60 minutes at a time, twice a day, 6 days a week. The entire rehabilitation program was supervised by skilled physiotherapists, and the specific therapy received was recorded in the participant's medical record.

Participants were kept non−weight-bearing for 6 weeks after transplantation surgery, followed by one-third weight-bearing, one-half weight-bearing, and two-thirds weight-bearing, progressing at 2-week intervals (see table 1). Full weight-bearing was permitted 12 weeks after treatment.

Before performing range-of-motion (ROM) exercises, pain level was assessed using a numeric rating scale. Passive flexion and extension ROM exercises were initiated 2 weeks after treatment on the transplant side. Passive adduction was initiated 3 weeks after treatment, and passive rotation ROM exercise was initiated 6 weeks after treatment. Active ROM exercise in all directions was initiated 12 weeks after treatment (see table 1). Passive and active ROM exercises in all directions were initiated 3 days after treatment on the nontransplant side (see table 1).

For isotonic flexion muscle-strengthening exercise, straight leg raising with no weight was started 6 weeks after treatment on the transplant side (see table 1). Straight leg raising with 2-kg weight was started after 10 weeks. The intensity of exercise was defined by pain level. Each position was held for 5 seconds and performed 5 times. For isokinetic flexion and extension muscle-strengthening exercises, resistance training was started 6 weeks after treatment on the transplant side. The intensity of exercise was increased by increasing the load by 40% to 80% of 10-repetition maximum (RM). Isokinetic adduction exercise was added at 8 weeks, rotation exercise at 10 weeks, and adduction exercise at 12 weeks after treatment. Isokinetic rotation exercise was performed using Coxa Link.[b] Squat and heel raise exercises were performed 12 weeks after treatment. On the nontransplant side, isometric and isokinetic exercises were started 3 days after treatment. If muscle weakness was present, the intensity of exercise was increased by increasing the load by 70% to 100% of 10RM for muscular hypertrophy. If muscle weakness was not present, exercise loading was increased by 60% to 70% of 15RM for muscular endurance. Nontransplant side squat and heel raise exercises were started 6 weeks after treatment. Upper limb muscle-strengthening exercises were performed using Shoulder Link[b] 1 week after treatment (see table 1).

Aerobic training was started 8 weeks after treatment. The intensity of exercise was defined as a target heart rate of 220×(age×0.6) by using an Aerobike Ai[c] for 30 minutes. After discharge, participants continued home exercises and were assessed once a month. Patients were allowed to resume sports and work 6 months after confirmation of bone ossification (see table 1).

Assessment

All participants underwent assessment before treatment and 6 and 12 months after treatment. Passive hip flexion, extension, abduction, and external rotation angles were measured using universal goniometry. Hip flexor, extensor, and abductor strengths were measured using a handheld dynamometer[d] during isometric contraction for 3 seconds with manual resistance. Knee extensor and flexor strengths and lower limb load were assessed using the Iso Force GT-330.[e] Torque was expressed as a percentage of body weight (Nm/kg). Values of lower limb load force were normalized to body weight (N/kg). In the Timed Up and Go test, the time (in seconds) that a participant required to stand from an armless chair (chair seat height, 45cm), walk a distance of 3m, turn, walk back to the chair, and sit down was measured. Health-related quality of life was evaluated using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36).[21]

Adverse events

Compliance with the rehabilitation program and adverse events were recorded in each participant's medical record. Adverse events were monitored by the Department of Clinical Trial Design and Management Translational Research Center. Serious adverse events were assessed by the External Data Monitoring Committee.

Statistical analysis

ROM, muscle strength, and SF-36 score were presented as the median with 25% to 75% quartiles. For follow-up assessment of changes in each outcome over time, the Friedman test was used to identify overall significant differences at 3 different time points (before treatment and 6 and 12mo after treatment) for each variable. Post hoc Scheffe test was used to assess which time points showed significant differences. A P value of $<.05$ was considered statistically significant for all analyses.

Results

Between November 2007 and June 2009, 10 participants were recruited into the clinical trial. All participants were men with an average age of 31.7 years (range, 20−48y). A history of steroid treatment was found in 4 participants (table 2). The pretreatment radiographic stage was 3A in 6 hips and stage 3B in 4 hips (see table 2). During the rehabilitation period (6mo after surgery), there was no progression of disease. At 1 year after surgery, 6 hips with stage 3A and 2 hips with stage 3B did not progress, but 2 hips with stage 3B (cases 3 and 7) progressed to stage 4.[17]

Hip ROM

While nearly all ROM measures improved after treatment, the only significant improvements were transplant-side external rotation at 6 months ($P<.05$) and nontransplant-side flexion at 12 months ($P<.01$) (table 3).

Muscle strength and function

While nearly all muscle strength measures improved after treatment, the only significant improvements were transplant-side extensor and abductor strength at 12 months after treatment ($P<.05$) (table 4).

On the nontransplant side, there was significant improvement in lower limb load strength ($P<.05$) (see table 4). The remaining subgroup scores showed posttreatment improvements that did not reach statistical significance.

SF-36 subgroup score

There were significant improvements in physical function, role physical, and bodily pain subgroup scores between the 3 time points (before treatment and 6 and 12mo after treatment) ($P<.05$) (table 5). There was also a significant difference in each score between values before and 12 months after treatment ($P<.05$).

Table 2 Baseline data of patients

Case	Age (y)	Sex	Height (cm)	Weight (kg)	Affected Side	Steroid Use	Class*	Stage†	History
1	27	M	170.9	66.5	R	Y	C2	3B	Nephritis
2	23	M	171.0	56.6	L	Y	C2	3A	Cushing syndrome
3	48	M	174.7	87.5	R	N	C2	3B	Meningioma
4	20	M	174.2	76.8	R	Y	C1	3A	Hepatitis
5	35	M	178.8	70.0	L	N	C2	3A	None
6	28	M	169.2	58.3	R	N	C2	3A	None
7	39	M	183.1	85.2	R	Y	C2	3B	Leukemia
8	26	M	175.1	66.4	R	N	C2	3B	None
9	33	M	174.2	61.0	R	N	C2	3A	None
10	38	M	166.7	52.9	R	N	C2	3A	None

Abbreviations: L, left; M, male; N, no; R, right; Y, yes.
* Radiographic clinical classification proposed by Japanese Investigation Committee.
† Radiographic staging score by Japanese Investigation Committee.

Adverse events

All participants completed the 12-week rehabilitation program. There were 5 cases of muscle pain, 2 cases of muscle stiffness, and 1 case of ankle pain on initiation of load bearing, but no serious adverse events were associated with rehabilitation. Radiography showed no evidence of progression in femoral head collapse during the rehabilitation period.

Discussion

In the current study, we designed a rehabilitation program that focused on 3 aspects: (1) improving hip joint function, (2) avoiding collapse of the femoral head, and (3) promoting bone formation from transplanted cells by using a physical therapy protocol.

In the field of rehabilitation, the relationship between pursuing functional improvement and risk reduction becomes a trade-off in some cases, but compatibility between them is important. To accomplish this trade-off, it is helpful to simultaneously assess the etiologic factors and radiologic findings of these patients in order to treat ION.[22,23] Further, lesion size, lesion location, and radiographic staging can help determine the natural course of ION.[22] In our patients, necrotic lesion size was broad, and radiographic stage had progressed (see table 2). The prognosis for steroid-induced ION is better than that for ION associated with sickle cell anemia.[22] In our study, among the 10 participants, 4 had a history of steroid use, while the other 6 had idiopathic ION (see table 2). The rehabilitation program in patients with ION should consider these aspects and should be planned carefully to avoid collapse of the femoral head.

Weight-bearing was prohibited until 6 weeks after treatment (see table 1), and full-weight sitting-to-standing actions were prohibited until 12 weeks after treatment because of the high pressure placed on the top of the femoral head.[24-26] Not only weight-bearing, but also muscle activity increases the acetabular contact pressure. Isometric hip extension and active hip flexion generate high pressure on the femoral head, equal to weight-bearing and walking.[25,26] By comparison, the pressure generated by isotonic and isokinetic exercises is much less.[25,26] Such joint-

Table 3 Comparison of hip ROM between pretreatment, 6 months after treatment, and 12 months after treatment (N=10)

Hip ROM	Pretreatment	6mo After Treatment	Effect Size (Pre/6mo)	12mo After Treatment	Effect Size (Pre/12mo)	*P* at 3 Time Points (Pre/6mo/12mo)
Flexion (deg)						
Transplant side	97.5 (95.0–107.5)	107.5 (96.3–110.0)	.58	107.5 (100–113.8)	.74	.19
Nontransplant side	101.0 (100.0–110.0)	112.5 (100.0–113.8)	.31	112.5 (101.3–120.0)*	.47	<.01
Extension (deg)						
Transplant side	20.0 (15.0–20.0)	20 (16.3–20.0)	.12	15.0 (15.0–18.8)	.47	.34
Nontransplant side	20.0 (16.3–20.0)	20.0 (15.0–20.0)	.01	17.5 (15.0–20.0)	0	.92
Abduction (deg)						
Transplant side	30.0 (21.3–35.0)	35.0 (30.0–40.0)	.52	35.0 (30.0–38.8)	.38	.24
Nontransplant side	35.0 (31.3–38.8)	37.5 (31.3–40.0)	.23	35.0 (35.0–35.0)	.11	.53
External rotation (deg)						
Transplant side	45.0 (37.5–53.8)	50.0 (41.3–60.0)†	.43	50.0 (42.5–53.8)	.31	.09
Nontransplant side	40.0 (37.5–53.8)	50.0 (45.0–60.0)	.46	50.0 (45.0–60.0)	.42	.38

NOTE. Values are median (25%–75% quartiles) or as otherwise indicated. *P* values at 3 time points were calculated by Friedman test. Multiple comparison test was performed by Scheffe test.
* $P<.01$.
† $P<.05$ as calculated by comparison with pretreatment.

Table 4 Comparison of physical function between pretreatment, 6 months after treatment, and 12 months after treatment (N=10)

Measure	Pretreatment	6mo After Treatment	Effect Size (Pre/6mo)	12mo After Treatment	Effect Size (Pre/12mo)	*P* at 3 Time Points (Pre/6mo/12mo)
Hip flexor strength (Nm/kg)						
Transplant side	1.39 (1.01–1.65)	1.49 (1.35–1.86)	0.74	1.79 (1.58–1.91)	0.70	.12
Nontransplant side	1.30 (1.05–1.50)	1.82 (1.38–1.96)	1.14	1.73 (1.68–2.03)	1.12	.08
Hip extensor strength (Nm/kg)						
Transplant side	0.56 (0.43–0.78)	1.48 (0.84–1.56)	0.98	1.28 (0.86–1.69)*	1.00	<.05
Nontransplant side	0.64 (0.37–0.80)	1.13 (0.82–1.49)	1.18	1.61 (0.96–1.77)	1.62	.08
Hip abductor strength (Nm/kg)						
Transplant side	0.67 (0.51–1.29)	1.20 (0.81–1.43)	0.58	1.28 (1.05–1.78)*	0.86	<.05
Nontransplant side	0.66 (0.52–1.37)	1.21 (0.88–1.66)	0.53	1.28 (1.21–1.85)	0.71	.20
Knee flexor strength (Nm/kg)						
Transplant side	1.36 (1.18–1.79)	1.55 (1.32–1.81)	0.38	1.63 (1.37–1.71)	0.47	.15
Nontransplant side	1.36 (1.11–1.70)	1.50 (1.12–1.66)	0.29	1.55 (1.27–1.58)	0.37	.07
Knee extensor strength (Nm/kg)						
Transplant side	2.77 (2.24–3.37)	2.97 (2.42–4.09)	0.46	3.22 (2.93–3.69)	0.56	.10
Nontransplant side	2.71 (2.50–4.00)	3.38 (2.98–3.83)	0.49	3.51 (2.72–4.10)	0.36	.19
Lower limb load (N/kg)						
Transplant side	10.61 (8.01–14.58)	15.78 (9.16–20.02)	0.99	15.34 (12.04–19.74)	0.98	.06
Nontransplant side	14.16 (10.36–20.65)	17.61 (12.49–21.72)	0.47	18.04 (14.12–23.50)*	0.70	<.05
Timed Up and Go test (s)	7.06(5.82–7.31)	6.11 (4.96–7.00)	0.51	5.40 (5.00–6.50)	0.77	.15

NOTE. Values are median (25%–75% quartiles) or as otherwise indicated. *P* values at 3 time points were calculated by Friedman test. Multiple comparison test was performed by Scheffe test.
* *P*<.05, as calculated by comparison with pretreatment.

preserving, muscle-strengthening exercise has been reported in physical therapy for osteoarthritis.[27,28] We designed the rehabilitation program so that isotonic and isokinetic exercises could be performed on the transplant side before isometric exercises (see table 1). All participants completed the 12-week rehabilitation program without excessive pain. Functional improvement was observed, and there were no serious adverse events associated with rehabilitation. These results suggest that the first 2 aims of our study were achieved.

Although we could not show clear evidence that the current rehabilitation program promotes bone formation, mechanical stimulation may be important for bone formation of transplanted cells. Lack of mechanical loading causes bone loss and fractures in the elderly.[29] During physical activity, mechanical forces are placed on the bones through ground reaction forces and the contractile activity of muscles.[30,31] Adapting physical forces to bone structure results in maintenance and prevention of fractures in the elderly.[30] Fluid flow, strain, and hydrostatic pressure are mechanotransducers of physical force to osteocytes.[29,31,32] Stimulated mechanoreceptors on osteocytes activate the prostaglandin and Wnt pathways.[33] Mechanical loading stimulates not only osteocytes but also osteoblasts[34,35] and MSCs.[36,37] Oscillatory fluid flow promotes the proliferation and differentiation of marrow MSCs.[37] Furthermore,

Table 5 Comparison of SF-36 subgroups scores between pretreatment, 6 months after treatment, and 12 months after treatment (N=6)

SF-36 Subgroups	Pretreatment	6mo After Treatment	Effect Size (Pre/6mo)	12mo After Treatment	Effect Size (Pre/12mo	*P* at 3 Time Points (Pre/6mo/12mo)
Physical function	45 (36.3–65)	90 (78.8–95)	1.54	92.5 (78.8–95)*	1.58	<.05
Role-physical	40.6 (36.3–78.1)	68.8 (57.8–93.8)	0.71	96.9 (93.8–100)*	1.63	<.05
Bodily pain	52 (51.3–52)	72 (64.5–72)	2.83	73 (64.5–81.5)*	3.18	<.05
General health	59.5 (49.5–77)	77 (61.8–90.8)	0.66	79.5 (62–88)	0.72	.31
Vitality	71.9 (54.7–84.4)	68.8 (62.5–84.4)	0.22	71.9 (62.5–85.9)	0.11	.58
Social function	31.3 (25–84.4)	100 (71.9–100)	0.90	93.8 (78.2–100)	1.00	.21
Role-emotion	50 (37.5–87.5)	100 (100–100)	0.89	100 (100–100)	1.15	.13
Mental health	80 (71.2–88.8)	90 (82.5–90)	0.52	80 (80–83.4)	0.44	.27

NOTE. Values are median (25%–75% quartiles) or as otherwise indicated. *P* values at 3 time points were calculated by Friedman test. Multiple comparison test was performed by Scheffe test.
* *P*<.05 as calculated by comparison with pretreatment.

mechanical signals inhibit adipogenesis and promote the anabolism of osteogenesis.[36] A report by Ambrosio et al[38] reveals important information about this issue. Treadmill running has a synergistic effect on healing injured skeletal muscle after muscle-derived stem cell transplantation,[38] in addition to the positive effects of improved weight management, cardiovascular health, and metabolic profile.[39] Our previous report[40] suggested that adequate exercise promotes muscle remodeling after bilateral broad necrosis of the soleus muscles. It is hypothesized that suitable mechanical stimulation drives the differentiation of MSCs, while the beneficial paracrine effect may induce a synergistic effect between MSC transplantation and rehabilitation. However, further basic and clinical research is required to prove this hypothesis.

Evaluation of the effect of nonsurgical procedures on ION is important. Mont et al[18] compared the effect of core decompression surgery with nonsurgical management of ION and reported a 63.5% satisfactory clinical result with core decompression, but only 22.7% with nonsurgical management. However, this study was not an adjusted case-control study but was a literature review. Therefore, etiologic factors and radiographic findings were not fully assessed.[18] In multicenter, randomized controlled studies, physical therapy has similar effects in ION patients with sickle cell disease as does core decompression surgery with physical therapy.[19,41] Basic studies to design the rehabilitation protocol and further clinical studies are needed, but the information provided from the current study may aid in the development of rehabilitation protocols after cell transplantation for the treatment of ION.

Study limitations

The current study has several major limitations. This was a small-scale, single-group, pre-post preliminary study. Case-control and large-scale studies are needed to demonstrate the efficacy of the rehabilitation protocol. The current study was based on the original clinical trial, so it is not an individual study. The population size of the clinical trial itself was limited because it was a feasibility study.

Conclusions

The present study demonstrated the feasibility and safety of an intensive multiplex rehabilitation program after MSC transplantation in individuals with ION. Despite this, future studies should investigate dosing and timing parameters, as well as the mechanistic basis for improvements in outcomes when a combination therapy is used.

Suppliers

a. Olympus Terumo Biomaterials Co.
b. Senoh Co.
c. KONAMI Co.
d. Nihon Medix Co Ltd.
e. OG Giken Co Ltd.

Keywords

Mesenchymal stromal cells; Osteonecrosis; Rehabilitation

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Appendix 1 Assessment of Necrotic Lesions and Stages

Radiographic classification proposed by the SDIC in Japan[20]:

- Type A lesions occupied the medial one third or less of the weight-bearing portion.
- Type B lesions occupied the medial two thirds or less of the weight-bearing portion.
- Both types C1 and C2 lesions occupied more than the medial two thirds of the weight-bearing portion.
- Type C2 lesions extended laterally to the acetabular edge, but type C1 lesions did not.

The ION staging proposed by the SDIC used in Japan is a modified version of the system proposed by the Association Research Circulation Osseous Committee.[20]

- *Stage 1:* Specific findings of osteonecrosis are not observed on magnetic resonance imaging, bone scintigram, histology, or radiographs.
- *Stage 2:* Demarcating sclerosis is seen without collapse of the femoral head.
- *Stage 3:* Collapse of the femoral head, including the crescent sign, is seen without joint-space narrowing. Mild osteophyte formation of the femoral head or acetabulum may be seen.
  - *Stage 3A:* Collapse of the femoral head $<$3mm
  - *Stage 3B:* Collapse of the femoral head $\geq$3mm
- *Stage 4:* Osteoarthritic changes are seen.

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Original Article

Arterial Stiffness Predicts Cognitive Decline in Japanese Community-dwelling Elderly Subjects: A One-year Follow-up Study

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Aim: The purpose of this study was to determine whether arterial stiffness can be used to predict one-year changes in the cognitive function in Japanese community-dwelling elderly subjects.
Methods: A total of 103 Japanese community-dwelling elderly patients joined this study. Information regarding the age, height, weight, gender and past medical history of each participant was obtained. Additionally, arterial stiffness was determined according to the cardio-ankle vascular index (CAVI), and the cognitive function was assessed with the Mini-Mental State Examination (MMSE). One year later, we performed the MMSE in the same subjects. After dividing the cohort according to the 80th percentile of the CAVI (normal and arterial stiffness [AS] groups), we examined whether the degree of cognitive decline, as determined using the pre- and post-MMSE, was significantly different based on the severity of arterial stiffness, adjusted for age, BMI, gender and the pre-MMSE scores.
Results: Of the 103 subjects who participated in the pre-data collection, 74 (38 men and 36 women, 73.4 ± 4.0 years) joined the post-data collection. We found a significant difference in the change in the post-MMSE scores between the normal and AS groups (pre-MMSE: normal group [27.4 ± 2.1] and AS group [26.9 ± 2.4] and post-MMSE: normal group [27.2 ± 2.1] and AS group [25.5 ± 2.3], F = 5.95, p = 0.02). For each domain of the MMSE, the changes in MMSE-attention-and-calculation (F = 5.11, p = 0.03) and MMSE-language (F = 4.32, p = 0.04) were significantly different according to an ANCOVA.
Conclusions: We found that arterial stiffness predicts cognitive decline in Japanese community-dwelling elderly subjects regardless of the initial level of the global cognitive function. This finding indicates the potential use of the degree of arterial stiffness as an indicator for preventing or delaying the onset of dementia in the elderly.

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Key words: Arterial stiffness, Cognitive impairment, Elderly, Dementia

Introduction

Dementia is a serious issue, especially in community-dwelling elderly subjects[1)]. Thirty-five million people worldwide suffered from dementia in 2012 according to the World Health Organization. Approximately 48% of patients with Alzheimer's disease (AD), the most common form of dementia, are estimated to live in Asia, and this percentage is expected to increase to 59% by 2050[2)]. Elderly people with dementia are typically frail due to their poor mobility and body composition, and the transitional stage between normal aging and AD, called mild cognitive impairment (MCI), results in frailty[3)], depression[4)], lower levels of physical activity[1)] and higher mortality[5)]. Preventing cognitive decline is therefore crucial.

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Of risk factors for cognitive decline, cardiovascular risk factors have received more attention in recent years[6, 7]. High blood pressure[8], dyslipidemia[8], obesity[9] and diabetes mellitus[9] have been proposed to be risk factors for cognitive decline. Among these factors, arterial stiffness is a comparatively easy-to-modify risk factor in community-dwelling elderly subjects. Madden *et al*. reported that three months of aerobic training reduces the degree of multifactorial arterial stiffness without generating any significant improvements in aerobic fitness, weight, BMI, waist-to-hip ratio or blood pressure in community-dwelling older individuals[10]. Additionally, previous studies have demonstrated the effectiveness of antihypertensive agents in improving arterial stiffness in both short- and long-term trials[11]. Community-dwelling elderly can improve their arterial stiffness; therefore, focusing on treating arterial stiffness may be effective for preventing cognitive decline.

Most older adults with MCI live in the community, and more than half of MCI cases progress to dementia within five years[12]. Therefore, a desired goal is the early detection of cognitive decline, especially in the community-dwelling elderly. When evaluating the degree of arterial stiffness in community-dwelling elderly subjects, the most important property is the ease of measurement. Arterial stiffness is one of the most easily measured vascular risk factors in community-dwelling elderly patients due to its non-invasive nature; therefore, it can be used as a predictor of cognitive decline in this population. Previous studies have also shown arterial stiffness to be a predictor of cognitive decline. However, the subjects in these studies were not elderly individuals living in the community[13, 14]. Additionally, other authors have reported that they were unable to validate arterial stiffness as an independent risk factor for cognitive decline, as measured according to the global cognitive function using the Mini-Mental State Examination (MMSE)[15-17]. Yamamoto *et al*. reported a relationship between the cognitive function and arterial stiffness determined according to the CAVI in community dwelling elderly[18], although the mean age was approximately 80 years, which is a bit high considering the mean age of community-dwelling elderly individuals in Japan. It may be more important to focus on healthier and younger older adults when discussing community-dwelling elderly[19]. The efficacy of arterial stiffness as a predictor of cognitive decline, especially in community-dwelling elderly patients, is less well investigated[4].

The purpose of this study therefore was to address whether the degree of arterial stiffness can be used to predict one-year changes in the cognitive function in Japanese community-dwelling elderly subjects. We used the CAVI to assess arterial stiffness, as this parameter was found to significantly correlate with cognitive decline in a cross-sectional study[18, 19].

Methods

Participants

Participants were recruited for this study through local press that requested healthy community-dwelling volunteers 65 years of age or older, and data collection was performed on two occasions: November 2012 (pre-data collection) and November 2013 (post-data collection). Interviews were conducted to exclude participants from both data collections based on the following exclusion criteria: severe cardiac, pulmonary or musculoskeletal disorders; comorbidities associated with a higher risk of falls, such as Parkinson's disease or stroke; and the use of psychotropic drugs. Written informed consent was obtained from each participant in accordance with the guidelines approved by the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1995 during both data collection periods. The study protocol was approved by the ethics committee of Kyoto University Graduate School of Medicine.

Measurements — *Pre-data Collection*

Demographic Data

Each patient's age, height, weight, gender, past medical history (cardiovascular disease, hypertension, diabetes mellitus and hyperlipidemia), smoking status (number of cigarettes smoked per day and total number of years smoked) and educational background (elementary school, junior high school, high school, career college or university) were obtained as demographic data. All data were collected at the first data collection time point. We directly asked about each participant's age and gender and measured their height and weight using standardized height and weight scales.

Arterial Stiffness

The degree of arterial stiffness was determined based on the CAVI using the VaSera-1500 device (Fukuda Denshi Co., Ltd., Tokyo, Japan). The details of this procedure have been described previously[20, 21]. After the participants had rested for five minutes in the sitting position, we obtained these measurements as previously described. Higher CAVI values indicate a higher degree of arterial stiffness. The measurements were obtained once, and the mean values of the right

Table 1. Baseline characteristics and post-MMSE scores in the study population

	All (n = 74)		
	Normal group n = 59	AS group n = 15	p
Demographic data			
Age, year	72.8 ± 3.8	76.1 ± 3.6	< 0.01
BMI, kg/m^2	23.2 ± 2.6	23.2 ± 3.2	0.99
Gender, male	28 (47.5%)	10 (66.7%)	0.25
Mean CAVI	8.83 ± 0.61	10.6 ± 0.51	< 0.01
Cognitive function			
Pre-MMSE	27.4 ± 2.1	26.9 ± 2.4	0.40
Post-MMSE	27.2 ± 2.0	25.5 ± 2.3	< 0.01
Pre-MMSE (orientation)	9.6 ± 0.6	9.7 ± 0.5	0.89
Post-MMSE (orientation)	9.7 ± 0.7	9.7 ± 0.5	0.89
Pre-MMSE (registration)	2.9 ± 0.4	3.0 ± 0.0	0.53
Post-MMSE (registration)	2.9 ± 0.3	3.0 ± 0.0	0.49
Pre-MMSE (attention and calculation)	3.2 ± 1.7	2.9 ± 1.8	0.55
Post-MMSE (attention and calculation)	3.4 ± 1.7	2.3 ± 1.5	0.03
Pre-MMSE (recall)	2.6 ± 0.6	2.4 ± 0.8	0.30
Post-MMSE (recall)	2.5 ± 0.6	2.4 ± 0.7	0.69
Pre-MMSE (language)	8.9 ± 0.3	8.9 ± 0.4	0.73
Post-MMSE (language)	8.7 ± 0.5	8.2 ± 1.3	0.15
Comorbidities			
Cardiovascular disease	6 (10.2%)	4 (26.7%)	0.11
Hypertension	23 (39.0%)	8 (53.3%)	0.39
Diabetes mellitus	5 (8.5%)	4 (26.7%)	0.08
Hyperlipidemia	9 (15.3%)	2 (13.3%)	1.00
Brinkman index	0 (0-800)	0 (0-400)	0.63
Educational background			n.s.
Elementary school	0 (0.0%)	1 (6.7%)	
Junior high school	16 (27.1%)	4 (26.7%)	
High school	35 (59.3%)	9 (60.0%)	
Career college	3 (5.1%)	0 (0.0%)	
University	5 (8.5%)	1 (6.7%)	

Mean CAVI = mean value of the right and left CAVI scores. The mean ± SD is shown for age, BMI, mean CAVI and pre- and post MMSE. n (%) is shown for gender, cardiovascular disease, hypertension, diabetes mellitus, hyperlipidemia and educational background. The median (25% quartile-75% quartile) is shown for the Brinkman index. AS: arterial stiffness; n.s.: not significant.

and left CAVI scores for each patient were used for the analysis[19].

Cognitive Function Measurements

The cognitive function was assessed using the Mini-Mental State Examination (MMSE)[22]. The MMSE is a short screening test that consists of the following five areas for detecting cognitive impairment: orientation, registration, attention and calculation, recall and language. The scores range from 0 to 30, with higher scores indicating better cognitive performance. The MMSE was performed at both the pre- and post-data collection time points.

Measurements—*Post-data Collection*

Cognitive Function Measurements

One year later, the cognitive function was also assessed using the MMSE[22]. We performed the MMSE using the same inclusion and exclusion criteria as that used at the pre-data collection time point.

Statistical Analysis

The patients were divided into two groups based on the 80th percentile of the CAVI values: the normal

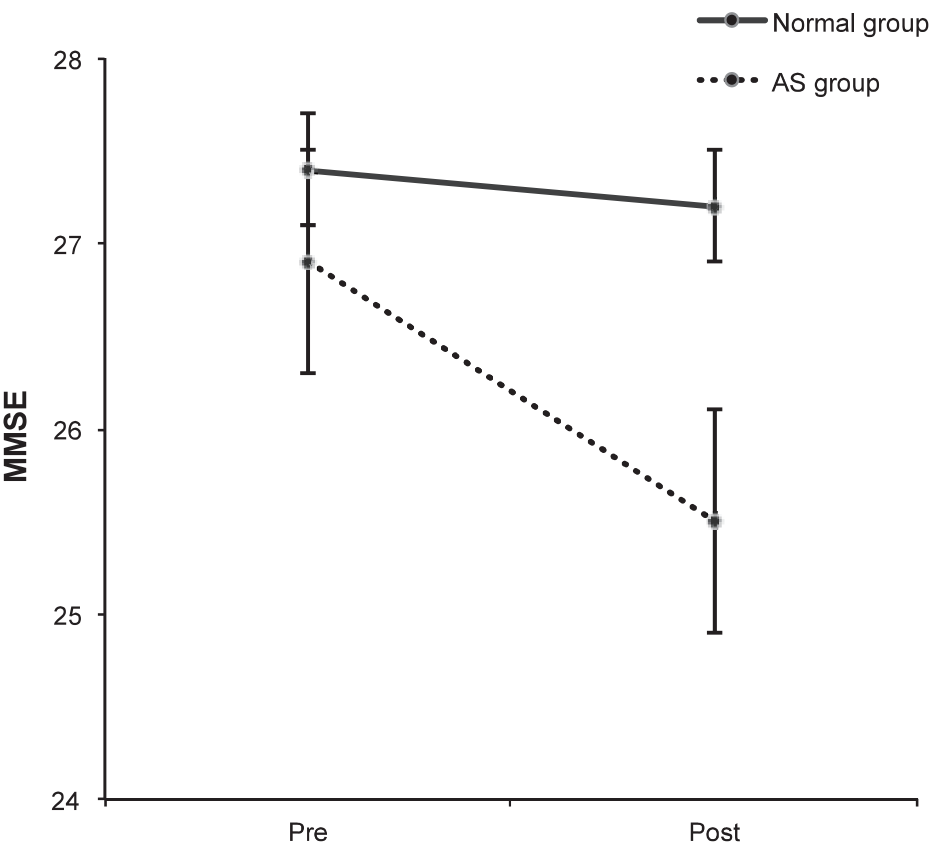

Fig. 1. Two-way analysis of variance showing the differences in the changes in the post-MMSE scores between the normal and AS groups. These findings indicate that the elderly subjects in the AS group experienced greater cognitive decline than those in the control group ($F=5.95$, $p=0.02$).

and arterial stiffness [AS] groups. We analyzed the differences between these two groups using the unpaired t-test for age, body mass index (BMI), mean CAVI values on both sides and the pre- and post-MMSE scores (total score and scores for each domain), the χ^2 test for gender, past medical history and educational background and the Mann Whitney U-test for the Brinkman index (number of cigarettes smoked per day × total number of years smoked). A repeated measures two-way analysis of covariance (ANCOVA) was used to analyze whether the degree of cognitive decline determined according to the pre- and post-MMSE scores (total score and scores for each domain) differed significantly according to the severity of arterial stiffness, adjusted for age, BMI, gender and the pre-MMSE score. A p value of <0.05 was considered to be statistically significant for all analyses.

Results

In total, 74 individuals (38 men and 36 women, 73.4 ± 4.0 years) participated in both data collection events. Of these individuals, none were excluded. We assigned 59 elderly individuals (28 men and 31 women) to the normal group and 15 (10 men and five women) to the AS group. **Table 1** shows the differences in each variable between the two groups. While there were no significant differences in BMI, gender, pre-MMSE, educational background or past medical history, we found significant differences in age ($p<0.01$) and the mean CAVI values ($p<0.01$). Additionally, the normal group had a significantly higher total post-MMSE scores (normal group: 27.2 ± 2.1, AS group: 25.5 ± 2.3, $p<0.01$) and higher post-MMSE scores for the attention-and-calculation domain (normal group: 3.4 ± 1.7, AS group: 2.3 ± 1.5, $p=0.03$) than the AS group.

The ANCOVA adjusted for age, BMI, gender

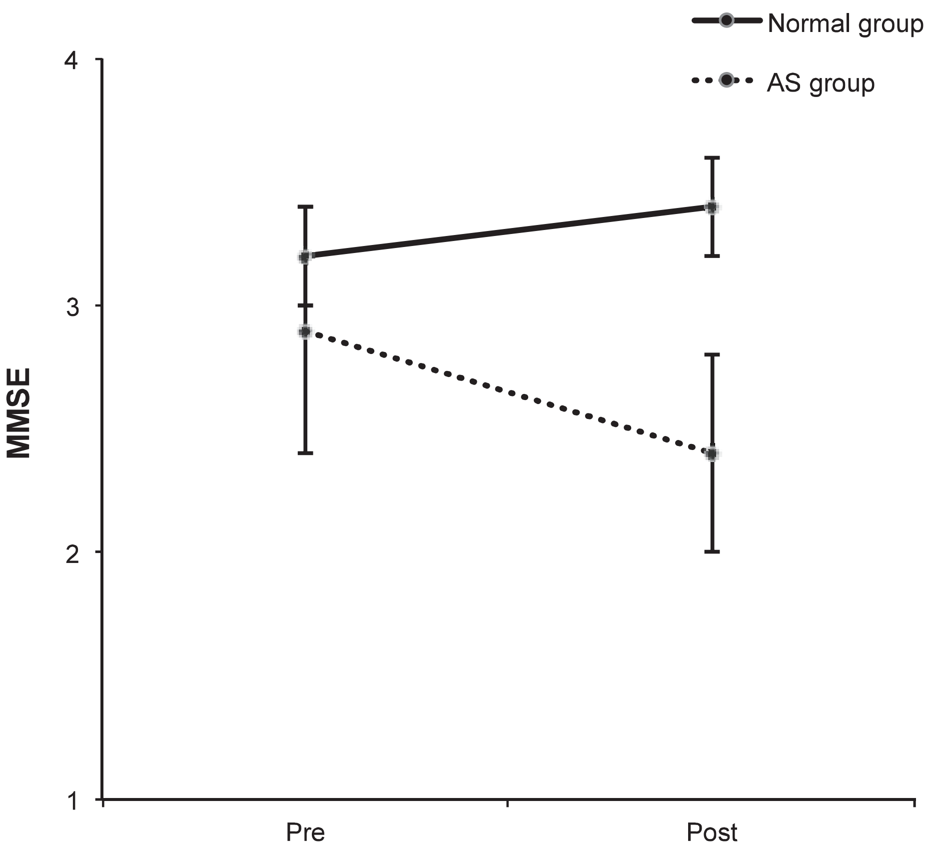

Fig. 2. Two-way analysis of variance showing the differences in the changes in the post-MMSE (attention and calculation) scores between the normal and AS groups. These findings indicate that the elderly subjects in the AS group experienced greater cognitive decline than those in the control group ($F=5.11$, $p=0.03$).

and pre-MMSE showed a significant difference in the changes in the post-MMSE scores between the normal and AS groups ($F=5.95$, $p=0.02$) (**Fig. 1**), indicating that elderly individuals with a higher degree of arterial stiffness may experience greater levels of cognitive decline, even after adjusting for age, BMI, gender and the pre-MMSE score. Additionally, the changes in the MMSE-attention-and-calculation ($F=5.11$, $p=0.03$) (**Fig. 2**) and MMSE-language ($F=4.32$, $p=0.04$) (**Fig. 3**) domains were shown to be significantly different according to the ANCOVA. The other areas did not show any differences between the two groups (orientation; $F=0.27$, $p=0.60$: registration; $F=2.69$, $p=0.11$, recall; $F=0.16$, $p=0.69$).

Discussion

In this study, we analyzed whether the degree of cognitive decline differs significantly according to the severity of arterial stiffness, adjusted for age, BMI, gender and the cognitive function at baseline and at the one-year follow-up. Consequently, we found that arterial stiffness predicts cognitive decline in Japanese community-dwelling elderly subjects, regardless of the initial level of the global cognitive function. Previous studies have demonstrated that arterial stiffness has a predictive effect on cognitive decline in the non-community-dwelling elderly[13-15, 18]; however, few reports have found arterial stiffness to be a predictor of cognitive decline in this group.

There are hypotheses regarding pathways linking arterial stiffness and cognitive decline, wherein augmented pressure pulses penetrate and damage small cerebral vessels in the global brain[23]. Brain lesions, such as ischemic lesions and white matter abnormalities resulting from augmented pressure, are thought to cause cognitive decline, thereby leading to dementia[24]. The augmented pressure caused by arterial stiffness independently predicts cognitive performance[25], and many previously published studies evaluating the

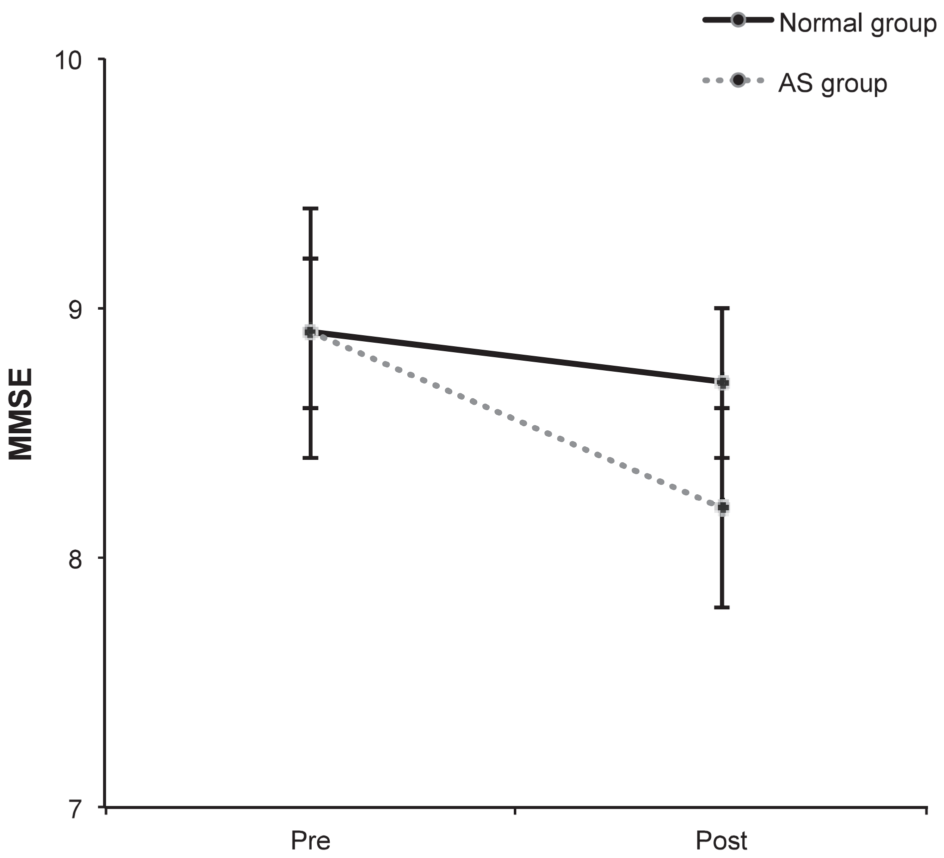

Fig. 3. Two-way analysis of variance showing the differences in the changes in the post-MMSE (language) scores between the normal and AS groups. These findings indicate that the elderly subjects in the AS group experienced greater cognitive decline than those in the control group ($F=4.32$, $p=0.04$).

association between arterial stiffness and the cognitive function have discussed the causal relationship with this phenomenon[14, 17, 18, 23].

Several studies have examined whether the severity of arterial stiffness longitudinally predicts cognitive decline. For example, one study targeting people older than 80 years of age in nursing homes showed results similar to the current findings[13]. The mean baseline MMSE score of these subjects was 23.7 ± 4.9, which is lower than that observed in the current study. Another study, in which the subjects were older patients in the hospital with complaints of memory loss, also reported that arterial stiffness has a strong predictive ability for cognitive decline[14]. Furthermore, Yamamoto *et al.* performed a similar analysis in community-dwelling elderly patients; however, the mean age was higher than that noted in our study[18]. Notably, we found that arterial stiffness predicts cognitive decline in community-dwelling elderly subjects with a comparably preserved cognitive function, even after adjusting for age, gender, BMI and the baseline cognitive function. In addition, we observed the scores for the attention-and-calculation and language domains of the MMSE to be significantly decreased in the AS group. It has been reported that these MMSE domains are not affected by impairment of the hippocampus[26]. Therefore, we assume that the cognitive dysfunction resulting from arterial stiffness is not attributed to dysfunction of the hippocampus. However, other studies have reported that measurements of arterial stiffness do not predict performance for the global cognitive function, as measured according to the MMSE[15-17]. There are various possible reasons for this discrepancy: 1) the mean age of the subjects was 57.1 years and the participants were relatively high functioning (ceiling effect of the MMSE)[15]; 2) many participants dropped out from the follow-up survey and selection bias may have affected the results for the change in the cognitive function[16]; 3) memory tasks that are more demanding for the executive function and attention may be more sensitive to cerebrovascular alterations due to aging and the MMSE may be too insensitive to accurately detect cognitive changes[17, 27]. As a result, further studies are needed to establish evidence clarifying the association between arterial stiffness and the cognitive function.

The most important clinical implication of our findings is that one of the most easily measured and non-invasive parameters, especially in community-dwelling elderly individuals, arterial stiffness, predicted cognitive decline after one year. These results imply that maintaining the arterial function may prevent or delay the onset of dementia in the community-dwelling elderly. Additionally, it may be possible to identify individuals at risk of dementia by evaluating the degree of arterial stiffness. Interventional and longitudinal studies examining improvements in arterial stiffness with the aim of preventing cognitive decline are required to establish effective strategies for inhibiting the onset of dementia.

This study is associated with several limitations. First, because we were unable to perform neuroimaging assessments, it was not possible to make a specific diagnosis of dementia subtypes. In addition, we only performed MMSE as a cognitive test, and the cognitive function was not fully investigated. There may be asymptomatic brain lesions and specific cognitive domains that exhibit a strong relationship with arterial stiffness. Second, the age at baseline in the AS group was significantly higher than that observed in the normal group. Although we tried to minimize the impact of this difference by adjusting for age, the effect may have been insufficient. Third, the small number of subjects may also have affected the results, and more samples are needed to confirm the results of this study. Finally, many studies have investigated the relationship between arterial stiffness and the cognitive function; therefore, this study may not have adequate novelty. Nevertheless, we regard our findings as providing evidence that strengthens the close relationship between arterial stiffness and cognitive decline.

Conclusions

This study showed that arterial stiffness predicts cognitive decline in Japanese community-dwelling elderly subjects regardless of the initial level of the global cognitive function. These findings indicate the potential of improving arterial stiffness in order to prevent or delay of the onset of dementia in the elderly.

Acknowledgments

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Conflicts of Interest

None.

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Original article

Spot the Difference for Cognitive Decline: A quick memory and attention test for screening cognitive decline

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ABSTRACT

Background: Dementia is currently one of the most common conditions in older adults, and early detection of cognitive decline is crucial for identifying dementia. We developed a new type of short-term memory and attention test that uses a spot-the-difference task: Spot the Difference for Cognitive Decline (SDCD). The purpose of the present study was to examine the accuracy of the SDCD test for the identification of cognitive impairment in community-dwelling older adults.
Methods: The participants were 443 Japanese community-dwelling older adults. The SDCD test uses two scenery pictures. Participants were instructed to memorize the details of the first picture for 30 seconds, after which the first picture was taken away and the second picture was shown. Next, the participants were asked to identify as many differences as possible between the first and second pictures, which were presented sequentially. The number of correct responses comprises the SDCD score (scores: 0–10). The Mini-Mental State Examination and Scenery Picture Memory Test were used to measure the participants' cognitive function. We used receiver-operating characteristic analysis to examine the power of the SDCD test and identify the optimal cutoff value of the SDCD score.
Results: Of the 443 participants, 30 (6.77%) had some cognitive impairment based on the Mini-Mental State Examination scores. Participants without cognitive impairment had higher SDCD scores than those with cognitive impairment ($p < 0.001$). The SDCD scores were significantly associated with the Mini-Mental State Examination ($r = 0.333$) and Scenery Picture Memory Test ($r = 0.402$) results. The receiver-operating characteristic curve used for the identification of cognitive impairment had a comparatively high area under the curve (0.798) for the SDCD score with a cutoff value of 1/2 (with >1 being normal; sensitivity: 70.5%; and specificity: 80.0%).
Conclusion: The present study found that the SDCD test could be an effective clinical tool for the identification of cognitive impairment in older adults.
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1. Introduction

Dementia can drastically influence one's daily life and is currently one of the most common conditions in older adults. Dementia affects 5–8% of the population over 65 years of age[1] and up to 30% of the people aged ≥85 years.[2] Currently, the number of people with dementia is increasing. It has been estimated that approximately 48% of the patients with Alzheimer's disease (AD), the most common form of dementia, live in Asia, and this percentage is projected to grow to 59% by 2050.[3] Dementia and AD have been associated with mortality[4]; therefore, prevention and early detection of cognitive decline are crucial.

The presence of cognitive decline increases the risk of progression to mild cognitive impairment (MCI) and AD.[5,6] It is generally agreed that older adults with early AD, compared to healthy older adults, exhibit a greater decline in memory function[7] and working memory[8] than in other major domains of cognitive function._ENREF_7 A central feature of AD is the decline in episodic memory.[9] Visual memory, which is included in episodic memory, is

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an important component of daily life. There are several well-established visual memory tests, such as the Benton Visual Retention Test[10] and the Rey–Osterrieth Complex Figure Test,[11] that can be used to assess nonverbal visual memory. However, these tests are not reflective of situations and activities encountered in daily life, are time consuming, and have complex scoring systems.

Deficits in working memory functions (e.g., attention and executive function) caused by AD are thought to contribute to a range of significant problems such as impairments in performing everyday tasks (e.g., keeping track of conversations, walking while talking, and packing a bag). Thus, the attentional function would appear to be important for the early detection of cognitive decline, as this function decreases with the progression of cognitive decline.[12]

We developed a new short-term visual memory and attention test called the Spot the Difference for Cognitive Decline (SDCD) test. The SDCD test is a brief and simple test that uses pictures of familiar-looking sceneries. Examinees are asked to find the differences between two scenery pictures. This test can be used in clinical or community-based settings with a large population. In a previous study, it was reported that poor visual memory predicts the onset/progression of dementia.[13] The spot-the-difference task has been used as a cognitive test in previous studies,[14–16] although its usefulness for detecting cognitive impairment had not been described. These spot-the-difference tasks have often been used in memory function training for older adults with dementia in many countries, including Japan. However, the effects of this training have not been examined empirically. We hypothesized that the SDCD score would be associated with cognitive function, and this test would be able to identify community-dwelling older adults with cognitive impairment. The purpose of the present study, therefore, was to examine the accuracy of the SDCD test for the identification of cognitive impairment in community-dwelling older adults.

2. Methods

2.1. Participants

Participants for this study were recruited through advertisements in the local newspaper. A total of 443 Japanese people aged $\geq$65 years (mean age, 73.1 $\pm$ 5.3 years) responded. We included only community-dwelling older adults who were able to perform their activities of daily living independently. A screening interview was conducted to exclude participants with severe cardiac, pulmonary, or musculoskeletal disorders, as well as those using medications that affect attention (e.g., psychoactive drugs or drugs prescribed for sleep). Written informed consent was obtained from each participant in accordance with the guidelines of the Kyoto University Graduate School of Medicine, Kyoto, Japan and the Declaration of Helsinki, 1975. The study protocol was approved by the Ethics Committee of the Kyoto University Graduate School of Medicine.

2.2. SDCD test protocol

The SDCD test uses two scenery pictures (Figs. 1 and 2) on A4 size papers. Fig. 1 is called the “first picture” and Fig. 2 the “second picture”. There are 10 differences between the two pictures: the shape of the chimney smoke, shape of the doorknob, height of the fountain, shape of the mountain (seen between the house and the fountain), number of fruits on the tree, direction that the dog on the right is facing, shape of the leftmost flower, shape of the child's mouth, presence of a bird versus a butterfly, and presence of the father's backpack. First, the examinees are instructed to memorize

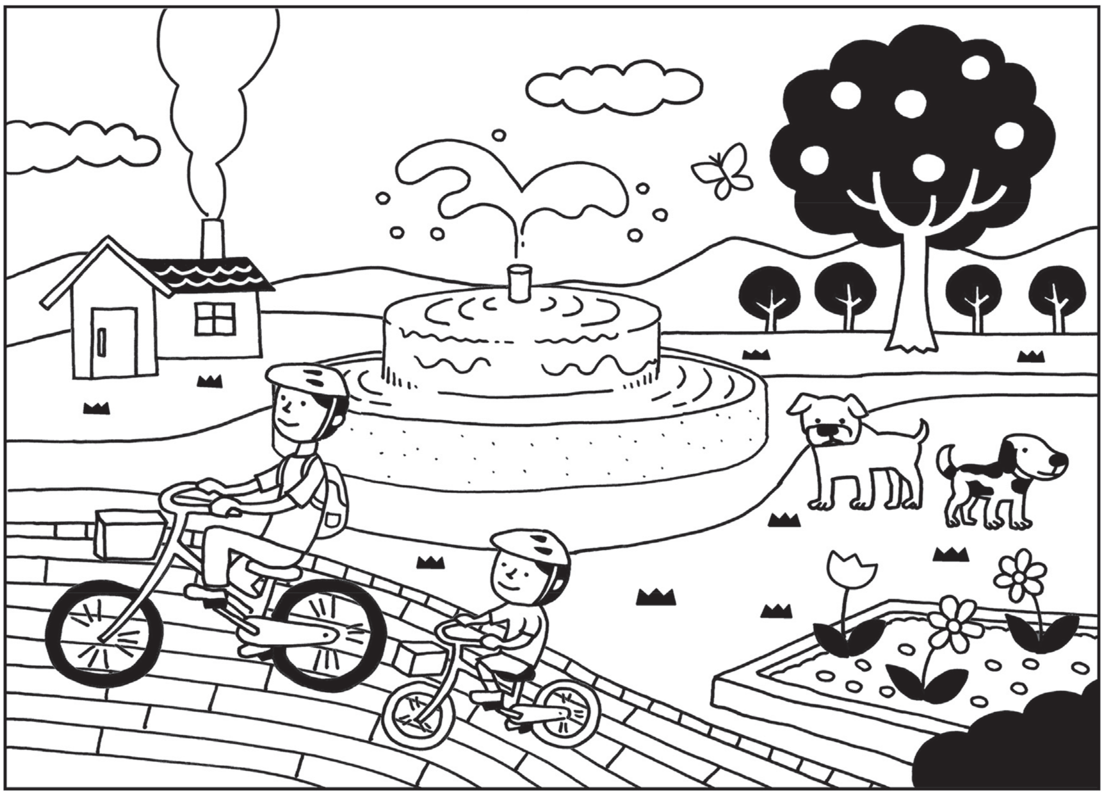

Fig. 1. First picture used in the Spot the Difference for Cognitive Decline test. The examinees were instructed to memorize the details of the picture, which was presented for 30 seconds.

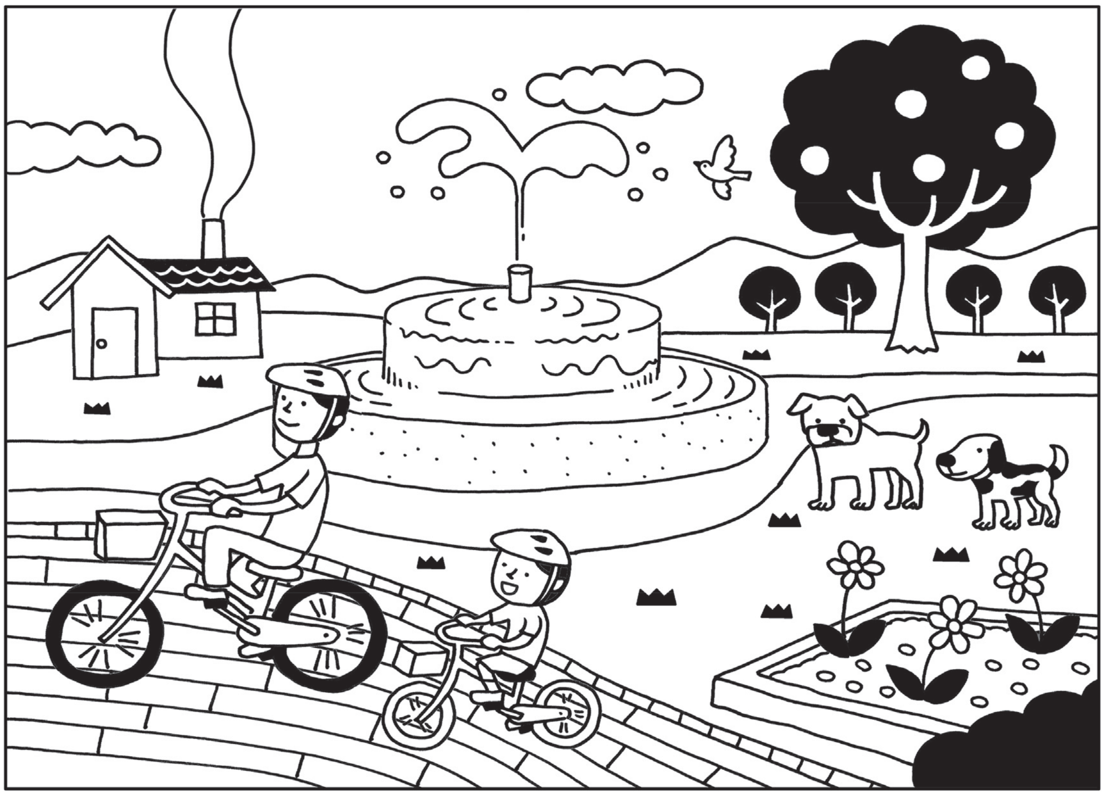

Fig. 2. Second picture in the Spot the Difference for Cognitive Decline test. This picture has 10 differences when compared with the first picture (Fig. 1). After studying the first picture for 30 seconds, the examinees were asked to find as many of the differences between the first and second pictures as they could within 1 minute.

the details of the first picture for 30 seconds. They are also told that there are "some" differences between the first and second pictures. The examiners do not inform the participants that there are 10 differences in total. After showing the first picture, the examiner takes the first picture away and shows the participants the second picture. The examinees are then asked to find the differences in the second picture, within 1 minute and without any hints. The number of the correct answers is then counted to determine the SDCD score. If the examinees' answers are close but not exactly correct (e.g., a flower type or increase in the fruit), these answers are marked as incorrect and not included in the SDCD score. In a sample of 21 participants, the SDCD had a high test–retest reliability [intertrial correlation coefficient (ICC) = 0.801; $p < 0.001$] between the two measurements with a 1-week interval.

2.3. Cognitive function

Participants' cognitive function was measured by two neuropsychological tests: the Mini-Mental State Examination (MMSE)[17] and the Scenery Picture Memory Test (SPMT).[18]

Global cognitive function was assessed using the MMSE, a standard test used in cognitive aging research for assessing mental status. Five areas of cognitive function—orientation, registration, attention and calculation, recall, and language—are tested. It has 11 questions in total and a maximum possible score of 30.

The SPMT is a simple memory test that assesses visual memory combined with verbal responses. This test uses a line drawing of a living room in a house on an A4-size paper, depicting 23 objects that are commonly observed in daily life. The examinee is instructed to look at the picture for 1 minute and remember the items. After this encoding period, participants are given a distractor task (a brief forward digit-span test). Participants are then asked to recall the objects in the picture without a time limit. Recall of the items usually takes approximately 2 minutes. The number of items recalled is the SPMT score. Higher scores indicate a better cognitive function.

2.4. Statistical analysis

We divided the participants into two groups (normal and cognitive impairment groups) based on the cutoff score of the MMSE (23/24). Differences between these two groups were statistically analyzed, using the unpaired *t* test for continuous variables and the χ^2 test for categorical variables. Differences between the SPMT and SDCD scores were examined using an analysis of variance. When a significant effect was found, the Tukey–Kramer *post hoc* test was used to examine the differences. In addition, the criterion-related validity was determined by evaluating the correlation between the SDCD score and the two neuropsychological tests using Spearman's rank correlation coefficient. Following this, we performed a multiple logistic regression analysis to determine whether the SDCD score was associated with cognitive impairment independently. For this analysis, the two groups (i.e., the normal group and the cognitive impairment group) were the dependent variables, and the SDCD score was the independent variable. We controlled age, sex, body mass index, medications, and the length of education. Furthermore, a receiver-operating characteristic (ROC) analysis was used to examine the power of the SDCD score and determine the optimal cutoff value of the SDCD score as a state variable. The area under the curve, sensitivity, and specificity of the SDCD score were calculated based on the ROC curve. The cutoff value for the SDCD score was determined based on the optimal sensitivity and specificity. Consequently, we performed a univariate logistic regression analysis to determine the correlation between the SDCD and the five subtests of the MMSE (orientation, registration, attention and calculation, recall, and language). For this analysis, the groups formed on the basis of the cutoff value of the SDCD were the dependent variables and each subtest of the MMSE was the independent variable.

Data were analyzed using SPSS Statistics for Windows, version 20.0 (SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered statistically significant.

3. Results

Of the 443 participants, 30 (6.77%) were identified as having cognitive impairment based on an MMSE cutoff score of 23/24. Demographic characteristics of the participants are shown in Table 1. The normal group had a higher SDCD score (2.21 ± 1.38) than the cognitive impairment group (0.77 ± 0.86; $p < 0.001$). The normal group also had a higher SPMT score than the cognitive impairment group ($p < 0.001$). The education level of the normal group was also higher than that of the cognitive impairment group ($p = 0.002$). There were no significant differences in age, sex, body mass index, or the use of medication between the two groups.

The participants were reclassified into five groups according to their SDCD scores; differences in the MMSE and SPMT scores between the groups are shown in Figs. 3 and 4. There were significant differences in the MMSE scores ($F = 15.7$, $p < 0.001$) as well as in the SPMT scores ($F = 22.6$, $p < 0.001$) between the five groups. Results of the *post hoc* tests are shown in Figs. 3 and 4. In addition, the SDCD scores were moderately and positively correlated with the MMSE ($r = 0.333$) and SPMT ($r = 0.402$) scores ($p < 0.001$). These analyses indicated that a higher SDCD score was associated with higher cognitive function. In the logistic regression analysis, the SDCD score was significantly associated with cognitive impairment after adjusting for age, sex, body mass index, medications, and the length of education (odds ratio: 0.388; 95% confidence interval: 0.257–0.584; $p < 0.001$).

The ROC curve for the SDCD scores used for the identification of cognitive impairment was based on the MMSE cutoff score (23/24). The area under the curve was comparatively high for the SDCD scores (0.798, $p < 0.001$), and the cutoff value of the SDCD score was 1/2 (with ≥1 being considered normal) with a 70.5% sensitivity and 80.0% specificity. A univariate logistic regression analysis showed that there were significant correlations between the SDCD scores and the four subtests of the MMSE ($p < 0.05$), except for the registration subtest (refer to Table 2).

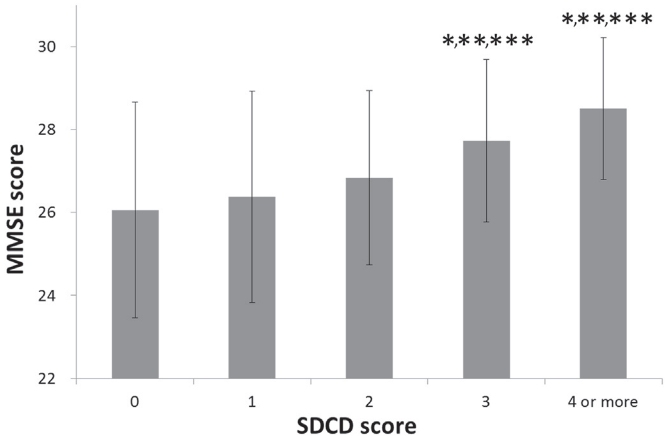

Fig. 3. Comparison of the MMSE scores between the groups formed based on the SDCD scores. There were significant differences in the MMSE scores across the five groups ($F = 15.7$, $p < 0.001$). * Significant difference from Group 0. ** Significant difference from Group 1. *** Significant difference from Group 2. MMSE = Mini-Mental State Examination; SDCD = Spot the Difference for Cognitive Decline.

4. Discussion

We examined a new type of short-term memory and attention test, the SDCD, which used a spot-the-difference task to identify cognitive impairment. In the present study, we showed that the SDCD test is a very quick and reliable screening tool for the identification of cognitive impairment in community-dwelling older adults.

The SDCD test is moderately and positively correlated with global cognitive and memory functions. The SDCD test includes a "memory" phase and a "recall and name the differences" phase. These phases require not only memory functions, but also other cognitive functions, such as attention. Some studies in the past have used similar spot-the-difference tasks as cognitive tests,[14,15] and only one previous study[16] has investigated brain activation in a test

Table 1
Characteristics of participants with and without cognitive impairment.[a]

	Normal ($n = 413$, MMSE ≥ 24, 27.4 ± 2.0)	Cognitive impairment ($n = 30$, MMSE < 24, 22.4 ± 1.1)	p
Age, y	72.9 ± 5.3	74.4 ± 5.3	0.160
Female	269 (65.3%)	20 (66.7%)	> 0.99
BMI, kg/m^2	22.7 ± 3.1	22.2 ± 2.8	0.384
Number of medications taken, n	2.53 ± 2.59	2.48 ± 2.46	0.237
Education			0.002**
<6 y	3 (0.7%)	0	
6–9 y	98 (23.7%)	17 (56.7%)	
10–12 y	212 (51.3%)	10 (33.3%)	
>12 y	100 (24.2%)	3 (10.0%)	
SDCD	2.21 ± 1.38	0.77 ± 0.86	<0.001**
SPMT	13.8 ± 3.5	10.1 ± 2.8	<0.001**

Data are presented as n (%) or mean ± SD.
* $p < 0.05$.
** $p < 0.01$.
BMI = body mass index; MMSE = Mini-Mental State Examination; SDCD = Spot the Difference for Cognitive Decline; SPMT = Scenery Picture Memory Test.
[a] Normal and cognitive impairment groups were defined according to the MMSE cutoff score of 23/24.

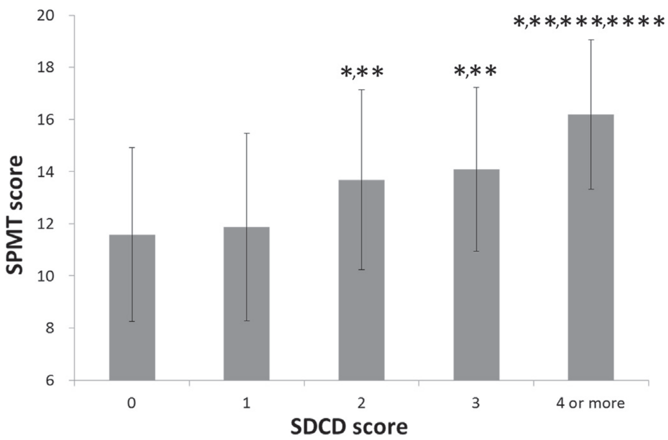

Figure 4. Comparison of the SPMT results between the groups formed based on the SDCD scores. There were significant differences in the MMSE scores across the groups ($F = 22.6$, $p < 0.001$). * Significant difference from Group 0. ** Significant difference from Group 1. *** Significant difference from Group 2. **** Significant difference from Group 3. MMSE = Mini-Mental State Examination; SDCD = Spot the Difference for Cognitive Decline; SPMT = Scenery Picture Memory Test.

Table 2
Correlation between SDCD score and subtests of MMSE.[a]

Subtests (total score)	Subtest score	SDCD score < 2 (n = 146) n (%)	OR (95% CI)
Orientation (10)	≤8	20 (13.7)	Reference
	9	30 (20.5)	0.26 (0.11–0.62)**
	10	96 (65.8)	0.21 (0.10–0.46)**
Registration (3)	≤2	4 (2.7)	Reference
	3	142 (97.3)	0.61 (0.16–2.30)
Attention and calculation (5)	≤2	69 (47.3)	Reference
	3	10 (6.8)	1.10 (0.47–2.59)
	4	18 (12.3)	1.19 (0.61–2.34)
	5	49 (33.6)	0.57 (0.36–0.88)*
Recall (3)	≤1	22 (15.1)	Reference
	2	51 (34.9)	0.21 (0.09–0.50)**
	3	73 (50.0)	0.13 (0.06–0.31)**
Language (9)	≤7	14 (9.6)	Reference
	8	38 (26.0)	0.18 (0.06–0.59)**
	9	94 (64.4)	0.12 (0.04–0.36)**

* $p < 0.05$.
** $p < 0.01$.
CI = confidence interval; MMSE = Mini-Mental State Examination; OR = odds ratio; SDCD = Spot the Difference for Cognitive Decline.
[a] For each univariate logistic regression analysis, SDCD scores <2 or ≥2 were the dependent variables and each subtest of the MMSE was the independent variable.

using a spot-the-difference task. Although the abovementioned test did not include a memory phase (unlike that included in the SDCD test), the results indicated that the brain areas related to visual information and attention was activated while carrying out the task. Our results indicated that the SDCD was associated with most of the subtests of the MMSE. Thus, the SDCD test appears to be associated not only with attention and memory, but also with global cognitive function. We need to minutely assess and investigate other cognitive functions (e.g., executive function and processing speed) and their association with the SDCD test in future studies.

The ROC curve for the SDCD score indicated that the SDCD test identified cognitive impairment with a high degree of accuracy. Previous studies have reported that some picture-based memory tests can reliably detect dementia.[18–20] These studies support the results of the present study. Moreover, the SDCD test is able to detect dementia in less time compared to other tests studied previously. Picture-based memory tests have some advantages over verbal memory tests. First, pictures are remembered better than words, a phenomenon known as the "picture superiority effect".[21] Previous studies showed that superiority of memory for pictorial material was often applied as a mnemonic aid for older adults.[22,23]_ENREF_17. Second, picture-based memory tests are not limited by the patient's level of education. Some verbal memory tests cannot be used for a population that has a low level of education.[19] Most of the verbal-based screening measures have not been validated in people with low education levels or illiterate individuals,[24,25] and it has been shown in previous studies that a low level of education can result in cognitively unimpaired people screening positive for dementia.[24] Furthermore, the SDCD test takes only approximately 2 minutes to assess short-term memory and attention functioning, in addition to its abovementioned merits. In the present study, the participants took approximately 10 minutes and approximately 5 minutes to complete the MMSE and the SPMT, respectively. The SDCD test appears as an easy game for patients, because of the simplicity of the differences, but it is actually quite a difficult cognitive task. It is possible that this characteristic makes the SDCD test fun for the participants to complete, thereby making its widespread use possible. Thus, we believe that the SDCD test can be used to identify cognitive impairment in older adults in a clinical or community-based setting.

The present study has several limitations. First, although we assessed global cognitive and memory functions with the MMSE and the SPMT, other cognitive functions, such as executive functions and processing speed, were not assessed in this study. We need to assess these cognitive functions and investigate their association with the SDCD test in future studies. Second, participants in the present study were community-dwelling older adults who had not received a diagnosis of dementia or MCI, and we did not confirm the test–retest reliability for older adults with dementia or MCI. In the future, we need to include older adults diagnosed with dementia to ascertain whether the SDCD test can discriminate between normal cognitive function and MCI in older adults.

5. Conclusion

We developed a new type of short-term memory and attention test that uses a spot-the-difference task for the identification of cognitive impairment. The present study indicates that the SDCD test can be an effective clinical tool for the identification of cognitive impairment in older adults.

Conflicts of interest

The authors declare no conflicts of interest.

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Original Article

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Children with flat feet have weaker toe grip strength than those having a normal arch

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Abstract. [Purpose] This study investigated the relationship between toe grip strength and foot posture in children. [Subjects and Methods] A total of 619 children participated in this study. The foot posture of the participants was measured using a foot printer and toe grip strength was measured using a toe grip dynamometer. Children were classified into 3 groups; flatfoot, normal, and high arch, according to Staheli's arch index. The differences in demographic data and toe grip strength among each foot posture group were analyzed by analysis of variance. Additionally, toe grip strength differences were analyzed by analysis of covariance, adjusted to body mass index, age, and gender. [Results] The number of participants classified as flatfoot, normal, and high arch were 110 (17.8%), 468 (75.6%), and 41 (6.6%), respectively. The toe grip strength of flatfoot children was significantly lower than in normal children, as shown by both analysis of variance and analysis of covariance. [Conclusion] A significant difference was detected in toe grip strength between the low arch and normal foot groups. Therefore, it is suggested that training to increase toe grip strength during childhood may prevent the formation of flat feet or help in the development of arch.

Key words: Flatfoot, Toe grip strength, Children

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INTRODUCTION

Foot misalignment (flatfoot and high arch) is one of the common orthopedic issues in pediatric health[1–3)] and it causes many injuries in the foot, knee, and lower back[3–5)]. Almost all children are born with flatfoot and normal foot posture develops during the first decade of life[6, 7)]. However, some children have misaligned feet even after10 years of age. An estimated 19.1% of children, aged 10–13 years, have flatfoot[8)]. The incidence of high-arched foot is reportedly 14.6–25.8%[9, 10)]. If normal foot posture does not develop created during the elementary school period, foot misalignment continues to during adolescence and into adulthood. Therefore, development of normal foot posture during childhood is important.

Flatfoot and high arch are caused by many factors such as neurological disorders, congenital conditions, and structural anomalies[1, 3)]. However, flatfoot and high arch can also be found in otherwise healthy individuals, and in the absence of injury, they can be caused by structural issues such as ligament tension and muscle strength[1, 3)]. Ligament laxity typically improves as bones lengthen with age, and the majority of children develop an arch in the first decade of life[11)]. In early childhood, the intrinsic and extrinsic foot muscles are usually strengthened through walking and running. However, if the intrinsic and extrinsic foot muscles are not used enough in early childhood, they remain weak. Therefore, improving muscle strength in the foot is one method of treating foot misalignment.

Recently it was revealed that toe grip strength is related to foot posture. Toe grip strength is the strength of the toe flexor muscles, such as the flexor hallucis longus and flexor digitorum longus. These muscles are related to the creation of the foot arch. Hashimoto et al.'s study revealed that toe grip strength training can increase the foot arch in adolescents[12)]. Toe grip strength is related to foot posture in adolescents[13)]. However, it is not known if the same relationship between toe grip strength and foot posture is present in children. The authors hypothesized that there was a relationship between toe grip strength and foot posture in children. The demonstration of a relationship between foot posture and toe grip strength would highlight the importance of toe grip strength

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in creation normal foot posture during childhood. Therefore, the authors investigated the relationship between toe grip strength and foot posture in this study.

SUBJECTS AND METHODS

A total of 619 children (boys, n = 311, age = 11.2 ± 0.7 years; girls, n = 308, age = 11.3 ± 0.7 years; age expressed as mean ± SD) participated in this study. Signed consent was obtained from the principals of five elementary schools in Nara Prefecture in Japan for inclusion of their schools in the study. Demographic data were collected from the returned consent forms, as were the inclusion (age 10–12 years) and exclusion (no history of foot surgery or congenital disorders) criteria. The purpose and methods of the current study were explained to the participants and elementary school teachers in detail in a verbal statement and document. The local ethics committee approved the study (H26-6).

Foot posture was measured using a foot printer (Bauerfeind Co. LTD, Germany). A static footprint was obtained as each child stood barefoot on the foot printer, with weight normally distributed between both feet. The dominant foot was identified as that preferred for kicking a ball and we used the posture of the dominant foot in the analysis. Children stood with their feet shoulder width apart and placed their foot at whatever angle they preferred. The width of the foot at the arch and the width of the heel were measured. The arch index for each foot was calculated by dividing the former number by the latter, as described by Staheli et al[14].

Toe grip strength was measured using a T.K.K.3362 toe-grip dynamometer (Takei Scientific Instruments, Niigata, Japan) (Fig. 1). The protocol for measuring toe grip strength was as described in the studies by Uritani et al[15, 16]. Participants sat upright on a chair without leaning on the backrest throughout the toe grip strength measurements. Both of the hips and knees were flexed at about 90° and the ankles were placed in a neutral position and fixed with a strap. The first proximal phalanx was positioned at the grip bar, and the heel stopper was adjusted to fit the heel of each participant. The bar was then gripped with the toes using maximal effort, for about 3 seconds. Toe grip strength of the dominant foot was measured twice. The maximum strength from the two measurements was recorded.

At first, participants were classified into flatfoot, normal, and high arch categories, based on the arch index, as measured by their footprint. An arch index value between 0.44 and 0.89 was defined as a normal foot, an index <0.44 was classified as a high arch, and an index, >0.89 was classified as a low arch[14]. Differences in age, body mass index (BMI), toe grip strength, and gender between the three groups were examined using analysis of variance (ANOVA) and a χ^2 test. Differences in toe grip strength among the 3 groups were examined using analysis of covariance (ANCOVA) adjusted for age, BMI and gender. When a significant effect was found, differences were determined using the Turkey-Kramer post-hoc test for ANOVA, and the Bonferroni post-hoc test for ANCOVA. Statistical analysis were carried out using the SPSS version 20.0 software package (SPSS, Chicago, IL, USA), with a p value < 0.05 accepted as significant.

Fig. 1. T.K.K.3362 toe-grip dynamometer

RESULTS

Table 1 shows the characteristics of the participants. The ANOVA results showed that there was a significant difference in toe grip strength among the 3 groups ($p < 0.01$). The values for toe grip strength were 11.0 ± 3.9 kg in flatfoot, 12.6 ± 4.1 kg in normal, and 11.4 ± 3.6 in high arch (Table 2). The toe grip strength of the low arch group was significantly lower than the normal group ($p < 0.01$) and that there was no significant difference between the high arch group and other groups. In addition, ANCOVA showed a significant difference in toe grip strength among the 3 groups when adjusted for age, BMI, and gender ($F = 5.22$, $p = 0.01$). Post-hoc tests indicated that the toe grip strength of the low arch group was significantly lower than in the normal group ($p < 0.01$).

DISCUSSION

Our study revealed that toe grip strength was related to foot posture in children and that the toe grip strength of the flatfoot group was weaker than that of the normal group. However, there was no significant difference between high arch group and the other groups. In addition, toe grip strength was related to foot posture after adjustment for BMI, age, and gender.

Foot posture of children is related to BMI, age, and gender[17, 18], however in this study toe grip strength was related to foot posture, when measurements were adjusted for these factors. Moreover, muscle strength and physique differ with age and gender as children go through their growth period[19], as does the prevalence of flatfoot[17]. Foot posture in children is flexible, so the foot arch can easily be decreased by the body weight load. Evan found that foot posture was not related to weight in children[20]; nevertheless, many other studies have identified a correlation between BMI and foot posture[17, 18, 21, 22]. Pfeiffer et al.'s study revealed that flatfoot was present in 62% of obese, 51% in overweight, and 42% of young children with normal body weight[17]. In the present study, toe grip strength was related to foot posture adjusted for BMI, age, and gender.

Two possible explanations for the relationship between toe grip strength and foot posture are proposed here. First, toe flexor muscles lift up the navicular and make a medial longitudinal arch. Toe grip strength comes from the toe flexor muscles, such as the flexor hallucis longus and flexor digito-

Table 1. Subject characteristics by foot posture group

	All subjects (N = 619)					
	Flatfoot (n = 110)	SD	Normal (n = 468)	SD	High arch (n = 41)	SD
Age (yrs)	11.1	0.8	11.3	0.7	11.1	0.7
BMI (kg/m^2)	17.9	3.0	17.4	2.6	16.8	2.3
Gender (n boy / %)	66 / 60.0		225 / 48.1		20 / 48.8	

The parameters above were analyzed by ANOVA and χ^2 test, * $p < 0.05$
There were no significant differences between any of these parameters between groups

Table 2. Toe grip strength differences by foot posture group

	All subjects (N = 619)						
	Flatfoot (n = 110)	SD	Normal (n = 468)	SD	High arch (n = 41)	SD	Post-hoc
Toe grip strength (kg) *†	11.0	3.9	12.6	4.1	11.4	3.6	a

[a]significant differences between flatfoot and normal
*analyzed for ANOVA ($p < 0.01$, post-hoc; a)
†adjusted for subject age, BMI and gender (ANACOVA) ($p = 0.01$, post-hoc; a)

rum longus, and these muscles pass under the navicular. The navicular height is the index of the longitudinal medial arch and by definition, flatfoot children have a diminished or absent longitudinal medial arch. Osseous structures, ligaments, tendons, and muscles create navicular height[23, 24)], and toe grip strength is one of the factors in creating the foot arch. This is supported by Hashimoto's study, which revealed that toe grip strength training increases the foot arch height in adolescents[12)]. Therefore, toe grip strength is related to foot arch, and toe grip strength is different between flatfoot and normal children.

Second, toe flexor muscles are stretched in flatfoot children, so the muscles cannot contract with maximal strength. Muscles contraction strength exhibits a length-tension relationship[25–27)], where optimal contraction occurs when the muscle is at the appropriate length and not overly stretched or compressed. In our study, toe grip strength of flatfoot children was lower than that of normal children. When the foot arch is low, toe flexor muscles are stretched. Therefore, toe flexor muscle cannot contract at maximum strength. Conversely, toe flexor muscles are looser in high arch children. However, subjects who had severe high arch due to neurological disorders were excluded from our study, and no significant differences were seen between the high arch group and the other groups. This is the second reason why toe grip strength of low arch feet was low.

The present study revealed that there was a significant difference in toe grip strength between flatfoot and normal children. A recent systematic review of current research demonstrated that there is very limited evidence for the efficacy of nonsurgical interventions in children with flatfoot[28)]. Usually, a shoe or insole is used to treat symptomatic flatfoot in children. However, these treatments cannot permanently correct foot alignment[1, 29)]. Flatfoot in children is caused by ligament laxity or foot muscle weakness, and ligament laxity is not changeable after foot posture develops. However, muscle strength is changeable, so increasing toe grip strength has the possibility to improve flatfoot. This idea is supported by the present study, which reveals that toe grip strength is related to foot posture in children. Therefore, training to increase toe grip strength during childhood may prevent flatfoot and improve foot posture.

There were several limitations in the present study. First, this study was a cross-sectional design, so the relationship between cause and effect is unknown. Therefore, further research is needed to reveal whether correlated change in grip strength and foot posture can be seen with individuals. Second, foot postures were measured using only a foot printer. The foot is a complex structure, so more detailed measurements of foot posture should be evaluated. Third, foot posture is related to genetics and ethnicity, but these factors were not considered. Despite these limitations, the findings from the present study provide valuable information and illustrate the importance of toe grip strength.

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Research Article Open Access

The Association between Pregnancy-Related Discomforts and Pre-Pregnancy Body Mass Index in Japanese Women

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Abstract

Objective: To determine the association between pregnancy-related discomforts and pre-pregnancy body mass index in a longitudinal study.

Methods: The study included 355 pregnant women (age, 31.1 ± 4.1 years). Participants were divided into three groups according to their pre-pregnancy body mass index: the low body mass index group, normal body mass index group, and high body mass index group. The occurrence of pregnancy-related discomforts during the second and third trimesters was investigated. Binomial logistic regression analysis was used to examine the association between pre-pregnancy body mass index and pregnancy-related discomforts experienced during the last two trimesters.

Results: The occurrence of most pregnancy-related discomforts increased in the third trimester, while that of constipation and shoulder stiffness or headache decreased. Based on logistic regression analysis, pre-pregnancy body mass index was significantly associated with various discomforts. The occurrence of hip joint or pubis pain (odds ratio/95% confidence interval = 2.38/1.14–4.95) during the second trimester, and sleeping difficulty (2.00/1.09–3.67), hand or finger stiffness (3.00/1.36–6.45), leg cramps (2.29/1.32–3.98), low back pain (2.20/1.29–3.75), hip joint or pubis pain (2.14/1.23–3.73), and shoulder stiffness or headache (2.01/1.06–3.82) during the third trimester was significantly higher in the high body mass index group than in the normal body mass index group. The low body mass index group exhibited a significantly a higher occurrence of shoulder stiffness or headache (2.84/1.35–5.96) during the second trimester and constipation (2.28/1.08–4.82) during the third trimester than the normal body mass index group.

Conclusion: The occurrence of discomforts decreased or increased during pregnancy. Furthermore, both pre-pregnancy high and low body mass index represent important risk factors for many pregnancy-related discomforts, compared with a pre-pregnancy normal body mass index.

Keywords: Health promotion; Pregnancy; Pregnancy-related discomforts; Pre-Pregnancy BMI; Prevention

Introduction

Methods

Anatomical, physiological, hormonal, and psychological changes occur in woman during pregnancy [1,2], causing a variety of discomforts such as low back pain, ligament pain, fatigue, and headache [3]. These pregnancy-related discomforts negatively impact mother and child health and affect the quality of life and limit the daily activities of mothers [4,5]. Despite a number of researchers investigating the management of pregnancy-related discomforts [6,7], there are several limitations to the treatments available during pregnancy. For example, non-prescribed medicines are usually unsuitable because of their adverse effects on pregnant women themselves and on the developing fetus [8,9]. Therefore, a longitudinal study is necessary to collect information on the prevalence of discomforts through the stages of pregnancy. Such information will increase the knowledge of the measures that can be taken to protect women from pregnancy-related discomfort and will be essential to prevent their onset.

Before pregnancy, it is important for women to maintain an appropriate body mass index (BMI) to avoid hormone imbalance and its negative impact on fertility [10]. Furthermore, some research indicates that the pre-pregnancy BMI is a predicting factor for conditions such as gestational diabetes, and thus for adverse pregnancy outcomes [11,12]. Pre-pregnancy obesity may also be a modifiable risk factor for intellectual disability in children [13]. On the other hand, women with pre-pregnancy low weight are at an increased risk of intrauterine growth restriction, perineal tears, preterm birth (spontaneous and induced), and low birth weight [14,15]. These results suggest that both pre-pregnancy high and low BMI negatively

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affect the progress of the pregnancy. Information about the occurrence of discomforts at each gestational period is necessary for their prevention. Moreover, a normal BMI before pregnancy promotes an uneventful progress through pregnancy. However, to date, very few studies have been conducted on the association between pre-pregnancy BMI and pregnancy-related discomforts. Accordingly, we conducted a longitudinal study aimed to identify pregnancy-related discomforts throughout pregnancy and to identify possible associations between these discomforts and the pre-pregnancy BMI.

Settings

We collected information from 355 women (age, 31.1 ± 4.1 years) at the obstetrics and gynecology clinics in the Aichi Prefecture, Japan, between 2009 and 2013. When the pregnant women visited the clinic for their periodic health examination, the information was collected by the hospital staff such as nurses. The inclusion criteria for the survey were the lack of serious orthopedic disorders, neurological diseases, and high-risk pregnancy. At the first medical examination, we recorded the personal information (age and BMI before pregnancy) of each participant by using a questionnaire.

Questionnaire about Pregnancy-Related Discomforts

The subjects of this study were asked to complete a questionnaire during the second trimester (22.4 ± 2.1 weeks of gestation) and third trimester (33.7 ± 2.1 weeks of gestation). We used the Medical Check Sheet to track pregnancy-related discomforts during gestation. The sheet, developed by the Japan Maternity Fitness Association, is a self-entry questionnaire for the management of physical conditions, to be completed before exercise. Questions were related to the expected date of birth, weeks of gestation, blood pressure, and 10 different pregnancy-related discomforts (i.e., sleeping difficulty, constipation, hand or finger stiffness, swelling, leg cramps, low back pain, hip joint or pubis pain, shoulder stiffness or headache, rib pain, and anorexia or heartburn), reported to commonly occur and to have an adverse effect on pregnancy. If the participants had felt discomfort due to any of the items on the list, those items were checked.

Ethical Considerations

After the purpose of the study had been explained, written informed consent was obtained from each participant in accordance with the guidelines approved by the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1975. The protocol was approved by the Ethics Committee of Kyoto University Graduate School of Medicine (protocol approval E-2110).

Statistical Analyses

Participants were divided into three groups (low BMI group, normal BMI group, and high BMI group) according to their pre-pregnancy BMI (<18 kg/m^2, ≥18 kg/m^2, and <22 kg/m^2 or ≥22 kg/m^2, respectively). We statistically calculated the differences in age between these three groups using analysis of variance. Based on the Medical Check Sheet completed during the second and third trimester, we determined the occurrence of each symptom during the second and third trimesters and analyzed this using descriptive statistics. Binomial logistic regression analysis was used to examine the association between each discomfort and the pre-pregnancy BMI for each trimester. We referred to discomforts as the dependent variables, to low and high BMI groups as the independent variables (with the normal BMI group as reference), and to age as the adjustment variable. Data were entered and analyzed using the Statistical Package for the Social Sciences (Windows version 20.0; SPSS Inc., Chicago, IL, USA). For all analyses, $p<0.05$ was considered statistically significant.

Result

Information on 355 women (pre-pregnancy BMI= 20.3±2.1 kg/m^2) who met the inclusion criteria was collected. We assigned 37 women to the low BMI group (BMI= 17.4±0.6 kg/m2), 246 women to the normal BMI group (BMI= 19.8 ± 1.0 kg/m2), and 72 women to the high BMI group (BMI= 23.5±1.8 kg/m^2). There were no significant differences between the three groups (low, normal, and high BMI groups) in age (30.4 ± 4.2 years, 31.2 ± 4.0 years, and 31.2 ± 4.2 years, respectively).

The occurrence of most of the pregnancy-related discomforts analyzed increased from the second to third trimester, in contrast to that of constipation and shoulder stiffness or headache that showed a decrease (Figure 1).

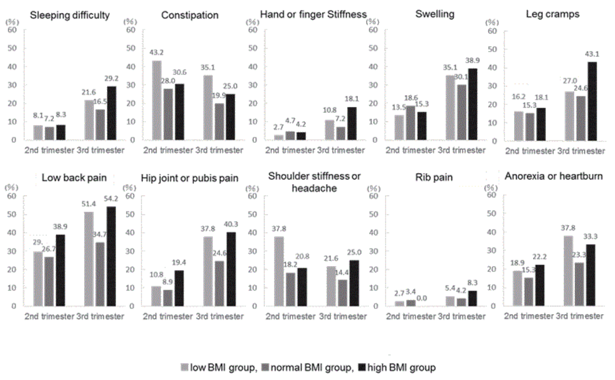

Figure 1: The prevalence of pregnancy-related discomforts during second and third trimester.

Multivariate analysis revealed that pre-pregnancy BMI was significantly associated with some of the discomforts during pregnancy (Table 1). The occurrence of hip joint or pubis pain (odds ratio/95% confidence interval=2.38/1.14–4.95) during the second trimester, and sleeping difficulty (2.00/1.09–3.67), hand or finger stiffness (3.00/1.36–6.45), leg cramps (2.29/1.32–3.98), low back pain (2.20/1.29–3.75), hip joint or pubis pain (2.14/1.23–3.73), and shoulder stiffness or headache (2.01/1.06–3.82) during the third trimester was significantly higher in the high BMI group than in the normal BMI group ($p<0.05$). The occurrence of shoulder stiffness or headache (2.84/1.35–5.96) during the second trimester, and constipation (2.28/1.08–4.82) during the third trimester was significantly higher in the low BMI group than in the normal BMI group ($p < 0.05$). No significant differences were observed in swelling, rib pain, and anorexia or heartburn.

Discussion

We analyzed the changes in the occurrence of pregnancy-related discomforts throughout pregnancy and whether their occurrence was significantly associated with pre-pregnancy BMI. We observed a different trend in the occurrence of the pregnancy-related discomforts analyzed; in fact, while some of them tended to decrease, others appeared to increase during pregnancy progression. Furthermore, we found that both low and high BMI before pregnancy represent important risk factors for many pregnancy-related discomforts, compared with normal BMI.

		second trimester		second trimester	
Discomforts	**BMI group**	**Odds ratio**	**95%CI**	**Odds ratio**	**95% CI**
sleeping difficulty	**low BMI** **normal BMI** **high BMI**	1.13 1[reference] 1.15	0.32-4.01 0.44-3.02	1.32 1[reference] 2.00*	0.57-3.11 1.09-3.67
constipation	**low BMI** **normal BMI** **high BMI**	1.92 1[reference] 1.13	0.95-3.91 0.64-2.00	2.28* 1[reference] 1.38	1.80-4.82 0.74-2.56
hand or finger stiffness	**low BMI** **normal BMI** **high BMI**	0.6 1[reference] 0.93	0.08-4.81 0.25-3.43	1.61 1[reference] 2.97*	0.74-2.09 1.36-6.45
swelling	**low BMI** **normal BMI** **high BMI**	0.68 1[reference] 0.51	0.25-1084 0.38-1061	1.25 1[reference] 1.45	0.60-2.58 0.84-2.51
leg cramps	**low BMI** **normal BMI** **high BMI**	1 1[reference] 1.14	0..39-2.55 0.57-2.26	1.1 1[reference] 2.29*	0.50-2.40 1.32-3.98
low back pain	**low BMI** **normal BMI** **high BMI**	1.15 1[reference] 1.74	0.54-2.45 1.00-3.01	1.98 1[reference] 2.20*	0.99-3.98 1.29-3.75
hip joint or pubis pain	**low BMI** **normal BMI** **high BMI**	1.27 1[reference] 2.38*	0.41-3.94 1.14-4.95	1.95 1[reference] 2.14	0.94-4.03 1.23-3.73
shoulder stiffness or headache	**low BMI** **normal BMI** **high BMI**	2.84* 1[reference] 1.21	1.35-5.96 0.63-2.33	1.63 1[reference] 2.14	0.69-3.86 1.06-3.82
rib pain	**low BMI** **normal BMI** **high BMI**	0.83 1[reference] 0	0.10-6.86 0	1.32 1[reference] 2.14	0.28-6.31 1.06-3.82 0.75-6.11
anorexia or heartburn	**low BMI** **normal BMI** **high BMI**	1.24 1[reference] 1.56	0.51-3.03 0.81-3.01	1.97 1[reference] 1.62	0.95-4.08 1.06-3.82 0.92-2.87

Table1: The influence of pre-pregnancy BMI on pregnancy related discomforts (logistic regression analysis). **Note:** The analysis for discomforts was adjusted for age. *: $p < 0.05$

The occurrence of most pregnancy-related discomforts increased from the second to third trimester, while the occurrence of constipation and shoulder stiffness or headache decreased. The tendency for the occurrence of the two discomforts of current study was almost equivalent to previous reports. A previous study in the United States showed that the occurrence of constipation decreased (26.3% to 15.7%) from the second to the third trimester [16], and in another cross-sectional study, the occurrence of headache decreased (44.9% to 37.6%) and that of constipation increased (38.6 to 45.2%) from the second to the third trimester [3]. Here, we observed a difference when compared with the previous study of Nazik and Eryilmaz, where the prevalence of constipation decreased in our study but increased in that study. However, it is worth noting that ours is a longitudinal study, and thus, we collected information during each trimester from the same participants, and that found that some discomforts might improve during the course of pregnancy. Therefore, pregnant women should pay attention to constipation and shoulder stiffness or headache during the early stages of pregnancy, especially during the second trimester, and of other discomforts thereafter.

We found significant differences in the occurrence of analyzed discomforts according to pre-pregnancy BMI. The occurrence of hip joint or pubis pain was higher during the second trimester, and the occurrence of sleeping difficulty, hand or finger stiffness, leg cramps, low back pain, hip joint or pubis pain, and shoulder stiffness or headache during the third trimester was higher in the high BMI group than in the normal BMI group. These discomforts are related to changes in the musculoskeletal and cardiovascular systems, common during pregnancy [17-21]. Overweight exposes the musculoskeletal system to excessive loads, resulting in conditions such as low back pain and hand pain (22,23). Overweight might also affect the cardiovascular system [24,25], leading to leg cramps and hand or finger stiffness.

Accordingly, discomforts, especially those related to the musculoskeletal and cardiovascular systems, might occur in the high BMI group. The occurrence of shoulder stiffness or headache during the second trimester, and constipation during the third trimester, was higher in the low BMI group than in the normal BMI group. These discomforts are related to fluctuations in hormones such as estrogen, occurring during pregnancy [26,27], and low weight might determine hormone imbalance, in particular by decreasing the effects of female hormones [28]. Therefore, pre-pregnancy low BMI might hamper the hormonal balance and lead to the observed pregnancy-related discomforts.

In recent years, the occurrence of obesity has increased worldwide [29],while women, especially young adults, attempt to lose weight despite being of normal weight or underweight [30,31]. In this respect, our study showed that both women with high or low pre-pregnancy BMI have a high risk of pregnancy-related discomforts that not only affect their quality of life and limit their daily activities, but might also have a negative impact on their children's health [4,5]. Hence, our findings suggest that young women should maintain an appropriate BMI before getting pregnant, in order to have a good pregnancy progression.

This study has several limitations. First, we could not obtain information on some factors that could affect pregnancy-related discomforts (e.g. living environment, parity, and hormonal fluctuations during pregnancy). These factors may have affected our results. Second, we could not investigate the occurrence of additional discomforts that occur during pregnancy: it is known that more than 30 discomforts might be experienced by pregnant women [3]. In the future, a similar study investigating various pregnancy-related discomforts should be conducted, taking into account the different factors related to the discomforts.

Conclusion

The current study showed that pregnancy-related discomforts have different trends in occurrence from the second to the third trimester. Therefore, pregnant women should pay attention to different discomforts depending on the pregnancy period. Moreover, pre-pregnancy low or high BMI might be a risk factor for pregnancy-related discomforts, regardless of age. These findings indicate that women should maintain an appropriate BMI before pregnancy to prevent potential discomforts during pregnancy.

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CLINICAL INVESTIGATIONS

A 12-Week Physical and Cognitive Exercise Program Can Improve Cognitive Function and Neural Efficiency in Community-Dwelling Older Adults: A Randomized Controlled Trial

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OBJECTIVES: To investigate whether a 12-week physical and cognitive exercise program can improve cognitive function and brain activation efficiency in community-dwelling older adults.

DESIGN: Randomized controlled trial.

SETTING: Kyoto, Japan.

PARTICIPANTS: Community-dwelling older adults (N = 48) were randomized into an exercise group (n = 24) and a control group (n = 24).

INTERVENTION: Exercise group participants received a weekly dual task–based multimodal exercise class in combination with pedometer-based daily walking exercise during the 12-week intervention phase. Control group participants did not receive any intervention and were instructed to spend their time as usual during the intervention phase.

MEASUREMENTS: The outcome measures were global cognitive function, memory function, executive function, and brain activation (measured using functional magnetic resonance imaging) associated with visual short-term memory.

RESULTS: Exercise group participants had significantly greater postintervention improvement in memory and executive functions than the control group ($P < .05$). In addition, after the intervention, less activation was found in several brain regions associated with visual short-term memory, including the prefrontal cortex, in the exercise group ($P < .001$, uncorrected).

CONCLUSION: A 12-week physical and cognitive exercise program can improve the efficiency of brain activation during cognitive tasks in older adults, which is associated with improvements in memory and executive function. **J Am Geriatr Soc 2015.**

Key words: cognitive improvement; physical and cognitive exercise program; fMRI; randomized controlled trial

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Dementia, which is common in older adults, affecting 5% to 8% of the population aged 65 and older[1] and up to 30% of people aged 85 and older,[2] can drastically influence daily life; its prevalence is also increasing. Approximately 48% of people with Alzheimer's disease (AD) are estimated to live in Asia, and this percentage is projected to grow to 59% by 2050.[3] Dementia, including AD, is associated with mortality,[4] so ways to prevent dementia onset are urgently needed.

Several meta-analyses have found that physical activity is associated with improvements in cognitive performance in older adults,[5–7] and cognitive activities reduce the risk of dementia.[8] A recent systematic review showed that combined cognitive and exercise training, including dual-task (DT) exercises, which involve concurrent cognitive and motor tasks, can improve cognitive function in older adults with and without cognitive impairment.[9] This review indicated that these interventions were beneficial to various components of cognitive function in older adults with healthy cognition,[10] mild cognitive impairment (MCI),[11] and AD.[12]

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In addition to the effect of multimodal exercise with physical and DT components on cognitive performance, recent functional magnetic resonance imaging (fMRI) studies have provided evidence that physical exercise changes brain activation. Some studies have reported less brain activation during memory-related[13] or conflict tasks,[14] which suggests that such reduced activation improves neural efficiency during cognitive tasks, but few studies have tested whether multimodal exercise affects neural activity, particularly cortical activation. Therefore, the present study used a randomized controlled trial combined with fMRI data from a visual short-term memory task, which requires frontal lobe function,[15] to investigate whether a 12-week multimodal exercise program, including physical and DT components, could improve cognitive function and the efficiency of brain activation in community-dwelling older adults. It was hypothesized that multimodal exercise would lead to less brain activation in the regions associated with visual short-term memory, especially the prefrontal cortex, because of the DT components of the exercise.

METHODS

Participants

Independently community-living individuals aged 60 and older who were willing to participate in group exercise classes for at least 3 months were recruited from the Kyoto City Silver Human Resources Center, Japan. An interview was used to exclude individuals with a history of major psychiatric illness; a serious neurological diagnosis; or severe cardiac, pulmonary, or musculoskeletal disorders according to self-report. Individuals with cognitive impairment (Mini-Mental State Examination (MMSE) score ≤23)[16] and those who showed major abnormalities on brain MRI scans, such as cerebral infarction or tumor, were also excluded. The study was conducted in accordance with the guidelines of the Declaration of Helsinki, and the ethics committee of the Kyoto University Graduate School of Medicine reviewed and approved the study protocol. The trial registration number is JMA-IIA00108.

Study Design and Randomization

Randomization via computer-generated random numbers was performed in blocks of four participants, stratified according to MMSE score. Participants were randomly assigned to the exercise intervention group (EG) or the control group (CG). EG participants received 90 minutes of group training sessions once per week for 12 weeks and were assigned a pedometer-based walking exercise. CG participants did not receive any intervention and were instructed to spend their time as usual during the intervention phase.

Required Sample Size

A previous study showed that 2 months of combined cognitive and exercise training can improve working memory in cognitively healthy older adults, with an approximate effect size of 0.9.[10] Considering participants' cognitive status and the intervention program used in this study, a sample size of 21 participants per group would be required to reach a power of 0.8, with an alpha set at 0.05 and beta at 0.2. Assuming a dropout rate of 15%, a final sample size of 24 per group was determined to be required.

Intervention Program

Subjects assigned to the EG received 90 minutes of group training sessions once a week for 12 weeks and pedometer-based walking exercise assignments supervised by physiotherapists.

Exercise classes followed a standardized format that included 15 minutes of stretching and moderate-intensity exercises, 15 minutes of progressive muscle strength training, and 60 minutes of DT exercise that included three DT categories.[17,18] The intensity of these exercises was based on recommendation from the American College of Sports Medicine and the American Heart Association.[19] In the first category, participants were instructed to perform a verbal fluency task during short-, fast-step exercises. In the second category, the supervisor assigned a number to various parts of the body (e.g., 1 = right shoulder, 2 = left shoulder), and participants were instructed to perform seated or standing step exercises at a tempo of 60 to 120 beats per minute according to the tempo of the accompanying music. During these exercises, the supervisor periodically stated a number, at which point participants were to touch the appropriate parts of their own body. In the third category, participants were instructed to perform standing step exercises at the same tempo as the second category exercise and to step in one of four directions indicated verbally by the supervisor (right, forward, back, left). The intensity and difficulty of the three exercises were gradually increased over the 12-week period.

During the 12-week intervention phase, the EG received walking exercises, using a pedometer (Yamax Power Walker EX-300; Yamasa Tokei Keiki Co., Ltd, Tokyo, Japan) to measure daily step counts. Participants were instructed to increase the number of daily steps by 15% each month and to record the number of steps taken by the end of each day on a calendar. At the end of every month, a sheet was given to each participant to collect brief feedback about the month's exercises and to provide reminders to record the exercises. The feedback responses were used to assist in setting the number of daily steps assigned for the next month. Walking exercise intensity was not clearly defined. During the first month, EG participants were instructed to increase their steps by approximately 15% relative to baseline (100% → 115%). During the second and third months, they were also instructed to do so relative to the previous month (115% → 132.3% → 152.1%). That is, their steps would have increased by approximately 50% relative to baseline.

Outcome Measures

All participants underwent several evaluations upon entry into this study (preintervention) and at the end of the study (postintervention). Evaluations included measurements of daily step counts, clinical tests (physical and cognitive function), and MRI scans. Before the study, one of the authors (SN) trained all staff members on how to obtain the measurements included in the study. Physical therapists administered the physical function tests, and occupational therapists administered the cognitive function tests; therapists were blinded to group allocation.

Measurement of Average Daily Steps

Participants were instructed to wear the pedometer in a clothing pocket on their dominant leg for 14 consecutive days except when bathing, sleeping, or performing water-based activities. The averages of their daily step counts for 14 days were calculated.

Clinical Tests

All participants underwent a 10-m walking test,[20] the Timed Up and Go test (TUG),[21] and the Five Chair to Stand test (5CS)[22] to evaluate physical function. In the 10-m walking test, participants walked at their usual speed over a distance of 10 m. The time was recorded to yield 10-m walking speed. In the TUG, participants were instructed to stand up from a standard chair, walk 3 m and back, and sit down. The task was timed for speed. In the 5CS, participants were asked to stand up and sit down five times as fast as possible; the time was recorded. Each of the three tests was assessed once per participant using a stopwatch.

The MMSE, a standard test in cognitive aging research used to assess mental status, was administered to evaluate global cognitive function.[16] Modified versions of the logical memory subtest from the Wechsler Memory Scale Revised (WMS-R) were used to assess memory.[23] In the logical memory subtest, two short stories are read aloud to for immediate (LM-I; maximum score 50) and delayed (after 30 minutes; (LM-II; maximum score 50) recall. The Trail-Making Test (TMT) was administered as a test of executive function, divided attention, and cognitive flexibility.[24] The test is divided into two parts; Part A tests visual scanning and includes a numbered connect-the-dots task, and Part B measures cognitive flexibility with a more-complex connect-the-dots task that includes alternating letters and numbers. The time required to complete each task was recorded, with longer time indicating worse performance. Data were analyzed using a difference score between Parts A and B, ΔTMT, calculated as the difference between the times taken for each part (Part B–A).[25]

Image Acquisition

Whole-brain imaging was performed using a MRI scanner (3.0-Tesla Magnetom Verio, Siemens, Erlangen, Germany). A T2*-weighted echo planar imaging (EPI) sequence sensitive to blood oxygenation level–dependent contrast with 2,000-ms repetition time (TR), 25-ms echo time (TE), 75° flip angle, 64×64 acquisition matrix, 224-mm field of view, 3.5 mm^2 in-plane resolution, and 39 axial slices with a slice thickness of 3.5 mm was used for functional imaging. A high-resolution structural image was also acquired using a T1-weighted magnetization-prepared rapid-acquisition gradient echo pulse sequence (voxel size 1 mm^3). Firm padding was placed around the head of each participant to restrict head motion. The visual stimuli were projected onto a screen, and participant responses were collected using a MRI-compatible response box. The EPI images were acquired during the visual short-term memory task in two consecutive rungs (one for face memory and one for location memory, see below). The first five scans in each run were discarded to compensate for T1 equilibration effects.

fMRI Experimental Protocol

During fMRI scanning, based on a previous study,[26] participants performed the n-back task (n = 1, 0) for the location and face stimuli created.[27] Only 0- and 1-back tasks were used in the present study because 2- or 3-back tasks were thought to be too cognitively demanding for older adults. Because the memory effort for the 1-back task is low, the results of the present study should be interpreted with caution. The visual short-term memory tasks for face and location were conducted in separate fMRI runs. In the 1-back task, participants were required to monitor a series of stimuli (single dot location or faces) and to indicate whether the stimulus was the same as that presented in the previous trial. In the location 0-back task, participants were required to monitor a stimulus and to indicate whether it was located in the center of the screen. In the face 0-back task, participants were required to indicate the sex of a face stimulus. In the rest phase, participants were required to gaze at a fixation cross located in the center of the screen. The location stimuli were made up of a single black dot, which was presented in a randomly designated location. The face stimuli were made up of neutral faces of young Japanese people (university students), with an equal number of male and female faces. The stimulus duration and the interstimulus interval for each task were each 2 seconds. Each of the three conditions (1- and 0-back tasks and rest) was conducted in separate blocks. Each block, which had a duration of 32 seconds (8 trials for 1- and 0-back tasks), was presented four times (a total of 12 blocks), and there were equal numbers of each condition within the block. For the face and location tasks, the order of the 12 blocks was counterbalanced across participants.

Statistical Analysis for Behavioral Data

Baseline characteristics were compared between the EG and CG groups using the Student *t*-test and the chi-square test. The intervention effects on all outcome measures except for brain activation were determined using two-way repeated-measures analyses of variance (ANOVAs) with group (EG, CG) as a between-subject factor and time (pre- and postintervention) as a within-subject factor. Data were entered and analyzed using SPSS Windows version 20.0 (SPSS, Inc., Chicago, IL). For all analyses, $P < .05$ was considered statistically significant.

Image Preprocessing and Statistical Analysis for MRI Data

MRI data were analyzed using Statistical Parametric Mapping 8 (Wellcome Department of Imaging Neuroscience, London, UK). All of the functional images were spatially realigned to the first functional image to correct for head motion. The resulting volumes were normalized to a standard EPI template based on the Montreal Neurological Institute reference brain (resampled voxel size 2 mm^3). The normalized images were smoothed using an isotropic 8-mm full-width-at-half-maximum Gaussian kernel. A high-pass filter of 1/128 Hz was used to remove low-frequency noise, and a first-order autoregressive model was used to correct temporal autocorrelation.

The fMRI data were analyzed using the blocked design. Activated voxels in each experimental condition were identified using a statistical model containing a boxcar function convolved with a canonical hemodynamic response function. The experimental conditions consisted of a 1-back task, a 0-back task, and rest. In addition to analyzing the face and location conditions, the fMRI data were also analyzed by combining two tasks to maximize the statistical power. Linear contrasts were used to obtain participant-specific estimates for each effect. The brain activation associated with visual short-term memory was analyzed using the contrast of the 1- versus 0-back task. These estimates were then entered into a second-level analysis that treated the participant as a random effect. To identify regions in which brain activation associated with visual short-term memory increased or decreased after the 12-week intervention, brain activation before the intervention was compared with that after intervention in the EG using two-sample *t*-tests. The statistical threshold was set at $P < .001$ (uncorrected for multiple comparisons, cluster size >10 voxels).

The MarsBaR[28] software was also used to extract the signal changes of regions identified in the analysis described above. The signal changes were averaged across all voxels in a given cluster. The group-by-time interactions in the signal changes were determined using two-way repeated-measures ANOVAs using SPSS.

RESULTS

Overall, 70 participants were screened, 52 (74.3%) of whom met the inclusion criteria, agreed to participate, and were enrolled in the study; four of these were removed on the basis of the exclusion criteria, two with a MMSE score less than 24, one with apparent brain damage on structural MRI, and the other with missing fMRI signals, leaving 48 participants to complete the 12-week intervention phase and the postintervention assessment: 24 in the EG and 24 in the CG (Figure 1).

The baseline characteristics of both groups were well matched, and there were no significant differences in any variables between the groups at baseline, with the exception of reaction time in the 0-back tasks (Table 1). Twelve exercise sessions were scheduled during the intervention phase, and all were performed. Median adherence was 91.7% (25th–75th percentile 83.3–100%) in the EG over the 12 weeks. Physiotherapists monitored for adverse events; there were none.

Change in Average Daily Steps

Average daily steps increased in the EG by 54.1% (from 7,266 ± 3,001 to 11,189 ± 5,823) during the study period but not in the CG (from 6,269 ± 1,885 to 5,692 ± 1,654). There was a significant group-by-time interaction ($F = 30.2$, $P < .001$; Table 1). Median adherence for recording the step counts was 100% (25th–75th percentile 99.0–100%) in the EG over the 12 weeks.

Effect of Intervention on Physical and Cognitive Functions

There were significant group-by-time interactions in physical function, with EG participants having greater improvements in walking speed ($F = 9.37$, $P = .004$) and 5CS time ($F = 11.2$, $P = .002$) but not TUG time (Table 1).

There were significant group-by-time interactions in cognitive function, with EG participants having greater improvements in memory (WMS-LM I: $F = 7.44$, $P = .009$; WMS-LM II: $F = 7.80$, $P = .008$) and executive (ΔTMT: $F = 6.05$, $P = .018$) function. There was no group-by-time interaction for MMSE score (Figure 2, Table 1).

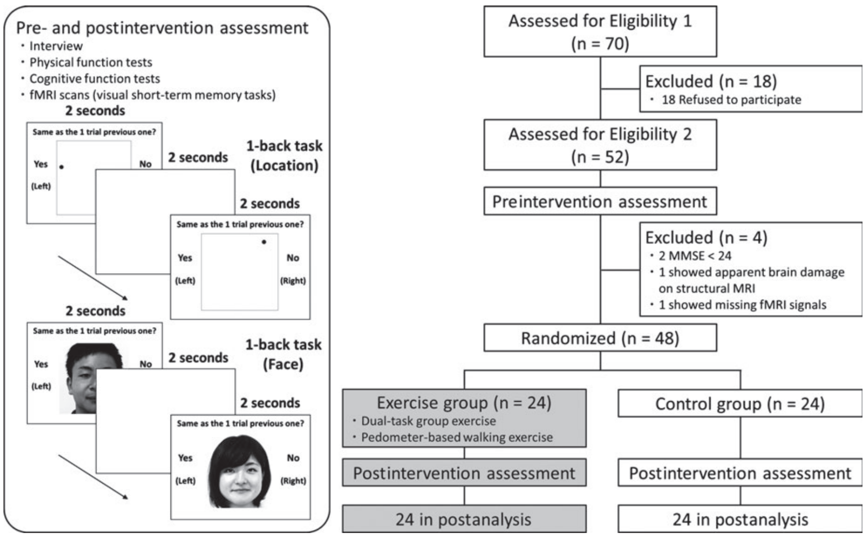

Figure 1. Flowchart of distribution of participants throughout the trial. fMRI = functional magnetic resonance imaging; MMSE = mini mental state examination.

Table 1. Participant Baseline Characteristics and Outcome Measures Before and After the Intervention

Characteristic and Outcome Measure	Exercise Group, n = 24	Control Group, n = 24	Baseline Difference *P*-Value	Group × Time Interaction	
				F-Value	*P*-Value
Age, mean ± SD	73.0 ± 4.8	73.5 ± 5.6	.76		
Female, n (%)	11 (45.8)	11 (45.8)	>.99		
Body mass index, kg/m^2, mean ± SD	21.0 ± 2.4	21.2 ± 2.9	.81		
Education, years, mean ± SD	12.2 ± 2.2	13.0 ± 2.5	.25		
Number of medications taken, mean ± SD	2.08 ± 1.91	2.13 ± 2.2	.94		
Physical function, mean ± SD					
Walking speed, m/s					
Before	1.33 ± 0.20	1.28 ± 0.14	.32		
After	1.40 ± 0.19	1.27 ± 0.13		9.37	.004
Timed Up and Go Test, seconds					
Before	6.79 ± 1.10	6.47 ± 1.23	.34		
After	6.54 ± 1.02	6.32 ± 1.17		0.15	.70
Chair stand test, seconds					
Before	7.46 ± 1.50	7.55 ± 2.06	.87		
After	6.88 ± 1.26	7.85 ± 2.14		11.2	.002
Cognitive function, mean ± SD					
Mini-Mental State Examination range (0–30)					
Before	27.4 ± 1.8	27.9 ± 2.0	.36		
After	28.2 ± 1.6	27.7 ± 2.3		1.90	.17
Wechsler Memory Scale logical memory subtest					
I					
Before	17.3 ± 4.5	20.0 ± 7.7	.14		
After	22.0 ± 5.9	21.3 ± 7.8		7.44	.009
II					
Before	12.8 ± 5.3	14.9 ± 7.9	.28		
After	18.0 ± 6.3	16.3 ± 8.0		7.80	.008
Change in Trail-Making Test, seconds					
Before	43.6 ± 26.1	37.9 ± 20.7	.41		
After	30.4 ± 16.1	41.5 ± 30.7		6.05	.02
Daily steps, mean ± SD					
Before	7,266 ± 3,001	6,269 ± 1,885	.18		
After	11,189 ± 5,823	5,692 ± 1,654		30.2	<.001
Correct responses, mean ± SD					
0-back (face + location), %					
Before	96.9 ± 3.0	97.5 ± 2.0	.42		
After	97.5 ± 3.8	98.7 ± 2.8		0.31	.58
1-back (face + location), %					
Before	90.2 ± 9.8	92.9 ± 5.1	.23		
After	94.3 ± 4.8	95.9 ± 3.3		0.29	.60
0-back (face), %					
Before	97.0 ± 2.5	97.3 ± 3.2	.76	0.16	.69
After	97.4 ± 2.2	97.3 ± 2.8			
1-back (face), %					
Before	87.8 ± 11.4	90.0 ± 7.0	.42	0.44	.51
After	94.3 ± 5.8	94.8 ± 4.5			
0-back (location), %					
Before	96.9 ± 4.2	97.8 ± 2.5	.37	0.05	.83
After	97.5 ± 3.8	98.7 ± 2.8			
1-back (location), %					
Before	92.6 ± 9.8	95.8 ± 4.7	.15	0.04	.84
After	94.2 ± 7.3	97.0 ± 3.4			
Reaction time, mean ± SD					
0-back (face + location), milliseconds					
Before	1,025 ± 109	1,122 ± 132	.009	0.68	.41
After	942 ± 148	1,014 ± 126			
1-back (face + location), milliseconds					
Before	1,181 ± 213	1,224 ± 179	.44	0.25	.62
After	1,118 ± 184	1,148 ± 157			

(Continued)

Table 1 (Contd.)

Characteristic and Outcome Measure	Exercise Group, n = 24	Control Group, n = 24	Baseline Difference *P*-Value	Group × Time Interaction *F*-Value	Group × Time Interaction *P*-Value
0-back (face), milliseconds					
Before	1,026 ± 93	1,120 ± 140	.009	0.90	.35
After	978 ± 142	1,037 ± 130			
1-back (face), milliseconds					
Before	1,207 ± 235	1,290 ± 211	.21	1.13	.29
After	1,155 ± 187	1,191 ± 175			
0-back (location), milliseconds					
Before	1,028 ± 164	1,125 ± 151	.04	0.16	.69
After	908 ± 166	991 ± 140			
1-back (location), milliseconds					
Before	1,154 ± 220	1,159 ± 189	.93	0.34	.56
After	1,081 ± 203	1,106 ± 163			

SD = standard deviation.

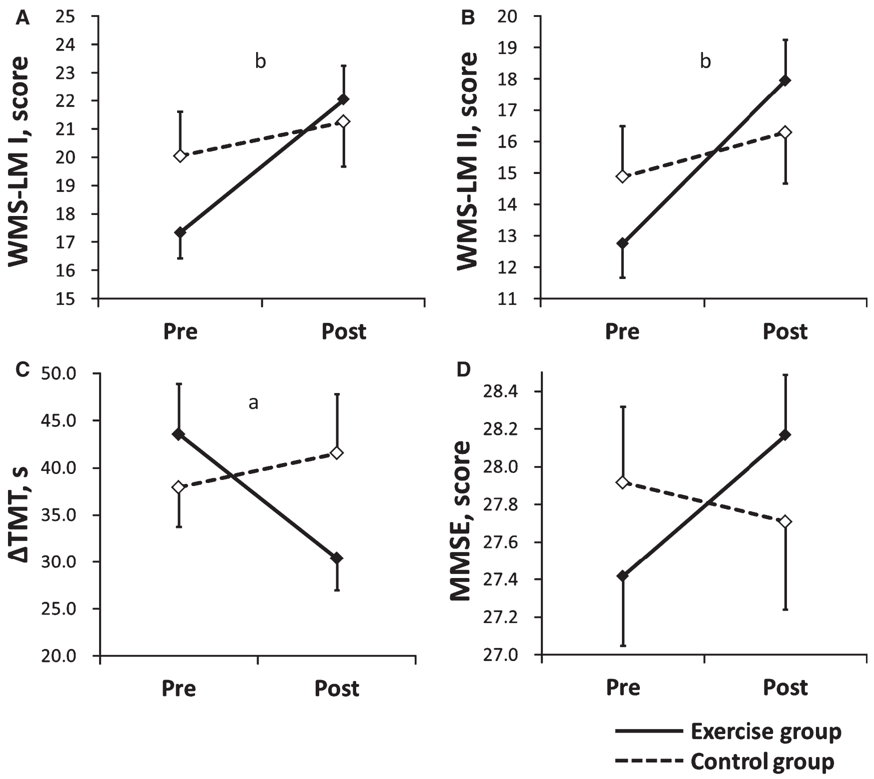

Figure 2. Group-by-time interactions in the cognitive functions before and after the intervention. Group mean differences and standard errors for Wechsler Memory Scale Revised logical memory subtest (WMS-LM) (A) I and (B) II, (C) Trail-Making Test Part A–B (ΔTMT), and (D) Mini-Mental State Examination (MMSE). $P <$ [a].05, [b] .01.

Effect of Intervention on Brain Activation Associated with Visual Short-Term Memory

There was no significant group-by-time interaction for visual short-term memory performance (face, location, face + location) after the intervention phase (Table 1), perhaps because of a ceiling effect.

The fMRI analysis showed that decreased brain activation was associated with each of the face and location tasks in several brain regions in the EG (Table 2). Although these results indicate that the exercise intervention might affect different neural networks (depending on the type of stimuli), these results were not a priori hypothesized, and these results are therefore not further discussed. After the intervention phase in the EG group, it was found that none of the regions showed significantly increased brain activation in association with the face and location tasks.

Table 2. Regions Showing Decreased Activation Associated with Visual Short-Term Memory After the Intervention

Region (Brodmann's Area)	Montreal Neurological Institute Coordinates x	y	z	Z-Value	Cluster Size
1–0 back (face + location)					
Left superior frontal gyrus (9)	−20	48	34	3.84	108
Right thalamus	6	−20	−2	3.52	51
Right superior frontal gyrus (10)	24	60	14	3.46	17
1–0 back (face)					
Right thalamus	2	−16	−4	3.84	35
1–0 back (location)					
Left superior temporal gyrus (22)	−50	10	−8	3.61	29
Left parahippocampal gyrus (36)	−38	−32	−16	3.57	23
Right superior temporal gyrus (38)	42	6	−22	3.42	13

$P < .001$ uncorrected, cluster size >10 voxels.

When combining the data from the two tasks, decreased brain activation was found to be associated with visual short-term memory in several brain regions, including the bilateral prefrontal cortex in the EG after intervention (Figure 3, Table 2), whereas no region showed significantly increased brain activation. The effects observed in the prefrontal cortex did not survive correction for multiple comparisons ($P < .001$ uncorrected, $k > 10$ voxels) and should therefore be interpreted with caution. Nevertheless, the fact that these effects were bilateral and consistent with a strong a priori hypothesis reduces the likelihood that they were due to chance. The region of interest analysis revealed that there were significant group-by-time interactions in the signal changes in the right ($F = 10.8$, $P = .002$) and left ($F = 7.71$, $P = .008$) superior frontal gyri (Figure 3). Although the interaction effect observed in the right superior frontal gyrus aligned with the prediction, greater activation during the 0-back task after the intervention phase drove the interaction in the left superior frontal gyrus. Therefore, the findings in the left superior frontal gyrus prevent us from drawing firm conclusions and should be interpreted cautiously. In the right superior frontal gyrus, the interaction was also observed for the face condition ($F = 7.71$, $P = .008$) but not for the location condition ($F = 0.77$, $P = .38$). In the left superior frontal gyrus, the interactions were also observed for the face ($F = 3.52$, $P = .048$) and location ($F = 3.81$, $P = .047$) conditions. The region of interest analyses to test a group-by-time interaction were performed independently of the whole-brain Statistical Parametric Mapping subtraction analysis (after vs before intervention) for the EG. Thus, the analysis successfully avoided the problems associated with double dipping.[29]

DISCUSSION

A 12-week multimodal exercise program with DT and walking exercises improved memory and executive function and led to decreased brain activation associated with short-term memory. These findings suggest that physical and cognitive exercise may improve the efficiency of brain function and thereby cognitive performance.

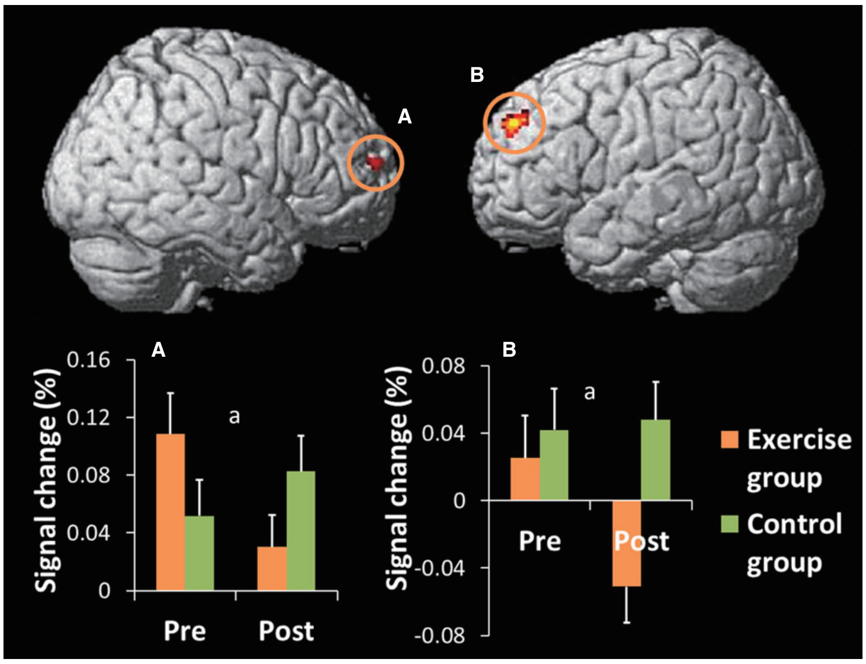

Figure 3. Bilateral prefrontal cortex showing decreased activation associated with visual short-term memory after intervention. The signal changes in these regions showed significant group-by-time interactions. Group mean differences and standard errors are shown. (A) Right and (B) left superior frontal gyrus. $P < {}^{a}.01$.

Participants in the EG had significant improvements in memory and executive function as well as physical performance. Physical activity alone[5–7] and combined cognitive and exercise training[9] can improve cognitive function in older adults. The results of this study support and expand these previous results. The physical and cognitive exercise program was performed for 12 weeks and involved changes in cognitive load using DT stimulation. Of previous studies that used physical and cognitive exercise interventions for 12 or fewer weeks,[10,30,31] only one whose participants exhibited normal cognition[10] showed positive effects on working memory and memory function. Short-term multimodal exercise with DT training could lead to cognitive improvement only in cognitively healthy elderly individuals. In the current study, EG participants performed daily walking exercise in addition to DT training; they also significantly increased their daily steps over the 12 weeks. Furthermore, there were significant correlations between percentage change in daily steps and percentage change in memory function in the EG (WMS-LM II: correlation coefficient = 0.622, $P = .001$). A previous study also indicated that physical activity and behavioral intervention improved memory and global cognitive function in older adults.[32] Because few studies have indicated cognitive improvements induced by short-term aerobic exercise alone,[5–7] the positive results in the present study may be attributed to the addition of walking to everyday life and DT training.

Despite similar pre- and postintervention task performance on the 0- and 1-back task (possibly due to a ceiling effect), it was found (on fMRI) that decreased brain activation was associated with short-term memory in the prefrontal cortex after the intervention, regardless of the type of stimulus. This finding can be interpreted as a marker of improved neural efficiency, given that a smaller amount of energy (prefrontal activity) was needed to perform the same amount of work (n-back task) after the intervention. The logic of neural efficiency (decreased activation at comparable performance levels) has been used in several previous studies in which performance was similar between groups but activation decreased in the experimental group.[33,34] This study hypothesized that multimodal exercise (DT training) would affect the efficiency of neural circuitry during the short-term memory task. It may have been that the higher cognitive loads that the DT exercise required resulted in reduced effort and improved brain activation during the short-term memory task.

Elderly adults with MCI or at risk of dementia tend to have greater brain activation than cognitively healthy elderly adults during interference[35,36] and memory[37] tasks, likely due to more-extensive, stronger cortical recruitment in task-related regions.[38] The compensation-related use of neural circuits hypothesis[39] assumes greater recruitment of neural resources at low levels of cognitive load in older adults than in younger adults, with a loss or reversal in age-related differences in compensatory mechanisms at higher levels of load. A similar difficulty-related reversal would also be observed in cognitively high- and low-risk older adults. The effect of physical exercise or cognitive training on task-related brain activation in cognitively healthy elderly adults has varied according to previous results.[40,41] One study found that DT training led to decreased activation in the bilateral dorsolateral prefrontal cortex and the right ventrolateral prefrontal cortex and increased activation in the left ventrolateral prefrontal cortex.[42] Although the results of the current study support the finding of decreased activation in the bilateral dorsolateral prefrontal cortex, it may be that the exercise training affects the asymmetric change of brain activation depending on the brain regions. Another study also reported that a multimodal intervention led to increased brain activation associated with interference tasks in cognitively high-risk older adults,[43] which may indicate that the effects of the exercise on brain activation differ according to the subject's cognitive level and the type of cognitive task. In the present study, it is likely that the cognitive health of participants and the low cognitive load of the fMRI task after the multimodal exercise were important factors in the decreased brain activation associated with improved cognitive performance. Further studies are necessary to investigate the effect of similar exercise on brain activation in elderly individuals with MCI or AD.

There were several limitations to this study. First, this trial was not double blinded. Second, a follow-up after the intervention was not arranged, so any longitudinal effects of the intervention remain unknown. Third, the control groups were not arranged to have only one component (physical or cognitive exercise) of the multimodal treatment. It is not known whether one or both components were necessary for the observed changes. Fourth, the greater social contact of the EG was not controlled for. Social engagement is known to affect cognitive functioning, and the social engagement in addition to physical activity may have partially affected the EG.

CONCLUSION

A 12-week physical and cognitive exercise program can improve the efficiency of brain activation in older adults; this result is consistent with improvements observed in memory and executive function. Future studies are needed to examine the longitudinal effect of the intervention and whether this program can be used to prevent the onset of dementia.

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Author Contributions: Nishiguchi, Yamada: study concept, participant recruitment, analysis, writing the manuscript. Sekiyama, Abe: study concept and design, participant recruitment, writing the manuscript. Tanigawa,

Kawagoe: acquisition, analysis, interpretation of data. Suzuki, Otsuka, Nakai: acquisition of data. Yoshikawa, Aoyama, Tsuboyama: writing the manuscript. All authors read and approved the final manuscript.

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Original Study

Mail-Based Intervention for Sarcopenia Prevention Increased Anabolic Hormone and Skeletal Muscle Mass in Community-Dwelling Japanese Older Adults: The INE (Intervention by Nutrition and Exercise) Study

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walking
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A B S T R A C T

Objective: The aim of the Intervention by Nutrition and Exercise (INE) study was to investigate the effects of a mail-based intervention for sarcopenia prevention on muscle mass and anabolic hormones in community-dwelling older adults.
Design: A cluster-randomized controlled trial.
Setting and Participants: This trial recruited community-dwelling adults aged 65 years and older in Japan. The 227 participants were cluster randomized into a walking and nutrition (W/N) group (n = 79), a walking (W) group (n = 71), and a control (C) group (n = 77). We analyzed the physical and biochemical measurements in this substudy.
Intervention: Six months of mail-based intervention (a pedometer-based walking program and nutritional supplementation).
Measurements: The skeletal muscle mass index (SMI) using the bioelectrical impedance data acquisition system, biochemical measurements, such as those of insulinlike growth factor (IGF-1), dehydroepiandrosterone sulfate (DHEA-S), and 25-hydroxy vitamin D (25[OH]D), as well as frailty, were assessed by the Cardiovascular Health Study criteria.
Results: Participants in the W/N and W groups had significantly greater improvements in SMI, IGF-1, and 25(OH)D ($P < .05$) than those in the C group. Participants in the W/N group had significantly greater improvements in DHEA-S ($P < .05$) than in the other groups. These effects were more pronounced in frail, older adults.
Conclusion: These results suggest that the mail-based walking intervention of the remote monitoring type for sarcopenia prevention can increase anabolic hormone levels and SMI in community-dwelling older adults, particularly in those who are frail.
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Sarcopenia is the age-dependent loss of skeletal muscle mass.[1] In 2014, the Asian Working Group for Sarcopenia recommended using the presence of both low muscle function and low muscle mass to diagnose sarcopenia.[2] Several epidemiologic studies have shown that sarcopenia is highly prevalent and a serious problem in older adults.[3,4] In addition, frailty is strongly associated with sarcopenia. Frailty is also highly prevalent with advanced age and is considered to be characterized by an impaired state of health with mortality.[5]

The mechanism underlying sarcopenia and frailty remains unclear. However, it may be related to the age-related loss of skeletal muscle mass due to multifactorial processes, such as a sedentary life, malnutrition, and changes in hormone levels.[6] Additionally, the age-dependent decrease in anabolic hormones, such as sex hormones and growth hormones, can result in increased skeletal muscle

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breakdown.[7,8] By contrast, age-dependent increases in inflammatory cytokines, such as tumor necrosis factor alpha and interleukin-6 (IL-6), may lead to skeletal muscle mass loss.[9]

A previous study reported that physical exercise can effectively increase anabolic hormone levels, such as those of testosterone and insulinlike growth factor (IGF-1). Several studies have also shown that testosterone is increased by resistance training.[10,11] Moreover, the dehydroepiandrosterone (DHEA) and IGF-1 levels showed a good correlation.[12]

The American College of Sports Medicine (ACSM) Position Stands indicate that usual walking for older adults corresponds approximately to high-intensity exercise for younger people.[13] Additionally, older adults exhibited greater activation of leg muscles for usual walking than young adults.[14] Furthermore, the ACSM reports that exercise with 40% to 50% of 1 repetition maximum for inactive older adults can improve muscle strength.[15] Therefore, it is possible that continuous walking can improve the muscle function in older adults. Indeed, body composition may be improved by light-to-moderate-intensity exercise, such as walking, in older adults.[16] The pedometer-based walking program in older adults also showed a significant increase in physical activity and physical function.[17,18]

The combination of physical exercise and nutritional supplementation is more effective in improving body composition and physical function than physical exercise by itself. Resistance training and amino acid supplementation, protein, β-hydroxy β-methylbutyric acid, or vitamin D together can improve muscle mass.[19–23] In addition, a more recent study showed that resistance training with a protein-enriched diet can effectively increase lean tissue mass and reduce IL-6 in older women.[24]

However, sarcopenia is highly prevalent in community-dwelling older adults (approximately 10%–20%), and there are several limitations in group-intervention programs. Therefore, we have developed the mail-based walking intervention for sarcopenia prevention (pedometer-based walking program and nutritional supplementation). Many older adults can participate in the intervention program at the same time in this program because it is a remote monitoring type. The aim of the Intervention by Nutrition and Exercise (INE) study was to investigate the effects of a mail-based intervention for sarcopenia prevention on muscle mass and anabolic hormones in community-dwelling older adults. This intervention of a remote monitoring type is the combination of a stepwise approach to increase physical activity and nutritional supplementation. In addition, we examined the relationship between frailty and trainability for this intervention program.

Methods

Participants

Ine-cho is a small town located in the northern part of Kyoto prefecture. The population and aging rate in Ine-cho are 2185 and 42%, respectively. Participants were recruited by an advertisement in the local press and in a poster. The following criteria were used to screen the participants in an initial interview: aged 65 years and older, community-dwelling, and able to walk independently (or with a cane). The exclusion criteria were severe cardiac, pulmonary, diabetes, or kidney disease or musculoskeletal disorders; comorbidities associated with a greater risk of falls, such as Parkinson disease and stroke; severe cognitive impairment (Mini-Cog <3)[25]; and the use of psychotropic drugs or regular supplementation of amino acids and vitamin D in the last 12 months. Written informed consent was obtained from each participant in accordance with the guidelines approved by the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 2000. The trial registration number is JMA-IIA00122.

Cluster Randomization

We used a 3-arm, cluster-randomized, controlled trial, and autonomous communities were randomly assigned to the walking and nutrition (W/N) group, walking (W) group, and control (C) group. Eleven autonomous communities were randomly allocated to each group and 79, 71, and 77 participants were enrolled in the W/N group, W group, and C group, respectively.

Intervention

Exercise program

Participants randomized to the W/N group and W group received pedometer-based walking programs for 6 months. A valid, accurate, and reliable pedometer, the Yamasa EX-300 (Yamasa Tokei Keiki, Ltd, Tokyo, Japan), was used to measure free-living step counts.[26]

We used a stepwise approach to increase physical activity in which the participants were instructed to increase the number of daily steps by 10% each month. In addition, the participants walked with an ankle weight (0.5 kg) at their own discretion. Written activity logs were averaged monthly to determine whether the participants were achieving their step goal. The intervention consisted of motivation for walking followed by goal setting, self-monitoring, and feedback. Participants were asked to record the step counts taken at the end of each day. A sheet for brief feedback and setting the number of daily steps was mailed to all of the participants to evaluate the recorded calendar monthly (Fig. 1).

Nutritional supplementation

Protein and a vitamin D supplement were provided every day for the participants in the W/N group for 6 months. Protein and the vitamin D supplement (200 kcal, 10.0 g of protein with branched chain amino acids 12.5 μg of vitamin D, and 300 mg of calcium [Resource PemPal Active; Nestle Japan Ltd, Tokyo, Japan]) were provided for the participants. Participants recorded the dietary supplementation and meal size per day on a calendar. The nutritional supplement was mailed to all participants monthly. Therefore, both the exercise and nutritional programs were remotely monitored by the researcher.

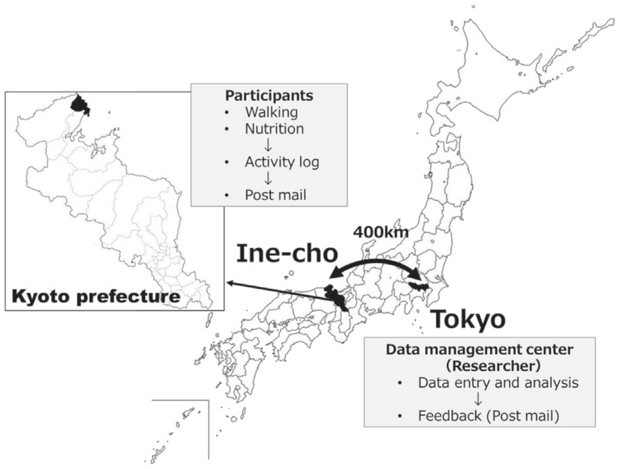

Fig. 1. Schematic representation of mail-based intervention of the remote monitoring type for sarcopenia prevention. Participants of the W/N and W groups were instructed to increase the number of daily steps by 10% each month. Protein and the vitamin D supplement were provided every day for the participants in the W/N group. Participants were asked to record the date on the calendar and steps taken at the end of each day. A sheet for brief feedback and setting the number of daily steps was mailed to all participants to evaluate the recorded calendar monthly.

Outcome Measures

Skeletal muscle mass index

A bioelectrical impedance data acquisition system (Inbody 430; Biospace Co, Ltd, Seoul, Korea) was used to determine bioelectrical impedance. This system uses electrical current at different frequencies (5, 50, and 250 kHz) to directly measure the amount of extracellular and intracellular water in the body. Participants stood on 2 metallic electrodes and held metallic grip electrodes. Using segmental body composition and muscle mass, a value for the appendicular skeletal muscle mass was determined and used for further analysis. Muscle mass was converted into the skeletal muscle mass index (SMI) by dividing by the muscle weight by height squared (kg/m^2).

Biochemical measurements

For all participants, the following 3 biomarkers were obtained: IGF-1, DHEA-S, and 25-hydroxy vitamin D (25[OH]D). Blood samples were drawn in the morning before physical exercise. The collected serum was stored at -80°C until the analysis. IGF-1 (ng/mL) was measured by immunoradiometric assay. Intra- and interassay coefficients of variance were 2.35% and 3.90%, respectively. DHEA-S (μg/dL) was measured by chemiluminescence enzyme immunoassay. Intra- and interassay coefficients of variance were 6.20% and 7.71%, respectively. Radioimmunoassay was used to measure 25(OH)D levels (ng/mL). Intra- and interassay coefficients of variance were 6.66% and 10.82%, respectively. All of the assays were performed in the same laboratory.

Definition of frailty

We defined frailty by the Cardiovascular Health Study criteria[27] with minor modifications by Shimada et al.[28]

We assessed weight loss by asking the single "yes or no" question, "Have you lost 5% or more of your body weight in the past 2 years?" Weakness was defined as a handgrip strength less than 26 kg in men and less than 18 kg in women. In the handgrip strength test, participants used a handheld dynamometer with the arm by the side of the body. The participant squeezed the dynamometer with the dominant hand using maximum isometric effort. No other body movement was allowed. The handgrip strength score was defined as the better performance of 2 trials. We assessed exhaustion by asking the single "yes or no" question, "Do you feel full of energy?" Slowness was defined as a usual walking speed less than 1.0 m/s identified in participants with a low physical performance. In the walking speed test, participants were asked to walk 11 m at a comfortable pace. A stopwatch was used to record the time required to reach the 5-m point (marked in the course). The time recorded in the 2 trials was averaged to obtain the data for the present analyses. We assessed low physical activity by the following 2 questions: "Do you engage in moderate levels of physical exercise or sports aimed at health?" and "Do you engage in low levels of physical exercise aimed at health?" Low physical activity was defined if the responses to these 2 questions were "no."

Required sample size

Several previous studies[19–23] showed that the effect size for physical exercise with nutritional supplementation on the skeletal muscle mass was approximately 0.65. Therefore, we designed the effect size of the current study to detect 0.65. With a significance level of 0.017 (0.05/3), a power of 80%, and an effect size of 0.65, 69 participants were needed in 3 groups. Accounting for a potential 10% attrition rate, a total of 228 participants were targeted for this study, a number that was sufficiently large to detect statistically significant differences.

Statistical Analysis

One-way analysis of variance (ANOVA) and post hoc test were used to test any differences in baseline measures between groups, and χ^2 test was performed on categorical variables. Bonferroni-adjusted *t* test was used to assess which group differed significantly from the others.

The effect of each intervention on outcome measurements was analyzed using a mixed 3 × 2 (group (W/N, W, and C group) × time (pretraining, posttraining) ANOVA. In addition, analysis of covariance (ANCOVA) with the baseline value as a covariate was used to determine the effect of the intervention on each outcome measure. ANOVA was used to test any differences in percentage changes of outcome measurements between the groups. Bonferroni-adjusted *t* test was used to assess which group differed significantly from the others.

For stratified analysis according to the level of frailty, we divided the cohort into 2 groups: nonfrail and frail. We compared the trainability in frailty-stratified and unstratified analyses for each outcome measure.

The data were managed and analyzed using SPSS (Statistical Package for the Social Sciences, Windows version 21.0; SPSS, Inc, Chicago, IL). A *P* value less than .05 was considered to indicate statistical significance for all analyses.

Results

Overall, 248 people were screened, and 227 (91.5%) who met the inclusion criteria for the trial and agreed to participate were enrolled (Figure 2). Most of the participants who were excluded had diabetes mellitus or severe musculoskeletal disorders. Twenty-one older adults who were eligible for the study withdrew from their participation after screening. Of 227 individuals selected for the study, 222 (97.8%) completed the 6-month follow-up, 77 in the W/N group (97.5%), 70 in the W group (98.6%), and 75 in the C group (97.4%). The baseline characteristics in the W/N, W, and C groups were comparable and well matched (Table 1). The median relative adherence was 80% (25th–75th percentile, 67%–92%) with nutritional supplementation; however, all of the participants completed the step count record during this study. No fall incident or health problems, including cardiovascular or musculoskeletal complications, occurred during the study period. A minor problem observed in both intervention groups was muscle aches in the first intervention month. This was easily managed by adjusting the intervention, and the muscle aches decreased over the course during the intervention. In both the W/N and W groups, the average daily steps were increased by 35.7% (from 4471 ± 2370 to 6067 ± 2967) and 42.1% (from 3795 ± 1913 to 5394 ± 2197), respectively ($P < .01$).

Significant time effects were found for IGF-1, DHEA-S, and 25(OH)D ($P < .05$) (Table 2). The pre- and postintervention group statistics and Group × Time interactions are shown in Table 2. Significant differences were observed among the 3 groups for SMI, IGF-1, and 25(OH)D with significant Group × Time interactions using ANOVA. Similarly, significant differences were observed among the 3 groups for SMI and 25(OH)D with significant Group × Time interactions using ANCOVA. Participants in the W/N and W groups had significantly greater improvement in SMI, IGF-1, and 25(OH)D ($P < .05$), but not in the C group (Table 2). Participants in the W/N group had significantly greater improvements in DHEA-S ($P < .05$) but not in the other 2 groups (Table 2).

We next analyzed nonfrail older adults. In this group, we also found significant time effects for IGF-1, DHEA-S, and 25(OH)D ($P < .05$) (Table 2). Significant differences were observed among the 3 groups for IGF-1 and 25(OH)D with significant Group × Time interactions. Participants in the W/N and W groups had significantly greater improvements in IGF-1 and 25(OH)D ($P < .05$) but not in the C group (Table 2).

We also performed subgroup analysis in frail older adults. In this subgroup, we found significant time effects for IGF-1 and 25(OH)D

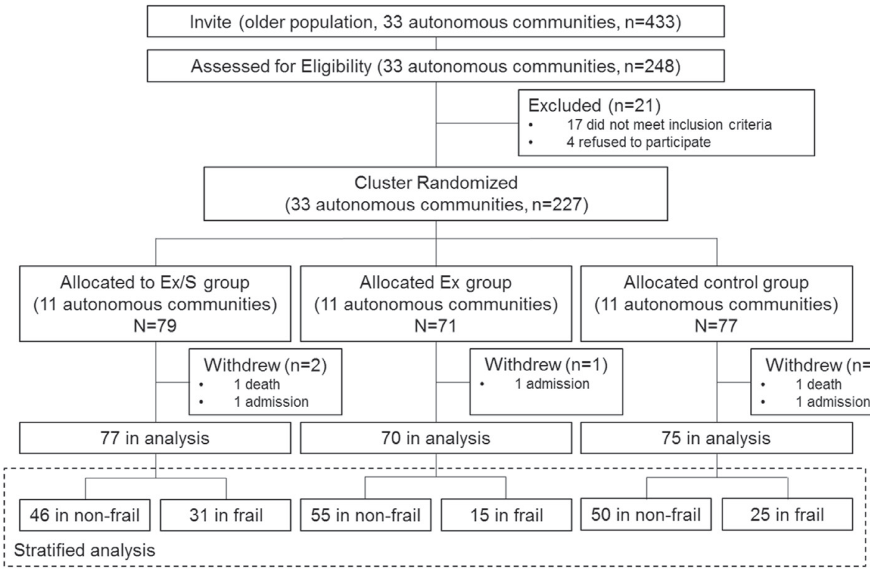

Fig. 2. A flowchart showing the distribution of participants throughout the trial.

($P < .05$) (Table 2). Significant differences were observed among the 3 groups for SMI, IGF-1, DHEA-S, and 25(OH)D with significant Group × Time interactions. Participants in the W/N and W groups had significantly greater improvements in SMI ($P < .05$) but not in the C group (Table 3). Participants in the W/N group had significantly greater improvements in IGF-1 and 25(OH)D ($P < .05$) but not in the others (Table 3).

Discussion

The 6-month mail-based walking intervention along with nutritional supplementation is an effective means to prevent sarcopenia in community-dwelling older adults. We have shown that participants in the W/N and W groups, but not in the C group, showed a significant increase in SMI, IGF-1, and 25(OH)D. The W/N group showed the largest increase in DHEA-S among the 3 groups. These results were more pronounced in frail older adults. These results suggested that the combination of walking exercise and nutritional supplementation may be beneficial for community-dwelling older adults to prevent and treat sarcopenia. In particular, this intervention program was useful for the muscle mass increase in frail older adults.

In this 6-month mail-based intervention for community-dwelling older adults, we have shown that the average daily steps were successfully increased by 35.7% and 42.1% in the W/N and W groups, respectively. We showed that the pedometer-based behavioral change program was very effective for the improvement of average daily steps. Goal setting and self-monitoring of behavior are crucial for behavioral change. In this study, pedometers and a record sheet

Table 1
Baseline Characteristics of the Study Participants in Each Group

	Walking + Nutrition		Walking		Control		F Value	*P* Value
	Mean	SD	Mean	SD	Mean	SD		
Overall	n = 77		n = 70		n = 75			
Age	76.3	5.9	75.8	5.2	75.7	6.5	0.38	.687
Height	153.5	8.4	152.8	8.3	155.1	9.3	2.67	.071
Weight	52.6	8.8	53.2	9.3	55.8	9.9	**4.49**	**.012***a*
BMI	22.3	3.2	22.7	3.2	23.1	2.8	2.08	.127
Women, n %	50	64.9%	48	68.6%	44	58.7%		.452
Nonfrail	n = 46		n = 55		n = 50			
Age	75.2	5.6	75.9	5.1	75.3	6.8	0.32	.724
Height	154.4	8.8	152.0	8.7	155.0	9.4	2.58	.078
Weight	53.6	8.9	52.9	9.5	55.3	9.3	1.52	.220
BMI	22.5	2.9	22.8	3.2	22.9	2.4	0.50	.609
Women, n %	31	67.4%	40	72.7%	29	58.0%		.452
Frail	n = 31		n = 15		n = 25			
Age	78.1	5.7	75.7	5.8	76.4	6.2	1.63	.199
Height	152.2	7.8	155.3	6.2	154.7	9.1	1.52	.222
Weight	51.3	8.6	54.5	8.7	55.7	10.1	2.94	.056
BMI	22.1	3.6	22.6	3.1	23.2	3.2	1.31	.272
Women, n %	19	61.3%	8	53.3%	15	60.0%		.452

BMI, body mass index.
*$P < .01$.
a, W/N group versus C group.

Table 2
SMI and Serum Biomarkers Before and After the Intervention in the Overall, Frail, and Nonfrail Groups

	Pre		Post		2-Way ANOVA				2-Way ANCOVA	
					Time Effect		Time × Group Interaction		Time × Group Interaction	
	Mean	SD	Mean	SD	F Value	*P* Value	F Value	*P* Value	F Value	*P* Value
Overall										
SMI										
Walking + Nutrition	6.5	0.9	6.4	0.9	0.21	.65	7.75	<.001**	5.98	.015*
Walking	6.5	0.9	6.4	0.9						
Control	6.6	0.9	6.7	1.0						
IGF-1										
Walking + Nutrition	77.1	24.3	95.4	32.7	105.73	<.001**	9.16	<.001**	3.13	.078
Walking	71.6	26.7	83.6	29.1						
Control	86.7	29.4	92.7	26.8						
DHEA-S										
Walking + Nutrition	72.8	47.4	80.8	45.3	24.54	<.001**	1.80	.168	1.32	.271
Walking	62.2	47.3	71.7	50.5						
Control	89.9	55.2	93.1	60.3						
25(OH)D										
Walking + Nutrition	31.0	10.3	41.0	12.4	58.35	<.001**	17.89	<.001**	18.33	<.001**
Walking	30.1	9.8	36.7	7.1						
Control	33.5	11.8	33.3	9.8						
Nonfrail										
SMI										
Walking + Nutrition	6.4	0.9	6.5	0.9	0.82	.367	2.60	.078	2.39	.095
Walking	6.3	0.8	6.4	0.8						
Control	6.7	0.9	6.7	0.9						
IGF-1										
Walking + Nutrition	80.6	23.2	96.3	27.8	75.59	<.001**	5.30	.006*	3.60	.030*
Walking	70.2	27.0	82.8	29.4						
Control	94.0	30.5	99.4	26.8						
DHEA-S										
Walking + Nutrition	79.2	48.3	68.7	48.7	24.10	<.001**	0.33	.720	0.26	.774
Walking	65.0	47.0	56.0	42.8						
Control	100.6	64.2	93.7	58.4						
25(OH)D										
Walking + Nutrition	30.9	11.1	41.2	12.9	43.47	<.001**	11.09	<.001**	10.45	<.001**
Walking	30.2	9.8	36.8	7.0						
Control	34.6	13.5	34.8	10.1						
Frail										
SMI										
Walking + Nutrition	6.3	0.9	6.5	0.9	0.10	.755	5.15	.008**	4.39	.016*
Walking	6.8	1.0	6.9	1.2						
Control	6.7	1.1	6.4	0.9						
IGF-1										
Walking + Nutrition	71.5	25.4	94.1	40.0	22.09	<.001**	4.56	.015**	4.48	.016*
Walking	75.3	27.0	84.3	29.7						
Control	75.7	26.1	81.1	25.1						
DHEA-S										
Walking + Nutrition	79.7	45.2	83.6	40.4	2.92	.093	3.60	.034*	3.76	.030*
Walking	86.2	57.3	97.8	57.1						
Control	84.6	51.9	80.6	53.9						
25(OH)D										
Walking + Nutrition	31.2	9.2	40.6	11.7	11.38	<.001**	6.39	<.001**	6.83	.002**
Walking	29.2	10.5	36.1	8.0						
Control	32.6	7.9	30.8	8.7						

*$P < .05$; **$P < .01$.

were primarily used as motivational tools, and our behavioral support seemed to have mainly affected the behavioral change toward increasing physical activity.

The W/N group showed a significant increase in the serum DHEA-S and IGF-1 levels. The W group showed a significant increase in the serum IGF-1 levels only, and a tendency for higher serum DHEA-S levels after intervention. The age-dependent decrease in anabolic hormones, such as DHEA and IGF-1, may lead to a loss of skeletal muscle mass.[7,8] However, a recent study suggested that physical activity is associated with the serum IGF-1 level, and physical activity training can effectively increase the serum IGF-1 level in premenopausal women.[29] Several studies have shown that an exercise training program greatly increases the serum DHEA levels in older adults.[10,11] In addition, the serum IGF-1 and DHEA can be maintained at a high level by long-term training in older adults.[30] The current trial shows that physical activity was increased in the W/N and W groups. Therefore, the W/N and W groups, but not the C group, showed a great increase in the IGF-1 and DHEA-S levels.

The W/N group showed the largest increase in 25(OH)D and SMI among the 3 groups. Several studies have suggested that a low 25(OH) D concentration is associated with lower muscle strength, reduced physical performance, and increased disability.[31–33] It has been shown that vitamin D supplementation may enhance muscle strength in frail older adults with vitamin D deficiency.[34] However, older adults have a high risk of inadequate protein intake,[35] and their

Table 3
Percentage Changes of Outcome Measurements in the Overall, Frail, and Nonfrail Groups

	Walking + Nutrition		Walking		Control		F Value	P Value
	Mean	SD	Mean	SD	Mean	SD		
Overall	n = 77		n = 70		n = 75			
Change of SMI	1.88	6.53	1.01	4.56	−1.85	6.90	**7.66**	**<.001**** *a, b*
Change of IGF-1	25.4	23.7	20.7	25.2	9.6	18.4	**8.03**	**<.001**** *a, b*
Change of DHEA-S	22.6	58.3	18.4	25.8	5.4	22.0	**3.26**	**.041*** *a*
Change of 25(OH)D	42.0	60.7	31.8	45.5	3.0	24.6	**12.50**	**<.001**** *a, b*
Nonfrail	n = 46		n = 55		n = 50			
Change of SMI	1.02	5.58	1.11	4.24	−0.86	5.72	2.32	.102
Change of IGF-1	21.4	20.3	22.5	25.5	8.6	17.1	**5.35**	**.006**** *a, b*
Change of DHEA-S	26.6	65.5	18.1	25.7	8.4	17.8	1.96	.145
Change of 25(OH)D	39.9	44.1	32.0	47.1	6.1	27.8	**7.35**	**<.001**** *a, b*
Frail	n = 31		n = 15		n = 25			
Change of SMI	3.16	7.66	0.64	5.76	−3.87	8.78	**5.63**	**.005**** *a, b*
Change of IGF-1	31.8	27.6	14.5	24.8	9.4	19.8	**4.70**	**.013**** *a*
Change of DHEA-S	15.9	44.2	19.7	27.3	−0.8	28.9	1.67	.197
Change of 25(OH)D	45.2	81.4	33.6	42.6	−5.6	16.5	**4.55**	**.015*** *a*

*$P < .05$; **$P < .01$.
a, W/N group versus C group; *b*, W group versus C group.

synthetic response to protein intake may be blunted.[36] Several studies have found a positive association between protein intake and muscle mass.[37,38] In fact, protein supplementation has been shown to augment the muscle strengthening effect of resistance exercise.[39,40] Therefore, the Society for Sarcopenia, Cahexia, and Wasting Disease (SSCWD) recently recommended the combination of exercise with protein and/or vitamin D supplementation for reducing the age-related skeletal muscle decline.[41] The results of the current study also supported the SSCWD recommendation, and the nutritional supplementation provided added benefits to those with walking exercise for increasing muscle mass.

The important point is that the effectiveness of this intervention was more pronounced in frail older adults. Recent frailty-related studies show that the frailty status is associated with muscle mass decline in older adults,[42] and regular physical activity may mitigate frailty in frail older adults.[43] Thus, it is possible that the intensity of our intervention was appropriate for frail older adults, but was low for nonfrail older adults. ACSM's recommendation is 40% to 50% of 1 repetition maximum for beginner or sedentary older adults, but the habitually exercising older adult requires 60% to 70% of 1 repetition maximum.[15]

Several limitations of the present study need to be mentioned. First, the intake of dietary food was not recorded. The nutritional supplement may have changed participants' dietary intake. Second, no follow-up after completion of the trial was conducted. Because there is a lack of evidence regarding the long-term effect of nutritional supplementation on sarcopenia treatment, this issue also needs to be addressed in future studies. Follow-up and cost-effective analyses are needed to confirm the present results and evaluate the most effective program for the prevention of sarcopenia and frailty.

In conclusion, the current study suggests that mail-based walking intervention of the remote monitoring type for sarcopenia prevention can increase anabolic hormone levels and SMI in community-dwelling older adults, particularly in frail older adults. This program is very simple and may be useful as a large population approach for the prevention of sarcopenia and frailty.

Acknowledgments

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Functional Movement Screen for Predicting Running Injuries in 18- to 24-Year-Old Competitive Male Runners

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Abstract

Hotta, T, Nishiguchi, S, Fukutani, N, Tashiro, Y, Adachi, D, Morino, S, Shirooka, H, Nozaki, Y, Hirata, H, Yamaguchi, M, and Aoyama, T. Functional movement screen for predicting running injuries in 18- to 24-year-old competitive male runners. *J Strength Cond Res* 29(10): 2808–2815, 2015—The purpose of this study was to investigate whether the functional movement screen (FMS) could predict running injuries in competitive runners. Eighty-four competitive male runners (average age = 20.0 ± 1.1 years) participated. Each subject performed the FMS, which consisted of 7 movement tests (each score range: 0–3, total score range: 0–21), during the preseason. The incidence of running injuries (time lost because of injury ≤ 4 weeks) was investigated through a follow-up survey during the 6-month season. Mann-Whitney *U*-tests were used to investigate which movement tests were significantly associated with running injuries. The receiver-operator characteristic (ROC) analysis was used to determine the cutoff. The mean FMS composite score was 14.1 ± 2.3. The ROC analysis determined the cutoff at 14/15 (sensitivity = 0.73, specificity = 0.54), suggesting that the composite score had a low predictability for running injuries. However, the total scores (0–6) from the deep squat (DS) and active straight leg raise (ASLR) tests (DS and ASLR), which were significant with the *U*-test, had relatively high predictability at the cutoff of 3/4 (sensitivity = 0.73, specificity = 0.74). Furthermore, the multivariate logistic regression analysis revealed that the DS and ASLR scores of ≤3 significantly influenced the incidence of running injuries after adjusting for subjects' characteristics (odds ratio = 9.7, 95% confidence interval = 2.1–44.4). Thus, the current study identified the DS and ASLR score as a more effective method than the composite score to screen the risk of running injuries in competitive male runners.

Key Words distance runner, screening, dynamic assessment, risk factor

Introduction

The functional movement screen (FMS) is a screening tool for injury risk that assesses the movement patterns of individuals and evaluates mobility and stability comprehensively. The FMS consists of 7 component tests; each scored based on the movement patterns within the kinetic chain, asymmetries between the sides, and compensatory movements. The validity of the FMS as a predictor of injury risk has been confirmed in several studies (5,10,11,17). The study by Kiesel et al. (10) examined the relationship between the FMS and serious injury in professional football players. They revealed that professional football players with an FMS score of ≤14 were at a greater risk of serious injury than those with higher scores (10). Other studies reported similar findings in other groups, such as officer candidates (11,17) and female collegiate athletes (5).

Recently, 2 studies investigated normative values of FMS scores for runners. Loudon et al. (12) reported the normative value for running athletes and Agresta et al. (1) reported the value for healthy runners (the mean FMS composite scores were 13.1 ± 1.8 and 15.4 ± 2.4, respectively). Additionally, Agresta et al. (1) investigated the association between FMS scores and injury history. However, no prospective cohort studies have investigated the association between the FMS and running injuries. Running injuries are a serious problem for most runners, especially for competitive runners (8). Unfortunately, some runners are forced to retire from running because of serious running injuries. Previous studies reported some risk factors for running injuries, such as inadequate flexibility (24), muscle weakness and imbalance (16), and deficits in neuromuscular coordination (19). Cook et al. (6,7) stated that these factors also caused poor movement

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patterns, which were reflected in the lower score of the FMS. Thus, runners with low FMS scores might have certain risk factors for running injury and become more prone to injury. In addition, although Parchmann and McBride (18) reported that the FMS was not significantly associated with sprinting, Chapman et al. (4) revealed that a high FMS score had a positive effect on performance in elite track and field athletes in the long view. Because athletes with a higher FMS score rarely suffered from injury, they could practice continuously and improve their performance. Therefore, we hypothesized that the FMS could predict running injuries.

The receiver-operator characteristic (ROC) curve is a plot of the sensitivity vs. 1 − specificity of a screening test; this analysis is useful in determining the cutoff where the sensitivity and specificity are maximized. In previous studies, the ROC curve was used to determine the validity of the FMS as a predictor of injury risk (3,10,17). In addition, a cutoff value allows determining more easily whether a runner has a potential injury risk simply based on the FMS scores. Therefore, the aim of the current study was to determine the cutoff value and to investigate if the FMS score during preseason could be used to predict running injuries in young competitive runners during season.

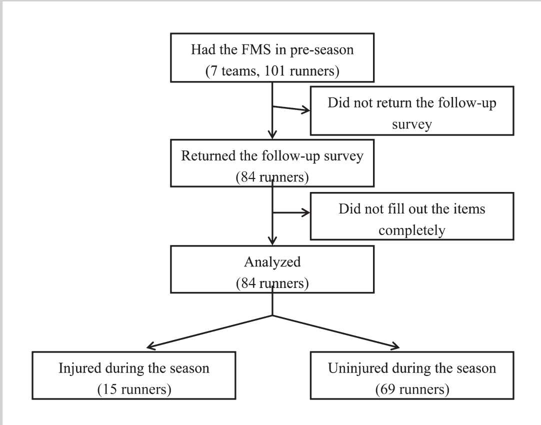

Figure 1. Flow chart illustrating the process of the study.

METHODS

Experimental Approach to the Problem

This study, using a prospective cohort design, investigated whether preseason FMS scores could predict serious running injuries during the season in 18- to 24-year-old competitive male runners. Figure 1 illustrates the process of this study in the form of a flow chart. The subjects performed the FMS at their college during preseason, February 2014. To minimize the influence of fatigue on performance, the FMS tests were conducted during the daytime on the day after a non-training day according to each team's schedule. No warm-up was included. The testing days added up to 7 days in total. After the FMS test, follow-up surveys were distributed to the subjects to investigate the incidence of running injuries during the 6-month season. The follow-up surveys were conducted twice at the end of May and August 2014 to reduce a recall bias. Statistical analyses were conducted using the data of the returned surveys. The ROC analysis determined the cutoff, and the logistic regression analysis determined if the FMS could be used for the prediction of running injuries.

Subjects

A total of 84 competitive male runners volunteered to participate in the study (mean age = 20.0 ± 1.1 years, range = 18–24 years, height = 171.6 ± 4.5 cm, weight = 57.5 ± 4.3 kg). For inclusion, subjects had to be competitive male runners belonging to collegiate track and field teams, were injury free at the time of FMS test in preseason, whose events were middle or long distance, and whose running experience exceeded 1 year. The purpose and methods of this study were explained to the subjects in detail in a verbal statement, and written informed consent was obtained from the subjects. The current study did not include athletes under the age of 18 years; thus, parental or guardian consent was not needed. This study was approved by the Institutional Review Board of Kyoto University (Approval No. E2023).

Procedures

Before the study, the physical therapists collecting data were instructed on the FMS evaluation method by an FMS specialist. The FMS scoring criteria were used as described by Cook et al. (6,7), and they discussed standardization of the testing.

On testing day, all subjects were questioned about their characteristics, such as age, height, weight, running experience, training sessions per week, weekly mileage, personal best time in their primary event in 2013, and injury history, by questionnaire. To allow comparison between different events, performances were normalized to a percentage of collegiate Japanese record performances (as of March 31, 2013) (4). To assess injury history, we asked the following question: "Have you ever suffered from musculoskeletal injury that was so severe that it required medical attention?" (5). Subsequently, all subjects were briefed on the FMS and were given a demonstration of the movements. After the demonstration, all subjects performed the FMS, which consisted of 7 movement tests to comprehensively assess mobility, stability, and coordination. The 7 tests were the deep squat (DS), hurdle step (HS), in-line lunge (ILL), shoulder mobility (SM), active straight leg raise (ASLR), trunk stability push-up (TSPU), and rotary stability (RS) tests. All tests were scored using standardized scoring criteria (6,7). Each movement test was scored on a 4-point scale (0–3), and the maximal FMS score that could be achieved was 21. A score of 3 was awarded for perfect form, a score of 2 was given for completing the test with compensations, a score of 1 was awarded for not completing the test accurately, and a score of 0 was given

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Table 1. Interrater reliability for the functional movement screen composite score.*

Intraclass correlation coefficient (2, 1)	95% CI	Bland-Altman plot: Fixed bias 95% CI	Fixed bias Presence/absence	Proportional bias Test for no correlation		Proportional bias Presence/absence	*SEM*	MDC_{95}	SEP
0.98	0.93–1.00	−0.83 to 0.43	Absence	$r = -0.44$	$p = 0.90$	Absence	0.31	0.87	0.44

*CI = confidence interval; MDC = minimum difference to be considered real; SEP = standard error of prediction.

if the subjects felt any pain during the test. Each test was performed 3 times, and the highest score was used. Of the 7 tests that comprise the FMS, 5 tests (HS, ILL, SM, ASLR, and RS) were performed and scored separately for the right and left sides of the body. For these bilaterally assessed tests, the lower score was used.

After the FMS test, follow-up surveys were distributed to all subjects through each team's manager to investigate the incidence of running injuries during the 6-month season. If information was missing in the questionnaires, we asked the subjects to answer the omitted questions by contacting them through the team's managers. For the current study, the definition of running injury was a musculoskeletal injury that met the following criteria: (1) the injury occurred as a result of participating in a practice or race in track and field (trauma injuries, such as sprains, were excluded) and (2) the injury was sufficiently severe to prevent participation for at least 4 weeks; this definition was based on that used in previous studies (10,17).

Reliability

Similar to a previous study (12), interrater reliability was assessed in a subgroup of 10 subjects by 2 physical therapists. Interrater reliability was calculated for the FMS composite score using the intraclass correlation coefficient (ICC, model 2, 1). On the basis of the reliability coefficients, the standard error of measurement ($SEM = SD \times \sqrt{1-ICC}$), the minimum difference to be considered real ($MDC = SEM \times 1.96 \times \sqrt{2}$), and the standard error of prediction ($SEP = SD \times \sqrt{1-ICC^2}$) were calculated (23). The Bland-Altman analysis was performed to determine whether systematic error was present. The weighted kappa statistic was used to establish the interrater reliability for each movement test of the FMS.

Statistical Analyses

We divided the subjects into 2 groups with and without running injuries according to the follow-up survey. Comparisons between the 2 groups were made using Student's *t*-tests (for parametric continuous variables), Mann-Whitney *U*-tests (for nonparametric continuous variables), or χ^2 tests (for categorical variables). The short version of the FMS was calculated from the movement tests that were significant

Table 2. Interrater reliability for each functional movement screen component test.

Test	Kappa	Strength of agreement
Deep squat	1.000	Excellent
Hurdle step	1.000	Excellent
In-line lunge	1.000	Excellent
Shoulder mobility	1.000	Excellent
Active straight leg raise	0.831	Substantial
Trunk stability push-up	0.836	Substantial
Rotary stability	1.000	Excellent

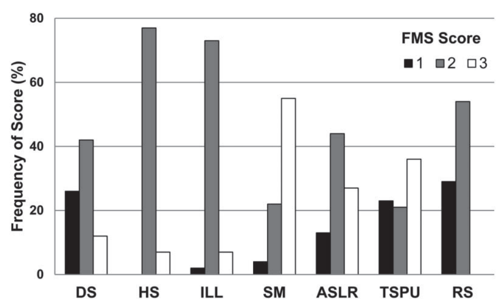

Figure 2. Distribution of scores for each functional movement screen (FMS) component test.

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TABLE 3. Comparison of runners with and without running injuries during the season.*

Variable	Serious running injury: Without ($n = 69$)	Serious running injury: With ($n = 15$)	p
Characteristics			
Age (y)†	20.1 ± 1.2	19.6 ± 0.9	0.15
Height (cm)	171.3 ± 4.3	172.7 ± 5.6	0.29
Weight (kg)	57.3 ± 4.2	58.4 ± 5.0	0.39
Running experience (y)†	6.9 ± 2.2	6.7 ± 2.4	0.64
Weekly training sessions ($d \cdot wk^{-1}$)‡	5.9 ± 0.6	5.9 ± 0.6	0.85
Weekly mileage ($km \cdot wk^{-1}$)†	80.9 ± 53.8	98.4 ± 57.3	0.26
Performance (%)	87.6 ± 4.1	88.7 ± 3.6	0.34
Injury history, *n* (%)§	34 (49.3)	8 (53.3)	1.00
FMS			
FMS total score†	14.4 ± 2.2	13.3 ± 2.7	0.10
Deep squat‡	1.8 ± 0.7	1.3 ± 0.7	0.01‖
Hurdles step‡	2.1 ± 0.3	2.0 ± 0.0	0.20
In-line lunge‡	2.0 ± 0.4	1.9 ± 0.7	0.26
Shoulder mobility‡	2.6 ± 0.8	2.5 ± 0.6	0.36
Active straight leg raise‡	2.3 ± 0.6	1.6 ± 0.5	<0.01¶
Trunk stability push-up‡	2.0 ± 1.0	2.5 ± 0.8	0.06
Rotary stability‡	1.6 ± 0.5	1.6 ± 0.6	0.97

*FMS = functional movement screen.
†Continuous data are expressed as the mean ± *SD* (tested by the student's *t*-tests).
‡Nonparametric data are expressed as the mean ± *SD* (tested by the Mann-Whitney *U*-tests).
§Categorical data are expressed as numbers (percentages) (tested by the χ^2 test).
‖$p \leq 0.05$.
¶$p < 0.01$.

according to the *U*-tests. The ROC curve was calculated by pairing the FMS score with running injury to determine the cutoff on the FMS that maximized sensitivity and specificity according to previous studies (3,5,10,17). In this context, the FMS can be thought of as a screening test that determines if a runner is at risk for a running injury. An ROC curve is a plot of the sensitivity (true positive) vs. 1 − specificity (false positive) of a screening test. The area under the curve (AUC) was calculated based on the ROC curve. The optimal cutoff was determined based on the Youden index, which consists of the following formula: Youden index = (sensitivity + specificity) − 1 (2). Maximizing this index allows finding the optimal cutoff value. Once the cutoff value was identified, a 2 × 2 contingency table was created dichotomizing those with and without injury and those above and below the cutoff on the FMS. To determine whether a runner, whose FMS score was below the cutoff, had potential injury risk during season, the multivariate logistic analysis was adjusted for each subject's characteristics, including age, height, weight, running experience, training sessions per week, weekly mileage, performance level, and injury history. A value of $p \leq 0.05$ was considered to be statistically significant for all analyses. All data were analyzed using the Statistical Package for the Social Sciences version 20.0 (SPSS, Inc., Chicago, IL, USA).

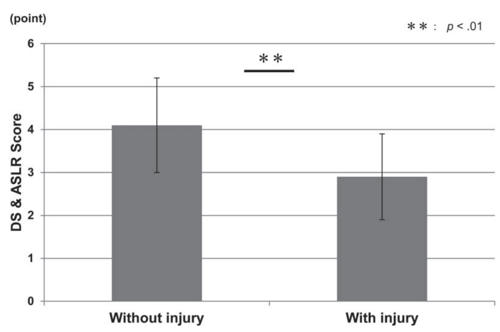

Figure 3. Comparison of the deep squat and active straight leg raise (DS and ASLR) scores between groups with and without injury.

RESULTS

In preseason, 101 runners from 7 teams participated in the FMS, of which 84 returned for the follow-up surveys (response rate was 83.2%).

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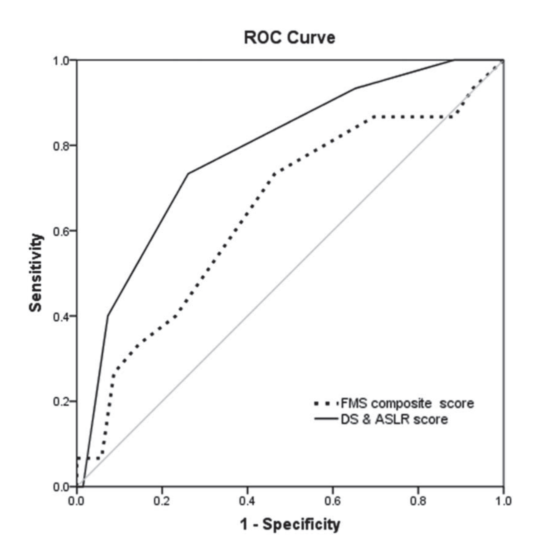

Figure 4. Receiver-operator characteristic (ROC) curves for functional movement screen (FMS) composite and deep squat and active straight leg raise (DS and ASLR) score.

Reliability

Interrater reliability for the FMS composite score is shown in Table 1. The ICC (2, 1) was 0.98 (95% confidence interval [CI] = 0.93–1.00), demonstrating excellent reliability, and the Bland-Altman analysis revealed that there was no systematic error present (both fixed bias and proportional bias). Interrater reliability (weighted kappa) for each component movement test is presented in Table 2 and shows that the majority of the FMS tests demonstrated a substantial to excellent agreement. These results were in accordance with the previous studies (9,15,21) and confirmed the reliability of the procedure in the current study.

Functional Movement Screen Score Distribution

The mean FMS composite score was 14.2 ± 2.3 with a range of 7–18. Of the 84 subjects, 43 (51.2%) scored ≤14 on the FMS composite score, indicating that they had a high injury risk according to Kiesel et al. (10). Among all the subjects, 4 reported pain in the DS and TSPU tests, 3 reported pain in the SM test, 2 reported pain in the ILL test, and 1 in the HS and RS tests, which resulted in a score of 0 for these tests.

The distribution of scores for each component movement test is presented in Figure 2. The SM test was the movement with the highest frequency of a score of 3 (65.5%). Conversely, the RS was the movement with the highest frequency of a score of 1 (34.5%); no subject achieved a score of 3 on this test. The DS, HS, ILL, and ASLR tests had the highest frequency of a score of 2 on each test.

Table 4. 2 × 2 contingency table: functional movement screen (FMS) composite score × running injuries.

	Running injuries	
	Without	With
FMS composite score ≤ 14	32	11
FMS composite score ≥ 15	37	4

Table 5. 2 × 2 contingency table: DS and ASLR score × running injuries.*

	Running injuries	
	Without	With
DS and ASLR score ≤ 3	18	11
DS and ASLR score ≥ 4	51	4

*DS = deep squat; ASLR = active straight leg raise.

Functional Movement Screen Score and Injuries

Among the 84 subjects, 15 (17.9%) experienced running injuries during the season. The comparisons between groups with and without running injuries are presented in Table 3. The mean FMS composite scores were 13.3 ± 2.7 and 14.4 ± 2.2 for subjects with and without any injury, respectively. Although there was a trend for the injury group to have a lower score, this difference was not significant (p = 0.07). Of the 7 tests, the scores on the DS and ASLR tests were significant with the *U*-test. Using the composite score of the 2 tests, we calculated a short version of the FMS, which was named "DS and ASLR" (score range: 0–6). Figure 3 shows the significant difference in the DS and ASLR score between the injured and the noninjured groups, whose scores were 2.9 ± 1.0 and 4.1 ± 1.1, respectively ($p < 0.01$).

The ROC curves for the FMS composite and DS and ASLR scores are presented in Figure 4. The cutoff of the FMS composite score was determined to be 14/15, which was consistent with a previous study (10). However, the ROC curve had a relatively low AUC (AUC = 0.65, p = 0.08), and at this point, the sensitivity was 0.73 and the specificity was 0.46. Subjects were dichotomized into groups with FMS composite scores ≤14 and ≥15, which are presented in Table 4. Conversely, the ROC curve for the DS and ASLR score had a relatively high AUC (AUC = 0.79, p = 0.01), and it determined the cutoff to be 3/4 with a sensitivity of 0.73 and a specificity of 0.74 (Figure 4). Subjects were again dichotomized into groups with DS and ASLR scores

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TABLE 6. Influence of the FMS on running injury.*

	Univariate			Multivariate†		
	OR	95% CI	p	OR	95% CI	p
FMS composite score ≤ 14	3.2	0.9–11.0	0.07	3.0	0.8–11.6	0.10
DS and ASLR score ≤ 3	7.8	2.2–27.6	<0.01‡	9.7	2.1–44.4	<0.01‡

*FMS = functional movement screen; OR = odds ratio; CI = confidence interval; DS = deep squat; ASLR = active straight leg raise.
†Adjusted for age, height, weight, running experience, weekly training sessions, weekly mileage, performance, and injury history.
‡$p < 0.01$.

≤3 and ≥4, which are presented in Table 5. Among the subjects with a score of ≤3, 11 out of 29 had been injured during the season (injury rate: 37.9%), whereas among the subjects with a score of ≥4, 4 out of 55 (injury rate: 7.3%) had been injured. The logistic regression analysis revealed similar results presented in Table 6. A score of ≤14 of the composite FMS did not significantly influence the incidence of running injuries (odds ratio [OR] = 3.0, 95% CI = 0.8–11.6, $p = 0.10$). However, the same analysis revealed that a runner with a DS and ASLR score of ≤3 was significantly more likely to become injured even when adjusting for each subject's characteristics (OR = 9.7, 95% CI = 2.1–44.4, $p < 0.01$).

DISCUSSION

The purpose of the current study was to investigate whether the FMS could predict running injuries in competitive male runners. The study revealed that the cutoff on the FMS was 14/15, which was in accordance with a previous study (10), but the composite score of ≤14 had low predictability for running injuries. In contrast, the current study also revealed that a DS and ASLR score of ≤3 during preseason was a more useful approach for predicting running injuries during season in 18- to 24-year-old competitive male runners. This is the first study to investigate the validity of the FMS as a predictor for running injuries and to establish the short version of the FMS (DS and ASLR) for screening running injuries.

The mean FMS composite score for the 18- to 24-year-old competitive male runners in the current study was 14.1 ± 2.3, which is similar to the results of college basketball, volleyball, and soccer athletes in the studies by Warren et al. (22) and Chorba et al. (5) (mean scores were 14.3 ± 2.5 and 14.3 ± 1.7, respectively). However, Loudon et al. (12) reported a mean score of 15.0 ± 2.4 for male running athletes, whereas Agresta et al. (1) reported a mean score of 13.1 ± 1.7 for healthy male runners. Although their findings slightly differ from ours, the runners in the current study had a comparable average performance as other runners. Additionally, our scores were relatively lower than the mean composite scores for professional football players (10) and officer candidates (17) (mean scores were 16.9 ± 3.0 and 16.6 ± 1.7, respectively). These differences are expected to occur because distance running mainly requires cardiorespiratory endurance and does not involve as much stability and power as required by football players or officer candidates.

Considering each movement test of the FMS, Figure 2 shows that the subjects performed the best on the SM test, which required mobility of the shoulder and scapula and thoracic spine extension. Because runners need to swing their arms frequently during running, SM is needed to minimize the burden from arm swing. However, the subjects performed the worst in the RS test, which requires multiplane trunk stability during a combined upper and lower extremity motion. This result was similar to the results of previous studies (1,17,20); there were only a few subjects who scored 3 on the RS test. Thus, these findings suggest that the RS test may be one of the more difficult tests of the FMS.

The ROC analysis revealed that sensitivity and specificity were 0.73 and 0.74, respectively. Subsequently, the multivariate logistic regression analysis revealed that subjects with a score of ≤3 on the DS and ASLR were approximately 10 times more likely to have running injuries than those with a score ≥4 after adjusting for each subject's characteristics. The relatively strong predictability of running injuries according to the DS and ASLR score was attributed to the following reasons. First, the DS test by itself had a strong predictability of injuries, which was in accordance with the result of the study by Butler et al. (3). The DS test assesses bilateral symmetrical mobility, especially mobility of hips, ankles, and thoracic spine, and coordination in the close kinetic chain. Renström (19) reported that poor flexibility and deficit in neuromuscular coordination can cause running injuries. Additionally, excessive pronation and knee-in during testing, which were the causes that decreased the score on the DS test (6), were also reported to be risk factors for injury (14). Second, the ASLR test was also found to be related to running injuries; it assesses active hamstring and gastric-soleus flexibility while maintaining a stable pelvis. This finding agreed with the study by Yagi et al. (24), who

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also reported that limited SLR ability increased the injury risk in high school runners. Additionally, Lysholm and Wiklander (13) reported that flexibility of the hamstrings was a risk factor for injury. Consequently, deficits in the DS and ASLR tests are likely to induce asymmetric or compensatory movement patterns and thus result in running injuries. Thus, the FMS contains both helpful and less helpful movement tests for predicting injury risk in competitive male runners. The HS test assesses stepping ability, which requires mobility and stability of the legs and also coordination. The ILL test requires mobility and stability in the split stance and also coordination. Although these 2 tests seem to be relevant for running, they were not significantly associated with incidence of running injury because most subjects received a score of 2 (91.7% for HS, 86.9% for ILL). Because of their ceiling effects, these 2 tests were ineffective in screening injury risk. As a result, the FMS composite score had low predictability. For the SM, TSPU, and RS tests, there is no solid evidence that SM and core stability influence the incidence of running injuries.

There were several limitations in the study. The first is the definition of injury as a running injury (lost training time $\geq$ 4 weeks). Although the current study revealed that the DS and ASLR could predict serious running injuries, it is unclear if it could successfully screen the risk of nonserious running injuries (lost training time $<$ 4 weeks). A second limitation was the mode of collecting injury data by a self-report questionnaire because of the absence of athletic trainers in all teams. As a result, relevant details, such as type of injury, were not collected. A third limitation was that the study was carried out among 18- to 24-year-old competitive male runners in Japan. It is unclear whether the results can be extrapolated to other running populations, such as female, older, or recreational runners. Therefore, further study is required to ensure the external validity of the DS and ASLR score for other runners.

Practical Applications

First, the study provided reliable normative data for FMS scores among 18- to 24-year-old competitive male runners. These data can be used as reference values for strength and conditioning by professional coaches when they need to assess the injury risk of similar groups using the FMS.

Additionally, the study revealed that a score of $\geq$4 or $\leq$3 of the DS and ASLR was more useful for predicting running injuries than the FMS composite score in the 18- to 24-year-old competitive male runners. This finding is meaningful for the strength and conditioning professional who supports a similar group of athletes. First, injury risks can be screened easily by using the DS and ASLR as it only takes approximately 5 minutes. This is an advantage because time is often limited and rather spent on training. Second, it allows the strength and conditioning professional to prevent serious problems in younger runners that could result in retiring from running because of injuries. Timely prediction of injury risks allows initiating strategies for preventing injury. For example, performing hamstring and gastric-soleus stretches are effective in improving scores on the ASLR (7). As to the DS test, the strength and conditioning professional or physical therapist should assess which deficit is limiting influence on this test before conducting corrective exercises. This is because the DS test is affected by many variables, such as the mobility of the hip, ankle, thoracic spine, and shoulder, the stability of the hip, and coordination (7). The current study suggests that, by improving scores on the DS and ASLR in preseason, the incidence of running injuries in 18- to 24-year-old competitive male runners could be reduced.

Acknowledgments

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A Preseason Checklist for Predicting Elbow Injury in Little League Baseball Players

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Investigation performed at Kyoto University, Kyoto, Japan

Background: Despite pitch count limits, the incidence of Little League elbow is increasing. A risk-evaluation tool capable of predicting which players are predisposed to throwing injury could potentially prevent injuries.

Purpose: To investigate the effectiveness of a risk factor checklist for predicting elbow injury in Little League baseball players during 1 season. The hypothesis was that a preseason risk-evaluation checklist could predict which players were predisposed to elbow injury.

Study Design: Case-control study; Level of evidence, 3.

Methods: A preseason risk-evaluation checklist was distributed to Little League baseball teams in Japan. Six months later, a follow-up questionnaire was mailed to determine injuries sustained during the season. Logistic regression analysis was performed, assigning presence or absence of elbow injury during the season as the dependent variable, and an injury risk score (IRS) was developed based on the statistically significant variables. Receiver operating characteristic (ROC) curve analysis was conducted to determine the predictive validity of the checklist and the optimal cutoff IRS.

Results: Data from 389 Little League players were analyzed. Among them, 53 players experienced an elbow injury requiring medical treatment during the season. Six checklist items associated with a medical history of throwing injury, pitch volume, and arm fatigue were found to be significant. Responses to the items could predict the players who were susceptible to injury during the season, with a two-thirds cutoff value for a 6-item checklist (area under the curve, 0.810; sensitivity, 0.717; specificity, 0.771).

Conclusion: Results from a 6-item preseason checklist can predict which Little League players are to sustain an elbow injury by the end of the season.

Clinical Relevance: The ability to predict which Little League baseball players are predisposed to elbow injury allows parents and coaches to initiate preventive measures in those players prior to and during the baseball season, which could lead to fewer elbow injuries.

Keywords: Little League elbow; prevention; checklist

Throwing injuries in young baseball players are a serious problem. Little League elbow, including epicondylitis and osteochondrosis dissecans, is one of the most severe throwing injuries, occurring in 20% to 40% of school-aged pitchers.[11,13-15] Such an injury can prematurely end a baseball career[4]; therefore, adults should do everything possible to protect children from these injuries.

Many studies have reported the risk factors for throwing injury. Ways to prevent such injuries, including limiting the number of pitches, have been suggested to protect players.[3,14,15,18] As a result, USA Baseball Medical and Safety Advisory Committee guidelines were developed in 2006 to provide recommendations for limiting pitch counts similar to recommendations made in Japan in 1995.[9,20,22] However, there are several problems with these recommendations. For one, these recommendations are meaningless without strict compliance, and a small proportion of coaches have complied with these recommendations. According to 2 recent studies, coaches in the United States answered 43% of questions regarding pitch count and rest periods correctly, whereas 28% of coaches complied with the recommendations in Japan.[1,22] Because few coaches follow these limits regularly, despite evidence that the number of pitches strongly influences development of Little League

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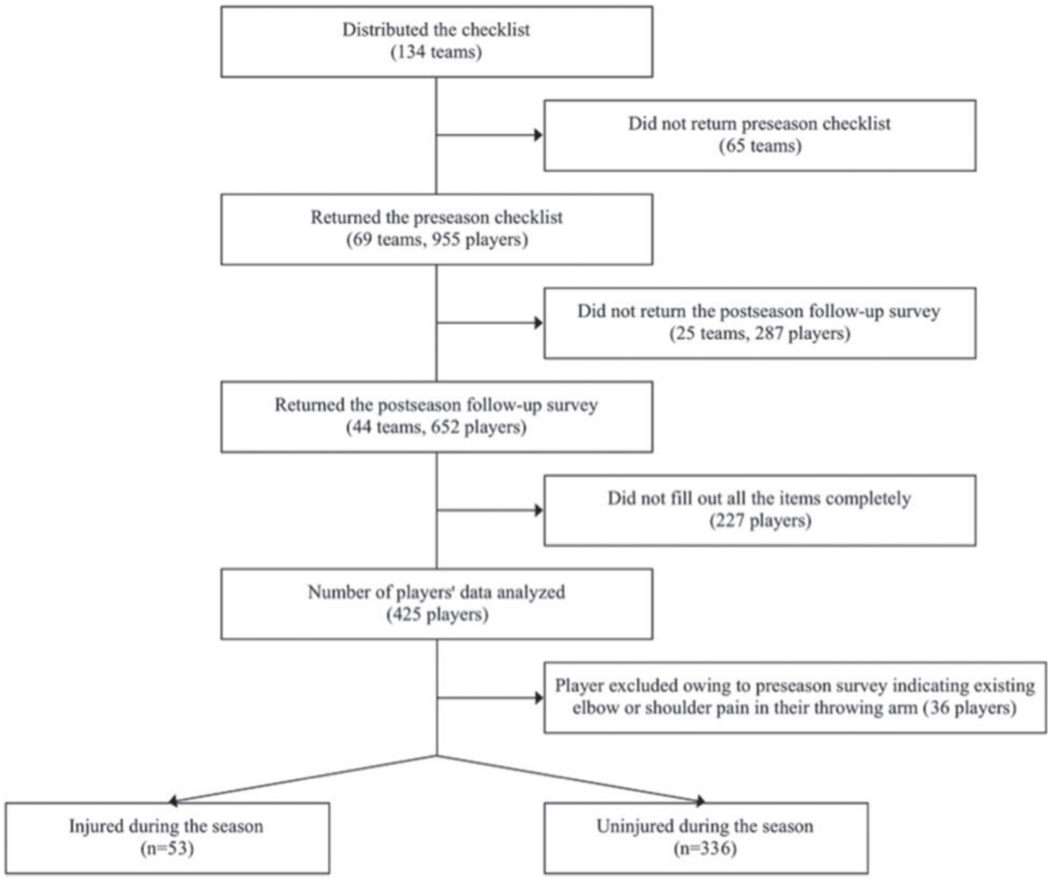

Figure 1. Flowchart showing the process of this research.

elbow, especially in Japan, another approach for prevention of elbow injury must be considered in addition to these limits.

When developing another strategy for primary prevention of youth baseball elbow injury, several things must be taken into account. First, it must be easy for coaches and parents to understand. Medical evaluation by experts, including medical doctors and physical therapists, has been reported to be an effective prevention strategy for throwing injury.[7] However, a large number of children play baseball worldwide: 5.7 million children in eighth grade or lower in the United States, and there are nearly 15,000 elementary school baseball teams in Japan.[2,8] With such large numbers, it is almost impossible for medical specialists to assess all of them. Therefore, coaches and parents, most of whom have no medical knowledge, inevitably have to be responsible for protecting children from injury. Second, the various factors must be evaluated comprehensively. Research has shown that the amount of force placed on a player's elbow is the principal risk factor for injury. Such force is influenced by pitching mechanics, pitch type, and pitch volume.[10] Other risk factors, including arm fatigue, playing baseball outside the league, and range of motion of the shoulder joint, also have been reported.[6,15,18] Thus, prevention cannot focus only on 1 factor, but various factors must be considered comprehensively to successfully prevent throwing injury.

Considering this, we created a checklist for predicting which Little League baseball players are predisposed to elbow injury. To our knowledge, studies using a checklist for injury prevention have not been performed for baseball or any other sport. The aim of the current study was to investigate the effectiveness of a risk factor checklist for predicting elbow injury in Little League baseball players during 1 season.

METHODS

This prospective cohort study investigated the effectiveness of a checklist for predicting elbow injury in young baseball players. Initially, we created an original checklist for predicting Little League elbow based on previous research that explored the risk factors for this injury. This checklist was distributed to each team's representative who participated in the annual tournament in Kyoto and Fukuoka in March 2013 (preseason). A total of 134 teams in 4 cities in Japan received the checklist (Figure 1). To increase response reliability, the players' parents were instructed to work with the players to help complete the

TABLE 1
Preseason Checklist for Little League Players

	Yes	No
Condition of the elbow of the pitching arm		
1. Is the angle of the elbow in full extension different between your arms?	1	0
2. Do you have pain in the elbow of the pitching arm when it is extended?	1	0
3. Is the angle of the elbow in full flexion different between your arms?	1	0
4. Do you have pain in the elbow of the pitching arm when it is flexed?	1	0
Information about baseball playing		
5. Are you a regular player?	1	0
6. Do you often throw more than 100 pitches per week?	1	0
7. Do you have an off-season (a period when you do not throw anything for at least 1 month)?	0	1
8. Does your pitching arm often feel fatigued while playing baseball?	1	0
9. Do you practice throwing breaking pitches often?	1	0
10. Are you more often satisfied than dissatisfied with your performance?	0	1
11. Do you often play catch or throw a ball in noncompetition settings?	1	0
12. Do you often participate in resistance training?	1	0
Pitching form		
13. Is your elbow in a straight line with your shoulders (horizontal shoulder abduction) when in the cocking stage of a pitch?	0	1
14. Is your elbow at or above shoulder level (abducted $\geq 90^\circ$) in the acceleration phase of a pitch?	0	1
15. Is your front foot pointed straight on an extension of the pitcher-catcher line or angled slightly toward third base (for a right-handed pitcher)?	0	1
16. Is your front foot angled straight toward or slightly inward from the catcher?	0	1
Flexibility		
17. When prone with knees flexed at 90°, is there a difference in the internal rotation angle of your hips?	1	0
18. Is there a difference in the height of your thumbs when the dorsum of your hand is placed at maximum height against your back on the line of the spine? (Reflecting range of motion of the shoulders when internally rotated.)	1	0
19. With your knee fully flexed, is the distance between your heel and buttock 0 cm for both legs? (Reflecting flexibility of the quadriceps.)	0	1
20. When you are fully flexed at the waist, is the distance between your fingers and the floor 0 cm? (Reflecting flexibility of the hamstrings.)	0	1

checklist. After the parents had verified the responses, the players/parents mailed back the completed checklist. The purpose and methods of this study were explained to the players' parents in detail in a verbal statement, and written informed consent was obtained from the coaches and parents. This study was approved by the Institutional Review Board of Kyoto University (Approval No. E1669).

Checklist

We designed a 20-item checklist (Table 1). These items were chosen according to 2 criteria: (1) whether the factors were already reported as risk factors for throwing-related elbow injury in previous studies and (2) whether the coaches and parents could easily evaluate the factors with reliability. This checklist consisted of 4 areas of risk: condition of the elbow of the throwing arm, information about the individual player's baseball playing and practice, pitching form, and flexibility. All questions had to be easily answered by parents without medical knowledge. Therefore, pitching form and flexibility were illustrated using photos, and alternative flexibility tests rather than direct range of motion or muscle flexibility tests were used because of the large size of the participants. In addition, each question was designed with a yes/no answer. Intrarater reliability of pitching form and flexibility evaluation was tested by 10 subjects who were not medical specialists, who assessed each variable twice on separate occasions. Pitching form was quoted from the pitching model developed by the American Sports Medicine Institute and American Baseball Foundation.[5,14] These intrarater tests revealed kappa coefficient consistency >0.60 (range, 0.73-1.00) for all 4 pitching form and flexibility variables. These data ranges suggested that coaches and parents with no medical knowledge could answer with substantial reliability.[12] In addition to the checklist questions, basic player information was investigated, including age, height, weight, number of months playing baseball, field position (fielder, pitcher, catcher, or pitcher who concomitantly plays catcher), number of team-training days per week (<4 or $\geq$4), number of self-training days per week ($\leq$6 or 7), presence or absence of pain with throwing in the shoulder or elbow in the preseason, pain in the shoulder or elbow of the throwing arm over the preceding 12 months, and elbow or shoulder injury that ever required medical treatment.

Follow-up Survey

Six months after distributing the preseason checklist, a follow-up questionnaire to determine injuries sustained during the season was distributed to players who had returned the preseason questionnaire. For this study, injury was defined as an elbow injury in the dominant arm sustained during the baseball season that required any medical treatment at least once. After the players' parents had verified the responses, the completed follow-up survey was returned.

Statistical Analysis

We excluded players who had ongoing throwing pain in the elbow or shoulder at the start of the season documented on the preseason questionnaire. We divided the players into 2 groups: those with occurrence of elbow injury during the season and those without injury. We statistically analyzed the differences between these 2 groups using the unpaired *t* test for interval items (age, height, weight, and number of months playing baseball) and the chi-square test for ordinal items.

Next, logistic regression analysis, performed in a stepwise manner, was carried out to examine whether the potential determinants were independently associated with occurrence of elbow injury during the season. In this analysis, presence or absence of elbow injury during the season was used as the dependent variable, and all items with a *P* value <.1 in univariate analyses were employed as independent variables.

Finally, we developed an "injury risk score" (IRS) based on the logistic regression analysis, distributing 1 point for significant variables to each individual. We then used receiver operating characteristic (ROC) curve analysis to examine the predictive validity of the checklist and the optimal cutoff IRS based on the Youden index,[21] assigning occurrence of elbow injury as a state variable. Area under the curve (AUC), sensitivity, and specificity of the IRS were calculated based on the ROC curve. The cutoff value for the IRS was determined based on optimal sensitivity and specificity. A *P* value <.05 was considered to be statistically significant for all analyses.

RESULTS

The 20-item preseason checklist was completed and returned by 69 teams representing 955 players (mean age, 10.0 ± 1.0 years). Of those, 25 teams failed to return the postseason follow-up survey, leaving us with pre- and postseason data from 44 teams, representing 652 players (mean age, 10.0 ± 1.0 years). After eliminating all players with incomplete surveys, data from 425 players remained. After eliminating 36 more players whose preseason surveys indicated existing elbow or shoulder pain in their throwing arm, data from 389 players remained (mean age, 10.1 ± 0.9 years) (Figure 1).

By the end of the season, 53 of 389 players had experienced an elbow injury, resulting in an injury rate of 13.6%. Basic information of these players is shown in Table 2. Results of the unpaired *t* test showed that age, height, weight, and length of time playing baseball were significantly different between the 2 groups, whereas results of the chi-square test showed that pain in the elbow or shoulder while throwing within the past 12 months (n = 37, 69.8%), throwing-related elbow or shoulder injury ever requiring medical treatment (n = 22, 41.5%), status of pitcher (n = 31, 58.5%), team training ≥4 days per week (n = 23, 43.4%), self-training 7 days per week (n = 10, 18.9%), and checklist items 5 (starting lineup member; n = 52, 98.1%), 6 (frequently throwing >100 pitches per week; n = 13, 24.5%), and 8 (frequently feeling fatigue in the throwing arm during the season; n = 23, 43.4%) were significantly different between players with and without elbow injury (Table 2).

Logistic regression analysis revealed that pain in the elbow or shoulder while throwing within the past 12 months

TABLE 2
Comparison of Players With and Without Elbow Injury Sustained During the Season[a]

	With Injury (n = 53)	Without Injury (n = 336)	*P* Value
Age, y, mean ± SD	10.4 ± 0.7	10.0 ± 1.0	<.01[b]
Height, cm, mean ± SD	141.5 ± 7.1	138.5 ± 7.6	<.01[b]
Weight, kg, mean ± SD	35.2 ± 7.6	32.6 ± 6.2	<.01[b]
Previous baseball experience, mo, mean ± SD	33.9 ± 16.0	28.0 ± 15.4	.01[c]
Has experienced shoulder or elbow pain while throwing in the preceding 12 months	37 (69.8)	108 (32.1)	<.01[b]
Has ever experienced an elbow or shoulder injury requiring medical attention	22 (41.5)	38 (11.3)	<.01[b]
Fielding position			
Pitcher	31 (58.5)	111 (33.0)	<.01[b]
Catcher	12 (22.6)	86 (25.6)	.74
Fielder	49 (92.5)	316 (94.0)	.55
Pitcher who concomitantly plays catcher	6 (11.3)	42 (12.5)	>.99
Team training ≥4 days per week	23 (43.4)	78 (23.2)	<.01[b]
Self-training 7 days per week	10 (18.9)	23 (6.8)	.01[c]
Checklist item			
No. 1	4 (7.5)	16 (4.8)	.33
No. 2	1 (1.9)	4 (1.2)	.52
No. 3	2 (3.8)	6 (1.8)	.30
No. 4	0 (0.0)	3 (0.9)	>.99
No. 5	52 (98.1)	266 (79.2)	<.01[b]
No. 6	13 (24.5)	37 (11.0)	.01[c]
No. 7	51 (96.2)	322 (95.8)	>.99
No. 8	23 (43.4)	52 (15.5)	<.01[b]
No. 9	1 (1.9)	8 (2.4)	>.99
No. 10	26 (49.1)	158 (47.0)	.88
No. 11	26 (49.1)	167 (49.7)	>.99
No. 12	7 (13.2)	52 (15.5)	.84
No. 13	17 (32.1)	133 (39.6)	.36
No. 14	11 (20.8)	47 (14.0)	.21
No. 15	10 (18.9)	66 (19.6)	>.99
No. 16	8 (15.1)	43 (12.8)	.66
No. 17	7 (13.2)	43 (12.8)	>.99
No. 18	19 (35.8)	100 (29.8)	.42
No. 19	5 (9.4)	32 (9.5)	>.99
No. 20	18 (34.0)	129 (38.4)	.65

[a]Values are reported as n (%) unless otherwise indicated.
[b]*P* < .01.
[c]*P* < .05.

TABLE 3
Factors Associated With Occurrence of Elbow Injury During the Season According to Stepwise Logistic Regression Analysis

	Odds Ratio	95% CI	*P* Value
Has experienced shoulder or elbow pain while throwing in the preceding 12 months	2.64	1.31-5.34	.007
Has ever experienced an elbow or shoulder injury requiring medical attention	4.10	1.96-8.54	<.001
Team training ≥4 days per week	2.58	1.30-5.12	.007
Self-training 7 days per week	3.15	1.23-8.09	.017
Checklist item No. 5	10.29	1.26-84.0	.030
Checklist item No. 8	3.01	1.48-6.11	.002

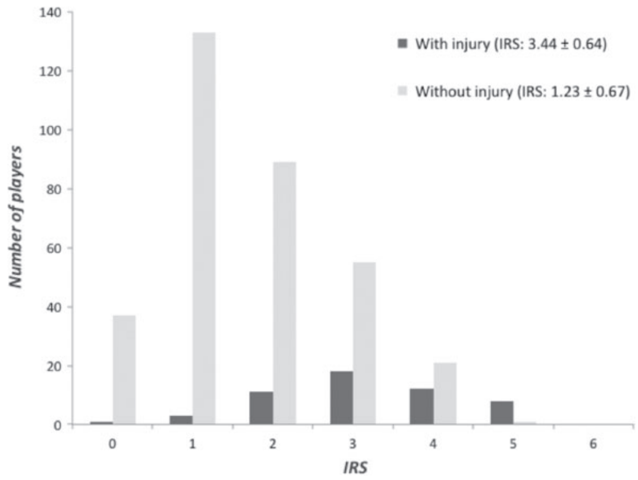

Figure 2. Injury risk score for players with and without elbow injury during the season. IRS, injury risk score.

(odds ratio [OR], 2.64; 95% CI, 1.31-5.34; P = .007), throwing-related elbow or shoulder injury ever requiring medical treatment (OR, 4.10; 95% CI, 1.96-8.54; P < .001), team training ≥4 days per week (OR, 2.58; 95% CI, 1.30-5.12; P = .007), self-training 7 days per week (OR, 3.15; 95% CI, 1.23-8.09; P = .017), checklist item 5 (OR, 10.29; 95% CI, 1.26-84.0; P = .030), and checklist item 8 (OR, 3.01; 95% CI, 1.48-6.11; P = .002) were independently associated with occurrence of elbow injury during the season (Table 3).

Using the 6 variables that were significant in the logistic regression analysis, we calculated the IRS going up to 6 points. In the injured player group, the mean IRS was 3.44 ± 0.64, whereas that in the noninjured player group was 1.27 ± 0.67 (P < .01) (Figure 2). The ROC curve had a relatively high AUC for the IRS (0.810), and we determined that a two-thirds cutoff point had a sensitivity of 0.717 and a specificity of 0.771 (Figure 3). Among players with an IRS of 3 to 6 (n = 115), 38 players had been injured during the season (injury rate, 33.0%). Among players with an IRS of 0 to 2 (n = 274), 15 players (injury rate, 5.5%) had been injured (Figure 2).

DISCUSSION

We developed a preseason checklist to predict predisposition to elbow injury in Little League baseball players. As a result, we could predict the players who would be injured during the season with a two-thirds cutoff value for a 6-item checklist. The final version of the checklist (Table 4) has some desirable features, such as being easy to answer for coaches and parents, and comprehensively considering the risk factors. Therefore, we believe this checklist will be helpful for primary prevention of Little League elbow in the future. To our knowledge, this is the first longitudinal study aimed to develop an injury-predicting checklist for Little League baseball players.

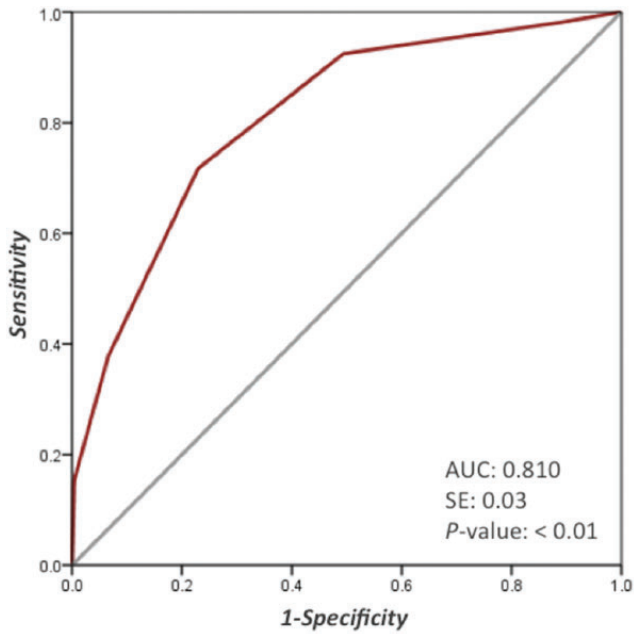

Figure 3. Receiver operating characteristic (ROC) curve analysis for injury risk score (IRS). ROC analysis was conducted to determine the predictive validity of the checklist and the optimal cutoff IRS, assigning occurrence of elbow injury as a state variable. We were able to predict the players who were injured during the season with a two-thirds cutoff value for a 6-item checklist (area under the curve [AUC], 0.810; sensitivity, 0.717; specificity, 0.771).

The IRS of this checklist is composed of 6 items. As demonstrated in many previous studies,[3,14,15,18] volume of playing baseball was a significant risk factor in our study. Playing baseball outside of league competition also has been reported to be a risk factor,[15,18] which might be close

TABLE 4
Final Version of Checklist

	Yes	No
1. Have you experienced shoulder or elbow pain while throwing in the preceding 12 months?	1	0
2. Have you ever experienced a shoulder or elbow injury requiring medical treatment?	1	0
3. Do you participate in team training $\geq$4 days per week?	1	0
4. Do you participate in self-training 7 days per week?	1	0
5. Are you in the starting lineup?	1	0
6. Does your pitching arm often feel fatigued while playing baseball?	1	0

to our finding: A similar measure, number of self-training days per week = 7, was found to be significant in our study. The more frequently baseball is played, the larger the amount of force a player's elbow receives. Players who spend a significant amount of time training outside the league competition should be monitored closely for signs of injury. Arm fatigue in the preseason also was found to be a significant risk factor. We cannot confirm whether this fatigue would continue during the season, but fatigue on a daily basis could affect the onset of injury. As shown in several studies,[15,18] coaches and parents may be able to use such fatigue as an easily observed predictor of elbow injury. In addition, a medical history of throwing injury was shown to be a significant factor. Some studies excluded players who had preexisting throwing injury or did not consider the history of injury[6,18]; therefore, the causal relationship between past medical history and new onset of injury remains unknown. Medical history may be misleading in players who continue to use their throwing arm despite known abnormalities on imaging studies or ongoing clinical symptoms.[7,16] These players often have worse outcomes[19] for several reasons: An injury that is not completely treated may become more severe with activity; an injury may have changed the player's pitching mechanics, making the player more susceptible to injury; and players who have experienced an injury in the past are more likely to sustain a new injury. Consequently, players with signs or symptoms of a previous or ongoing injury should be followed more closely for evidence of a new or worsening injury than players without a preexisting injury. In this study, one of the most important risk factors, pitching mechanics, was not shown to be significant. However, this may be because the checklist was designed to be easily answered by parents, and proper pitching motion analysis is quite complicated[17]; thus, only 4 of 24 items in the pitching model developed by the American Sports Medicine Institute and American Baseball Foundation were selected for evaluation. Incorporating pitching mechanics into our checklist will be considered in a future study.

Researchers have identified risk factors for Little League elbow, including age, height, weight, range of motion of the shoulder joint, pitch count, fatigue, pitching biomechanics, and pitch type.[3,6,14,15,18] Based on this information, several primary prevention strategies have been considered. Limiting pitch count is regarded as the most effective way to prevent throwing injury.[2,11] While we agree that this is true, these limits are meaningless without strict compliance.[1,22] One cause of poor compliance is that pitch count limits are monitored by coaches rather than parents, and coaches may have less interest in protecting players from injury than parents. We believe that parents have the potential to prevent children from being injured, and our checklist, which we have shown can predict predisposition to injury, was designed to be easy for parents to use. The most important clinical implication of this study is that parents can evaluate and follow their child's condition and determine whether the child is at risk of developing Little League elbow. When parents are aware that their child is at risk for elbow injury, they can monitor pitch count limits themselves and encourage coaches to apply the limits more strictly. Closer monitoring by parents may lead to earlier detection and prevention of Little League elbow. Players with an IRS of $\geq$3 on this checklist had only a 33% chance of injury; therefore, it might be exaggerated to suggest that use of this checklist only is effective for prevention of injury. However, this is a step in the right direction, and the checklist would be more valuable in combination with other preventive measures. We expect that use of our checklist in combination with pitch count limits or other preventive measures in collaboration between coaches and parents will be helpful for primary prevention of Little League elbow.

Our study has several limitations. First, selection bias might have influenced the results. Participants were lost to dropout, preexisting injury, and omissions on the follow-up survey. Second, pitching mechanics were not fully investigated in the study. Until the checklist is more comprehensive in its coverage of pitching mechanics, its usefulness for predicting risk of elbow injury may be limited. Finally, because the study was confined to Japanese children, the generalizability of this study to other populations or geographic areas is unknown. Further research is required to ensure the external validation of our checklist.

CONCLUSION

Our study showed that responses on a 6-item checklist of risk factors for elbow injury can predict which Little League baseball players are predisposed to elbow injury. The ability to predict which Little League baseball players are predisposed to elbow injury allows parents and coaches to initiate preventive measures in those players prior to and during the season, which could lead to fewer elbow injuries.

The 6-item checklist should be applied to all Little League baseball players in the preseason to determine their predisposition to elbow injury.

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中高年を対象としたウォーキングエクササイズの効果に関するエビデンスの検証

Verification of the effect of walking exercise on middle aged and elderly people

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Key words：ウォーキングエクササイズ (walking exercise)、エビデンス (evidence)、高齢者 (elderly)、リハビリテーション (rehabilitation)、システマティックレビュー (systematic review)、メタアナライシス (meta-analysis)

要旨

ウォーキングエクササイズは手軽に実施でき、合併症が少ない事から、高齢者や疾病を有する患者であっても比較的容易に取り組む事ができる。リハビリテーションにおいても歩行機能が低下した患者の移動能力の再獲得や向上を目的としてリハビリテーションプログラムの一つとして実施され、その効果についてのエビデンスも明らかにされている。しかしながらその目的は対象者によって異なることから、アウトカムや調査の方法が異なり、見解が異なる結果も少なくない。そこで本研究はウォーキングエクササイズが行われる目的別にシステマティックレビュー、メタアナライシスなどのエビデンスレベルの高い論文を抽出し、検証する事で、ウォーキングエクササイズの効果について検討した。この結果、高血圧、代謝異常、運動器疾患、神経疾患を有する患者に対する介入効果は高いが、高齢者のパフォーマンス向上や骨密度改善には効果が少ない事が明らかになった。

【背景及び目的】

一般的に運動は健康の維持、増進に良好な影響を与えると考えられている。さまざまな運動の中でもウォーキングエクササイズは特別な器具を必要とせず、どこでも簡便に行うことができ、運動時の外傷や呼吸循環動態に急激な変化をもたらすことが少ないことから、有疾病者や高齢者を含めて幅広い世代において安全に実施できる簡便なエクササイズである[1]。また、有酸素運動の一つとして捉えられているウォーキングエクササイズは運動器系だけでなく、呼吸器系、循環器系、代謝系、神経系を動員し、刺激を加えることから、全身の多くの器官に機能維持や亢進効果を与えることが期待される。

また視点を変えると、高齢者において歩行機能を維持する事は、介護予防の観点から重要視するべきポイントである。また高齢者に限らず、廃用予防あるいは廃用症候群の改善目的のリハビリテーションでは、早期離床に続いて実施されるプログラムの一つでもある[2]。さらに筋骨格系疾患[3]、パーキンソン病[4]、脳梗塞[5,6]などの歩行機能に障害をもたらす疾病に対して、歩行機能の再獲得や改善を目的としたリハビリテーションは臨床現場で積極的に行われている。

これらのことからウォーキングエクササイズの目的を、①健康維持及び向上、②歩行機能の維持及び改善、③歩行機能の再獲得と分ける事ができるが、その目的は少しずつ異なるため、何をアウトカムに効果を判定するかによって結果は少しずつ異なってくる。これまでにウォーキングエクササイズの効果については無作為抽出症例対象研究（randomized control study: RCT）やシステマティックレビュー、メタアナラ

イシスなどのエビデンスレベルの高い報告がなされ、エビデンスは着実に構築されており、統計学的にもその効果は示されている。しかしながら、それらのシステマティックレビューなどの中には異なる見解を示すものや効果に対する見解を明らかにしていないものも多い。これは抽出された論文の間で異なる結論が導かれていることやメタアナライシスにおいて統計学的な効果量がわずかであったりすることに起因する。これらの原因としては、それぞれの研究報告はエビデンスレベルの高い調査手法で実施されているが、実施する目的、対象や介入強度、アウトカムなどが調査研究間で異なる、あるいは研究デザインが目的と合致していない可能性がある。

そこで本研究においては中高年を対象にさまざまな目的で行われるウォーキングエクササイズの効果を明らかにするために、ウォーキングエクササイズによる介入効果検証目的で行われたシステマティックレビュー論文を渉猟し、目的別に整理、比較することで、明らかにされていない効果判定の見解の原因を探求することとする。

【方法】

2015年7月までのウォーキングエクササイズによる介入効果を検証する論文を、データベースであるPubMedにて、キーワード「((walking) AND (((intervention) OR training) OR exercise)) AND ((older adults) OR elderly))」を用いて検索した。ここで該当した論文(計16964編)より、エビデンスレベルの高い論文として位置づけられるメタアナリシスを含むシステマティックレビュー(計273編)を抽出した。さらに抽出した論文の抄録や本文からウォーキングエクササイズによる介入効果を検証している20編を最終的な検討対象とした(図1)。

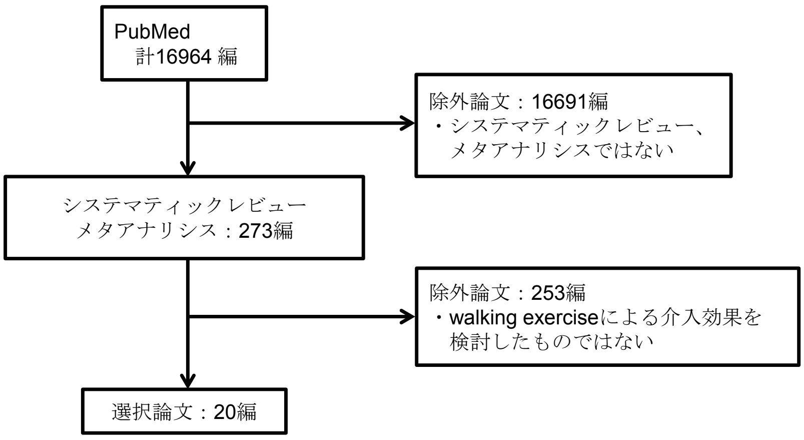

図1. 論文検索フローチャート

【結果】

1. 対象者に関して

それぞれのシステマティックレビュー論文において、RCTなどのエビデンスレベルの高い論文がピックアップされていた。

対象者は、健常高齢者のみを対象としたものが3編、閉経後女性を対象としたものが1編、疾病患者を含む健常成人〜高齢者を対象としたものが9編、肥満を有する成人を対象としたものが1編、疾病患者のみを対象としたものが6編であった。(表1)。

表１. walking exerciseによる介入効果に関するシステマティックレビューのまとめ

Number	Authors Journal	Design	Subjects	Intervention type	Outcome (effective)	Outcome (less effective)
1	Bolam KA Osteoporos Int. 2013; 24 (11): 2749-2762.	SR	middle-aged and older men	brisk walking (一部)		bone mineral density (BMD) (limited effect)
2	Fritschi JO Scand J Med Sci Sports. 2012; 22 (5): e70-78.	SR	any adults	pole walking	cardiospiratory outcomes functional status QOL	anthropometry muscle strength and flexibility fatigue gait parameters blood glucose levels
3	Lee LL Int J Nurs Stud. 2010; 47 (12): 1545-1561.	SR	any adults	walking	blood pressure	
4	Kang M Res Q Exerc Sport. 2009; 80 (3): 648-655.	MA	any people	pedometer-based walking	physical activity	
5	Murphy MH Prev Med. 2007; 44 (5): 377-385.	MA	any adults	walking	VO2 max decreased body weight BMI percent body fat resting diastolic blood pressure	
6	Palombaro KM J Geriatr Phys Ther. 2005; 28 (3): 102-107.	MA	adults aged over 50 years	walking	lumber BMD	femur and calcaneus BMD
7	Kelley GA Prev Cardiol. 2005; 8 (2): 102-107.	MA	any adults	walking	non-HDL-C	
8	Kelley GA Prev Med. 2004; 38 (5): 651-661.	MA	any adults	walking	LDL-C TC/HDL-C VO2max	TC HDL TG
9	Kelley GA Prev Med. 2001; 33(2 Pt 1): 120-127.	MA	any adults	walking	resting systolic and diastolic blood pressure	
10	Gómez-Cabello A Sports Med. 2012; 42 (4): 301-325.	SR	older adults	walking (一部)		BMD BMC
11	Howe Te Cochrane Database Syst Rev. 2011; (11): CD004963.	SR (Cochrane)	older adults	walking (一部)	FRT tandem	TUG OLS
12	Sherrington C J Am Geriatr Soc. 2008; 56 (12): 2234-2243.	SR and MA	older adults	walking (一部)		fall
13	Martyn-St James M Bone. 2008; 43 (3): 521-531.	SR and MA	postmenopausal women	walking	femoral neck BMD	lumber spine BMD
14	Richardson CR Ann Fam Med. 2008; 6 (1): 69-77.	MA	adults with overweight	pedometer-based walking	weight loss	
15	Grande AJ Cochrane Database Syst Rev. 2015; 6: CD010596.	SR (Cochrane)	acute respiratory infection	walking (一部)	ARI symptoms	
16	Mansi S BMC Musculoskelet Disord. 2014; 15: 231.	SR	musculoskeletal disorders	pedometer-based walking	physical activity physical function pain	
17	Peurala SH J Rehabil Med. 2014; 46 (5): 387-399.	SR and MA	stroke	walking	walking speed walking distance walking independence self-care	
18	Charalambous CC Neurorehabil Neural Repair. 2013; 27 (8): 709-721.	SR	stroke	treadmill-based walking	walking speed	
19	Thuné-Boyle IC Int Psychogeriatr. 2012; 24 (7): 1046-1057.	SR	dementia	walking (一部)	BPSD (mood and agitation)	
20	Mehrholz J Cochrane Database Syst Rev. 2010; (1): CD007830.	SR (Cochrane)	Parkinson's disease	treadmill-based walking	gait speed stride strength walking distance	cadence

SR: systematic review, MA: meta analysis, QOL: quality of life, VO2: maximum oxygen uptake, BMI: body mass index, BMD: bone mineral density, BMC: bone mineral content, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, TC: total cholesterol, FRT: functional reach test, ARI: acute respiratory infection, BPSD: behavioral and psychological symptoms of dementia, TUG: timed up and go test, OLS: one leg standing

２.介入方法に関して

ウォーキングエクササイズ単独は14編、さまざまなエクササイズと組み合わせてウォーキングエクササイズを行ったものが６編であった。このうち歩数計を用いたウォーキングエクササイズが３編、ポールウォーキングエクササイズが１編、トレッドミルウォーキングエクササイズは２編であった。対照群に対する介入としては何もしないといったものが多い。他のエクササイズの効果検証を目的としたものでは、ウォーキングエクササイズを対照群として設定してあるものもあった。

３.アウトカムに関して

健常な中高年に対するウォーキングエクササイズ介入のアウトカムとして、活動量や運動機能、転倒などのパフォーマンスが３編、骨密度改善が４編であった。

疾病者を対象としているものでは血圧などの循環機能が３編、体重やコレステロールなどの代謝マーカーが４編であった。また筋骨格系疾患でパフォーマンスや痛みを、急性呼吸器感染症で呼吸器症状の持続期間や再発回数を、認知症においては認知症に伴う周辺症状を、パーキンソン病では歩行スピードやストライドなどの歩行パフォーマンスを検証しているものがそれぞれ１編ずつあり、脳梗塞では歩行スピードなどの歩行パラメーターを検証しているものが２編あった。

４．効果

４．１．高齢者の身体的パフォーマンスに対する効果

歩数計の使用は歩数を増やす。

歩数計はウォーキングエクササイズを実施する際に、モチベーションを維持するのに有用なツールである。Kang Mらは歩数計を使用する前後での歩数変化を32論文のメタアナライシスによって検証した。この結果、歩数計を使用することで歩数が有意に増加する事が明らかになった（effect size 0.68, 95%CI 0.55 to 0.81）。女性においてその効果は顕著で（effect size 0.80, 95%CI 0.64 to 0.97）あるが、男性においてはあまり明らかではなかった（effect size 0.30, 95%CI -0.18 to 0.79）。歩数計を使用する事で2000歩／日の歩数増加効果を得る事ができ、歩数計は活動性を上昇するのに有効であると結論している[7]。

ウォーキングは高齢者のバランス機能向上に弱い効果を示す。

高齢者において、バランス機能の低下は身体機能の低下や転倒のリスクと関連する。Howe TEらは地域在住及び施設入所の高齢者（60歳以上）のバランス機能に対するエクササイズ介入の効果を、94論文をレビューすることで検証した。エクササイズの種類として、①歩行、バランス、機能訓練、②筋力強化、③太極拳、ダンス、ヨガなどの三次元エクササイズ、④ウォーキング、⑤サイクリング、⑥ビジュアルフィードバックを用いたコンピューターバランスエクササイズ、⑦不安定板、⑧様々なエクササイズの複合などに分類して検証したが、いずれにおいてもバランス機能向上にあまり強い効果を示すことはできなかった。④ウォーキング単独では統計的な有効性を示すことはなく、①歩行、バランス、機能訓練の複合エクササイズによってTimed up and Go test, Gait speed、Berg Balance Scaleなどのバランス指標の向上に対しては弱い効果を示すのみであった[8]。

ウォーキングは高齢者の転倒予防については有効な結果は得られなかった。

高齢者の転倒予防を目的に、ウォーキングを含むさまざまなエクササイズが試みられている。そこで、Sherrington Cらはさまざまなエクササイズの効果をメタアナライシスで検証した。転倒防止にもっとも有効であったハイチャレンジバランストレーニング（rate ratio 0.79 95%CI 0.66 to 0.95）と比較して、ウォーキング単独プログラムの効果は（rate ratio 1.19 95%CI 1.11 to 1.58）と有効な結果を得ることはできなかった[9]。

４．２．骨密度に対する影響

中高年の骨密度改善効果は性別、評価部位、介入方法、対象年齢によって異なり、一定の結論を得る事は困難である。

女性の閉経後には骨密度の低下により骨折のリスクが上昇する。骨密度改善の目的でエクササイズが行われているが、ガイドラインなどでも一定の見解を得ていない[10]。そこでウォーキングを含むエクササイズの骨密度改善効果を検証した。

Martyn St Jamesらは閉経後の女性の腰椎及び大腿骨の骨密度に対するウォーキングエクササイズの効果をメタアナライシスにより検証した。解析の結果、腰椎の骨密度については対照群と比較して改善効果はなく（weighted mean difference 0.007g/cm^2 95%CI -0.001 to 0.016, p=0.09）、大腿骨の骨密度には弱い改善効果（weighted mean difference 0.014g/cm^2 95%CI 0.000 to 0.028, p=0.05）を有していた[11]。

閉経後の女性及び50歳以上の男性を対象に、腰椎及び大腿骨の骨密度に対するウォーキングエクササイズの効果をメタアナライシスにより検証したもの[12]では、腰椎の骨密度改善に有効（p=0.03）ではあるが、大腿骨（p=1.00）及び踵骨（p=0.56）の骨密度改善効果は認めないという結果であった[12]。

またBolam KAらは中高年の男性及び女性の骨密度に対するウォーキングを含むエクササイズの効果をシステマティックレビューで検証した[13]。抽出された８論文のうち、ウォーキング単独は２論文、ウォーキングと抵抗運動を行ったものが１論文であった。ウォーキング単独を検証しているHuuskonen J[14]とPaillard T[15]においては、中高年の男性を対象にしたブリスクウォーキングの効果検証を行っている。このうちHuuskonen Jらは対照群と比較して腰椎、大腿骨の骨密度に対してウォーキングエクササイズの効果はない[14]としているが、Paillard Tらは対照群と比較して2.1％の股関節骨密度増加効果を有すると報告している[15]。ウォーキングと抵抗運動を行ったものは、介入群にウォーキングと抵抗運動、対照群にウォーキング単独を設定している。この論文の目的は抵抗運動の効果検証であるため、ウォーキングの効果については明らかにしていない[13]。

Gómez-Cabello Aらは高齢の男性と女性を対象としたウォーキングを含む有酸素運動の効果をシステマティックレビューで検証した。いずれの調査においても骨密度が増加したものはないが、骨密度低下を防止した可能性がある事を記載している[16]。また、骨密度に対するウォーキングの効果を検証したこれまでの調査は年齢、評価部位、骨密度測定方法、エクササイズの強度、頻度、期間などがばらばらで、現時点の調査ではその効果は明らかではないと結論している[16]。

４．３．心血管機能に対する影響

ウォーキングエクササイズは血圧低下効果を有する。

Lee LLらは降圧薬を内服中の高血圧患者だけではなく、高血圧ではない健常者を含む中高年者を対象にウォーキングエクササイズの血圧に与える効果をシステマティックレビューで検証した[17]。この論文においては27編のRCT論文が抽出され、このうちの９編でウォーキングエクササイズによる降圧効果を認める事ができた。この結果、ウォーキングは血圧低下に対して有効な効果を有すると結論した[17]。

またKelly GA（2001）らはウォーキングエクササイズ介入群と無介入の対照群と間で安静時血圧に与える影響をメタアナライシスで検証した[18]。この結果、ウォーキングエクササイズを行う事で、安静時の収縮期及び拡張血圧のいずれにおいても2％（収縮期：平均±SEM=-3±1mm Hg, 95%COI:-5 to -2mm Hg、拡張期：平均±SEM=-2±1mm Hg, 95%COI:-3 to -1mm Hg）の血圧減少効果を有する事が示された[18]。

ポールウォーキングエクササイズはさまざまな疾病者、健常中高年の循環機能、社会心理的健康の改善効果を有する。

Fritschi JOらは”pole walking”、”Nordic walking”、”stick walking”などのワード検索でポールウォーキングと総称するウォーキングプログラムの有効性について調査した。対象は健常高齢者だけなく、２型糖尿病、心血管疾患、筋骨格系疾患、慢性閉塞性呼吸器疾患、パーキンソン病、乳がんなど多岐にわたる疾病患者を含んでいる。持久力向上や血圧低下、脈拍減少などの心機能の改善が認められ、functional statusはベースラインより向上が認められた。また、筋骨格系疾患患者の背部痛、下肢痛、跛行などの痛みは減少した。Medical Outcomes Study 36 Item Short-Form Health Survey（SF36）などのQuality of Lifeの指標も改善するなど、心理社会的健康も向上した[19]。

４．４．代謝機能に対する影響

ウォーキングエクササイズは体重減少効果を有する。

Richardson CRらはデスクワーク従事者、BMIが25kg/cm^{2}以上の肥満者、２型糖尿病、乳がんのがんサバイバーなどを対象に歩数計を用いたウォーキングエクササイズの体重に対する効果を、９編のRCTのメタアナライシスを用いて検証した。平均年齢は43～60.5歳とやや若年者を対象にした結果である。この結果、平均の体重は-1.27 kg (95% CI, -1.85 to -0.70 kg)の体重減少を認め、ウォーキングエクササイズを実施している期間は、0.05kg/週の減量効果を認めた事を報告している[20]。

またMuphy MHらはデスクワーク従事者を対象に、循環器疾患の発症リスク因子である体重、BMI、体脂肪率、最大酸素摂取量、安静時血圧に対するウォーキングエクササイズによる変化をメタアナライシスにより明らかにした。平均34.9週のウォーキング介入の結果、体重(-0.95kg)、BMI (-0.28 kg/m^2)、体脂肪率(-6.3%)、最大酸素摂取量(2.73 ml/kg/min)、拡張期血圧(-1.54 mm Hg)などで有意な効果を認めた。これらの結果からデスクワーク従事者においてウォーキングエクササイズは心血管系のリスク因子を減らすと結論した[21]。

ウォーキングエクササイズは脂質代謝を改善する。

脂質代謝異常は心血管病のリスクを上昇する。Kelly GA(2004)らは総コレステロール、high and low density lipoprotein cholesterol (HDL-C、LDL-C)、トリグリセリドなどの脂質代謝マーカーに対するウォーキングエクササイズによる影響をメタアナライシスで検証した。この調査においては健常者、喫煙者、非喫煙者、アルコール愛好者、肥満者、投薬治療を受けている脂質代謝異常者など幅広い対象者を調査対象にしている。この結果、LDL-C (-5.5±2.2 mg/dL, 95% CI -9.9 to -1.2 mg/dL)、総コレステロール/HDL-C(-0.3±0.1%, 95% CI -0.6 to -0.1)は有意な改善を認めたが、総コレステロール、HDL-C、トリグリセリドは統計的に有意な改善を認めなかった[22]。

Non-High density lipoprotein cholesterol (non- HDC-C)は心血管病のリスク因子である。Kelly GA (2005)らはウォーキングエクササイズによるnon- HDC-Cの変化をメタアナライシスで検証している。この結果、平均22.5±17.8週、4.9±2.6日/週のウォーキングエクササイズで-5.6±1.6 mg/dL (95%CI, -8.8 to -2.4 mg/dL)のnon- HDC-C減少効果を示した[23]。

４．５．疾病者の機能改善、健康増進に与える影響

筋骨格系疾患に対して歩数計を用いたウォーキングエクササイズは活動性を向上する。

Mansi Sらは筋骨格系疾病者を対象に歩数計を用いたウォーキングエクササイズの効果をシステマティックレビューによって検証した。"musculoskeletal disorders"、"walking"、"pedometer"のワード検索を行い、RCTを用いた介入研究を抽出したところ、変形性膝関節症、慢性腰痛、線維筋痛症などの筋骨格系疾患を対象にRCTを行った７論文が抽出された。変形性膝関節症を対象にした４論文のうち３論文で有意な痛みの軽減、身体機能の向上効果が認められた。慢性腰痛を対象にした２論文ではいずれも腰痛のスコアであるRoland Morris Disability Questionnaireが有意に改善した。線維筋痛症を対象にした１論文では痛み(p=0.06)、疲労(p=0.85)、６分間歩行(p=0.92)などで有意な改善効果は得られなかった。これらの結果から、筋骨格系疾患者に対する歩数計を用いたウォーキングエクササイズは痛みや活動性の改善に強い効果を有すると結論している[3]。

急性呼吸器感染症の再発、重症化、罹患期間に対する有酸素エクササイズの効果は限定的である。

30日以内に沈静化する急性の呼吸器感染症は世界的にも多い疾患である。Grande AJらはウォーキングを含む有酸素エクササイズの効果を、急性呼吸器感染症の重症化、再発、罹患期間をアウトカムとしてシステマティックレビューで検証した。症状期間の短縮、再発や重症化防止については統計的に有意ではあるが弱い効果であり、副次アウトカムとして検証した白血球数、免疫グロブリン量、QOLなどは統計的に有意な改善効果を得る事は出来なかった。このことから急性呼吸器感染症に対する有酸素エクササイズの効果は限定的で、エビデンスの構築には更に多くの調査が必要であると結論している[24]。

認知症に伴う周辺症状(behavioral and psychological symptoms of dementia: BPSD)のいくつかの項目軽減にウォーキングを含むエクササイズは有効である。

BPSDは認知症患者、介護者の双方に苦痛を与え、施設収容や死へとつながる問題を引き起こす。これらの症状緩和には抗不安薬や抗うつ薬の投薬治療がおこなわれるが、投薬による副作用も多く、活動性の低下にもつながる[25]。そこでThuné-Boyle IC らはBPSD に対するウォーキングを中心にしたエクササイズの効果をシステマティックレビューで検証した。この結果、抑うつ気分、興奮、徘徊、不眠などには効果を示したが、不安、無気力、繰り返し動作などに対する効果は少なかった。エクササイズの方法や頻度については十分に示されていないが、週に何回か30分以上の歩行を行うことを推奨している[25]。

トレッドミルウォーキングはパーキンソン病における歩行パラメーターを改善する。

パーキンソン病においては歩行機能低下が問題になる事からリハビリテーションのプログラムの一つとして歩行訓練は行われる。Mehrholz Jらはパーキンソン病患者に対するトレッドミルウォーキングの効果についてシステマティックレビューを用いて検証を行った。8論文が抽出され、歩行スピード(MD 0.50, 95% CI 0.17 to 0.84; p=0.003)、ストライド長 (MD 0.42, 95%CI 0.00-0.84; p=0.05)、歩行距離 (MD 358m, 95% CI 289 to 426; p<0.001)などの歩行パラメーターは有意に改善したが、ケイデンスに関しては有意な改善効果を認めなかった(MD 1.06, 95% CI -4.32 to 6.44; p=0.07)。ドロップアウトのrisk difference は－0.07 (95%CI -0.18 to 0.05, p=0.70)で、対照群と比較してドロップアウトの差はなかった。これらの結果からパーキンソン病患者に対するトレッドミル歩行介入は低下した歩行運動能力を改善するが、対象となるパーキンソン病の重症度、トレーニング期間や頻度、効果継続期間については不明である[4]。

脳梗塞後のリハビリテーションとしてウォーキングは効果を有する

脳梗塞後のリハビリテーションプログラムの一つとしてトレッドミルウォーキングや荷重補助トレッドミルウォーキングが行われている。Charalambous CCはこれらの有効性の確認のため、システマティックレビューを行った。この結果、歩行速度の有意な改善効果を認めた事を報告している[5]。

Peurala SHらは脳梗塞後のリハビリテーションプログラムにおけるウォーキングトレーニングの効果をメタアナライシスによって検証した。プラセボもしくは介入なしと比較してウォーキングトレーニングは有意に歩行スピード(p=0.03)、6分間歩行テストによる歩行距離の延長(p=0.004)を認めた。ウォーキングトレーニングとセラピストが行う他の一般的な理学療法との比較では亜急性期にはわずかな効果(p=0.21)があるのに対して、慢性期には強い効果(p<0.001)を示した。歩行距離については有意な差を認めなかった(亜急性期p=0.53、慢性期p=0.34)。ウォーキングトレーニングにおいてセラピストが支える程度の通常の

ウォーキングトレーニングとトレッドミルやelectric assistedなどの特別なウォーキングトレーニングプログラムの比較では、特別なウォーキングトレーニングプログラムの方が歩行スピードにおいて急性期（p<0.001）、亜急性期（p=0.04）に強い効果を、慢性期（p=0.45）は弱い効果を有していた[6]。

4．6．有害事象について

有害事象について記載された論文はほとんどなく、記載されたものの中でもウォーキングエクササイズと関係のない有害事象や、ドロップアウトの原因としてウォーキングエクササイズによる有害事象は報告されていない（表1）ことから安全に実施できるものと考えられる。

【考察】

介入プログラムについて

全体を通してウォーキングエクササイズの介入プログラム（強度や頻度、期間）を規定していないものが多かった。ウォーキングエクササイズの効果がない、あるいは弱い効果と結論したレビュー調査においては、これらの介入プログラムが規定されていないことを効果が低いことの理由の一つに挙げている。これに対して歩数計、ポールやトレッドミルなどを用いたウォーキングエクササイズでは、介入プログラムが規定されており、比較的有効性の高い結果を示している。これらのことから介入プログラムを規定して実施する事がエビデンス構築には必要な事であるが、手軽に実施できるというウォーキングエクササイズの利点との二律背反を解消する必要がある。

対照群の設定について

何もしていないものを対照群としてウォーキングエクササイズの効果を比較している場合にはウォーキングエクササイズの効果は強い。しかし筋力強化や複合エクササイズとウォーキングエクササイズとを比較している場合にはウォーキングエクササイズの効果は弱い傾向にある。後者の場合には筋力強化や複合エクササイズなどの強度の高いエクササイズとの比較においては、介入強度の弱いウォーキングエクササイズの効果が示されにくい可能性がある。これらのことから対照群をどのように設定するかで結果は変わる可能性があることから対照群の設定に気を配る必要がある。

最近の調査ではウォーキングエクササイズにその他の要素を加えた介入研究を行い、それぞれの要素を除いた際の改善効果をRCTにて検証する「マルチドメインエクササイズ」が行われており[26,27]、この手法がウォーキングエクササイズのエビデンス構築には有用と考えられる。

効果について

ウォーキングエクササイズの効果が認められるものとして、血圧などの心血管系や体重や脂質代謝マーカーなどの代謝系、筋骨格系疾患、パーキンソン病、脳梗塞後の歩行指標などが挙げられる。これに対して、健常な高齢者のパフォーマンスや中高齢者の骨密度など健康維持に関連したものについては、ウォーキングエクササイズの効果は少ない。この理由として以下の二点が考えられる。一点目としては有疾病者においては歩行能力そのものが低下しており、また心血管、代謝系疾患におけるデスクワーク従事者などのベースラインの活動量が少ない対象者においては、ウォーキングエクササイズそのものがかなり強い介入になる。それに対して既に高い活動性を維持している健常者にとってはウォーキングエクササイズの介入はあまり強いものではない。この活動性のベースラインの違いが、有効性において異なる結果を導いていると考えられる。

二点目としてはウォーキングエクササイズの質と介入強度の違いが挙げられる。有疾病者に対するリハビリテーションとしてウォーキングエクササイズを行う際には、トレッドミルやセラピストの指導により体系だったプログラムとして実施される。これに対して健常者を対象にした場合には、ポールウォーキングエクササイズやブリスクウォーキングエクササイズなど、ウォーキングの質に関しては指導しているものはあるが、それらを規定していないものが多く、ウォーキングエクササイズの質に違いが生じている可能性がある。また強度、頻度などを規定していない場合には、介入強度が十分でない事もある。

これらのことからウォーキングエクササイズの有効性を得るためには、対象者の活動性のベースラインを評価し、それに合わせた質と強度を考慮したウォーキングエクササイズプログラムを立案する必要があると考える。

【結論】

ウォーキングエクササイズは心血管機能向上、代謝機能向上、筋骨格系疾患や神経疾患などの有疾患者の歩行能力向上に対してはエビデンスの強い効果を示すが、高齢者のパフォーマンスや骨密度などの指標においては強い効果を示すことはなかった。対象者、対照群、アウトカムの設定などの検討が、ウォーキングエクササイズの効果を示すためには必要である。

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