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シンポジウム 運動器リハビリテーションと健康寿命

運動器不安定症の評価法*

北　潔† 新村秀幸† 葉梨之紀‡ 浦門　操§ 吉良貞伸¶

はじめに

超高齢社会が到来し，高齢者の抱える疾病，障害あるいは不安が大きな社会問題としてますますクローズアップされている．活力ある社会の存続のために，健康寿命を延伸することがわれわれ整形外科医にとっても大きな課題となっている．われわれ日本臨床整形外科学会は介護保険が導入された直後より，介護予防の対象者は骨・関節に慢性疾患を抱えた高齢者であることから介護予防を課題として取り上げ，整形外科診療所こそ主戦場であると考え調査を企画してきた．主な調査は整形外科通院患者を対象にした運動療法の介入調査と患者特性の調査である．本稿は調査開始時のアンケート調査，機能評価および転倒リスクの相互関係を解析するものである．

対象および方法

1. 研究プロジェクトの構成

われわれの行ってきた調査は3つのプロジェクトからなる．

I. 日本臨床整形外科学会が行った運動器不安定症に対する運動療法の介入調査(平成15-17年)
対象施設：日本臨床整形外科学会会員が所属する施設，男性79例，女性315例，平均年齢77.7±5.9歳

II. 平成17-18年度厚生労働科学研究費補助金(長寿科学総合研究事業)のもとで行った転倒リスクの調査
対象：明石市医師会主催の健康講座参加者，男性83例，女性99例(不明49例)，平均年齢70.8±8.0歳

III. 平成16-18年度厚生労働科学研究費補助金(循環器疾患等生活習慣病対策総合研究事業)で行った患者特性調査
対象施設：山口県，静岡県および兵庫県の整形外科診療所，女性147例，平均年齢75.9±6.5歳

2. 機能テスト(performance test)

1)開眼片脚起立時間：文部科学省が示す新体力テスト[1]に準じ測定を行った．

2)Timed up & go(TUG)：Podsiadlo ら[2]は肘掛椅子を用いているが，われわれは通常用いられている丸椅子を用いた．

3)踏み台昇降：健脚度(奥泉ら)[3]の1つの測定項目である40 cm踏み台昇降を10 cm刻みに40 cmまで行い，もっとも高く昇降できた高さを記録した．全く不能の場合は0 cmとし，手を体に触れて支えるように昇降した場合は不可とした．

3. アンケート調査

1) 聞き取り調査：要介護認定に用いられる障害高齢者および認知症高齢者の日常生活自立度，介護度，過去1年間の転倒回数とした．転倒の定義は，意図せずに，地面，床もしくはその他の低い平面に体が接触すること；家具・壁もしくはその他の構造物によりかかることは含まない．また，乗り物が走行中の転倒や暴力による転倒は除外した[4]．

2) 記述調査：自記式でEuro QOLを調査し，完答者のデータを解析した．

4. 統計処理

アンケート調査の調査項目間の解析にはχ^2検定を行

Key words: Performance test, Feasibility, Fall prevention, Step-climbing test, One-leg balance

*Assessment of musculoskeletal instability

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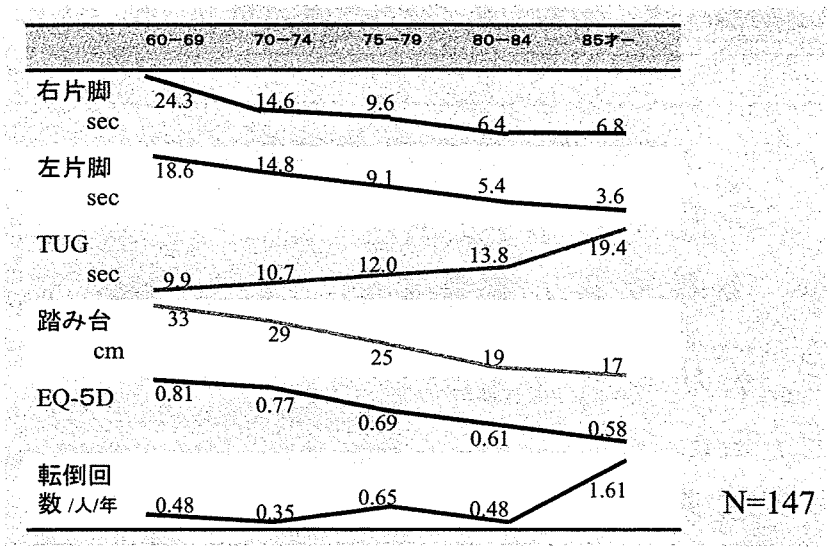

図1　年齢階層と各指標

った．相対リスクはクロス表を作成し，χ^2 検定を行い算出した．感度および特異度は2×2クロス表を作り算出した．平均値の差は等分散か否か検定後独立したt検定を行った．階層間の平均値の差の検定にはKruskal Wallis検定を行った．転倒率と機能テスト間の相関係数はPearsonの相関係数を用いた．階段昇降能力と踏み台昇降との相関はSpearmanの順位相関を用い，踏み台昇降の再現性の試験はKappa係数を用いた．転倒率は過去1年間の転倒回数÷人÷1年とした．

結　　果

1. 年齢階層別調査結果

地方健康増進の技術的支援の班会議(プロジェクトIII)で行った調査結果を図1に示す．片脚起立時間とEuro QOLは加齢とともに漸減している．TUGは加齢とともに漸増するが，80歳を過ぎると遅延傾向がはっきりしている．転倒回数は発生するイベント数が限られるため起伏を伴った図となっているが，80歳を過ぎると転倒は急増していることが分かる．数値は各階層の平均値を示す(図1)．

2. アンケート調査間の相関関係(プロジェクトIII)

各調査項目間の相関関係を χ^2 検定し，危険率5%以下のものを実線で示す(点線は $p=0.05$)．転倒は自立度，移動，普段の生活と痛みや不快と相関していた．また，Euro QOLのすべての項目間に相関を認めた．一方，痛みや不快と自立度の間には相関関係はなかった(図2)．

3. アンケート調査と転倒の有無(プロジェクトIII)

障害高齢者の日常生活自立度とEuro QOLの1つの項目である普段の生活を転倒経験の有無で2群に分け症例数を表1に示す．自立からJ1に外出能力が低下し，普段の生活にいくらか問題が生じると転倒経験の割合が著しく増加していることが分かる．これらのことから，障害が顕在化するにはかなりの潜伏期が存在するものと推測される(表1)．

4. アンケート調査と機能テスト(プロジェクトIII)

障害高齢者の日常生活自立度が自立と判定された高齢者の機能はかなり高いが，J1の高齢者では機能低下は著しく低下している．また，移動にいくらか問題が生じると，すでに機能は大きく低下していることが分かる．生活機能低下の観点からも障害が顕在化するまでにはかなりの潜伏期が存在するものと推測される(表2)．

5. 痛みや不快と調査結果(プロジェクトIII)

痛みが中程度と回答した高齢者の機能をみると，TUGと踏み台昇降で機能低下はなく，開眼片脚起立時間は低下しているものも，先に述べたADL(activities of daily living)にいくらか障害を生じた高齢者に比べ，平均約11秒と比較的バランス能力は保たれていた．すなわち，痛みを中程度自覚している高齢者の生活機能はまだ保たれており，疼痛管理が障害予防に直結する可能性を物語っている(図3)．

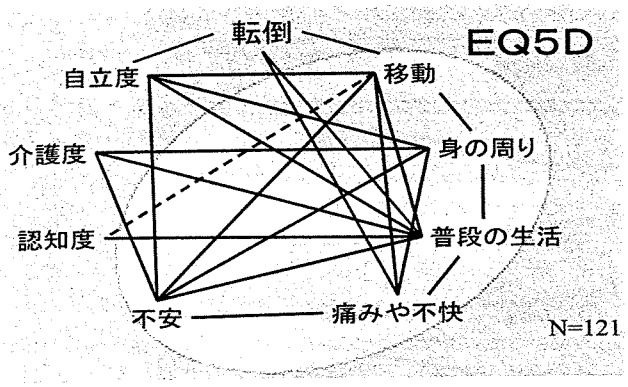

図2　調査項目と cross talk

表1　アンケート調査と転倒

N=121

	60-69才 自立	70-74才 自立	潜伏期	J1	J2
転倒群	7	7		17	12
非転倒群	26	23		18	11

普段の生活	問題なし	潜伏期	いくらか問題	できない
転倒群	10		21	3
非転倒群	47		19	2

表2　アンケート調査と Performance test

N=124	60-69才自立	70-74才自立	潜伏期	J1	J2
右片脚sec	15.7±14.0	16.8±13.3		5.7±4.9	2.7±3.5
左片脚sec	15.4±13.3	11.7±8.5		4.7±4.4	3.6±5.3
TUG sec	8.0±1.7	10.7±2.9		12.6±3.8	22.5±12.8
踏み台cm	36.5±6.3	29.2±10.4		19.3±11.6	10.6±11.2

移動 N=108	問題なし	潜伏期	いくらか問題	できない
右片脚 sec	21.7±16.1		7.0±9.8	—
左片脚 sec	20.6±14.4		6.1±7.7	—
TUG sec	8.5±2.0		14.4±8.8	—
踏み台 cm	33.9±9.5		20.8±12.5	—

6. 転倒回数と各機能テストの相関(プロジェクト III)

図4には転倒と各機能テストの Pearson の相関係数を示す．いずれも緩やかな相関を示した．

7. 機能テストの感受性と特異性(プロジェクト III)

片脚起立時間が左右いずれも15秒未満であるか，TUG が11秒以上かかるか，あるいは踏み台昇降が30 cm できないかでクロス表を作り，転倒に対する感受性および特異性を算出した．踏み台昇降は高齢者の女性を対象としたため，40 cm 踏み台は昇降できない高齢者が多く30 cm とした．感受性および特異性ともに踏み台昇降30 cm の値が高く，基準値としても適した値を示している(表3)．

8. 不安と調査項目(プロジェクト III)

Euro QOL では各項目は3段階(問題なし，いくらか問題あり，問題あり)で評価されるが，いくらか問題ありは問題ありに含め，問題なしと問題ありの2段階評価に組み換え，不安の有無との相対リスクを算出した．移動に問題が生じると，不安を抱えるリスクが24.9倍で，痛みや不快が生じると，不安を抱えるリスクが14.7倍に増加している．障害の発生や痛み・不快の発生が高齢者の不安に大きく影響を与えていることが分かる(図5)．

9. 介入前後の開眼片脚起立時間と転倒(プロジェクト I)

介入後8カ月後に追跡可能であった症例の開眼片脚起立時間と介入後の転倒との解析を行った．まず，開始時両側とも15秒未満であった361例の結果をみると，

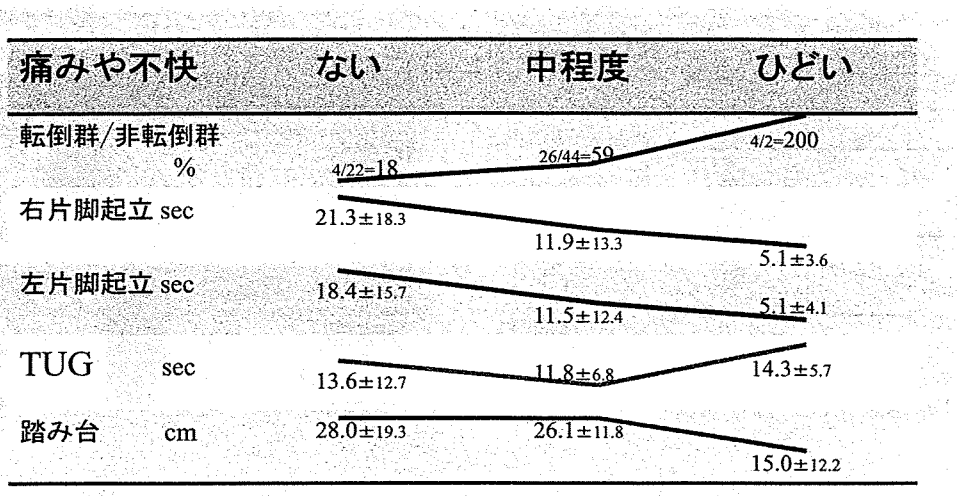

図 3　痛みと転倒と Performance test

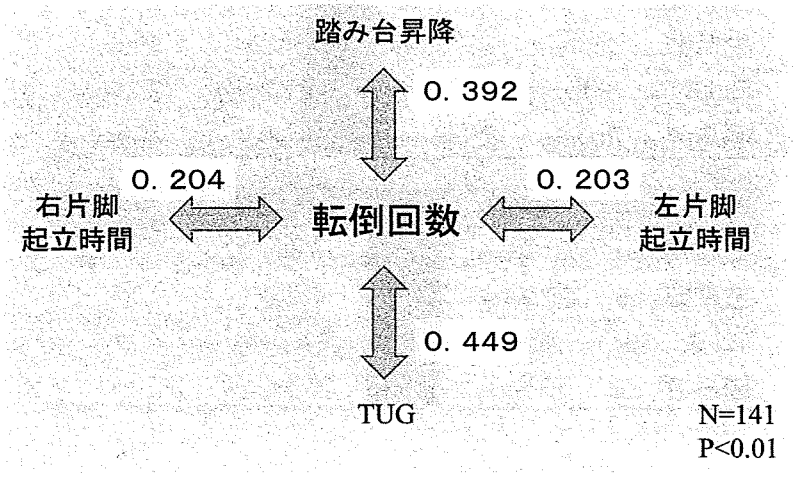

図 4　転倒と Performance test

表 3　転倒と Performance test

	感受性	特異性	
片脚起立が15秒未満	0. 91	0. 21	
30cm踏み台が登れない	0. 72	0. 69	P<0.01
TUGが11秒以上	0. 51	0. 59	
			N=141

介入後には約 3 分の 1 が介入後，左右いずれかが 15 秒以上に改善した．これと転倒回数を，介入後も両側とも 15 秒未満であった群と比較すると，有意に 50%転倒が減少することがわかった(図 6)．次に Tinneti がハイリスク患者の指標としてあげる開眼片脚起立時間 5 秒[5]を基準として，両側とも 5 秒未満，いずれか 5 秒以上，両側とも 5 秒以上の 3 群に分けると，開始時は各群均等な症例数であったが，介入後には両側とも 5 秒以上の症例が半数以上をしめた(表 4)．階層間の比較をみると，階層間に平均値の有意差があり，いずれかが 5 秒以上に改善した場合転倒は半減していることが分かる．

10. 階段昇降と踏み台昇降(プロジェクト II, III)

踏み台昇降が優れた指標であることから，階段昇降能力に注目した．しかし，踏み台昇降はテスト施行時に転倒するリスクがあることから，手軽で安全に行える階段昇降の聞き取り調査を企画した(N＝608)．調査

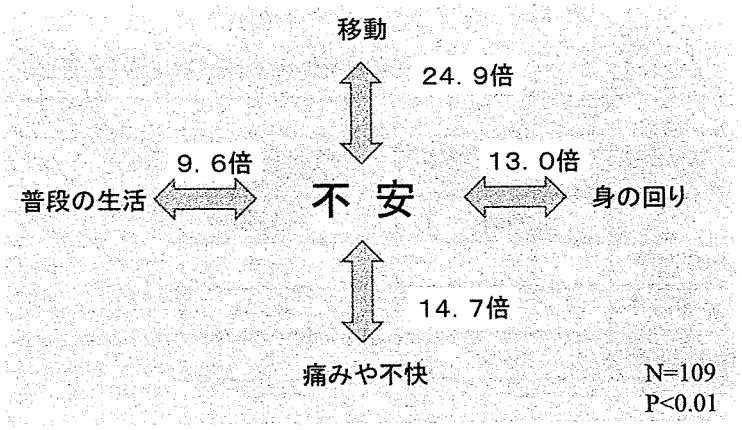

図 5　不安と相対リスク

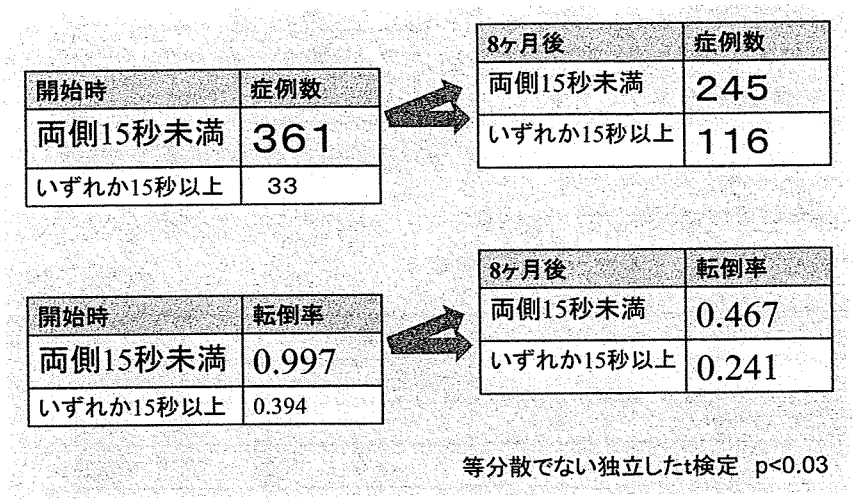

図 6　介入前後の開眼片脚起立時間と転倒

項目は生活機能低下を連続的に捕捉できるよう以下の10段階に細分した．1：小走りで階段昇降できる．2：駅の階段を不自由なく昇降できる．3：屋内の階段を不自由なく昇降できる．4：ゆっくりなら階段昇降できる．5：階段の上り下りは1段1段行っている．6：階段昇降は手すり，または，杖を用いている．7：階段昇降は手すりや杖をもって1段1段行っている．8：階段は昇れないが，低い段差や敷居などは支障がない．9：杖や手すりがあれば低い段差や敷居などもまたげる．10：バリアフリーなら杖や手すりを用い歩ける．この10項目と踏み台昇降の相関結果を表5に示す．Spearmanの順位相関係数は−0.73と強い相関を認めた．各項目の頻度と転倒率を基準に6項目に再編した．この再編した6項目と踏み台昇降，転倒回数とEuro 5Dの関係を図7に示す．いずれもKruskal Wallis検定で各階層間に有意差があり，指標として有用性があるといえた．

考　　察

高齢者の体力評価の課題は，生活機能低下のみならず，転倒リスクを視野に入れた評価方法の確立である．自己申告法は高齢者では精度が落ちる欠点がある．そこで客観的評価が可能なperformance testが臨床の場でも用いられるようになった．最近ではこのperformance testにおいても調査対象の特性を捉え，特性にあった簡便な方法を用いることが求められている(feasibility)[6]．

われわれの機能テストの年齢階層別の結果とGibbs[7]らのコホート調査の結果を図8に示す．

60-65歳の各指標の値を1として，加齢とともにいかに低下していくかをみている．開眼片脚起立時間は前期高齢者から早期に低下しているが，歩行速度は後期

表 4　5 秒できるか．Tinetti ME[5]

J Am Geriatr Soc 36:467-472,2006

	開始時
	症例数
両側5秒以上	118
いずれか	112
両側5秒未満	164

	8ヶ月後
	症例数
両側5秒以上	245
いずれか	74
両側5秒未満	75

	開始時
	転倒率
両側5秒以上	0.87
いずれか	0.68
両側5秒未満	1.18

	8ヶ月後
	転倒率
両側5秒以上	0.32
いずれか	0.30
両側5秒未満	0.65

Kruskal Wallis 検定　$p<0.05$

表 5

		踏台昇降					
		0cm	10cm	20cm	30cm	40cm	転倒率
アンケート	1				17	72	0.047
	2	1		4	32	73	0.228
	3			3	20	16	0.389
	4	1		13	30	21	0.220
	5	1	1	20	14	13	0.306
	6	2	9	31	36	16	0.560
	7	30	19	61	17	5	1.041
	8		4	1	1		1.167
	9	13	7				0.615
	10	4					1.500

Spearman順位相関係数	−0. 73
p値（両側）	<0. 001

高齢者で低下が著しいことが分かる．すなわち，前期高齢者の機能評価には開眼片脚起立時間が，後期高齢者には歩行速度が適していることが分かる．逆に床効果のため開眼片脚起立時間は後期高齢者の機能評価には不向きで，歩行速度は前期高齢者の機能評価には不向きである．一方，踏み台昇降は加齢とともに一様に低下し，前期高齢者から後期高齢者まで幅広く評価可能なことが分かる(図 8)．

踏み台昇降能力は転倒に対する感受性と特異性が高いだけでなく，加齢変化を経年的に捉えうる優れた指

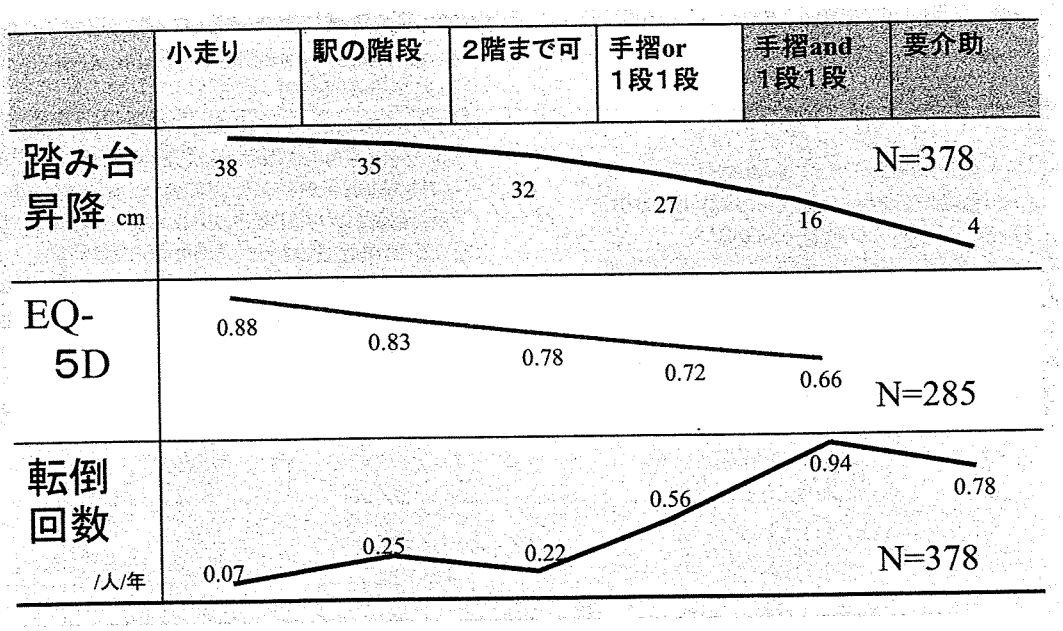

図 7 階段昇降能力と各指標

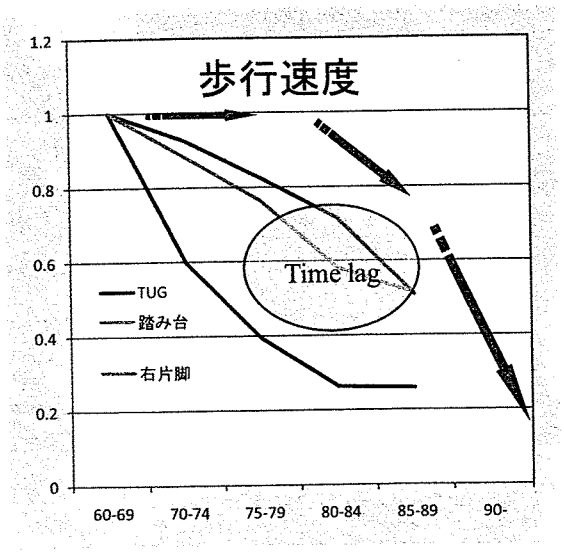

図 8 Performance test の経時的変化
Gibbs J et al.[7] J Am Geriatr Soc 1996; 44: 126-132

標であることがわかる．次に踏み台昇降能力は階段昇降能力に直結すると考え，われわれ日本臨床整形外科学会では階段昇降能力を詳しく聞き取ることにより高齢者の機能を評価できないかと想定し調査した．図 7 は階段昇降能力と踏み台昇降，Euro QOL と転倒回数の変化をみたものである．階段昇降能力の低下とともに，踏み台昇降能力と Euro QOL 値は著しい階級差を認めることなく漸減している．転倒は，手摺りを用いるようになるとリスクがかなり高まっていることが分かる．すなわち，階段昇降能力を詳細に聞き取ることにより，前期高齢者の機能的低下も早期から把握でき，転倒リスクの高い高齢者の聞き取り調査にも適していることが分かる (図 7)．

結　　語

1) これらの結果より，用途を踏まえた機能テストと調査項目の使い分け (feasibility) を考案した．早期診断には開眼片脚起立時間の測定と痛みの聞き取り調査が有効である．すでに広く用いられ他と比較しやすい (汎用性) Performance test は Timed up & go テストであり，階段昇降能力の聞き取り調査は，汎用性の高いアンケート調査として期待できる．信頼性の点ではそれぞれ踏み台昇降と Euro-5D が推奨できる．

2) 移動などの日常生活動作の障害と痛みや不快が，高齢者の不安に大きく関与していることが分かった．

3) 日本臨床整形外科学会で行った介入調査の結果，開始前開眼片脚起立時間が 5 秒未満の高齢者が左右いずれかの片脚起立時間が 5 秒以上に改善すると，あるいは，開始前開眼片脚起立時間が 15 秒未満の高齢者が左右いずれかの片脚起立時間が 15 秒以上に改善すると，転倒は半減することが分かった．

調査の機会を与えてくださった明石市医師会ならびに，長期間にわたり多くの課題の調査に参加してくださった日本臨床整形外科学会の先生方に深謝いたします．

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シンポジウム　変形性膝関節症のマネージメント　—最新の臨床エビデンスとエキスパートオピニオン—

変形性関節症の疫学研究の現状と問題点：ROAD (Research on Osteoarthritis Against Disability) 研究*

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はじめに

変形性関節症 (osteoarthritis, OA) は，全国民の自覚症状の上位を占め，多くの高齢者の健康寿命を短縮させている疾患であるにもかかわらず，国民はOAに対して良質かつ適切な医療の提供を受けていない．これはOA研究が国内外を通じて，他の生活習慣病はもとより，骨粗鬆症や関節リウマチなどの他の運動器疾患に比べても明らかに遅れているからである．その病因については，危険因子として力学的負荷の蓄積が指摘されている程度で，細胞・分子レベルのメカニズムに関してはほとんど解明されていない．したがって，その治療法が対症療法の域を出ていないのは当然の帰結である．重症度を客観的・定量的に評価する方法・指針がなく，診断基準も曖昧なままである．有病率・発症率などの基本的な疫学指標も確立されていない．したがって，もし画期的な予防・治療法が開発されたとしても，それをエビデンスとして評価する方法も基盤となるデータも存在しないのが現状である．OAに関する包括的・系統的な研究体制の確立は，いまや世界的に焦眉の課題と言える．

われわれは2005年に，OAの分子メカニズム解明から画期的な予防・治療法の開発を目指した戦略的OA統合研究計画ROAD (Research on Osteoarthritis Against Disability) を樹立した．ROAD研究の全体像は図1のとおりである．3つのサブテーマである「臨床情報とゲノム情報を網羅した大規模臨床データベースの構築」,「客観的・定量的な診断・評価基準の確立」,「分子生物学的検討による発症メカニズムの解明」を包括・融合して，OAの治療標的分子の同定と原因療法の確立を目指している．

大規模臨床データベースの構築

ROAD研究の第1の目的は，詳細な臨床情報とゲノム情報を網羅した世界に類を見ない規模のOA統合データベースを構築し，これを用いた観察疫学研究により疫学指標を確立し，ヒトゲノム疫学により遺伝・環境因子を探索することである．現在までに東京都板橋区 (都市部コホート)，和歌山県日高川町 (山村

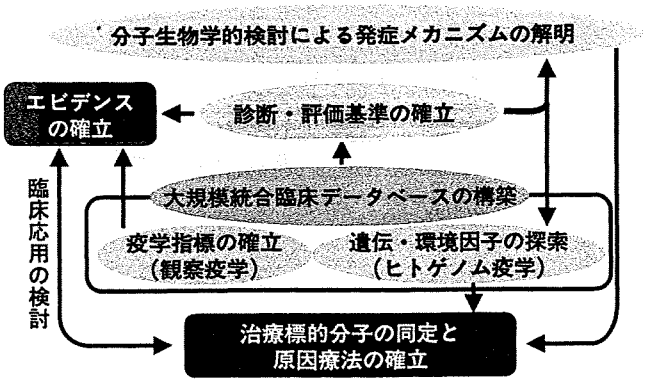

図1　ROAD研究の全体像

Key words: Osteoarthritis, Lumbar spondylosis, Epidemiology

*Update of epidemiologic study of osteoarthritis: the ROAD study

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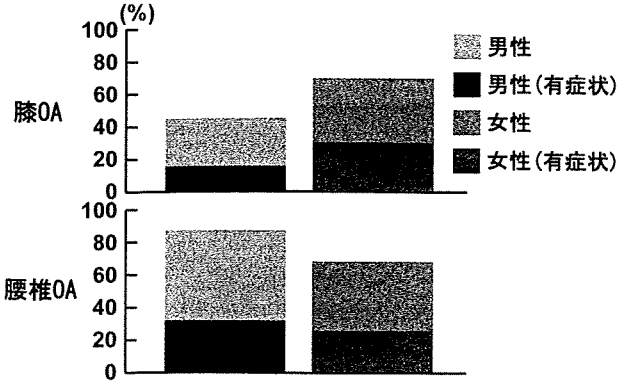

図2　OAの有病率(X線上 KL>=2 を基準)

部コホート)および和歌山県太地町(漁村部コホート)におけるベースライン調査を終了し，全3040例のうち50歳以上の2843例(男性1001例，女性1842例：平均年齢72.3歳)について解析を行った．それによると，変形性膝関節症(膝OA)の有病率は男性44.6%，女性66.0%，変形性腰椎症(腰椎OA)の有病率は男性82.6%，女性67.4%であった(図2)．ただし，これはX線上のKellgren Lawrence(KL)グレード2以上を基準としたものであり，この中で症状(主に膝痛と腰痛)のある者は1/3程度であった．ここから本邦のOA患者数を推定すると，膝OAの潜在患者数は2400万人，有症患者数は820万人，腰椎OAでは潜在患者数3500万人，有症患者数は1020万人であった．以上より，X線上のOAについて言えば従来の試算よりもはるかに多いものの，必ずしも症状を伴うわけではないことが示された．そこでKLグレードの重症度と症状の有無との相関を見ると，膝OAでは有意な正相関が見られるが，腰椎OAでは非常に弱かった．膝OAにおいてもKLグレード2以上の膝痛のオッズ比は低く，KLグレード3以上で明らかな危険因子となることがわかり，従来のKL2以上というOAの診断基準に疑問を投げかける結果となった[1),2)]．

次に山村，漁村コホートの50歳以上の住民1471人を対象に職業動作の関与を検討したところ，しゃがみ込む仕事，坂道を上り下りする仕事，重量物を持つ仕事などの膝に負荷の強い仕事は関節裂隙の狭小化(KL3以上)の危険因子であり，立ち仕事，歩く仕事などの比較的膝に負荷の少ない仕事が骨棘形成(KL2以上)の危険因子であることがわかり，変形性関節症のこの代表的な2つの病態に異なる背景が存在することが示唆された[3)]．

この大規模データベースを確立することによって初

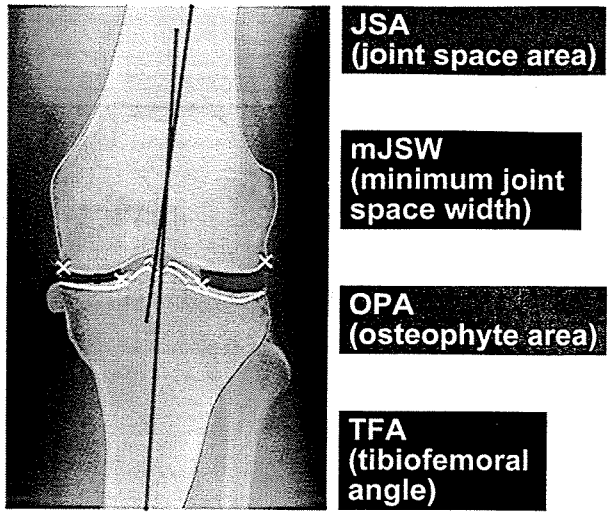

図3　KOACADパラメータ

めて，大きな検出力を要求される正確なゲノムワイド関連解析が可能となった．ROAD研究のヒトゲノム疫学解析は，候補遺伝子に限定して疾患の有無だけによる2群間比較のみを行ってきた従来の解析とは明らかに一線を画するものである．現在，この統合データベースを用いて，臨床情報によって詳細に層別化した各群における感受性遺伝子の探索，また逆にゲノム情報によって層別化した各群における環境因子の探索を行っている．

客観的・定量的な診断・評価基準の確立

上記のように，KL分類によるカテゴリカル分類では境界域での判定が主観的かつ曖昧になり，正確な診断基準・治療評価基準とはなりえない．ROADプロジェクトでは医用工学的手法を駆使して，膝OAのX線画像上の複数の重症度指標を自動的に計測できるコンピュータ支援診断システムKOACAD(knee OA computer assisted diagnosis)を開発し，その良好な精度を確認した[4)]．これは立位膝関節単純X線画像をデジタルフィルタによるノイズ除去，輪郭線の抽出，情報の統計処理による基準点標準化を経て，内・外側の関節裂隙の最小距離(mJSW)および面積(JSA)，内側の骨棘面積(OPA)および大腿脛骨角(FTA)を，自動的に瞬時に計測する画像解析ソフトである(図3)．ROADデータベースをKOACADで解析したところ，男女ともに内側関節裂隙の狭小化が膝痛と最も強い相関を示し，骨棘面積は有意な相関を示さなかった．近い将来に製品化される予定であり，骨粗鬆症における骨密度測定のように，膝OAの客観的な診断基準の確

立，および治療の正確な評価法として新薬の開発にも寄与することが期待される．

分子生物学的検討による発症メカニズムの解明

まず，遺伝子操作が汎用されるマウスにおいて膝OAの疾患モデルを作成したところ，力学的負荷によって関節軟骨においてX型コラーゲン(COL10)陽性の病的肥大軟骨細胞の出現と軟骨基質の分解が起こることを見出した[5]．さらに，軟骨細胞肥大分化因子Runx2によって永久軟骨であるはずの関節軟骨表層の軟骨細胞の肥大化が誘導されることがOA発症の引き金となることが示された[6]．また，carminerinはOA負荷や老化などの病的条件下における石灰化に重要であることが示された[7]．一方，オステオプロテジェリンはそのアポトーシス抑制作用を介してOAの発症を予防することが示された[8]．軟骨細胞の肥大分化もアポトーシスも，成長板軟骨の軟骨内骨化の過程で見られる現象である．永久軟骨であるはずの関節軟骨においても，過度のメカニカルストレスの蓄積に抗しきれなくなって軟骨内骨化をするために細胞の肥大分化・アポトーシスが起こるものと推察される．滑膜や靱帯に接して血管の侵入が可能な関節辺縁では軟骨内骨化が起こって力学的要請に応じた骨棘ができるが，関節の内部では血管侵入ができないために骨化することなく軟骨の破壊だけで終わってしまうと考えられる(図4)[9,10]．

一方，従来からそのOAへの関与が指摘されてきた炎症関連分子(PGES-1，TNF-αおよびIL-1)に関しては，どの欠損マウスにおいてもOAの発症・進行が抑制されておらず，炎症性因子はOAの原因分子としての可能性は低いと考えられた[11]．さらに，膝OA患者の関節液中の炎症性サイトカイン濃度を測定したところ，TNF-α，IL-1，IL-6ともに外傷患者と差がなかった[12]．この，炎症シグナルよりも，病的な軟骨内骨化シグナルがOA発症に重要であるという仮説は，ROAD研究が最初に提唱したものであるが，最近ではこれを裏付ける知見が国内外から続々と出ている．

おわりに

最近，世界的に骨軟骨研究のターゲットが骨粗鬆症や関節リウマチからOAにシフトしてきている．近い将来に，上記の軟骨内骨化シグナルのような標的分子の同定，さらにはMRIなどの診断法・評価法の確立によって，画期的なOAの予防法，治療法が開発されることが期待される．ROAD研究もさらに発展させて，多くの新知見を世界に発信し続けたいと考えている．

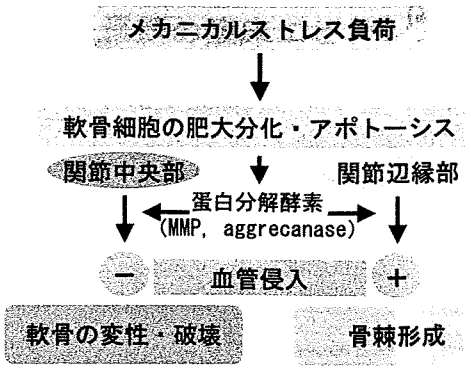

図4　軟骨内骨化を介するOA発症のメカニズム

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ORIGINAL ARTICLE

Association of Occupational Activity With Radiographic Knee Osteoarthritis and Lumbar Spondylosis in Elderly Patients of Population-Based Cohorts: A Large-Scale Population-Based Study

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Objective. To investigate the risk of radiographic knee osteoarthritis (OA) and lumbar spondylosis associated with occupational activity in elderly Japanese subjects using the large-scale population-based cohort of the Research on Osteoarthritis Against Disability (ROAD) study.

Methods. From the baseline survey of the ROAD study, 1,471 participants age ≥50 years (531 men and 940 women) living in mountainous and seacoast communities were analyzed. Information collected included a lifetime occupational history and details of specific work place physical activities. Radiographic severity at the knee and lumbar spine was determined by the Kellgren/Lawrence (K/L) grading system.

Results. The prevalence of K/L grade ≥2 knee OA and lumbar spondylosis among agricultural, forestry, and fishery workers was significantly higher than among clerical workers and technical experts in the overall population. For occupational activities, sitting on a chair had a significant inverse association with K/L grade ≥2 knee OA and lumbar spondylosis. Standing, walking, climbing, and heavy lifting were associated with K/L grade ≥2 knee OA, but were not associated with K/L grade ≥2 lumbar spondylosis. Kneeling and squatting were associated with K/L grade ≥3 knee OA.

Conclusion. This cross-sectional study using a population-based cohort suggests that sitting on a chair is a significant protective factor against both radiographic knee OA and lumbar spondylosis in Japanese subjects. An occupational activity that includes heavy lifting appears to have a greater effect on knee OA than on lumbar spondylosis.

INTRODUCTION

Osteoarthritis (OA) and spondylosis, which cause cartilage and disc degeneration and osteophyte formation at joints in the extremities and spine, are major public health issues causing chronic disability in the elderly in developed countries (1–6). Despite the urgent need for strategies to prevent and treat these conditions, epidemiologic data on OA and spondylosis are sparse. Established risk factors for knee OA in whites include older age, female sex, evidence of OA in other joints, obesity, and previous injury or surgery of the knee (7–12). Evidence is accumulating in whites that the disease is more common in people who have performed heavy physical work (13–18), particularly in those whose jobs have involved kneeling or squatting (19–24). However, published work has tended to concentrate on the knee, and few studies have focused on risk

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factors for lumbar spondylosis associated with occupational activity (25–28). In addition, there have been no large-scale population-based epidemiologic studies that have simultaneously evaluated the risk of both knee OA and lumbar spondylosis associated with occupational activity in the same population. Furthermore, most epidemiologic studies of OA and spondylosis associated with occupation are limited in terms of the quality of the information collected about occupational exposure. Occupational histories are not always complete, and exposure has often only been inferred from the subject's job title (13–18). To provide accurate data on the relationship of occupational activities with knee OA and lumbar spondylosis, collected information has to include a lifetime occupational history and details of specific work place physical activities.

With the goal of establishing epidemiologic indexes to evaluate clinical evidence for the development of disease-modifying treatment, we set up a large-scale nationwide OA cohort study called the Research on Osteoarthritis Against Disability (ROAD) study in 2005. In the present study, we used the data of participants living in mountainous and seacoast communities to investigate the association of job title and occupational activity with radiographic knee OA and lumbar spondylosis.

PARTICIPANTS AND METHODS

Participants. The ROAD study is a nationwide prospective study for bone and joint diseases consisting of population-based cohorts established in several communities in Japan. Because the Miyama cohort has been profiled in detail elsewhere (29), the characteristics of the participants are briefly summarized here. To date, we have created a baseline database including clinical and genetic information on 3,040 inhabitants (1,061 men and 1,979 women) ages 23–95 years (mean 70.6 years) who were recruited from listings of resident registrations in 3 communities. All participants provided written informed consent, and the study was conducted with the approval of ethical committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. Information collected about job title and occupational activity included a lifetime occupational history with details of 7 types of specific work place physical activities, including sitting on a chair, kneeling, squatting, standing, walking, climbing, and heavy lifting. Participants were asked whether they engaged in the following activities: sitting on a chair for ≥2 hours/day, kneeling for ≥1 hour/day, squatting for ≥1 hour/day, standing for ≥2 hours/day, walking ≥3 km/day, climbing up slopes or steps for ≥1 hour/day, and lifting loads weighing ≥10 kg at least once a week. Information on these activities was obtained for the principal job, defined as the job at which the participant had worked the longest. Anthropometric measurements included height, weight, bilateral grip strength, and body mass index (BMI; weight [kg]/height [m^2]). All participants were interviewed regarding knee pain and low back pain by asking them, "In the past 1 month, have you had knee pain on most days lasting?" and "In the past 1 month, have you had low back pain on most days lasting?" Participants who answered yes were defined as having knee pain or low back pain, respectively. From the baseline data of all participants, the present study analyzed 1,471 participants (531 men and 940 women) age ≥50 years living in mountainous and seacoast cohorts.

Radiographic assessment. All participants had a radiographic examination of both knees using anteroposterior and lateral views with weight-bearing and foot map positioning, and an examination of the lumbar spine, including intervertebral levels from L1–L2 to L5–S1 with anteroposterior and lateral views. Knee and lumbar spine radiographs were read without knowledge of participant clinical status by a single well-experienced orthopedist (SM) using the Kellgren/Lawrence (K/L) radiographic atlas, and the severity was determined by K/L grading (30). We defined knee OA and lumbar spondylosis as a K/L grade ≥2 in at least one knee and in one intervertebral level, respectively.

To evaluate the intraobserver variability of K/L grading, 100 randomly selected radiographs of the knee and the lumbar spine were scored by the same observer more than 1 month after the first reading. One hundred other radiographs were also scored by 2 experienced orthopedic surgeons (SM, HO) using the same atlas for interobserver variability. The evaluated intra- and intervariability were confirmed by the kappa analysis to be sufficient for assessment (0.86 and 0.80 for knee OA, 0.84 and 0.76 for lumbar spondylosis, respectively).

Statistical analysis. The differences of age and BMI between men and women were examined by the unpaired *t*-test. To compare the prevalence of radiographic knee OA and lumbar spondylosis between men and women, we performed a logistic regression analysis after adjustment for age and BMI. The percentage of each occupational activity was compared between men and women by a chi-square test. To determine risk factors for knee OA and lumbar spondylosis with K/L grades ≥2 as well as K/L grades ≥3, logistic regression analyses were used to estimate the odds ratio (OR) and the associated 95% confidence interval (95% CI) for variables such as job title and occupational activities after adjustment for age and BMI compared with K/L = 0 or 1 (for K/L grades ≥2) and K/L = 0, 1, or 2 (for K/L grades ≥3). Furthermore, the overall population was classified into 4 subpopulation groups based on the presence or absence of knee OA and lumbar spondylosis, and a multinomial logistic regression analysis was performed to determine factors associated with knee OA, lumbar spondylosis, and their combination after adjustment for age, sex, and BMI. The subpopulation with neither knee OA nor lumbar spondylosis was used as a reference group. Data analyses were performed using SAS, version 9.0 (SAS Institute, Cary, NC).

RESULTS

Characteristics of the 1,471 participants age ≥50 years in the 2 cohorts of the ROAD study are shown in Table 1. The

Table 1. Characteristics of participants*

	Overall	Men	Women
No. of subjects	1,471	531	940
Age, years	68.4 ± 9.2	69.1 ± 9.1	68.0 ± 9.2†
Height, cm	154.3 ± 9.3	162.3 ± 7.1	149.8 ± 7.2
Weight, kg	55.2 ± 10.5	61.0 ± 10.3	51.8 ± 9.1
BMI, kg/m^2	23.1 ± 3.3	23.1 ± 3.1	23.1 ± 3.5
Grip strength, kg	26.7 ± 9.3	34.7 ± 8.4	22.1 ± 6.1
K/L ≥2 knee OA, %	55.6	45.6	61.2‡
K/L ≥3 knee OA, %	23.0	16.8	26.5‡
K/L ≥2 lumbar spondylosis, %	65.3	79.1	57.6‡
K/L ≥3 lumbar spondylosis, %	38.7	38.8	38.7
Current smoker, no. (%)	169 (11.5)	140 (26.4)	29 (3.1)§
Current alcohol drinking, no. (%)	562 (38.2)	343 (64.6)	219 (23.3)§

* Values are the mean ± SD unless otherwise indicated. BMI = body mass index; K/L = Kellgren/Lawrence grading system; OA = osteoarthritis.
† $P < 0.05$ versus men by unpaired *t*-test.
‡ $P < 0.05$ versus men by logistic regression analysis after adjustment for age and BMI.
§ $P < 0.05$ versus men by chi-square test.

prevalence of K/L grade ≥2 and K/L grade ≥3 knee OA was significantly higher in women than in men, whereas that of K/L grade ≥2 lumbar spondylosis was significantly lower in women than in men. The prevalence of K/L grade ≥3 lumbar spondylosis was comparable between sexes.

There was great diversity in the job titles of the study participants (Table 2). Although a substantial proportion includes clerical workers and technical experts, there were many agricultural, forestry, and fishery workers. Among various occupational activities, agricultural, forestry, and fishery workers had the highest rates of kneeling, squatting, standing, walking, climbing, and lifting weights and the lowest rates of sitting on a chair, whereas clerical workers and technical experts had the lowest rates of kneeling, squatting, standing, walking, climbing, and lifting weights and the highest rates of sitting on a chair (Figure 1).

To determine factors associated with K/L grade ≥2 knee OA and lumbar spondylosis, we performed a logistic regression analysis to estimate ORs and 95% CIs (Tables 3 and 4). Analysis of job titles revealed that agricultural, forestry, and fishery workers had a significantly higher risk of knee OA and lumbar spondylosis compared with clerical workers and technical experts in the overall population. We then examined the association of occupational activities with knee OA and lumbar spondylosis (Tables 3 and 4). Sitting on a chair for ≥2 hours/day was a significant protective factor for knee OA and lumbar spondylosis

Table 2. Participants with job title and occupational activity reported as the principal job

	Overall	Men	Women
Job titles, no. (%)			
Clerical workers/technical experts	363 (24.7)	170 (32.0)	193 (20.5)
Agricultural/forestry/fishery workers	318 (21.6)	164 (30.9)	154 (16.4)
Factory/construction workers	153 (10.4)	68 (12.8)	85 (9.0)
Shop assistants/managers	132 (9.0)	25 (4.7)	107 (11.4)
Housekeepers	126 (8.6)	0 (0.0)	126 (13.4)
Teachers	82 (5.6)	42 (7.9)	40 (4.3)
Dressmakers	51 (3.5)	1 (0.2)	50 (5.3)
Clinical workers	41 (2.8)	1 (0.2)	40 (4.3)
Hairdressers	17 (1.2)	6 (1.3)	11 (1.2)
Others (cooks, taxi drivers, etc.)	72 (4.9)	22 (4.1)	50 (5.3)
No answer	116 (7.9)	32 (6.0)	84 (8.9)
Occupational activities, no. (%)			
Sitting on a chair ≥2 hours/day	657 (44.7)	254 (47.8)	403 (42.8)
Kneeling ≥1 hour/day	292 (19.9)	96 (18.1)	196 (20.9)
Squatting ≥1 hour/day	386 (26.2)	131 (24.7)	255 (27.1)
Standing ≥2 hours/day	1,235 (84.0)	456 (85.9)	779 (82.9)
Walking ≥3 km/day	673 (45.8)	268 (50.5)	405 (43.1)
Climbing ≥1 hour/day	346 (23.5)	185 (34.8)	161 (17.1)*
Lifting weights ≥10 kg at least once a week	788 (53.6)	347 (65.3)	441 (46.9)*

* $P < 0.05$ versus men by chi-square test.

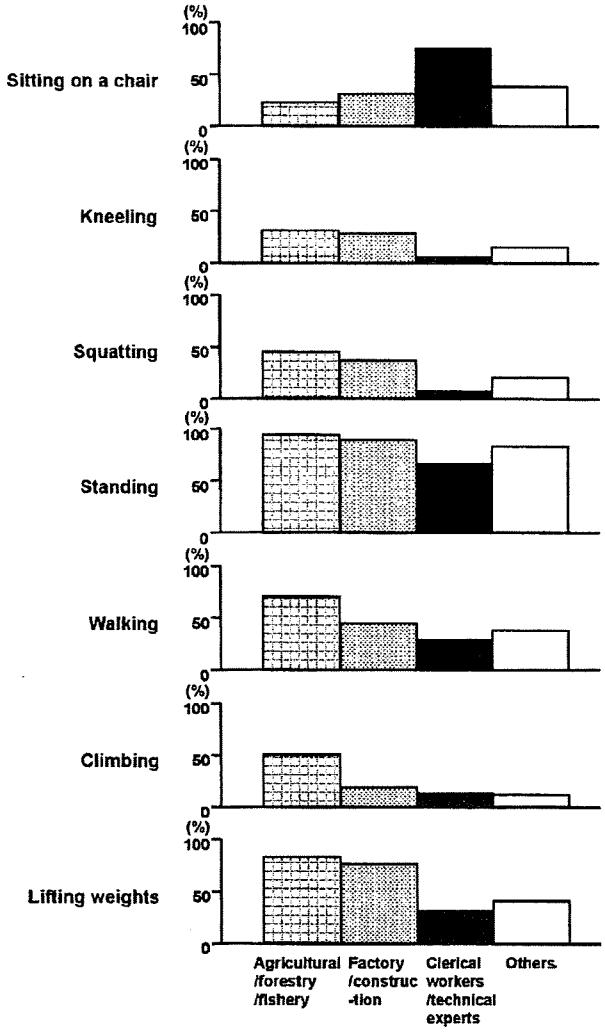

Figure 1. Percentages of participants engaged in each occupational activity: sitting on a chair ≥2 hours/day, kneeling ≥1 hour/day, squatting ≥1 hour/day, standing ≥2 hours/day, walking ≥3 km/day, climbing ≥1 hour/day, or lifting weights ≥10 kg at least once a week among agricultural, forestry, and fishery workers; factory and construction workers; clerical workers and technical experts; and others.

in the overall population and in men. Neither kneeling for ≥1 hour/day nor squatting for ≥1 hour/day was associated with knee OA in the overall population. Standing for ≥2 hours/day, walking ≥3 km/day, climbing for ≥1 hour/day, and lifting weights ≥10 kg at least once a week were significantly associated with knee OA in the overall population and in both sexes (Table 3). A multiple logistic regression analysis after adjustment for age, BMI, sex, and the above 4 occupational activities showed that climbing and lifting weights were significantly associated with knee OA overall (OR 1.65, 95% CI 1.18–2.32 and OR 1.51, 95% CI 1.16–1.95, respectively) and in men (OR 1.75, 95% CI 1.10–2.80 and OR 1.76, 95% CI 1.14–2.73, respectively), suggesting that among the 4 activities that required a standing position, climbing and lifting weights had an independent association with knee OA. In contrast, these occupational activities had no significant association with lumbar spondylosis except for lifting weights in women (Table 4).

We next performed a multinomial logistic regression analysis to determine factors associated with K/L grade ≥2 knee OA, lumbar spondylosis, and their combination after adjustment for age, sex, and BMI. Sitting on a chair was confirmed to be a significant protective factor for the presence of both knee OA and lumbar spondylosis (OR 0.62, 95% CI 0.45–0.86). Although neither kneeling nor squatting was associated with the presence of knee OA or lumbar spondylosis, standing (OR 2.03, 95% CI 1.32–3.12), walking (OR 1.56, 95% CI 1.12–2.17), climbing (OR 2.14, 95% CI 1.38–3.40), and lifting weights (OR 2.05, 95% CI 1.48–2.86) were associated with the presence of both knee OA and lumbar spondylosis. For the subpopulation group with knee OA and without lumbar spondylosis, standing (OR 1.69, 95% CI 1.04–2.79), climbing (OR 2.34, 95% CI 1.39–3.97), and lifting weights (OR 1.92, 95% CI 1.31–2.81) were also significantly associated, although there were no significant associations of the subpopulation group with lumbar spondylosis and without knee OA compared with the subpopulation group without knee OA or lumbar spondylosis.

We further analyzed the association of K/L grade ≥2 knee OA and lumbar spondylosis with job titles and occupational activities according to the presence of knee pain and low back pain at the baseline examination (Supplementary Tables A and B, available in the online version of this article at http://www3.interscience.wiley.com/journal/77005015/home). Although some of the job titles and occupational activities showed higher ORs in the subpopulation with knee pain, the direction of association was similar regardless of the presence of pain, and the results did not differ between the overall population and the subpopulation without knee pain or low back pain.

We next determined factors associated with K/L grade ≥3 knee OA and lumbar spondylosis using logistic regression analysis after adjustment for age and BMI. Analysis of occupational activities revealed that sitting on a chair was a significant protective factor for lumbar spondylosis in men (OR 0.58, 95% CI 0.40–0.84). In the overall population and in women, kneeling (OR 1.40, 95% CI 1.01–1.93 and OR 1.69, 95% CI 1.16–2.47, respectively), squatting (OR 1.34, 95% CI 1.00–1.80 and OR 1.51, 95% CI 1.06–2.15, respectively), and lifting weights (OR 1.60, 95% CI 1.21–3.12 and OR 1.73, 95% CI 1.25–2.43, respectively) were associated with knee OA. A multinomial logistic regression analysis also showed that sitting on a chair was a protective factor for the presence of both K/L grade ≥3 knee OA and lumbar spondylosis, as well as for the presence of lumbar spondylosis and the absence of knee OA in men (OR 0.46, 95% CI 0.23–0.87 and OR 0.63, 95% CI 0.42–0.94, respectively). Lifting weights (OR 1.57, 95% CI 1.10–2.23) was associated with the presence of both knee OA and lumbar spondylosis. For the subpopulation group with knee OA and without lumbar spondylosis, kneeling (OR 1.76, 95% CI 1.13–2.72), squatting (OR 1.85, 95% CI 1.23–2.77), and lifting weights (OR 1.77, 95% CI 1.19–2.65) were significantly associated, although there were no

Table 3. Association of K/L grade ≥2 knee OA with job title and occupational activity*

	Overall, OR (95% CI)	Men, OR (95% CI)	Women, OR (95% CI)
Job titles (vs. clerical workers/technical experts)			
Agricultural/forestry/fishery workers	1.69 (1.19–2.41)	1.58 (0.98–2.56)	1.90 (1.14–3.20)
Factory/construction workers	1.52 (0.99–2.36)	1.33 (0.72–2.47)	1.64 (0.90–3.06)
Other†	1.18 (0.88–1.60)	1.21 (0.73–2.00)	1.20 (0.82–1.76)
Occupational activities			
Sitting on a chair ≥2 hours/day	0.73 (0.57–0.92)	0.63 (0.44–0.92)	0.80 (0.60–1.09)
Kneeling ≥1 hour/day	1.11 (0.83–1.48)	0.79 (0.49–1.26)	1.36 (0.93–1.97)
Squatting ≥1 hour/day	1.23 (0.94–1.61)	0.89 (0.58–1.35)	1.50 (1.06–2.13)
Standing ≥2 hours/day	1.97 (1.43–2.72)	2.31 (1.32–4.17)	1.78 (1.21–2.63)
Walking ≥3 km/day	1.80 (1.42–2.29)	2.17 (1.49–3.16)	1.59 (1.17–2.16)
Climbing ≥1 hour/day	2.24 (1.65–3.04)	2.43 (1.64–3.60)	1.85 (1.19–2.96)
Lifting weights ≥10 kg at least once a week	1.90 (1.50–2.42)	2.26 (1.52–3.40)	1.68 (1.24–2.26)

* ORs were calculated by a logistic regression analysis after adjustment for age, sex, and BMI in the overall population, and for age and BMI in both sexes. K/L = Kellgren/Lawrence grading system; OA = osteoarthritis; OR = odds ratio; 95% CI = 95% confidence interval; BMI = body mass index.
† Includes all participants except for agricultural/forestry/fishery workers, factory/construction workers, and clerical workers/technical experts.

significant associations of the subpopulation group with lumbar spondylosis and without knee OA compared with the subpopulation group without knee OA or lumbar spondylosis.

DISCUSSION

Using baseline data from the ROAD study, the present investigation evaluated the risk of occupational activity for radiographic knee OA and lumbar spondylosis, and revealed that sitting on a chair was a significant protective factor for both radiographic knee OA and lumbar spondylosis in Japanese subjects. For other occupational activities, kneeling, squatting, standing, walking, climbing, and heavy lifting were significantly associated with radiographic knee OA, whereas there was no significant occupational activity for radiographic lumbar spondylosis in the overall population. To our knowledge, this is the first epidemiologic study using a large-scale population-based cohort to determine the risk of occupational activity for both knee OA and lumbar spondylosis simultaneously in the same population. Information on occupational activities was collected by direct inquiry rather than being inferred from the job title.

In the present study, agricultural, forestry, and fishery workers had a significantly higher prevalence of both radiographic knee OA and lumbar spondylosis compared with clerical workers and technical experts in the overall population. These jobs have historically been among the first to be identified in relation to knee OA in whites (31,32), which is also compatible with our data in this Japanese population. As other authors have hypothesized, the combination of intense exposure to heavy labor of varied nature and repeated local stresses, especially at a young age, could contribute to some systemic mechanism in the development of OA (33). This argument would support the implementation of preventive measures as a priority to reduce the intensity of physical labor in this sector, particularly for young male and female farm workers.

For occupational activities, standing, walking, climbing, and heavy lifting were associated with K/L grade ≥2 knee OA in the overall population, whereas kneeling and squat-

Table 4. Association of K/L grade ≥2 lumber spondylosis with job title and occupational activity*

	Overall, OR (95% CI)	Men, OR (95% CI)	Women, OR (95% CI)
Job titles (vs. clerical workers/technical experts)			
Agricultural/forestry/fishery workers	1.46 (1.02–2.11)	1.49 (0.83–2.68)	1.42 (0.89–2.28)
Factory/construction workers	1.05 (0.68–1.55)	1.52 (0.76–3.22)	0.84 (0.49–1.44)
Other†	1.22 (0.91–1.64)	1.53 (0.87–2.76)	1.11 (0.78–1.58)
Occupational activities			
Sitting on a chair ≥2 hours/day	0.78 (0.62–0.99)	0.48 (0.30–0.76)	0.93 (0.71–1.23)
Kneeling ≥1 hour/day	0.96 (0.72–1.28)	0.95 (0.55–1.70)	0.97 (0.70–1.35)
Squatting ≥1 hour/day	1.05 (0.81–1.38)	0.95 (0.58–1.61)	1.09 (0.80–1.48)
Standing ≥2 hours/day	1.11 (0.81–1.50)	1.14 (0.61–2.04)	1.10 (0.77–1.57)
Walking ≥3 km/day	1.00 (0.79–1.26)	0.89 (0.57–1.40)	1.04 (0.79–1.37)
Climbing ≥1 hour/day	1.02 (0.76–1.38)	1.09 (0.68–1.78)	0.98 (0.67–1.44)
Lifting weights ≥10 kg at least once a week	1.15 (0.91–1.45)	1.09 (0.69–1.72)	1.23 (1.01–1.55)

* ORs were calculated by a logistic regression analysis after adjustment for age, sex, and BMI in the overall population, and for age and BMI in both sexes. See Table 3 for definitions.
† Includes all participants except for agricultural/forestry/fishery workers, factory/construction workers, and clerical workers/technical experts.

Table 5. Comparison of characteristics of epidemiologic studies

Author, ref.	Ethnicity/country	Age, years	Total no.	Men:women
Muraki et al, current study	Japan	≥50	1,471	531:940
Yoshimura et al, 34	Japan	≥45	202	0:202
Lau et al, 35	Chinese		1,316	332:984
Anderson and Felson, 19	Blacks and whites/US	55–64	1,250	606:644
Felson et al, 20	Whites/US	≥63	1,376	569:807
Cooper et al, 21	UK	≥55	327	90:237
Coggon et al, 22	UK	≥47	1,036	410:626
Sandmark et al, 23	Sweden	≥55	1,173	589:584
Manninen et al, 24	Finland	≥55	805	195:610

ting were not, which was similar to previous studies in Japan and China (34,35). Comparison of characteristics and ORs for knee OA associated with occupational activity among epidemiologic studies is shown in Tables 5 and 6. The present study showed different results from other previously published studies (Table 6). Because each study defined knee OA and cases somewhat differently (in some studies, a case was defined as a subject with K/L grade ≥3 OA with knee pain, while it was defined as a subject with K/L grade ≥2 or K/L grade ≥3 OA in the present study), our results are not directly comparable with those of other studies. Even so, studies of whites have suggested that occupational activities of kneeling and squatting and job titles that required kneeling and squatting were associated with knee OA (19–24), whereas these activities were not associated with K/L grade ≥2 OA in this study. The discrepancies between white and Japanese subjects may be partly explained by the Japanese traditional lifestyle, which includes sitting on the heels on a mat and using the Japanese-style lavatory, where subjects have to take a deep squatting position. These positions may cause mechanical stress to the knee joint and possibly lead to the acceleration of knee OA. Among elderly Japanese subjects, kneeling and squatting are common postures in daily life, which could obscure the association between knee OA and occupational activities of kneeling and squatting.

The direction of the association of kneeling and squatting with knee OA was also different between sexes in the present study, although these differences were not signif-

Table 6. Comparison of odds ratios for knee osteoarthritis associated with occupational activity among epidemiologic studies*

	Muraki et al (current study)		Yoshimura et al (34), K/L ≥3 with knee pain	Lau et al (35), K/L ≥3	Anderson and Felson (19), K/L ≥2	Felson et al (20)		Cooper et al (21), K/L ≥3 with knee pain	Coggon et al (22), listed for knee surgery	Sandmark et al (23), TKA	Manninen et al (24), TKA
	K/L ≥2	K/L ≥3				K/L ≥2	K/L ≥3				
Sitting on a chair	0.7†	0.8	–					1.2		–	
Men	0.6†	0.8	–					–		0.7	
Women	0.8	0.8	0.4†					–		0.9	
Kneeling	1.1	1.4†	–	–				3.4†	1.8†	–	1.7‡
Men	0.8	0.9	–	1.4				–	1.7†	2.1†	1.7
Women	1.4	1.7†	1.0	0.9				–	2.0†	1.5	1.8†
Squatting	1.2	1.3†	–	–	–	–	–	6.9†	2.3†	–	1.7‡
Men	0.9	1.0	–	1.2	2.5†	2.2†	2.0	–	2.2†	2.9†	1.7
Women	1.5†	1.5†	1.1	1.1	3.5†	0.4	0.7	–	2.8†	1.1	1.8†
Standing	2.0†	1.4	–					0.8		–	0.6†
Men	2.3†	1.1	–					–		1.7†	0.4†
Women	1.8†	1.5	1.2					–		1.6†	0.7
Walking	1.8†	1.1	–	–				0.9	1.9†		1.1
Men	2.2†	0.9	–	2.2†				–	1.7		1.5
Women	1.6†	1.1	0.9	1.4†				–	2.1†		1.1
Climbing	2.2†	1.3	–	–				2.7†	1.5†	–	1.6
Men	2.4†	1.0	–	4.1†				–	2.3†	1.2	2.8
Women	1.9†	1.5	0.9	6.1†				–	0.7	1.4	1.5
Lifting weights	1.9†	1.6†	–	–				1.4	1.7†	–	1.0
Men	2.3†	1.3	–	1.7				–	1.9†	3.0†	0.9
Women	1.7†	1.7†	1.0	1.5†				–	1.5†	1.7†	1.1

* K/L = Kellgren/Lawrence grading system; TKA = total knee arthroplasty.
† $P < 0.05$.
‡ $P < 0.05$. Kneeling or squatting.

icant, except for squatting in women. Because men are known to have greater muscle strength than women of all ages and muscle strength has a protective effect on knee OA (36–38), it might be that the greater muscle strength obscures the harmful effects of kneeling and squatting on knee OA in men, resulting in lower ORs for knee OA than in women.

For K/L grade ≥2 lumbar spondylosis, there were no occupational activities associated with the increased prevalence except for heavy lifting in women. Few studies have focused on risk factors for lumbar spondylosis associated with occupational activity (25–28), and no increased risk of lumbar osteophytes due to physical activities has been reported (25,39,40).

In the present study, the occupational activity of sitting on a chair was inversely associated with both K/L grade ≥2 knee OA and lumbar spondylosis. For knee OA, our previous small-scale study showed that prolonged sitting on a chair at work was associated with a reduced prevalence of knee OA (34) (Table 5). Regarding the relationship between sedentary work and OA, the results of studies investigating the influence of sedentary work on knee OA are controversial (21,22). Although sitting on a chair clearly involves reduced load on many joints compared with other working activities, no other studies have reported a relationship between sedentary activity and knee OA. Sitting on a chair as a physical activity in the work place appears to represent a characteristic protective factor for OA in Japan.

Contrary to K/L grade ≥2 knee OA, occupational activities of kneeling and squatting were significantly associated with K/L grade ≥3 knee OA, whereas those of standing, walking, and climbing were not. Considering the definition of the K/L grade, this may suggest distinct risk factors between osteophytosis and joint space narrowing. In this population-based cohort study, the prevalence of K/L grade ≥2 knee OA was 45.6% in men and 61.2% in women, which was higher than that in whites, whereas that of K/L grade ≥3 was 16.8% and 26.5%, which is comparable with that in whites (41), suggesting that the Japanese lifestyle may be associated with osteophytosis rather than joint space narrowing. Therefore, regarding K/L grade ≥2 knee OA, the Japanese lifestyle could obscure the association between knee OA and occupational activities of kneeling and squatting as mentioned above. Furthermore, the discrepancy between risk factors for K/L grade ≥2 and K/L grade ≥3 knee OA may also be due to differences between the mechanism of osteophytosis and joint space narrowing. There is accumulating evidence that osteophytosis and joint space narrowing have distinct etiologic mechanisms (25,42–47). A previous prospective study using a large-scale OA cohort reported that there was no association between the 2 representative features of knee OA (44). A recent cross-sectional study also showed that osteophytosis was unrelated not only to joint space narrowing on plain radiographs, but also to cartilage loss measured by quantitative magnetic resonance imaging (45). Furthermore, our study on an experimental mouse model for OA has identified a cartilage-specific molecule, carminerin, which regulates osteophytosis without affecting joint cartilage destruction during OA progression (46,47). Further clinical and basic research will disclose the distinct backgrounds of these 2 features of OA.

There are several limitations in the present study. First, this is a cross-sectional study on factors associated with knee OA and lumbar spondylosis, so a causal association with occupational activity could not be determined. However, information collected included a lifetime occupational history and details of specific work place physical activities; therefore, ample evidence on the background of knee OA and lumbar spondylosis could be obtained. Second, information regarding past occupational exposures was obtained by self-report and there is a possibility that both self-selection bias and recall bias may have occurred. People with painful conditions may choose work that allows them to avoid aggravation of their conditions, so the impact of job titles and occupational activities on knee OA and lumbar spondylosis may be underestimated in the present study. Conversely, people with painful knee and lumbar conditions are likely to look for and assign a cause when asked about past work exposures. To determine the impact of working conditions on knee OA and lumbar spondylosis independently of the presence of pain at the examination, we analyzed the association of knee OA and lumbar spondylosis with job titles and occupational activities according to the presence of knee pain and low back pain at the baseline examination. The direction of association was similar regardless of the presence of pain, and the results between the overall population and the subpopulation without knee pain or low back pain were not different, suggesting that pain at the examination may not affect the results of the overall population very much in this study.

In conclusion, the present cross-sectional study using a large-scale population from the ROAD study revealed distinct risk factors of occupational activities for radiographic knee OA and lumbar spondylosis in Japanese subjects. Sitting on a chair was a significant protective factor for both radiographic knee OA and lumbar spondylosis. Other occupational activities of kneeling, squatting, standing, walking, climbing, and heavy lifting were risk factors for radiographic knee OA, but not for radiographic lumbar spondylosis. Further studies, along with longitudinal data in the ROAD study, will elucidate the environmental backgrounds of OA and spondylosis and clarify clinical evidence for the development of disease-modifying treatments.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Muraki had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Muraki, Akune, Oka, Mabuchi, En-yo, Yoshida, Saika, Nakamura, Kawaguchi, Yoshimura.

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Analysis and interpretation of data. Muraki, Akune, Oka, Mabuchi, En-yo, Yoshida, Saika, Nakamura, Kawaguchi, Yoshimura.

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