表1　1981年　厚生省血液研究事業の基準

			第1日		第2～3日	第4～7日	第8～14日
			術前	術後12時間			
血友病A	大手術	目標レベル(%)	100	100	50～100	50～100	50
		投与量(U/kg)	50	50	40	40	25
		回　数(回/日)			2～3	1～2	1
	小手術	目標レベル(%)	80	50～80	30～50	20～30	
		投与量(U/kg)	40	30	20	15	
		回　数(回/日)	1	1	2	1～2	
	抜歯	目標レベル(%)	40		30		
		投与量(U/kg)	20		15		
		回　数(回/日)	1		1		

後1～3日目までは1000単位を1日2回投与，4～6日目までは500単位を1日2回投与し，7日目より中止した．しかし術後10日目左股関節周囲の強い腫脹と疼痛を認めたため，2000単位・1000単位を投与したところ症状は消失し，術後14日目に全抜糸した．

両肘関節鏡時は3000単位・1500単位を投与，術後1～3日目までは1500単位を1日2回投与，4～13日目までは500単位を1日2回投与した．術中術後，出血は少量で術後14日目に全抜糸した．

考　　察

血友病性関節症に対する滑膜切除の効果についてはこれまで多数の報告がある．関節内出血の止血効果が89～97%に有効であり，出血頻度は1/3～1/10に減少し，再手術は極めて稀であるとされている．しかし関節症変化は緩徐に進行するとの報告が多い[1)2)]．本症例においては術後早期より疼痛の改善および関節内出血の改善を認め，関節症変化の進行もほとんどないように思われた．両肘関節に関しても術後早期より疼痛の改善・関節内出血の改善を認めているが，術後経過期間が短く関節症変化の進行の有無については今後の経過を注意深く観察する必要がある．このように諸家の報告のとおり滑膜切除術は止血効果・徐痛に優れており極めて有用な方法であると考えられた．

重度の血友病性関節症に対するTHAは徐痛・ADLの改善に有用であるとの報告が多いが，長期成績は不透明である．NelsonらはTHAを施行した22症例（平均年齢48.1歳，平均観察期間7.6年）のうち8症例に緩み（THA生存率63.6%）を観察したと報告した[3)]．本症例は術後5年しか経過しておらず長期成績は不明であるが現在ADLは改善し，疼痛もなく日常生活をおくっている．若年者の人工関節置換術には意見が分かれるところであるが，血友病という特異な疾患においては著明なADLの改善が見込まれ極めて有用であると考える．

血友病性関節症の観血的加療を行ううえで凝固因子補充療法は極めて重要である．1981年厚生省血液研究事業が発表した凝固因子補充に関する基準がある（表1）．今回左足関節鏡および両肘関節鏡時には出血による合併症は認められなかったが，THA時には術後1週で凝固因子補充を中止したために関節内出血を引き起こすこととなった．迅速な補充療法の再開により大事には至らなかったが，THAのように侵襲が大きな手術を施行する場合は基準に基づき最低でも2週間は十分な凝固因子レベルを維持する必要があると反省した．

ま　と　め

血友病性関節症において滑膜切除術は止血・徐痛に極めて有用な方法であり，また重度の関節症に対しては人工関節置換術も積極的に選択するべき治療法であると考えられた．しかし，観血的治療を施行する場合は十分な凝固因子補充を行う必要がある．

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特集 Dupuytren 拘縮の基礎と臨床

Dupuytren 拘縮の病因
−オステオポンチン発現の検討−

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要旨：Dupuytren 拘縮（DC）の病態メカニズムには組織修復の中心である筋線維芽細胞（MF）が関与すると考えられており，腱膜内での創傷治癒反応の可能性が示されている。Osteopontin（OPN）は増殖，接着，遊走といった創傷治癒過程の各段階で機能することが報告されている。本研究では DC 腱膜の OPN 発現を検討した。対象は DC 腱膜 11 例で，免疫組織化学的に OPN，αSMA，CD68，tryptase の発現を評価した。培養細胞でも OPN と αSMA を蛍光二重免疫染色で検討した。コントロールは手根管症候群の腱膜を用いた。OPN 発現は nodules に認め，cord やコントロールでは認めなかった。連続切片において OPN と αSMA の発現部位は有意に相関し，*in vitro* でも共発現していた。一方，CD68 や tryptase とは発現部位が異なっており，OPN は MF が発現していると考えられた。MF の OPN 発現は組織修復の際に瘢痕形成に関与し，ノックアウトマウスでは瘢痕形成が減弱することが報告されている。OPN の DC 病態メカニズムへの役割を解明することで新しい治療の展開が期待される。

はじめに

Dupuytren 拘縮（Dupuytren contracture；DC）は手掌腱膜の線維腫で，病態の進行とともに手指の屈曲拘縮きたす疾患であるが，現在もその病態メカニズムについては不明である。病理組織学的には線維芽細胞活性の変化が大きく関与していると考えられており，1971 年 Gabbiani[1] は線維芽細胞の phenotype である筋線維芽細胞（myofibtoblast；MF）の存在を示した。MF は組織障害後に間質の線維芽細胞から形質転換をすると考えられており，細胞内には発達したアクチン線維が認められ，α 平滑筋アクチン（αSMA）などの平滑筋細胞に特異的な蛋白を発現する線維芽細胞と平滑筋細胞との中間的な性質を持つ細胞である。これは自ら強い収縮力を発生するとともに，コラーゲン合成から瘢痕収縮を起こすことで創部を縮小し，組織修復の中心的な役割を果たすと考えられている[2]。DC においても MF は nodules を腱膜内に形成し，同部での収縮が手指拘縮をきたすと考えられている。そのため DC の病理組織学的分類は MF 活性をもとに行われ，DC の病態進行は MF と密接に関係していると考えられている[3]。

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Expression of osteopontin in Dupuytren contracture

Key words：Dupuytren contracture，Osteopontin，Myofibroblast

DCの病勢やMF増殖にはTGF-β, PDGF, FGFなどの様々な創傷治癒関連因子が関与することが報告されている[4)5)]。このことも肺，腎，心臓などの他臓器における線維化疾患での報告と同様である。Osteopontin（OPN）は分子量約32,000の分泌型の糖タンパク質であり，当初骨基質で同定された。OPNは細胞接着配列であるRGDドメインを有しており，細胞表面のインテグリンと結合することで，細胞増殖，接着，遊走などの創傷治癒過程の各段階において発現・機能することが報告されている[6)7)]。実際に肺線維症，創傷治癒，肝硬変などの様々な線維化病変において高発現していることが報告されており，線維化において重要な役割を果たすと考えられている[8)~10)]。

さらに，これらの疾患においてOPNがMFへの形質転換を促進する報告やOPNのノックアウトマウスを用いた研究では，MFの出現が遅れることが示されており，線維化病変におけるMF活性にOPNが主要な因子であると考えられている[11)]。DCは手の外科疾患における代表的な線維化病変であるが，現在までにOPNを対象とした研究はない。

そこでわれわれは，DC腱膜においてOPN発現の検討を行った。本研究の目的はDC腱膜におけるOPN発現を正常コントロールと比較検討すること，DC腱膜おけるOPN発現部位を検討すること，さらにOPN発現細胞を評価するために*in vitro*で検討を行うことである。

I．対象と方法

1．対　象

2004年以降にDCにて観血的治療を施行した11例11手で，手術は全例に部分腱膜切除術を施行した。平均年齢は67.1歳（58～82歳）で，女性2例・男性9例であった。罹患側は右8例・左3例であった。また糖尿病の合併を4例に認めた。術後に摘出部に結節を認めたものはあったが，拘縮により再手術となった例はなかった。摘出組織はホルマリン固定後にパラフィン包埋とした。またコントロールとして特発性手根管症候群の5例（平均年齢52.8歳）で，手根管開放術の際に摘出した腱膜を用いた。

2．組織学的検討

パラフィン包埋された腱膜を4 μmに薄切し，HE染色を行い，光学顕微鏡にnodulesとcordを観察した。Luck分類にて病理組織学的にproliferative, involutional, residualの病期分類を行った[2)]。

3．免疫組織化学的検討

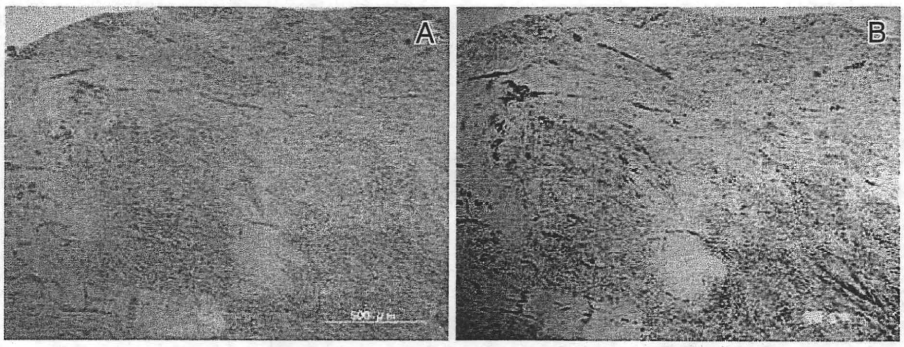
上記のごとくパラフィン包埋された腱膜の連続切片を作製し，アミノ酸ポリマー法にて免疫染色を行った。まず抗原性賦活化のためにmast cell-tryptaseは0.04% proteinase Kで酵素処理を，他はクエン酸緩衝液（pH 6.0）を用いて熱処理を行った。一次抗体として抗αSMAマウスモノクローナル抗体（Dako），抗OPNラビットポリクローナル抗体（IBL），さらにOPNの発現細胞を検討するために抗CD68マウスモノクローナル抗体（Dako），抗mast cell-tryptaseマウスモノクローナル抗体（大日本住友製薬）を用いた。二次抗体はHRP標識抗マウス・ラビット抗体を用い，DABにて発色させ，光学顕微鏡下に評価を行った。

4．αSMA発現とOPN発現の評価

1標本につき任意の5視野にて発現領域を画像解析ソフト（Lumina Vision ver.1.11, Mitani Shoji co.）を用いて面積率を算出した。

5．細胞培養

摘出されたDCの腱膜を肉眼的にnodulesの中心部分から約7 mm^3ほどを切り出し，これをメスにてmincing後，collagenaseを300units/m*l*（St. Louis）とdispaseを5,000units/m*l*（Sankojunyaku）混入させた10% fetal bovine serum（FBS, Canadian International）入りのF-12 Ham's medium（GIBCO）にて腱膜細胞を単離させた。その後，10% FBS入りのDulbecco's modified Eagle's medium（DMEM）にて初代培養を行い，コンフルエントとなってから，細胞5×10^3個/m*l*をスライドガラス上に10% FBS入りのDMEMにて培養を行った[12)]。また同様に手根管開放術の際に摘出した腱膜からも細胞培養を行



HE 染色　　αSMA の免疫染色

図 1

細胞密度の高く，αSMA 発現の強い proliferative phase と考えられる部位から，ほとんどαSMA 発現を認めない residual phase と考えられる部位までが混在していた。

い，コントロールとした。

6．二重蛍光免疫染色

培養 5 日目に 2%パラフルムアルデヒドと 0.1% Triton-X にて固定後に一次抗体に抗αSMA 抗体，抗 OPN 抗体を，二次抗体に Alexa488 標識抗マウス抗体，Alexa546 抗ラビット抗体を用い，benzimide にて核染色し，蛍光顕微鏡下に観察した。

7．統計解析

StatView 5.0 for Windows を用いて Spearmann の順位相関で $p<0.05$ にて統計学的有意とした。

表 1

病期分類	症例数
Proliferative	2
Involutional	0
Residual	1
Proliferative/ Involutional	2
Involutional/ Residual	1
Proliferative/ Involutional/ Residual	5

Ⅱ．結　果

1．DC の組織学的病期分類

炎症細胞浸潤を認めたものはなく，各標本において高い細胞密度で配列した nodules の形成を認めた。Luck 病期分類では明確に proliferative, involutional, residual の各段階を認めるものは少なく，ほとんどの標本において様々な段階が混在していた（図 1, 表 1）。Cord と正常腱膜においては線維芽細胞が散在して配列していた。

2．腱膜での OPN 発現

OPN は DC 腱膜の nodules に発現を認め（図 2 A），発現部位は連続切片でみたαSMA 発現と類似したパターンであった（図 2 D・E）が，αSMA 発現を血管平滑筋細胞にも認めたのに対して OPN 発現は結合織のみに発現していた。またαSMA 発現は認めないものの形態的に fibroblast とは異なる細胞で OPN を発現するものが認められた。一方でコントロールや cord では，血管にαSMA 発現を認める以外には OPN の発現は認められなかった（図 2 B・C）。

3．OPN 発現細胞の検討

αSMA 以外に腱膜内の単球/マクロファージと mast cell の評価のため CD68, mast cell- tryptase の発現を検討したが，両者の発現は腱膜内に散在して認めるものの（図 3 C・D），強く OPN 発現を認める nodules 内では発現は少なく，OPN

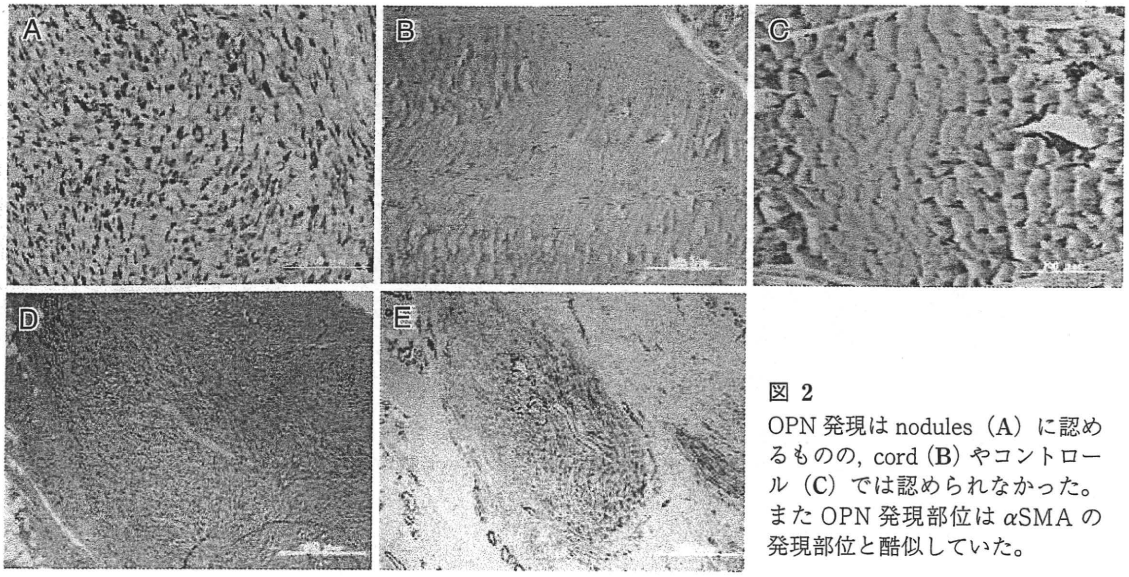


図 2
OPN 発現は nodules（**A**）に認めるものの，cord（**B**）やコントロール（**C**）では認められなかった。また OPN 発現部位は αSMA の発現部位と酷似していた。

発現を認めない nodules 周囲や cord にも同様な密度で存在していた。このことから，単球/マクロファージや mast cell は OPN 発現のみならず，病態への関与も少ないと思われた。一方で αSMA 発現細胞と OPN 発現は nodules に強く発現を認めており，発現様式も酷似していた（図 3 A・B）。連続切片でのそれぞれの画像解析による発現領域の統計学的検討では，有意な相関関係を認めた（図 4）。さらに *in vitro* における蛍光免疫染色では αSMA 発現を認めたものでは二重蛍光免疫染色にて OPN 発現も認めており，その周囲には OPN 発現を認める細胞が多数認められた（図 5）。コントロールでも αSMA 発現を認めるものはあったが少なく，OPN 発現も DC 細胞より少ない傾向であった。

Ⅲ. 考　察

本研究において OPN が DC 腱膜内に発現することが示された。一方でコントロール（手根管症候群の手掌腱膜）では，その発現は明らかでなかった。現在までに DC において OPN 発現に言及したものは渉猟し得た限りはない。当初 OPN は骨基質で同定されたが，近年では炎症性サイトカインとしての役割が注目されており，様々な炎症性疾患，線維化病変で病態進行に関与することが示されている[6)13)]。関節炎において IL-1β，IL-6，TNF-α といった炎症性サイトカインとともに OPN 発現の増大が認められている[6)7)]。またマウスの関節リウマチモデルでは OPN が病態の中心的役割を担っていることが報告されている[14)]。さらに虚血性心疾患後の瘢痕部における *in vitro* 研究において，線維化の中心的役割を担う TGF-β が MF への形質転換を促進することが示され，その MF 活性能に OPN が必須であることが示されている[15)]。今回の研究から，DC の主病変と考えられる nodules に OPN 発現を強く認めており，TGF-β などの創傷治癒関連因子とともに病態の進行に関与するものと推察された。

DC は特徴的な組織学的形態により，3 つの段階に分類される[2)16)17)]。① Proliferative phase では線維芽細胞が増殖し，MF への形質転換が認められる。② Involutional phase では細胞密度の減少が認められ，MF も減少し，長軸に配列する。③ Residual phase において MF はほとんど消失する。DC で認められるこの組織学的変化は創傷治癒で認められる肉芽形成の過程と酷似してお

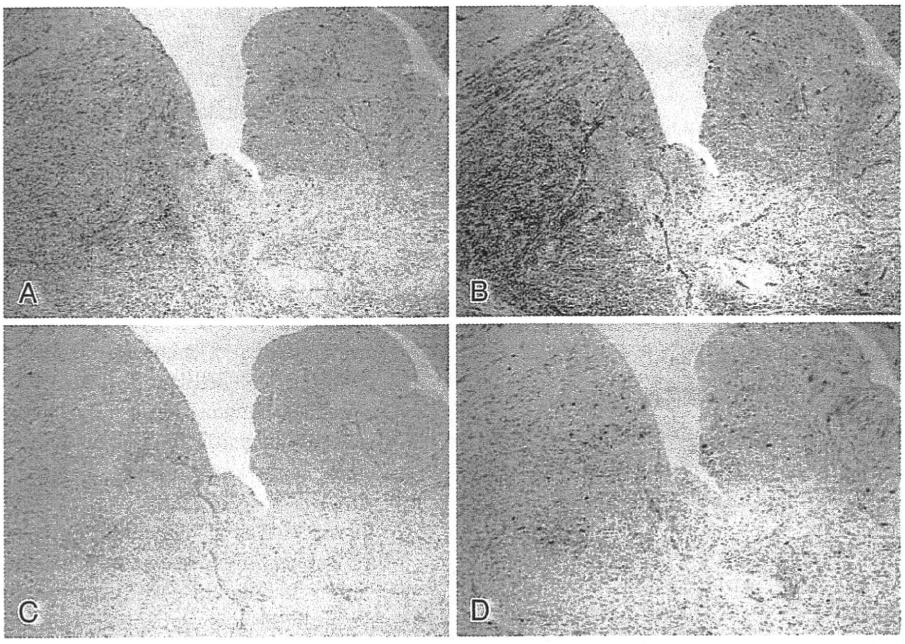


図 3

連続切片にて OPN の発現領域（**A**）は αSMA 発現（**B**）と同様の部位であったが，CD68（**C**）や mast cell-tryptase（**D**）とは部位が異なっており，DC 腱膜において筋線維芽細胞が OPN を発現していると考えられた。

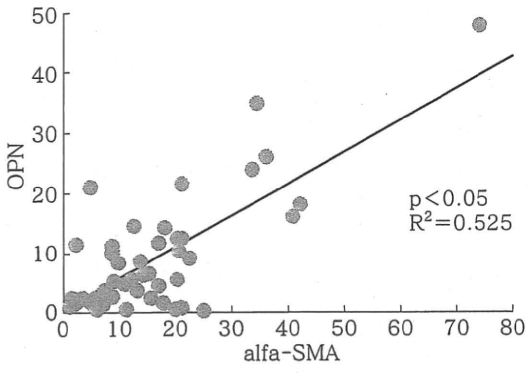


図 4

OPN と αSMA の発現部位を各々面積率で評価したところ，統計学的に有意な相関関係にあった。

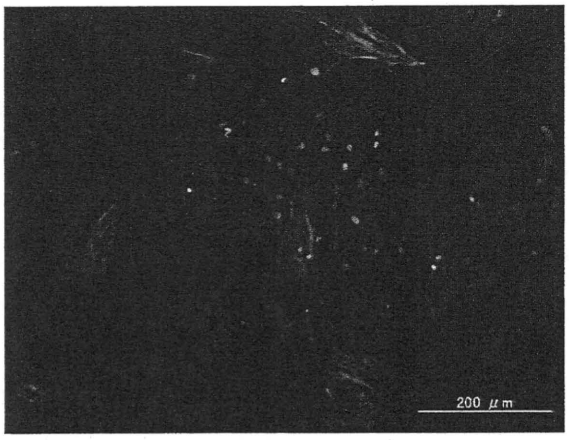


図 5

培養細胞においても αSMA 発現陽性細胞（緑）は OPN 発現（赤）を認めた。また周囲には OPN 発現を認める線維芽細胞が多数認められた（青：核）。

り，生化学的検討においても病勢により collagen 組成が変化するなど急速な組織改変が関与することが示されている[4]。

創傷治癒においてノックアウトマウスを用いた研究では，OPN が欠損した状態では損傷部での MF への転換が強く抑制されており[11)15)]，DC においても OPN が MF への形質転換から病態の進行に関与すると仮設された。そこで病勢に関して病理組織学的分類を行い，OPN 発現との関連性の評価を試みたが，Luck 分類に準じて明確に分けることは困難であり，1つの標本に各段階が混在するものが多かった。そのため病期での OPN 発現は評価できなかったが，各標本で病勢の強い部位，proliferative phase と考えられる部位には発現が強い印象であり，OPN が MF 活性に関与する可能性が考えられた。

実際に MF と OPN は発現領域において有意に相関しており，OPN を発現する多くが MF であると考えられ，さらに *in vitro* でも MF と思われる αSMA 陽性細胞には OPN が発現していた。これまでの報告では OPN 発現を認めるものはマクロファージや肥満細胞が多く，それらから炎症が惹起されると考えられている。今回の免疫組織化学的検討ではマクロファージと肥満細胞は OPN 発現より明らかに少なく，組織学的にもこれまでの報告と同様，炎症細胞浸潤は認められなかった。しかし Mori ら[11)]は創傷治癒過程の *in vitro* 研究において，線維芽細胞にマクロファージと肥満細胞の cell line から得た conditioned medium を添加することで線維芽細胞に OPN 発現が誘導されたことを報告している。本研究においても DC 腱膜の OPN 発現細胞は MF であったが，その引き金となるのはマクロファージや肥満細胞である可能性も考えられた。

今回の研究では病態メカニズムにおける OPN の役割には言及しておらず，今後 OPN の MF への関与について研究を行うが，その結果 OPN が病態進行の抑制や再発率低下のための標的分子となる可能性があり，さらに検討を重ねる必要がある。

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Body Mass Index Misclassification Due to Kyphotic Posture in Japanese Community-Dwelling Adults Aged 65 Years and Older

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Background. In older adults, kyphosis (slouching posture) can lead to underestimation of height, which may in turn lead to overestimation of body mass index (BMI). We investigated the extent to which inaccurate BMI assessments led to misclassification of elderly people as normal weight (when they were actually underweight) or overweight (actually normal weight).

Methods. Anthropometric measurements were taken in 2005 and 2006 for 842 residents aged 65 years or older (women: 491; men: 351). We calculated BMI from measured height and weight (observed BMI) and then predicted BMI from height as determined by demi-span, which is unaffected by kyphosis (predicted BMI). Kyphosis was assessed by the number of blocks placed under the occiput required for the supine participant to achieve a neutral head position. Participants were classified as underweight (BMI < 18.5), normal weight, or overweight (BMI ≥ 25.0) according to both observed and predicted BMI; classification accordance was investigated by cross-tabulation.

Results. Kyphosis was present in 17.2% of the participants overall and in 23.6% of those aged 75 years or older. Predicted BMI measurements showed that 11% of participants with kyphosis requiring ≥ 3 blocks were misclassified as normal weight and that 10% were erroneously classified as overweight. In those aged 75 years or older, the corresponding figures were 15% and 12%.

Conclusions. Our results suggest that inaccurate BMIs due to kyphosis lead to substantial numbers of older adults being misclassified as normal weight or overweight, which can cause significant distortions in data on the impact of underweight and overweight on health outcomes.

Key Words: Body mass index—Kyphosis—Demi-span—Aged.

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MAINTAINING proper weight is an important public health issue not only for children and middle-aged persons but also for older people. In fact, underweight in older adults is reportedly associated with increased mortality (1–5). In contrast, the association between overweight and mortality among older adults is less consistent than it is among middle-aged adults (6,7). To determine overweight and underweight, body mass index (BMI) is commonly used worldwide. However, accurate BMI assessment require accurate height measurements, which can be problematic in older persons with kyphosis, shortening of the spinal vertebrae, or thinning of weight-bearing cartilage (8,9).

BMI is calculated as weight divided by the square of height, so small changes in height have a significant effect on BMI. Because height is generally measured with the participants in a standing position, measured height can be underestimated if the examinee has kyphosis. Examinees are asked to stand as straight as possible when measured, but this does not necessarily compensate for postural kyphosis. Any resulting underestimation of height leads to overestimation of BMI, which causes weight-category misclassifications.

The combined effects of osteoporotic vertebral fractures, disk degeneration, and weakness of the back muscles make kyphosis common in elderly populations (10). Progressed kyphosis is reportedly associated with ventilatory dysfunction (11), diminished daily physical function (12,13), injurious falls (14), impaired quality of life (15), subjective poor health (16), and increased mortality (17,18). Overestimation of BMI due to kyphosis may therefore cause significant distortions in data on the impact of underweight and overweight on health outcomes, including mortality. Nevertheless, weight-category misclassifications due to kyphosis have rarely been investigated.

In an attempt to rectify this situation, we calculated BMI in 842 Japanese aged 65 years or older, first using measured height and then height as determined by measurement of the demi-span, which is unaffected by kyphosis. The values

were compared. We also evaluated the participants for kyphosis and investigated the extent to which inaccurate BMI assessments led to the misclassification of underweight participants as normal weight and of normal weight participants as overweight.

Methods

Study Population

The Kurabuchi study is an ongoing community-based cohort study of aging involving functional assessment of an older population in Kurabuchi Town, Takasaki City (approximately 100 km north of Tokyo, Japan), a rural mountainous area where a quarter of the population work in the primary sector of industry (19,20). In 2005 and 2006, all residents aged 65 years or older, excluding those hospitalized or institutionalized, were enrolled (n = 1,294), and 842 (491 women and 351 men) of them (65.1%) participated in detailed health examinations, including anthropometric measurements and kyphosis evaluation, carried out in eight community centers.

The study protocol was approved by the Ethics Committee of the School of Medicine, Keio University (Tokyo, Japan), and written informed consent was obtained from all participants.

Measurement of Height, Weight, and Demi-span

Height was measured with a portable stadiometer. Participants were asked to remove their shoes and socks and stretch to maximum height with their backs to the stadiometer. Readings were recorded to the nearest 0.1 cm. Weight was measured in all participants (lightly clothed) to the nearest 0.1 kg by having them stand on an electronic scale (WB-110; Tanita Co., Tokyo, Japan) placed on a firm surface. Demi-span was measured with a tape from the finger root to the sternal notch; participants were seated, with the arm stretched out laterally (Figure 1) (21). The left arm was measured, unless it could not be stretched fully or was injured or deformed; measurements were recorded to the nearest 0.1 cm. The interrater reliability of the demi-span was good (interclass correlation: .96) (21).

Evaluation of Kyphosis

Kyphotic posture was evaluated with a modified version of the method described by Kado and colleagues (17). Participants were asked to lie flat on a table with their eyes directed toward the ceiling, and the distance from the occiput to the table (OTD) was measured. Kyphotic individuals are unable to lie flat with their heads in a neutral position (ie, neither hyperextended nor hyperflexed) on a flat surface. In Kado's method, the degree of kyphotic posture is evaluated according to the number of blocks placed between the occiput and the table that is required to achieve a neutral head position in the participant: the larger the number of blocks, the greater the degree of kyphotic posture. In the original method, 1.7-cm blocks are used, but in the present study, 1.5-cm blocks were used to compensate for the smaller body size of Japanese. The interrater reliability, assessed by interclass correlation, of OTD was .9 (Dr Deborah Kado, personal communication).

Figure 1. Assessment of demi-span. Demi-span was measured with a tape from the finger root to the sternal notch; participants were seated with the arm stretched out laterally.

Calculation of BMI

Observed BMI was calculated as weight (kilograms) divided by the square of observed height (meters). Predicted BMI was calculated on the basis of height as predicted by measurement of the demi-span; separate prediction equations were used for men and women, as described below. The equations reported by Bassey (21) and used in other studies rely on data concerning the stature of Europeans, so we used regression equations derived from our study participants with straight posture. Participants with 1-block OTD were classified, like those with 0-block OTD, as having straight posture because including them in this category did not significantly alter the equations. The equation for women was predicted height (cm) = (1.44 × demi-span in cm) + 48.23; for men, it was predicted height (cm) = (1.39 × demi-span in cm) + 55.56.

Statistical Analysis

We used STATA version 11 (STATA Corporation, College Station, TX) for all data analyses. First, scatter plots were drawn to show the relationship between observed BMI and predicted BMI in association with the presence of kyphotic posture. The differences between observed BMI and predicted BMI were also calculated by subtracting predicted BMI from observed BMI. Finally, the participants

Table 1. Characteristics of the Study Population

	Women (n = 491)	Men (n = 351)	Women and Men (n = 842)
Age (years old)*			
65–69	99 (20.2)	76 (21.7)	175 (20.8)
70–79	252 (51.3)	188 (53.6)	440 (52.3)
80 or more	140 (28.5)	87 (24.8)	227 (27.0)
Height (cm)†	145.8 ± 6.5 (119.2–164.7)	159.4 ± 6.0 (141.2–179.5)	151.5 ± 9.2 (119.2–179.5)
Weight (kg)†	48.6 ± 8.0 (28.0–75.5)	58.1 ± 8.8 (38.0–90.0)	52.6 ± 9.5 (28.0–90.0)
Demi-span (cm)†	68.6 ± 3.0 (58.5–77.5)	74.9 ± 3.1 (63.8–83.3)	71.2 ± 4.3 (58.5–83.3)
Occiput-to-table distance (number of blocks)*			
0	153 (31.2)	47 (13.4)	200 (23.8)
1	183 (37.3)	143 (40.6)	326 (38.7)
2	76 (15.5)	95 (27.1)	171 (20.3)
3	34 (6.9)	46 (13.1)	80 (9.5)
4	19 (3.9)	9 (2.6)	28 (3.3)
5	14 (2.9)	4 (1.1)	18 (2.1)
6 or more	12 (2.4)	7 (2.0)	19 (2.3)

*Number (percent) is shown.
†Mean ± *SD* (range) is shown.

were classified as underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), or overweight (BMI ≥ 25.0) on the basis of observed BMI and predicted BMI, respectively. The results were cross-tabulated, and accordance/discordance was investigated. The results did not vary by sex, so the findings shown are those for men and women combined.

Results

Table 1 shows the characteristics of the study population by sex; more than half of both sexes were in their 70s. Kyphosis measurements ranged from 0 to 11 blocks, with 1 block being the most prevalent in both sexes. With a cutoff of greater than or equal to 2 blocks versus 1 or 0 blocks, kyphosis was present in 31.6% of the women and 45.9% of the men. With the cutoff set at greater than or equal to 3 blocks, the corresponding figures were 16.1% and 18.8%, respectively.

The differences between observed BMI and predicted BMI according to the grade of kyphosis are shown in Figure 2. Observed BMI was virtually identical to predicted BMI in those with 0-, 1-, and 2-block OTD. However, observed BMI was higher than predicted BMI in those with greater than or equal to 3-block OTD. The mean difference (95% confidence interval) between observed BMI and predicted BMI was −0.010 kg/m^2 (−0.109 to 0.090) for those with 0- or 1-block OTD, 0.149 kg/m^2 (−0.054 to 0.352) for those with 2-block OTD, and 0.965 kg/m^2 (0.673–1.256) for those with greater than or equal to 3-block OTD; the difference was statistically significant only in those with greater than or equal to 3-block OTD. If BMI is overestimated on the basis of observed height, those with kyphosis may easily be misclassified as (1) normal weight when they are actually underweight if BMI is calculated on the basis of predicted height or (2) overweight when predicted BMI places them in the normal weight range. To clearly demonstrate the potential for misclassification, cross-tabulations of underweight, normal weight, and overweight as calculated on the basis of observed BMI and predicted BMI are shown in Table 2. In some cases, predicted BMI was lower than observed BMI due to imperfections in the equations, so the higher of the two was used as predicted BMI. According to

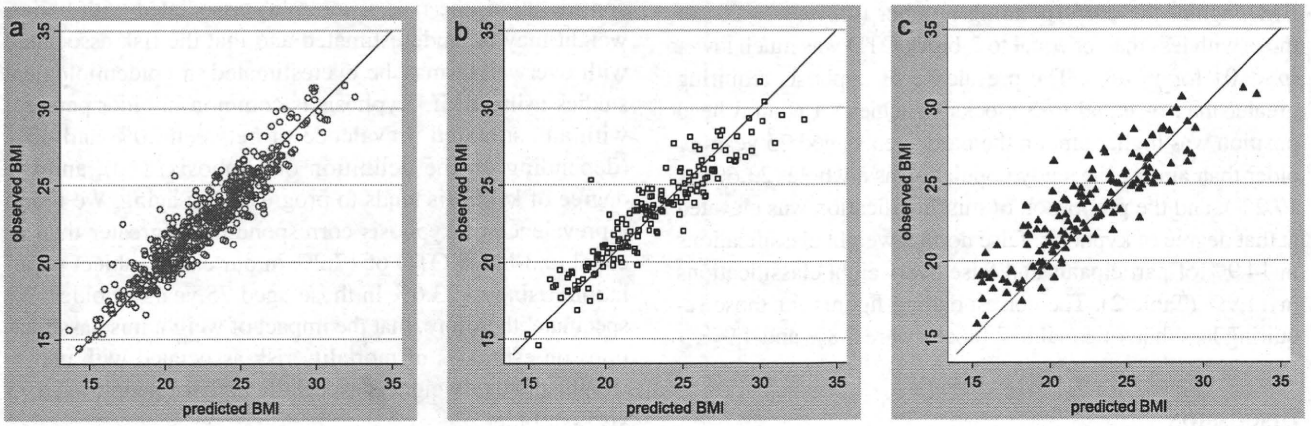

Figure 2. Scattergram of observed body mass index (BMI) against predicted BMI. (**a**) Participants with 0–1 block for the occiput-to-table distance. (**b**) Participants with 2 blocks for the occiput-to-table distance. (**c**) Participants with 3 blocks or more for the occiput-to-table distance.

Table 2. Cross-Tabulations of Underweight, Normal Weight, and Overweight Calculated by Observed BMI and Predicted BMI

	Predicted BMI		
	Underweight (BMI < 18.5)	Normal (18.5 ≤ BMI < 25.0)	Overweight (25.0 ≤ BMI)
All participants (n = 842)			
Participants with 0–2 blocks for the occiput-to-table distance (n = 697)			
Observed BMI			
Underweight (BMI < 18.5)	56 (8.0)	0 (0)	0 (0)
Normal (18.5 ≤ BMI < 25.0)	27 (3.9)	450 (64.6)	0 (0)
Overweight (25.0 ≤ BMI)	0 (0)	29 (4.2)	135 (19.4)
Participants with ≤ 3 blocks for the occiput-to-table distance (n = 145)			
Observed BMI			
Underweight (BMI < 18.5)	9 (6.2)	0 (0)	0 (0)
Normal (18.5 ≤ BMI < 25.0)	16 (11.0)*	75 (51.7)	0 (0)
Overweight (25.0 ≤ BMI)	0 (0)	14 (9.7)†	31 (21.4)
Participants aged 75 and older (n = 428)			
Participants with 0–2 blocks for the occiput-to-table distance (n = 327)			
Observed BMI			
Underweight (BMI < 18.5)	32 (9.8)	0 (0)	0 (0)
Normal (18.5 ≤ BMI < 25.0)	19 (5.8)	212 (64.8)	0 (0)
Overweight (25.0 ≤ BMI)	0 (0)	16 (4.9)	48 (14.7)
Participants with ≤ 3 blocks for the occiput-to-table distance (n = 101)			
Observed BMI			
Underweight (BMI < 18.5)	7 (6.9)	0 (0)	0 (0)
Normal (18.5 ≤ BMI < 25.0)	15 (14.9)‡	54 (53.5)	0 (0)
Overweight (25.0 ≤ BMI)	0 (0)	12 (11.9)§	13 (12.9)

Notes: BMI = body mass index.
*$p < .01$ for χ^2 test when comparing with the prevalence of the same misclassification (3.9%) among those with 0–2 blocks.
†$p < .01$ for χ^2 test when comparing with the prevalence of the same misclassification (4.2%) among those with 0–2 blocks.
‡$p < .01$ for χ^2 test when comparing with the prevalence of the same misclassification (5.8%) among those with 0–2 blocks.
§$p = .01$ for χ^2 test when comparing with the prevalence of the same misclassification (4.9%) among those with 0–2 blocks.

the result shown in Figure 1, cross-tabulations were done separately for those with less than or equal to 2-block OTD and for those with greater than or equal to 3-block OTD: The results were compared.

Among the participants with greater than or equal to 3-block OTD, 16 (11.0%) were classified as normal weight, although they were underweight on the basis of predicted BMI; only 3.9% (n = 27) of those with less than or equal to 2-block OTD were similarly misclassified (11.0% vs 3.9%, $p < .01$ for χ^2 test). Fourteen (9.7%) of the participants with greater than or equal to 3-block OTD were classified as overweight when they were normal weight according to predicted BMI; again, the corresponding number (4.2%, n = 29) of those with less than or equal to 2-block OTD was much lower ($p < .01$ for χ^2 test). The prevalence of kyphosis requiring greater than or equal to 3 blocks to achieve a neutral head position was higher among the participants aged 75 years or older than among the study population as a whole (23.6% vs 17.2%), and the proportion of misclassification was elevated at that degree of kyphosis: false normal weight classifications in 14.9% of participants and false overweight classifications in 11.9% (Table 2). The corresponding figures for those requiring less than or equal to 2 blocks were 5.8% and 4.9%.

Discussion

This study shows that there is a distinct risk of weight misclassifications due to kyphosis in adults aged 65 years or older: 11% of our participants with kyphosis corresponding to greater than or equal to 3-block OTD were classified as normal weight when they were actually underweight and 10% were erroneously classified as overweight. The corresponding figures for those aged 75 years or older were 15% and 12%, respectively. Such misclassifications may result in some underweight elderly people failing to receive nutritional support and in others of normal weight being put on unnecessary weight reduction programs. One study indicated that persons with hyperkyphosis have a 1.4 times higher rate of mortality after adjustment for possible confounders than those without (17). When taking this into consideration, the risk of mortality associated with underweight may be underestimated and that the risk associated with overweight may be overestimated in epidemiological studies using BMI. Kyphosis is common in older persons, with an estimated prevalence of between 20% and 40% (depending on the definition of kyphosis) (10), and the degree of kyphosis tends to progress with aging. We found a prevalence of kyphosis corresponding to greater than or equal to 3-block OTD of 17.2% in our entire subject population, rising to 23.6% in those aged 75 years or older. We speculate, therefore, that the impact of weight misclassifications on estimates of mortality risk associated with underweight and overweight is especially high for people aged 75 years or older.

Kyphosis can be measured from radiographs or with noninvasive methods, including the kyphosis index (22),

occiput-to-table distance (17), occiput-to-wall distance (11), and qualitative visual measurements (23,24). Height is generally measured with the participant standing with their back stretched against the stadiometer, as in this study. Elderly people are often able to correct their posture so that height is measured correctly. However, those with uncorrected rigid kyphosis cannot compensate for it, so their height is underestimated. We selected OTD for this study because measurements are made with the participant in a supine position on a table, allowing us to evaluate uncorrected kyphosis.

Various measures to prevent weight misclassifications due to kyphosis exist. First, alternatives to height measurements, such as demi-span, arm span, and knee height, can be used to calculate BMI. We selected demi-span because it offers the following advantages: Undressing is not required; the number of joints included is smaller than with the arm span (21); and measurements are known to decrease slowly with age (25). Second, instead of BMI, nutritional markers, like mid-arm circumference and calf circumference, can be used if the purpose is to screen for malnutrition. Aging is associated with changes in body composition, and the reliability of BMI itself as a surrogate marker of body fat in later life needs further discussion.

Few studies have investigated BMI overestimation due to age-related height loss. Sorkin and colleagues (8) estimated that the artifactual increase in BMI caused by cumulative height loss from age 30 to 80 was 1.2 U in men and 1.6 U in women. Hirani and Mindell (26) calculated BMIs in adults aged 65 years or older, using both measured height and demi-span equivalent height. In women, the prevalence of underweight was 1.2% when BMI was calculated on the basis of measured height and 2.8% when BMI was calculated according to demi-span equivalent height; the figures for overweight were 66.5% and 60.1%, respectively. No such differences were found in men. Our findings expand on these earlier studies, but we think, we are the first to include accurate evaluations of kyphosis and demonstrate that the proportion of misclassification varies according to the degree of kyphosis. We will continue to collect detailed data on our participants to further assess the impact of weight misclassifications on the association between BMI and health outcomes, including mortality.

One limitation of this study is that 65% of the target population participated, and as previously reported, the participants were younger and better educated than the nonparticipants (19). Both younger age and better education can be associated with a reduced prevalence of osteoporotic fractures, and the prevalence and degree of kyphosis, so the proportion of misclassification in our study might be underestimated (27). Another limitation is that our equations for predicted height were derived from data on the nonkyphotic study population. Because age-related stature shrinking also occurs in nonkyphotic participants, predicted height, and therefore the proportion of misclassification, might still be underestimated in this study. Also, only community-dwelling older Japanese were studied, so our findings may not apply to other populations, including institutionalized people.

In conclusion, this study suggests that inaccurate BMI due to kyphosis lead to substantial misclassifications of older people as normal weight or overweight. Options to prevent such misclassifications include the use of alternative methods of measuring height for BMI calculations and, indeed, the use of alternatives to BMI itself for classifying underweight and overweight.

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Original Article

Knee Pain and Future Self-Reliance in Older Adults: Evidence From a Community-Based 3-Year Cohort Study in Japan

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ABSTRACT

Background: Although knee pain is common in older persons and can cause ambulatory limitation, its impact on self-reliance has rarely been examined in Japan, particularly in a community setting. The aim of this 3-year cohort study was to investigate the association of knee pain with dependence in activities of daily living (ADL) and mortality in community-dwelling older Japanese adults.

Methods: In 2005, presence of knee pain was assessed by a home visit survey of 1391 older adults aged 65 years or older (participation proportion = 97.3%). A total of 1265 participants who were ADL-independent at baseline were followed for 3 years, and information on outcomes, namely death and dependence in ADL, was collected.

Results: Participants who always had knee pain were more likely to become dependent in ADL than those who reported no knee pain (multivariate-adjusted OR, 1.98; 95% CI, 1.03–3.83); however, always having knee pain was not associated with mortality or a composite outcome of ADL dependence and death. Further analyses of each component of ADL dependence revealed that knee pain was associated with a need for assistance at home (long-term care eligibility, bathing, dressing, and transferring), but not with institutionalization.

Conclusions: The participants were highly representative of the target population and the rate of follow-up was almost perfect (99.4%). The results suggest that knee pain is associated with future dependence in ADL, particularly a need for assistance at home.

Key words: joint diseases; activities of daily living; mortality; cohort studies; aged

INTRODUCTION

Knee pain is common in older adults.[1,2] However, there is considerable discordance between knee pain and radiographic knee osteoarthritis (OA).[3,4] The proportion of individuals with both knee pain and radiographic OA was reported to range from 15% to 76%, and, among those with radiographic knee OA, the proportion of individuals with pain ranged from 15% to 81%.[3] It is usually the perception of pain, rather than the presence of pathology, that troubles patients, and pain is the principal reason for seeking treatment.[1] In addition, assessment of perceived pain is more straightforward, less expensive, and faster than measuring radiographic changes of OA, which is obviously advantageous for an epidemiologic study that hopes to attain a high participation proportion of the target population.

The self-reliance of older adults is an increasingly important public health concern as the global population ages. Knee pain can cause ambulatory limitation.[2] Therefore, it is an important factor in loss of independence in activities of daily living (ADL), and even death, because ambulation is a good predictor of mortality in older persons.[5] Many studies of the association between knee OA, including knee pain, and dependence in ADL have been conducted.[6–8] In Japan, however, evidence is limited. Watanabe et al reported that mobility was significantly lower in patients with knee OA than in control subjects,[9] and Kondo et al investigated risk factors associated with knee pain and functional limitation.[10,11] In both these studies, the subjects were hospital-based patients with knee OA. However, a recent population survey in the United Kingdom found that among 3023 adults aged 50 years or older who reported knee pain within the previous year, only 33% reported visiting their general practitioner for this complaint during the same period.[12] Therefore, community-based studies are desirable to produce less biased estimates of the association between

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knee pain and dependence in ADL. Moreover, because body composition in Asian and Western populations is very different[13] and lifestyle factors including kneeling and squatting in daily life also differ between Japan and Western countries, associations observed in whites may not be applicable to Japanese populations. If knee pain were shown to be associated with dependence in ADL among community-dwelling older populations, intervention in the form of exercise programs, for example, could be aimed at maintaining self-reliance in those with knee pain.

Therefore, the aim of this 3-year cohort study, in which the participants were highly representative of the target population, was to investigate the association of knee pain with dependence in ADL and mortality in community-dwelling older Japanese adults.

METHODS

Study population

This study is part of the Kurabuchi study, an ongoing community-based longitudinal study of aging that involves functional assessment of an older population in Kurabuchi Town, Takasaki City, a community approximately 100 km north of Tokyo, Japan. The details of the study have been described elsewhere.[14–16] Briefly, from April through July 2005, trained public health nurses and local welfare commissioners conducted a home-visit health survey of residents aged 65 years or older, using a structured questionnaire with items on many aspects of health. Of the 1429 eligible residents, excepting those admitted to a hospital or an institution at the time of the survey, 1391 (97.3% of 1429) participated in the survey, and 1273 who were independent in ADL at baseline were followed as a cohort until September 2008, a period of approximately 3 years. Eight subjects moved out of the study area during follow-up; therefore, the associations between knee pain and the study outcomes were analyzed in 1265 residents (573 men, 692 women, follow-up rate: 99.4%). The median (range) age at baseline was 74 (65–97) years in men and 75 (65–98) years in women. The study was approved by the Medical Ethics Committee of the Keio University School of Medicine, Tokyo, Japan.

Evaluation of knee pain

Presence of knee pain was assessed using the following question in the home-visit survey, "Have you had pain in the last year in or around the knee?,"[17] with answer choices of "never," "occasionally," "often," and "always." This simple question seemed more suitable in a community setting than a complicated disease-specific instrument for measurement of knee pain, such as the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC).[18] Moreover, the English version of this question has been validated,[18] although the Japanese version has not. In addition, to determine if subjects had gone to a physician for treatment of their knee pain, we asked the question, "Have you had a medical consultation regarding knee pain in the last year?," with answer choices of "yes" or "no."

Outcome measurements

We defined dependence in ADL as either admission to a nursing home or need of assistance at home during the follow-up period. The latter was defined as long-term care (LTC) eligibility or a need for help in any of 6 basic ADL items on the Katz Index of Independence in ADL.[19]

LTC eligibility is a requirement for receiving LTC insurance services in Japan, which began in 2000. In this study, any of the 7 levels of LTC insurance services was considered LTC-eligible. However, not all residents who are dependent in ADL apply for LTC insurance services. We added the Katz ADL measures to address this possibility. The Katz ADL is based on self-reported performance levels for 6 basic ADL items (bathing, dressing, toileting, transferring, continence, and feeding), each of which has 3 answer options (without help, with partial help, with help). On the Katz ADL, dependence in ADL is defined as a need for partial or full help in performing any of the 6 items.

Information on death, nursing home admission, and LTC eligibility was obtained from the Kurabuchi Branch Office of Takasaki City Hall. Information on Katz ADL was obtained from repeat face-to-face home interviews conducted every year (in 2006, 2007, and 2008), and occurrence of ADL decline in any year was defined as an ADL decline.

Covariates

Information on age, sex, marital status (married vs widowed/separated/single), education (junior high vs high school or higher), support by relatives, neighbors, and friends (yes vs no), smoking status (current vs former/never), alcohol drinking (current vs former/never), and current/past history of major diseases, including stroke, myocardial infarction/angina, chronic obstructive pulmonary disease, diabetes mellitus, and cancer (summary answer of yes or no), was also collected at the baseline survey, because these factors have been reported to be related to the study outcomes.[8,20]

Statistical analyses

Stata 10.0 (Stata Corporation, College Station, TX, USA) was used for all analyses. Analyses were carried out by first conducting crude analyses, followed by multivariate analyses using logistic regression models. The initial basic model included only age (as a continuous variable) and sex. Then, the second and final models were constructed by adding marital status, education, smoking status, and current/past history of major diseases. There was no interaction between knee pain and medical consultation, and this was included in the model as an independent variable. Support by relatives, neighbors, and friends and alcohol drinking did not confound the observed association (the effect on the estimate was less

Table 1. Characteristics of the study population

	Knee pain				*P* value[a]
	Never (*n* = 667) No. (column %)	Occasionally (*n* = 303) No. (column %)	Often (*n* = 128) No. (column %)	Always (*n* = 167) No. (column %)	
Age group, yrs					
65–69	198 (29.7)	63 (20.8)	14 (10.9)	13 (7.8)	<0.001
70–79	315 (47.2)	153 (50.5)	69 (53.9)	87 (52.1)	
≥80	154 (23.1)	87 (28.7)	45 (35.2)	67 (40.2)	
Sex					
Male	337 (50.5)	131 (43.2)	50 (39.1)	55 (32.9)	<0.001
Female	330 (49.5)	172 (56.8)	78 (60.9)	112 (67.1)	
Marital status					
Married	489 (73.6)	193 (64.3)	83 (65.9)	100 (60.6)	0.001
Widowed/separated/single	175 (26.4)	107 (35.7)	43 (34.1)	65 (39.4)	
Education					
Junior high school	502 (75.7)	241 (80.6)	99 (78.0)	144 (86.8)	0.014
High school or higher	161 (24.3)	58 (19.4)	28 (22.0)	22 (13.3)	
Consultation due to knee pain					
Yes	0 (0.0)	85 (28.1)	67 (52.3)	119 (71.3)	<0.001
No	659 (100.0)	217 (71.9)	61 (47.7)	48 (28.7)	
History of major disease[b]					
Yes	177 (26.7)	84 (27.9)	41 (32.3)	52 (31.5)	0.448
No	485 (73.3)	217 (72.1)	86 (67.7)	113 (68.5)	
Current smoking					
Yes	164 (24.6)	78 (25.8)	25 (19.7)	36 (21.7)	0.482
No	503 (75.4)	224 (74.2)	102 (80.3)	130 (78.3)	
Current alcohol drinking					
Yes	238 (36.2)	118 (39.3)	41 (32.5)	45 (27.8)	0.079
No	419 (63.8)	182 (60.7)	85 (67.5)	117 (72.2)	

[a]On χ^2 test.
[b]Stroke, myocardial infarction/angina, chronic obstructive pulmonary disease, diabetes mellitus, or cancer.
Due to missing values, the totals of stratified subgroups are not equal.

than 10%[21]) and were thus not included in the model. Because there was no interaction by sex, all analyses were carried out with combined data for men and women. This analytic method was repeated for dependence in ADL, for the single outcome of mortality, and for the composite outcome of dependence in ADL and death. In the analysis of dependence in ADL, residents who died during the follow-up period were excluded. Finally, we analyzed each component of ADL dependence, including institutionalization, LTC eligibility, and the 6 items on the Katz basic ADL. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to describe the strength of associations. Goodness of fit of all logistic models was assessed and confirmed by using the Hosmer–Lemeshow goodness-of-fit statistic (*P* values, 0.604–0.761).[22]

RESULTS

The characteristics of the study population by knee pain status are shown in Table 1. A total of 667 (52.7%), 303 (24.0%), 128 (10.1%), and 167 (13.2%) participants reported never, occasionally, often, and always having knee pain, respectively. Furthermore, among the latter 3 groups, 28.1%, 52.3%, and 71.3%, respectively, reported seeking treatment from a physician for their knee pain. Participants who always had knee pain tended to be older, female, unmarried, and less educated than those in other categories. There was no difference among groups in history of major diseases, smoking status, or alcohol drinking.

Table 2 summarizes the associations of knee pain with the study outcomes. During the 3-year follow up, 109 participants died and 126 became dependent in ADL; thus, 235 in total (18.6% of 1265) experienced a study outcome. As the frequency of knee pain increased, the odds of being dependent in ADL increased. Those who always had knee pain were almost twice as likely to experience dependence in ADL as those who never had knee pain, even after adjustment for potential confounders (adjusted OR, 1.98; 95% CI, 1.03–3.83). Always having knee pain was associated with the composite outcome of ADL dependence and death in the crude analysis; however, after adjusting for covariates, the odds ratio became statistically insignificant. Knee pain was not associated with mortality. Requesting treatment from a physician for knee pain was not related to any outcome in this study population.

The association between knee pain and each component of dependence in ADL was further examined (Figure). Among 126 subjects who were dependent in ADL, 36 were institutionalized. Of the remaining 90 who needed assistance at home, 76 were LTC-eligible and 48 were judged as dependent using the Katz index (35 in bathing, 27 in dressing, 17 in transferring, 18 in toileting, 27 in continence, and 7

Table 2. Association of knee pain with dependence in activities of daily living (ADL) and death

	No. (%)	Crude OR (95% CI)	Age- and sex-adjusted OR (95% CI)	Multivariate-adjusted OR[a,b] (95% CI)
Dependence in ADL[c]				
Never	57/609 (9.4)	1.00	1.00	1.00
Occasionally	22/279 (7.9)	0.83 (0.50–1.39)	0.61 (0.35–1.06)	0.64 (0.36–1.16)
Often	14/116 (12.1)	1.33 (0.71–2.47)	0.83 (0.42–1.63)	0.89 (0.42–1.88)
Always	33/152 (21.7)	2.69 (1.67–4.31)	1.84 (1.10–3.08)	1.98 (1.03–3.83)
Death				
Never	58/667 (8.7)	1.00	1.00	1.00
Occasionally	24/303 (7.9)	0.90 (0.55–1.48)	0.74 (0.44–1.26)	0.75 (0.43–1.33)
Often	12/128 (9.4)	1.09 (0.57–2.09)	0.81 (0.40–1.63)	0.76 (0.35–1.67)
Always	15/167 (9.0)	1.04 (0.57–1.88)	0.83 (0.44–1.56)	0.72 (0.32–1.61)
Death and dependence in ADL				
Never	115/667 (17.2)	1.00	1.00	1.00
Occasionally	46/303 (15.2)	0.86 (0.59–1.25)	0.64 (0.42–0.97)	0.67 (0.43–1.04)
Often	26/128 (20.3)	1.22 (0.76–1.97)	0.84 (0.50–1.43)	0.85 (0.47–1.52)
Always	48/167 (28.7)	1.94 (1.31–2.86)	1.45 (0.94–2.23)	1.46 (0.84–2.54)

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Model included age, sex, marital status, education, medical consultation, current/past history of major disease, and smoking.
[b]Due to missing data, only 1125 subjects for dependence in ADL and 1227 for death or composite outcome were included in the analyses.
[c]Participants who died during follow-up were excluded from this analysis.

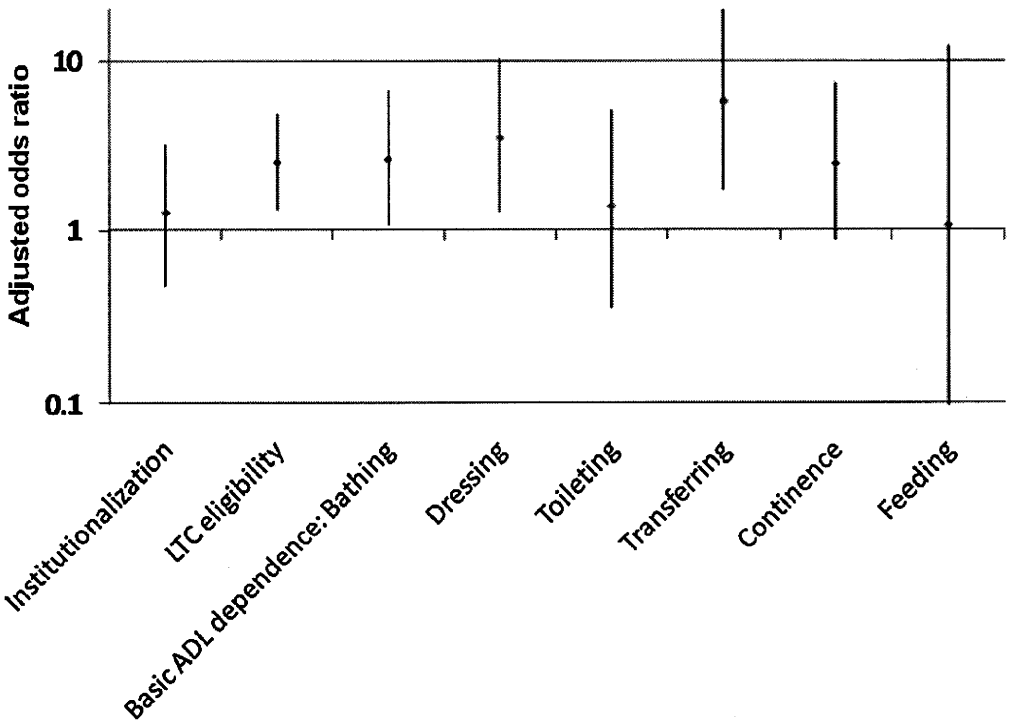

Figure. Multivariate-adjusted odds ratios and 95% confidence intervals for always having knee pain as compared with never/occasionally/often having knee pain were plotted using a logarithmic scale, after adjusting for age, sex, marital status, education, medical consultation, current/past history of major disease, and smoking. Participants who died during follow-up were excluded. Additionally, participants who were institutionalized during follow-up were excluded from the estimation of odds ratios of LTC eligibility and basic ADL dependence on the Katz ADL.

in feeding, with some participants dependent in more than 1 activity). In this analysis of a smaller number of event occurrences, "never," "occasionally," and "often" were grouped together because there was no difference in the risk of ADL dependence, as shown in Table 1. As compared with never/occasionally/often having knee pain, always having knee pain was associated with LTC eligibility (adjusted OR, 2.61; 95% CI, 1.34–5.07) and dependence in bathing (2.71, 1.08–6.82), dressing (3.65, 1.30–10.28), and transferring (5.90, 1.78–19.50).

DISCUSSION

Knee pain was clearly associated with dependence in ADL, but not with the single endpoint of mortality or the composite outcome of dependence in ADL and death. To minimize bias, much attention was placed on attaining high representation and a high follow-up proportion. Another strength of this study is that many potential confounders were included in the analysis. To the best of our knowledge, this is the first community-based epidemiological study of the association of knee pain with dependence in ADL and mortality.

Participants who reported always having knee pain were more likely to become ADL-dependent. This result was in line with earlier studies, which reported a clear association of knee pain with functional decline in ambulatory activities.[6,23] Constant pain, regardless of whether the individual seeks medical treatment, can be a good marker of future dependence in ADL. This marker requires only one, simple question and can be very useful in both clinical and community settings. Further analyses revealed that knee pain was associated with need of assistance at home, but not with institutionalization. Bathing and transferring undoubtedly require mobility/ muscular strength of the lower extremities; dressing may involve walking to get clothes from a closet.[19] Thus, the association of a need for assistance in these activities with knee pain was expected. It should also be noted that this is, to the best of our knowledge, the first report to assess the relationship between LTC eligibility and knee pain. Information revealed by our study on future care needs should be useful for caregivers. However, because we were unable to consider multiple comparisons in this analysis, caution is warranted in interpreting the present results.

Knee pain was not associated with an increased risk of death. Although the lack of an association between knee pain and mortality has previously been reported,[24] such a result is counterintuitive because ADL dependence is generally a good predictor of mortality.[25,26] Indeed, in the present study, knee pain tended to be inversely associated with mortality. A possible explanation for this finding is that 71% of subjects with knee pain were regularly consulting physicians for this complaint, thus increasing the chance that risk factors for mortality, such as hypertension and hyperlipidemia, would be detected and treated early. In any event, further studies with longer follow-up periods are needed to elucidate the association between knee pain and death.

The present study illustrates how knee pain plays a key role in the self-reliance of older adults and highlights the importance of preventing knee pain. The effect of exercise in alleviating knee pain has been reported.[27,28] Enlightenment of the general public regarding the importance of preventing musculoskeletal problems, and knee pain in particular, should be continued and even expanded. Our findings also suggest that intervention programs that foster self-reliance should be aimed at older people with knee pain. In fact, exercise programs for reducing knee pain are cited in the preventive approach manual issued in conjunction with LTC insurance services. However, the checklist used for screening candidates does not include the presence of knee pain itself, although it does include mobility limitation.

A limitation of this study is that knee pain was assessed at only 1 time point, and the course of pain was not evaluated. In a Dutch study, 44% of patients presenting to a general practice with knee complaints recovered within 12 months.[29] The difference in knee pain prognosis after treatment is an important issue that requires further study. Another limitation in the present study is the possibility of confounding by unmeasured factors, such as body mass index and occupation. Overweight in particular can be a risk factor for future ADL dependence,[30,31] so further discussion of this variable is needed. If overweight is the result of inactivity due to knee pain, it should not be included in models as a covariate. However, Kondo et al suggested that overweight precedes knee OA and is a predictor of stair-climbing limitation rather than an outcome of knee OA.[11] Because overweight is sometimes associated with ADL dependence through pathways other than knee pain, eg, hip pain or ankle pain, adjustment for overweight is necessary, and the OR observed in this study might thus have been overestimated. However, Lamb et al suggested that overweight modified the association between knee pain and mobility limitation.[32] Obviously, in such a case, analysis stratified by BMI category would be appropriate. Furthermore, relatively crude classification of a covariate such as education category might cause residual confounding. Also, we could not determine whether knee pain resulted from OA, rheumatoid arthritis, or other causes.

In conclusion, after nearly perfect follow-up of participants that were highly representative of the target population, we found that knee pain was clearly associated with dependence in ADL, and with a need for assistance at home (LTC-eligibility, bathing, dressing, and transferring) in particular, but not with the single endpoint of mortality or the composite outcome of dependence in ADL and death.

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