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same individuals over several decades. He found that only a certain proportion of subjects who had with-the-rule astigmatism in their youth changed to against-the-rule astigmatism by way of oblique astigmatism. However, there is no report that certifies the relation between previously reported factors and the change in corneal astigmatism. Therefore, further longitudinal studies on the age-related change in corneal astigmatism are required to investigate related factors of previous hypotheses.

Although much information on the prevalence of refractive errors with aging is available,[19] little is known about decreased vision caused by undercorrection of refractive error. Liou et al.[14] and our group[15] reported that the most frequent cause of visual impairment in daily living is undercorrected refractive error. Weih et al.[47] also reported that uncorrected refractive error was the most common cause of bilateral visual impairment among individuals 40 years of age and older, rising from 0.5% in 40- to 49-year-olds to 13% among 80-year-olds and older. Visual acuity is considered to be important, especially in the elderly, because it is associated with activities of daily living.[12] The undercorrected refractive errors may include undercorrected astigmatism. In the present study, the prevalence of either total astigmatism or corneal astigmatism ≧0.5 D was nearly 90%, and that of astigmatism ≧2.0 D was nearly 20% in the eldest age group. However, elderly people are less likely to have regular ocular examinations than younger people. Thus, the elderly may unknowingly have various degrees of visual impairment, and decreased mobility, quality of life, and independence are consequences of such impairment. Therefore, it is necessary to treat decreased vision due to astigmatism to improve their daily life.

In this cross-sectional study, we evaluated age-related astigmatic change by the polar value method[30] in Japanese residents over the age of 40 in small communities. Our conclusion is that the age-related change is mainly associated with changes in the cornea. The findings in this study add some useful information to our knowledge of astigmatic refractive errors and refractive error development. We consider these findings to be important for further investigation of the relationship between visual function and other functions such as physical or psychosocial functions. Also, these age-related astigmatic changes need to be taken into consideration in order to minimize postoperative astigmatism induced by cataract or corneal refractive surgery.

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References

1. Tielsch JM, Sommer A, Witt K, Katz J, Royall RM. Blindness and visual impairment in an American urban population. The Baltimore Eye Survey. Arch Ophthalmol 1990;108:286–290.
2. Klein R, Klein BE, Linton KL, De Mets DL. The Beaver Dam Eye Study: visual acuity. Ophthalmology 1991;98:1310–1315.
3. Attebo K, Mitchell P, Smith W. Visual acuity and the causes of visual loss in Australia. The Blue Mountains Eye Study. Ophthalmology 1996;103:357–364.
4. Klaver CC, Wolfs RC, Vingerling JR, Hofman A, de Jong PT. Age-specific prevalence and causes of blindness and visual impairment in an older population. The Rotterdam Study. Arch Ophthalmol 1998;116:653–658.
5. Marsiske M, Klumb P, Baltes MM. Everyday activity and sensory functioning in old age. Psychol Aging 1997;12:444–457.
6. Klein BE, Klein R, Lee KE, Cruickshanks KJ. Performance-based and self-assessed measures of visual function as related to history of falls, hip fractures, and measured gait time. The Beaver Dam Eye Study. Ophthalmology 1998;105:160–164.
7. Wang JJ, Mitchell P, Smith W, Cumming RG, Attebo K. Impact of visual impairment on use of community support services by elderly persons: the Blue Mountains Eye Study. Invest Ophthalmol Vis Sci 1999;40:12–19.
8. Lee PP, Smith JP, Kington RS. The associations between self-related vision and hearing and functional status in middle age. Ophthalmology 1999;106:401–405.
9. Lee PP, Spritzer K, Hays RD. The impact of blurred vision on functioning and well-being. Ophthalmology 1997;104:390–396.
10. Uhlmann RF, Larson EB, Koepsell TD, Rees TS, Duckert LG. Visual impairment and cognitive dysfunction in Alzheimer's disease. J Gen Intern Med 1991;6:126–132.
11. Lindenberger U, Baltes PB. Sensory functioning and intelligence in old age: a strong connection. Psychol Aging 1994;9:339–355.
12. Rubin GS, West SK, Munoz B, et al. A comprehensive assessment of visual impairment in a population of older Americans. The SEE study. Salisbury Eye Evaluation Project. Invest Ophthalmol Vis Sci 1997;38:557–568.
13. Tielsch JM, Javitt JC, Coleman A, Katz J, Sommer A. The prevalence of blindness and visual impairment among nursing home residents in Baltimore. N Engl J Med 1995;332:1205–1209.
14. Liou HL, McCarty CA, Jin CL, Taylor HR. Prevalence and predictors of undercorrected refractive errors in the Victorian population. Am J Ophthalmol 1999;127:590–596.
15. Nomura H, Asano K, Tanabe N, et al. Presenting and best-corrected visual acuity in Japanese over forty years of age. Rinsho Ganka (Jpn J Clin Ophthalmol) 2002;56:293–296.
16. McKendrick AM, Brennan NA. Distribution of astigmatism in the adult population. J Opt Soc Am A 1996;13:206–214.
17. Gudmundsdottir E, Jonasson F, Jonsson V, Stefánsson E, Sasaki H, Sasaki K, the Iceland–Japan Co-Working Study Groups. "With the rule" astigmatism is not the rule in the elderly. Reykjavik Eye Study. Acta Ophthalmol Scand 2000;78:642–646.
18. Jackson E. Norm of Refraction. JAMA 1932;9:132–137.
19. Katz J, Tielsch JM, Sommer A. Prevalence and risk factors for refractive errors in an adult inner city population. Invest Ophthalmol Vis Sci 1997;38:334–340.
20. Wong TY, Foster PJ, Hee J, et al. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. Invest Ophthalmol Vis Sci 2000;41:2486–2494.
21. Saunders H. Age-dependence of human refractive errors. Ophthalmic Physiol Opt 1981;1:159–174.
22. Saunders H. A longitudinal study of the age-dependence of human ocular refraction. III. The mediation of changes from direct to inverse astigmatism examined by means of matrices of transition probabilities. Ophthalmic Physiol Opt 1987;7:175–186.
23. Leighton DA, Tomlinson A. Changes in axial length and other dimensions of the eyeball with increasing age. Acta Ophthalmol 1972;50:815–826.
24. Fledelius HC. Prevalences of astigmatism and anisometropia in adult Danes. Acta Ophthalmol 1984;62:391–400.
25. Saunders H. Changes in the orientation of the axis of astigmatism associated with age. Ophthalmic Physiol Opt 1986;6:343–344.
26. Saunders H. A longitudinal study of the age-dependence of human ocular refraction. I. Age-dependent changes in the equivalent sphere. Ophthalmic Physiol Opt 1986;6:39–46.

27. Fledelius HC, Stubgaard M. Changes in refraction and corneal curvature during growth and adult life. A cross-sectional study. Acta Ophthalmol 1986;64:487–491.
28. Saunders H. Changes in the axis of astigmatism. A longitudinal study. Ophthalmic Physiol Opt 1988;8:37–42.
29. Lam AK, Chan CC, Lee MH, Wong KM. The aging effect on corneal curvature and the validity of Javal's rule in Hong Kong Chinese. Curr Eye Res 1999;18:83–90.
30. Naeser K. Conversion of keratometer readings to polar values. J Cataract Refract Surg 1990;16:741–745.
31. Kamiya S. Age-dependence of human corneal astigmatism and corneal radius. Nihon Ganka Kiyo (Folia Ophthalmol Jpn) 1984;35: 2011–2018.
32. Hayashi K, Masumoto M, Fujino S, Hayashi F. Change in corneal astigmatism with aging. Nippon Ganka Gakkai Zasshi 1993;97: 1193–1196.
33. Shimokata H, Ando F, Niino N. A new comprehensive study on aging—the National Institute for Longevity Sciences, Longitudinal Study of Aging (NILS-LSA). J Epidemiol 2000;10:S1–9.
34. Nomura H, Tanabe N, Nagaya S, Ando F, Niino N, Miyake Y, Shimokata H. Eye examinations at the National Institute for Longevity Sciences–Longitudinal Study of Aging: NILS-LSA. J Epidemiol 2000;10:S18–25.
35. Attebo K, Ivers RQ, Mitchell P. Refractive errors in an older population: the Blue Mountains Eye Study. Ophthalmology 1999;106: 1066–1072.
36. SAS language guide for personal computers, version 6.03. Cary, NC, USA: SAS Institute, 1988.
37. Thompson JR, Gibson JM, Jagger C. The association between visual impairment and mortality in elderly people. Age Aging 1989; 18:83–88.
38. Klein BE, Klein R, Linton KL. Prevalence of age-related lens opacities in a population. The Beaver Dam Eye Study. Ophthalmology 1992;99:546–552.
39. Toulemont PJ. Multivariate analysis versus vector analysis to assess surgically induced astigmatism. J Cataract Refract Surg 1996;22: 977–982.
40. Naeser K, Behrens JK. Correlation between polar values and vector analysis. J Cataract Refract Surg 1997;23:76–81.
41. Naeser K, Hjortdal J. Multivariate analysis of refractive data. Mathematics and statistics of spherocylinders. J Cataract Refract Surg 2001;27:129–142.
42. Naeser K, Hjortdal J. Polar value analysis of refractive data. J Cataract Refract Surg 2001;27:86–94.
43. Marin-Amat MM. Les variations physiologiques de la courbure de la cornée pendant la vie. Leur importance et transcendance dans la réfraction oculaire. Bull Soc Belge Ophtalmol 1956;113:251–293.
44. Mori I, Handa T, Mukuno K, et al. Effect of extraocular muscles on the aging shift in corneal astigmatism. Atarashii Ganka (J Eye) 2002;19:1345–1347.
45. Duke-Elder S. Simple refractive errors. In: Duke-Elder S, editor. System of ophthalmology. Vol. V. Ophthalmic optics and refraction. London: Henry Kimpton; 1970. p. 254–295.
46. Waardenburg PJ. Total refraction and the variability of its individual components. In: Waardenburg PJ, editor. Genetics and ophthalmology. Vol. II. Neuro-ophthalmological part. Oxford: Blackwell Scientific; 1963. p. 1201–1286.
47. Weih LM, VanNewkirk MR, McCarty CA, Taylor HR. Age-specific causes of bilateral visual impairment. Arch Ophthalmol 2000;118: 264–269.

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中高年者における余暇身体活動および青年期の運動経験と骨密度との関連

Relationship of bone mineral density with leisure-time physical activity and adolescent exercise in the middle-aged and elderly

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Purpose: The aim of this study was to assess the relationships of bone mineral density (BMD) with current leisure-time physical activity (LTPA) and adolescent exercise (AEX) among the middle-aged and elderly in Japan.
Methods: The data for the present study were derived from the baseline data of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA). Subjects consisted of 1017 male (58.5±10.8 years) and 577 postmenopausal female (62.6±8.4 years). Those who had osteoporosis, rheumatoid arthritis or cancer were excluded from the subjects. Those who used thyroid hormone or parathyroid hormone were also excluded. Subjects were interviewed about their physical activity habits during leisure time throughout the past twelve months and about exercise they engaged in during adolescence (12 to 20 years). Subjects were divided into 3 groups according to the intensity of LTPA, 'no LTPA', 'light LTPA' and 'moderate or heavy LTPA'. They were also divided into 2 groups, with or without AEX. BMD was measured with a dual energy X-ray absoptiometry (DXA; Hologic QDR-4500A), in g/cm^2. Measurement sites were the whole body (WT), L2-L4 lumber spine (L24), femur neck (FN), Ward's triangle (WT), and trochanter (TR). Relationships of BMD with LTPA and AXE were analyzed using analysis of covariance controlled for age, height and weight. Significant probability levels were less than 0.05.
Results: Average BMD (SD) at WB, L24, FN, WT, TR were 1.09(0.10), 0.99(0.16), 0.76(0.11), 0.56(0.13), 0.67(0.11) in male and 0.93(0.11), 0.82(0.16), 0.66(0.10), 0.47(0.14), 0.55(0.10) in female, respectively. The proportion of subjects with LTPA was 75.5% in male and 67.7% in female. The subjects that engaged in AEX represented 65.7% in male and 39.5% in female. The result of analysis of covariance controlled for age, height and weight was as follows; in male, LTPA showed significant main effect on BMD at FN, WT and TR. AEX showed significant main effect on BMD at all sites. However, there was no interaction effect on BMD at all sites. As for female, LTPA showed significant main effect on BMD at FN and TR. AEX showed significant main effect on BMD at TR. There was a significant interaction effect on BMD at WB and FN.
Conclusion: The results suggested that not only current leisure-time physical activity but also adolescent exercise benefits bone mineral density among middle-aged and elderly people in Japan.

1．緒言

我が国の高齢者における寝たきりの原因の第2位は転倒による骨折であり[14]、骨折は高齢者の自立を妨げ、生活の質（Quality of life; QOL）を脅かす要因の一つと考えられている。また、高齢者に多くみられる骨密度の低下による骨折は脆弱性骨折と呼ばれ、World Health Organization（WHO）では、骨密度（Bone Mineral

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Density; BMD）が若年成人平均値（Young Adult Mean; YAM）の−2.5SD以下であると脆弱性骨折が急増することを報告している[22]。従って、中高年期における骨密度低下の要因を明らかにし、その予防法を確立することは高齢社会における急務の課題と考えられる。

骨密度の低下には、年齢や性あるいは遺伝的因子など制御できない要因の影響が大きいとされる一方、運動、栄養、嗜好などの生活習慣や日照時間などの環境因子など制御可能な要因も影響するといわれる[7]。運動については、運動不足など身体活動量の減少が骨密度低下の危険因子とされており、骨粗鬆症の予防には運動が推奨されている[7]。しかし、骨密度増加に対する運動介入の効果は多く確認されているものの[10),12),13)]、日常生活における運動習慣と骨密度との関連については、運動により骨密度が増加したという報告[3),6),27)]に対し、骨密度は変化しなかったという報告もみられ[4),5)]、一致した結論に至っていない。

一方、中高年期の骨量には若年期の骨密度（peak bone mass）も影響を与える。骨は成長期に著しく発達して骨量のピークに達することから、この時期にピークをいかに高めるかは、それ以降の骨密度を予測する上で重要な因子と考えられている[26)]。運動は成長期においても骨密度増加と関連することが報告されており[15),16),20)]、現在の運動習慣だけでなく、青年期の運動習慣も併せて検討することは、中高年期の骨密度低下の予防を考える上で重要なことと思われる。

そこで、本研究では地域在住中高年者の日常生活における余暇身体活動状況および青年期の運動と骨密度を調べ、各々の身体活動と骨密度との関連について横断的に検討することを目的とした。

2．方法

対象

本研究は、国立長寿医療センター疫学研究部が行う「老化に関する長期縦断疫学調査（National Institute for Longevity-Longitudinal Study of Aging; NILS-LSA）」の一環として行われた。NILS-LSAは、老化および老年病の予防法の確立や機序の解明を目的に、医学、形態学、栄養学、心理学、運動生理学などの分野から調査、検討を行う学際的な研究である。詳細は他論文を参照にされたい[25)]。NILS-LSAの参加者は、国立長寿医療センター周辺の愛知県大府市、東浦町に在住する地域住民より性・年代別に層化無作為抽出された人の中で、調査・検査内容とその継続の意義を十分に理解し、文書による了承（インフォームドコンセント）の得られた40〜79歳までの男女2267名である。本研究では、調査参加者の中から骨密度に影響すると考えられる疾患（骨粗鬆症、リュウマチ・関節炎、がん）や服薬（甲状腺・副甲状腺ホルモン剤）のない男性1017名（平均年齢58.5±10.8歳）、閉経後の女性577名（平均年齢62.6±8.4歳）について検討した。尚、NILS-LSAは、「疫学調査に関する倫理指針」を遵守し、国立長寿医療センター倫理委員会の承諾を受けた上で実施されている。

測定項目

骨密度（Bone mineral density; BMD, g/cm^2）は、Dual energy X-ray absoptiometry（DXA：Hologic社製、QDR-4500A）を用いて測定した。測定部位は、全身（Whole Body; WB）、腰椎L2-4（Lumber2-4; L24）、右下肢の大腿骨頸部（Funeral Neck; FN）、ワード三角（Word Triangle; WT）、大転子部（Trochanter Region; TR）とした。骨密度測定において、別に行った再現性の検討では、10名の被験者（男性6名、女性4名、平均年齢38.3±6.8歳）に対し、測定を3回繰り返した際の各測定項目の変動係数（coefficient of variation; CV）は、WB＝0.9%、L24＝0.9%、FN＝1.3%、WT＝2.5%、TR＝1.0%であった。

身体活動量は、余暇身体活動（Leisure-time physical activity; LTPA）と青年期の運動経験（Adolescent exercise; AEX）について質問票を用いた聞き取り調査を行った[11)]。余暇身体活動は、過去1年間に余暇時間に定期的な身体活動（週1回、1回10分以上）を行ったかを聞き取り、その活動内容を「低強度＝2.5METs（metabolic equivalents）程度」、「中強度＝4.5METs程度」、「高強度＝6.5METs以上程度」に分類した。青年期の運動経験は、12—20歳の間にクラブ活動などで定期的な運動（週1回、1年以上）を行ったか否かを調べた。

対象者の基礎的身体特性として、身長、体重を測定し、体重を身長の二乗で除したBody Mass Index（BMI; kg/m^2）を算出した。体脂肪率および除脂肪量は、骨密度と同じくDXAにて測定した。

統計解析

骨密度は性別に平均値を算出した。現在の余暇身体活動および青年期の運動と骨密度の関連を検討するために、余暇身体活動のレベルを、「活動を行っていなかったもの＝LTPA（N）」、「低強度の活動のみを行っていたもの＝LTPA（L）」、「中強度以上の活動を行っていたもの＝LTPA（H）」の3段階、青年期の運動経験を、「なし＝AEX（−）」、「あり＝AEX（+）」の2段階に分け、各骨密度への余暇身体活動および青年期の運動の影響について年齢、身長、体重を調整変数とした共分散分析を行った。尚、余暇身体活動レベルについては、高

強度の活動に従事した人の数が少なかったため、中強度の活動に従事した人と合わせてLTPA（H）とした。解析にはSAS（Statistical Analysis System, release.8.2）を用い[24]、有意水準はすべて5％未満とした。

3．結果

対象者の身体特性はTable 1に、DXAで測定した部位別の骨密度はTable 2に示した。本研究の対象者の骨密度は、日本骨粗鬆学会の提示する骨密度の各性・年代別標準値と大きな差は認めなかった[19]。

強度別の余暇身体活動および青年期の運動に従事した者の割合は、Table 3に示した。過去1年間に余暇身体活動に従事したものは男性で75.5%、女性で67.7%であった。強度別の余暇身体活動従事者の割合をみると、低強度のみの活動に従事していた人は男性30.5%、女性33.8%、中強度以上の活動に従事していた人は男性45.0%、女性33.9%であった。男性は女性に比べ強度の高い余暇身体活動に参加する人の割合が高かった。一方、青年期の運動経験のある者は、男性65.7%、女性39.5%であり、女性は男性に比べ青年期の運動経験のある人の割合が低かった。

余暇身体活動および青年期の運動と各部位の骨密度との関連を検討するために、余暇身体活動レベルをLTPA（N）、LTPA（L）、LTPA（H）の3段階、青年期の運動をAEX（−）、AEX（+）の2段階に分け、年齢、身長、体重を調整変数とした共分散分析を行った。その結果、男性では、余暇身体活動の主効果はFN、WT、TRの大腿骨近位部において有意であり、青年期の運動の主効果は全ての部位において有意であった。余暇身体活動と青年期の運動との交互作用は、いずれの部位にもみとめられなかった（Table 4）。男性において、余暇身体活動のレベルの高い人は大腿骨近位部の骨密度の高いこと、青年期の運動経験のある人は測定した全ての部位において骨密度の高いことが示された。女性では、余暇身体活動の主効果はFNとTRにおいて有意であり、青年期の運動の主効果はTRにおいて有意であった。余暇身体活動と青年期の運動の交互作用は、WBとFNにおいて有意であった（Table 5）。女性において、余暇身体活動レベルの高い人は大腿骨頸部と大転子部の骨密度が高く、青年期の運動経験のある人は大転子部の骨密度の高いことが示された。女性ではさらに、全身と大腿骨頸部において青年期の運動経験の有無により余暇身体活動レベルと骨密度との関連に差のあることが示され、青年期の運動経験のないものは余暇身体活動レベルの高いもので骨密度の高い傾向が認められたが、運動経験のあるものではその傾向は認められなかった。

余暇身体活動および青年期の運動と骨密度との関連は、性や部位により異なったものの、大腿骨近位部、特に大転子部においては男女に共通して各々の身体活動の高いもので骨密度の高いことが認められた（Fig. 1）。

Table 1. Charactaristics of the subjects

		Male	Postmenopausal female
Height	(cm)	164.8±6.3	150.7±6.0
Weight	(kg)	62.4±9.1	52.0±8.4
BMI	(kg/m^2)	22.9±2.8	22.9±3.3
% Body fat	-	21.3±4.3	32.1±5.0
Fat free mass	(kg)	49.2±5.9	35.4±4.3

Mean±S.D.

Table 2. The average of bone mineral density (BMD) at each site in boch genders

	BMD (g/cm^2)	
site	Male	Postmenopausal female
Whole Body	1.09±0.10	0.93±0.11
Lumber 2-4	0.99±0.16	0.82±0.15
Femoral neck	0.76±0.11	0.66±0.10
Ward Triangle	0.56±0.13	0.47±0.14
Trochanter Region	0.67±0.11	0.55±0.10

Mean ± S.D.

Table 3. The participation rates of LTPA and AEX

	Levels	Male	Postmenopausal female
LTPA	Total†	75.5	67.7
	Light	30.5	33.8
	Moderate and Heavy	45.0	33.9
AEX	Total†	65.7	39.5

Note. †total number of the subjects who participated in LTPA or AEX. LTPA, leisure-time physical activity; AEX, adolescence exercise. Values are expressed in percentage.

Table 4. The analysis of covariance controlled for age, height and weight in male

Male	WB		L24		FN		WT		TR	
	df	F value	df	F value	df	F value	df	F value	df	F value
LTPA	2	1.66	2	0.27	2	**5.65***	2	**5.15***	2	**4.96***
AEX	1	**6.21***	1	**12.90***	1	**4.42***	1	**5.93***	1	**15.59***
LTPA×AEX	2	1.11	2	0.55	2	1.79	2	1.86	2	0.80
Age	1	8.09*	1	11.07*	1	26.22*	1	122.31*	1	0.45
Height	1	0.44	1	5.13*	1	0.76	1	1.77	1	12.71*
Weight	1	73.03*	1	141.54*	1	184.34*	1	91.91*	1	217.78*
error	1008		1007		1007		1007		1007	
r^2	0.15		0.15		0.29		0.30		0.24	

Note. LTPA, leisure-time physical activity; AEX, adolescence exercise; WB, Whole body; L24, Lumber2-4; FN, Femoral Neck; WT, Ward Triangle; TR, Trochanter region. *p <0.05

Table 5. The analysis of covariance controlled for age, height and weight in postmenopausal female

Female	WB		L24		FN		WT		TR	
	df	F value	df	F value	df	F value	df	F value	df	F value
LTPA	2	0.70	2	0.70	2	**3.14***	2	1.98	2	**3.98***
AEX	1	1.02	1	1.42	1	2.81	1	2.10	1	**6.40***
LTPA·AEX	2	**3.50***	2	0.71	2	**4.55***	2	2.13	2	2.31
Age	1	232.89*	1	89.64*	1	162.37*	1	245.02*	1	149.47*
Height	1	2.23	1	0.01	1	1.11	1	2.85	1	7.42*
Weight	1	19.57*	1	86.31*	1	92.60*	1	42.12*	1	120.05*
error	566		566		564		564		564	
r^2	0.43		0.34		0.42		0.42		0.42	

Note. LTPA, leisure-time physical activity; AEX, adolescence exercise; WB, Whole body; L24, Lumber2-4; FN, Femoral Neck; WT, Ward Triangle; TR, Trochanter region. *p <0.05

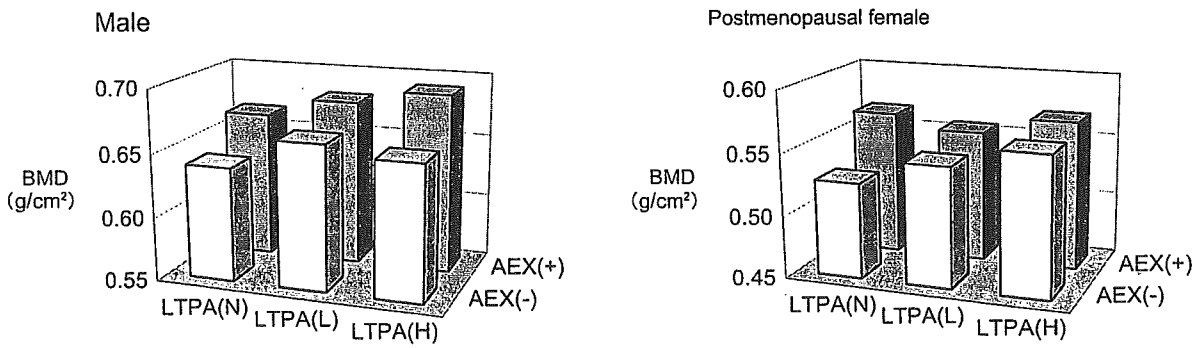

Fig. 1. The relationships of LTPA and AEX with BMD at TR controlled for age, height and weight deviding by gender. LTPA(N), no leisure-time physical activity; LTPA(L), light leisure-time physical activity; LTPA(H), moderate and heavy leisure-time physical activity; AEX(–), without adolescent exercise; AEX(+), with adolescent excercise; BMD, bone mineral density, TR, trochanter region.

4．考察

本研究では、地域在住中高年者における現在の余暇身体活動状況および青年期の運動経験と骨密度を調べ、各々の身体活動と骨密度との関連について、年齢や体格を調整した検討を行った。その結果、男女ともに余暇身体活動のレベルの高いもので大腿骨近位部の骨密度の高いこと、青年期の運動経験のあるもので男性における全ての部位の骨密度、および女性における大転子部の骨密度の高いことが示された。

余暇身体活動と大腿骨の骨密度との関連が認められたことは、Vuillemin らの健康な高齢男女を対象とした報告[27]や閉経女性を対象とした Blanchet らの報告を支持する結果である[3]。身体活動は大腿骨への力学的あるいは筋肉の収縮による負荷により、この部位の骨密度の維持向上に関連したと考えられた。

これまで、運動習慣と骨密度との関連が先行研究[4),5)]において明確でなかった理由の一つには、身体活動の定量や分類方法が異なることがあげられる。Coupland らは、閉経女性における歩行と骨密度との関連の検討から、骨密度は歩行量よりも歩行速度との関連の強いことを示し[5]、骨密度は活動の量よりも強度に依存することを示唆した。また Kerr らは、12ヶ月の運動介入の研究において低負荷・高頻度のトレーニングに比べ、高負荷・低頻度の活動でより骨密度の高まることを報告し、骨密度に対する強度の高いトレーニングの有効性を示した[13]。本研究では余暇身体活動の分類に、metabolic equivalents（METs）を指標として用いた。METs は、酸素摂取量を基準とした強度設定であるため[2]、加重負荷の程度は明確ではないが、METs により分類された活動内容をみると、低強度では散歩や庭仕事などが含まれたのに対し、中強度以上の活動ではスポーツ活動などが含まれた。従って、本研究の活動分類は加重負荷の強弱をある程度反映しており、余暇身体活動レベルによる骨密度の違いに結びついたと考えられた。

余暇身体活動と骨密度との関係が部位により異なった点、すなわち全身や腰椎、女性におけるワード三角部の骨密度と余暇身体活動との関連が認められなかった点については、次のような理由があげられる。大腿骨近位部は運動の影響を受けやすく[10),13)]、特に最近の身体活動が反映しやすい部位であることが指摘されている[27]。本研究では女性において特に骨量低下の危険性の高い閉経女性に関して検討を行ったが、NILS-LSA の未閉経女性においても大腿骨近位部でのみ余暇身体活動との関連が認められた（データ未発表）。そのため、大腿骨近位部では全身や腰椎に比べ現在の余暇身体活動の効果が表れやすかったと考えられた。一方、腰椎は加齢に伴い骨や血管の石灰化を起こしやすい部位とされており[18]、70歳以上の人も多く含む本研究の対象者においては、このような見かけ上の骨密度の高さが腰椎において、また全身において身体活動の影響を捉えにくくしたことが考えられた。女性のワード三角部については、骨の構成要素による説明が考えられる。ワード三角部は皮質骨に比べ海面骨の割合が高く、海面骨を含む部位は加齢の影響を受けやすいとされている[1),18),23)]。従って、女性において加齢による顕著な海面骨の減少が身体活動の影響を上回ったことが考えられた。ただし、先行研究ではこれらの部位において運動の影響を認める報告もあるため[8),17)]、身体活動の影響が部位により異なる点については、今後さらなる研究が必要である。

青年期の活動と骨密度との関連については、男性では全ての部位において、女性では大転子部において、青年期の運動経験のあるもので骨密度の高いという結果が認められた。先行研究において、Florindo らは50歳以上のブラジル人男性を対象に行った研究から、10歳から20歳までの運動は最近1年間の活動と同様に全身、腰椎、大腿部近位部の骨密度を高めるための独立した因子となることを報告した[6]。女性については、Puntila らが閉経前後の女性の骨密度と11―17歳の運動との関連の検討から、青年期のスポーツ活動は腰椎骨密度の維持に関連すること[21]、また Ward らは高齢女性において大腿骨頸部の骨密度と発育期の身体活動との関連を報告した[28]。本研究はこれらの結果を支持するものであり、青年期の運動経験が中高年期の骨密度の維持向上に影響する可能性を示した。

健常者において、腰椎や股関節部の骨塩量は思春期後期に最大になるとされ、骨塩量増加のピークは女子で13歳前後、男子で16歳前後といわれている[26]。従って、この骨形成時期の環境因子の影響は非常に重要であると考えられている[26]。成長期の運動はこの時期の骨密度を高める[15),16),20)]。また、高められた骨密度は一定期間維持されることが縦断研究により報告されている[9),15)]。本研究では、男性において青年期の運動経験のあるものでは有意に骨密度が高いという結果が得られたが、骨の成長の著しい12―20歳の間に積極的に運動を行い、骨量のピークを高めたことが中高年期の骨密度の維持に結びついた可能性がある。

一方、女性における青年期の運動と骨密度との関連は大腿骨近位部内でも部位により異なり、その関係性は明らかではなかった。これは、女性においては青年期に行った運動の強度が男性ほど強くない可能性のあることや、骨密度に対する年齢の影響の大きいこと、

さらには出産や閉経などダイナミックな性ホルモンの変動のあることなどが影響したのではないかと考えられる。その中で、大転子部において影響が認められたことは、この部位が筋肉との接合部であり、特に運動の影響を受けやすい部位であるという指摘のあることから[5),13)]、他の大腿骨近位部に比べ大転子部で青年期の運動の影響が強く表れたことが考えられた。

女性においては、さらに全身と大腿骨頸部の骨密度において青年期の運動経験の有無により余暇身体活動と骨密度との関連の異なることが示された。各身体活動レベルの骨密度の平均値を確認すると、青年期の運動経験のない群では余暇身体活動レベルが上がるにつれ骨密度も高まるが、運動経験のあるものは余暇身体活動のレベルによらず比較的骨密度が高値に維持されることが推察された。しかし、本研究のみでこの結果を解釈することは難しく、さらに検討を重ねる必要がある。

以上のように、余暇身体活動および青年期の運動は、性や部位により異なるものの骨密度との有意な関連が認められた。特に大腿骨近位部では、男女共に各々の活動レベルの高いもので骨密度は高値を示した。大腿骨近位部は転倒による骨折を起こしやすい部位であるため、この部位の骨密度の維持向上は高齢になるに従い非常に重要となる。また、転倒は筋力や平衡機能の低下と密接に結びついており[17)]、転倒予防の観点からも現在および青年期における積極的な身体活動はこれらの運動機能の維持向上に有効である。

本研究には、いくつかの問題点も考えられた。一つは、身体活動量の測定方法に関する点である。本研究では身体活動量は聞き取り法による測定を行ったため、信頼性や再現性を考慮する必要があった。対象者の記憶の曖昧さや回答に対して何らかのバイアスの入ることなどは、聞き取り法に共通した対象者側の問題点である。一方、聞き取る側の問題点となる部分に関して、本研究では信頼性の確認された質問紙を用い、トレーニングされた面接者が面接を行うことで対応した。また、二つ目として身体活動のレベルの分類では強度による検討のみを行ったため、運動を行う上で重要な頻度や時間などは考慮されていない。骨密度低下の予防に対する至適運動を提唱していくためには、今後この点についても検討していくことも必要である。三つ目は、骨密度への他の因子の関与に関する点である。骨密度には様々な関連因子があるとされ、性ホルモンや成長ホルモンといった内分泌や遺伝子などの内的要因、嗜好品やカルシウム補助食品の摂取といった栄養摂取量、あるいは仕事活動量などの生活環境要因などがあげられている。骨粗鬆症の予防策を確立していくためには、今後これらを含めた総合的な検討をしていく必要がある。

本研究は多数の一般地域住民を対象に、余暇身体活動および青年期の運動経験と骨密度を調べ、各々の身体活動と骨密度との関連を検討した。その結果、現在および青年期の積極的な身体活動は、中高年期における大腿骨近位部の骨密度の維持向上に関連することが示された。本研究の結果は、高齢者における骨折の予防法を確立するための一助となることが示唆された。

5．要約

本研究では、地域在住中高年者を対象に、余暇身体活動および青年期の運動と骨密度を調べ、各々の身体活動と骨密度との関連について検討した。骨密度の測定はDXAを用い、全身、腰椎L2-4、大腿骨骨頭、ワード三角、大転子部を測定した。余暇身体活動状況と青年期の運動経験は聞き取り調査により調べた。余暇身体活動および青年期の運動と骨密度との関連について、余暇身体活動を「活動なし」、「低強度の活動のみ」、「中強度以上の活動」の3段階、青年期の運動経験を「なし」、「あり」の2段階に分け、年齢、身長、体重を調整した共分散分析を用いて検討した。以下に結果を示す。

1）余暇身体活動に従事していた人の割合は男性75.5％、女性67.7％であり、強度別では低強度、中強度以上の順に男性30.5％、45.0％、女性33.8％、33.9％であった。青年期の運動経験のある人の割合は、男性65.7％、女性39.5％であった。

2）余暇身体活動と骨密度との関連では、男性において余暇身体活動のレベルの高いもので大腿骨近位部の骨密度の高いこと、同じく女性でもワード三角部を除く大腿骨近位部の骨密度の高いことが示された。

3）青年期の運動と骨密度との関連では、男性において青年期の運動経験のあるもので全ての部位における骨密度の高いこと、女性では大転子部の骨密度の高いことが示された。女性ではさらに全身と大腿骨頸部において、青年期の運動経験の有無により余暇身体活動と骨密度との関連の異なることが示された。

以上の結果より、余暇身体活動と青年期の運動経験は骨密度の維持向上に関連し、加齢に伴う骨密度の低下や骨折の予防に繋がることが示唆された。

文　献

1）Adami, S., D. Gatti, V. Braga, D. Bianchini, and M. Rossini:

Site-specific effects of strength training on bone structure and geometry of ultradistal radius in postmenopausal women. *J. Bone Miner. Res.* **14**(1): 120-124, 1999.
2) アメリカスポーツ医学会編　日本体力医学会体力科学編集委員会監訳　運動処方の指針　運動負荷試験と運動プログラム　原著第6版　南江堂　p143-151, 2001.
3) Blanchet, C., Y. Giguère, D. Prud'homme, L. Turcot-Lemay, M. Dumont, G. Leduc, S. Côte, N. Laflamme, F. Rousseau, and S. Dodin: Leisure physical activity is associated with quantitative ultrasound measurements independently of bone mineral density in postmenopausal women. *Calcif. Tissue Int.* **73**(4): 339-349, 2003.
4) Brahm, H., H. Mallmin, K. Michaëlsson, H. Ström, and S. Ljunghall: Relationships between bone mass measurements and lifetime physical activity in a Swedish population. *Calcif. Tissue Int.* **62**: 400-412, 1998.
5) Coupland, C.A.C., S.J. Cliffe, E.J. Bassey, M.J. Grainge, D.J. Hosking, and C.E.D. Chilvers: Habitual physical activity and bone mineral density in postmenopausal women in England. *Int. J. Epidemiol.* **28**: 241-246, 1999.
6) Florindo, A.A., Mdo.R. Latorre, P.C. Jaime, T. Tanaka, M.G. Pippa, and C.A. Zerbini: Past and present habitual physical activity and its relationship with bone mineral density in men aged 50 years and older in Brazil. *J. Gerontol.* **57A**(10): M654-657, 2002.
7) 藤原佐枝子　骨粗鬆症　危険因子と予防対策　日本臨床 **56**(6): 211-215, 1998.
8) Greendale, G.A., M.H. Huang, Y. Wang, J.S. Finkelstein, M.E. Danielson, and B. Sternfeld: Sport and home physical activity are independently associated with bone density. *Med. Sci. Sports. Exerc.* **35**(3): 506-512, 2003.
9) Gstavsson, A., K. Thorsen, and P. Nordström: A 3-year longitudinal study of the effect of physical activity on the accrual of bone mineral density in healthy adolescent males. *Calcif. Tissue Int.* **73**: 108-114, 2003.
10) Heinonen, A., P. Kannus, H. Sievänen, M. Pasanen, P. Oja, and I. Vuori: Good maintenance of high-impact activity-induced bone gain by voluntary, unsupervised exercises: An 8-month follow-up of a randomized controlled trial. *J. Bone Miner. Res.* **14**(1): 125-128, 1999.
11) Iwai, N., N. Yoshiike, S. Saitoh, T. Nose, T. Kushiro, H. Tanaka, and the Japan Lifestyle Monitoring Study Group: Leisure-time physical activity and related lifestyle characteristics among middle-aged Japanese. *J. Epidemiol.* **10**: 226-233, 2000.
12) Kelley, G.A., K.S. Kelley, and Z.V. Tran: Exercise and bone mineral density in men: a meta-analysis. *J. Appl. Physiol.* **88**: 1730-1736, 2000.
13) Kerr, D., A. Morton, I. Dick, and R. Prince: Exercise effects on bone mass in postmenopausal women are site-specific and load-dependent. *J. Bone Miner. Res.* **11**(2): 218-225, 1996.
14) 厚生省　監修　厚生労働白書（平成12年度版）ぎょうせい　p71-74, 2000.
15) Lloyd, T., V.M. Chinchilli, N. Johnson-Rollings, K. Kieselhorst, D.F. Eggli, and R. Marcus: Adult female hip done density reflects teenage sports-exercise patterns but not teenage calcium intake. *Pediatrics* **106**(1): 40-44, 2000.
16) MacKelvie, K.J., K.M. Khan, and H.A. McKay: Is there a critical period for bone response to weight-bearing exercise in children and adolescents? a systematic review. *Br. J. Sports Med.* **36**: 250-257, 2002.
17) 真野行生　編　高齢者の転倒とその対策　医歯薬出版株式会社　p2-7, 1999.
18) 森田陸司　監修　骨粗鬆症と骨塩定量—DXAによる骨塩定量—　メディカルレビュー社　p48-62, 1994.
19) 折茂肇　原発性骨粗鬆症診断基準—2000年度改訂版（概要）—　*Osteoporosis Japan* **9**(1): 9-14, 2001.
20) Pettersson, U., P. Nordström, H. Alfredson, K. Henriksson-Larsén, and R. Lorentzon: Effect of high impact activity on bone mass and size in adolescent females: A comparative study between two different types of sports. *Calsif. Tissue Int.* **67**(3): 207-214, 2000.
21) Puntila, E., H. Kröger, T. Lakka, R. Honkanen, and M. Tuppurainen: Physical activity in adolescence and bone density in peri- and postmenopausal women: A population-based study. *Bone* **21**(4): 363-367, 1997.
22) Report of WHO Study Group: Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. p2-7, 1994.
23) Riggs, B.L., H.W. Wahner, E. Seeman, K.P. Offord, and W.L. Dunn: Changes in bone mineral density of the proximal femur and spine with ageing. *J. Clin. Invest.* **70**: 716-723, 1982.
24) SAS Procedures Guide, Release 8.2 Edition. SAS Institute Inc. Cary, NC, USA, 2001.
25) Shimokata, H., F. Ando, and N. Niino: A new comprehensive study on aging – the National Institute for Longevity Science, Longitudinal Study of Aging (NILS-LSA). *J. Epidemiol.* **10**: S1-S9, 2000.
26) 田中弘之　青壮年期の最大骨量の調節機構　*Medical Practice* **19**(10): 1645-1649, 2002.
27) Vuillemin, A., F. Guillemin, P. Jouanny, G. Denis, and C. Jeandel: Differenttial influence of physical activity on lumber spine and femoral neck bone mineral density in the elderly population. *J. Gerontrol.* **56A**(6): B248-253, 2001.
28) Ward, J.A., S.R. Load, P. Williams, K. Anstey, and E. Zivanovic: Phisiologic, health and lifestyle factors associated with femoral neck bone density in older women. *Bone* **16**(4); s373-s378, 1995.

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ORIGINAL ARTICLE

Lack of correlation between total lymphocyte count and nutritional status in the elderly

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KEYWORDS
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Summary *Background & aims*: Malnutrition is a widespread but largely unrecognized problem in aged people. Although absolute total lymphocyte count (TLC) has been proposed as a useful indicator of nutritional status, there is little evidence that low TLC levels reflect malnutrition in the elderly. To examine whether TLC is a suitable marker of malnutrition in the elderly.

Methods: A total of 161 elderly subjects (44 males and 117 females, mean age±SD: 77.9±7.4; range: 65–95 years) were enrolled from geriatric clinical settings. The participants were categorized according to severely low, low, or normal TLC. Anthropometry measurements, serum albumin, total cholesterol levels, and total score on the mini-nutritional assessment (MNA) were determined.

Results: There were no significant differences among the three TLC groups with regard to anthropometry measurements, serum albumin, total cholesterol levels, or MNA score. There was a significant negative correlation of TLC with age, but not with other nutritional markers. The clinical nutritional screening tool, MNA score, was well correlated with all of the nutritional parameters used in the present study except for TLC.

Conclusion: TLC is not a suitable marker of malnutrition in the elderly.

Introduction

Malnutrition is a common finding in the elderly, not only in institutionalized populations but also in community-dwelling elderly, with prevalence rates ranging from 12% to 85%.[1,2] Malnutrition is associated with increased hospitalizations, increased susceptibility to infection, decreased wound healing, reduced quality-of-life, and increased mortality in the elderly.[3,4] However, it remains difficult to define malnutrition for the elderly precisely. Therefore, malnutrition is

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often unrecognized and subsequently goes untreated.

Anthropometry measurements such as body mass index (BMI), mid-arm circumference (MAC), calf circumference (CC), and skin fold thickness are generally considered as the single most easily obtainable, inexpensive, and noninvasive method by which to assess nutritional state. Biochemical measurements such as serum albumin and total cholesterol are also well known as markers for the protein energy malnutrition (PEM), and are the most commonly used laboratory tests.[5,6]

Multidimensional screening tools for nutritional assessments in the clinical situation have been developed. Among those, the mini-nutritional assessment (MNA) is a simple clinical scale for the evaluation of the nutritional status of frail elderly subjects.[7,8] It has been validated in various countries by comparing its results with a clinical assessment performed by expert geriatric nutritionists.

Total lymphocyte count (TLC) has been also proposed as a useful indicator of nutritional status and outcome. It has been proposed that TLC decreases with progressive malnutrition and correlates with morbidity and mortality in hospitalized patients.[5,6] It has also been proposed that regardless of age, a decrease in TLC to less than 1500/mm^3 or less than 900/mm^3 reflects malnutrition or severe malnutrition, respectively.[5,6] Although TLC is one of the most commonly obtained nutritional markers, there is little evidence that low TLC levels reflect malnutrition in the elderly, and it remains uncertain whether TLC can be used as a marker of malnutrition in elderly subjects.

In the present study, we evaluated the relationship of TLC with other nutritional markers including MNA score, anthropometry measurements, serum albumin, and total cholesterol levels as an indicator of nutritional status in the Japanese elderly.

Methods

Subjects

We enrolled 235 elderly subjects (67 males and 168 females, mean age$\pm$SD: 78.6$\pm$7.6; range: 65–95 years) from our geriatric outpatient clinic ($n = 69$), a nursing home ($n = 56$), geriatric hospitals ($n = 72$), and home care patients ($n = 38$). All participants provided written informed consent. Subjects diagnosed with infection, inflammation, liver disorders, kidney disorders, cancer, or bone marrow proliferative disorders were not included in the 235 participants. The analysis on TLC described herein was limited to the 161 (44 male and 117 female) participants (mean$\pm$SD: 77.9$\pm$7.4 years; range: 65–95 years) whose TLC measurements were obtained, since some participants did not approve blood sampling for TLC measurement.

Anthropometric measurements and biochemical markers

BMI is defined as weight in kilograms divided by height in meters squared. Triceps skinfold (TSF) was measured with Harpenden callipers over the triceps muscle at the midway point between the acromion and the olecranon process. MAC and CC were measured on the left arm and calf with a tape measure. Three repeat measurements were taken to the nearest 0.5 mm, with the mean taken as the true value. All anthropometric measurements were taken at least twice by two different investigators, and the reported values are the means of the repeated measurements. Blood samples were collected after an overnight fast. Serum albumin and total cholesterol levels were determined using automated analysers. Blood was collected into tubes containing EDTA, and TLC was measured with use of a Coulter counter.

Definition of malnutrition

A BMI of less than 20 is widely accepted to indicate that the subject is underweight, particularly in well-developed countries, and 18.5 is recommended as a practical lower limit for most populations.[9] Therefore, a diagnosis of malnutrition was made when BMI was less than 18.5 kg/m^2. Serum albumin and total cholesterol levels were used as the biochemical markers of undernutrition: levels less than 3.5 g/dl of albumin or 150 mg/dl of total cholesterol were taken to indicate malnutrition. Participants were categorized into three groups according to lymphocyte count, as follows: severely low lymphocyte ($<$900 count/mm^3), low lymphocyte (900–1499 count/mm^3), and normal lymphocyte count ($\geqslant$1500 count/mm^3). The relationship of each group to various respective nutritional markers has been examined. In addition, participants were classified according to the cutoff of each nutritional parameter and comparisons were made among groups in terms of anthropometric markers, nutritional proteins, and MNA score.

MNA, a comprehensive, noninvasive, well-validated screening tool for malnutrition in elderly persons, has been also used as an indicator of

malnutrition. The MNA includes 18 items, including the anthropometrical measurements BMI, MAC, and CC, weight loss, a global assessment (six questions related to lifestyle, medication, and mobility), a dietary questionnaire (eight questions related to the number of meals, types of food, and fluid intake), and a subjective assessment (self-perception of health and nutrition). The MNA assigns points on nutritional adequacy with a maximum score of 30 points.[7] The MNA score distinguishes between elderly patients with adequate nutrition (scores of 24 and up), protein-calorie undernutrition (lower than 17), and risk of malnutrition (between 17 and 23.5).[7]

Statistical analysis

Differences between groups (TLC: <900, 900–1499, ⩾1500) were determined by one-way analysis of variance, Chi-square test or the Kruskal–Wallis test, as appropriate. The Kolmogorov–Smirnov test was used to check the normal distribution of variables. Chi-square test, Mann–Whitney *U* test, or Student's unpaired *t*-test was used to test differences between normal and malnutrished groups, as appropriate. Partial rank correlation coefficients adjusted for age were used to measure the relationships between TLC and variables, or between MNA score and variables. The significance level was set at 0.05. Data evaluation was carried out using the SPSS software package (SPSS Inc., Chicago, USA).

Results

Table 1 shows the mean results of variables, which are expressed according to the classification of lymphocyte count (< 900, 900–1499, ⩾1500). There were significant differences between classes with regard to MAC, but there was no trend toward greater MAC values in the group with 900–1499 TLC compared to those in the <900 TLC group. No significant differences were observed between classes in terms of age, BMI, TSF, CC, serum albumin, total cholesterol, or MNA score. There was a weak but statistically significant negative correlation between lymphocyte count and age ($r = -0.21$, $P = 0.0006$). There were no correlations between TLC and any other nutritional indices.

When levels of less than 18.5 kg/m^2 of BMI, 3.5 g/dl of albumin or 150 mg/dl total cholesterol, and 17 points on MNA score were taken to indicate malnutrition, the relationship among these parameters and anthropometric measurements were examined (Table 2). The groups with <18.5 kg/m^2 of BMI, <3.5 g/dl of serum albumin, <150 mg/dl of total cholesterol, and <17 of MNA score had significantly lower values than those of the well-nourished groups with respect to most of the nutrition-related variables except for lymphocyte count.

The score on MNA, a commonly used comprehensive malnutrition screening for the elderly, was correlated with BMI, MAC, TSF, CC, serum albumin, and total cholesterol levels ($r = 0.52$, 0.36, 0.26, 0.28, 0.61, and 0.34, respectively; $P \leqslant 0.0001$

Table 1 Lymphocyte count and nutritional characteristics.

	Lymphocyte (count/mm^3)			*P*-value*
	<900	900–1499	⩾1500	
n	9	51	101	
Men/women	1/8	12/39	31/70	0.343
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	79.1 (9.8)	79.1 (6.4)	77.2 (7.7)	0.287
BMI (kg/m^2)	21.8 (3.1)	21.2 (3.9)	22.6 (3.7)	0.074
MAC (cm)	25.0 (2.8)	23.6 (3.1)	25.2 (3.2)	0.013
TSF (mm)	10.6 (4.9)	11.4 (8.2)	14.6 (8.6)	0.052
CC (cm)	30.3 (2.2)	31.2 (3.8)	31.5 (4.0)	0.666
Albumin (g/dl)	4.0 (0.4)	4.1 (0.3)	4.1 (0.5)	0.526
Total cholesterol (mg/dl)	186.4 (38.3)	203.8 (33.8)	205.3 (41.3)	0.380
MNA score	20.9 (2.3)	20.6 (4.2)	21.0 (4.1)	0.901

BMI: body mass index; MAC: midarm circumference; TSF: triceps skinfold; CC: calf circumference; MNA: mini-nutritional assessment.

*One-way analysis of variance was conducted except for the gender difference (χ^2-test) and MNA score (Kruskal–Wallis test).

Table 2 Comparison among various nutritional markers.

	BMI (m/kg^2), $n = 235$			Albumin (g/dl), $n = 179$			Total cholesterol (mg/dl), $n = 177$			MNA score, $n = 235$		
	<18.5	⩾18.5	*P*-value*	<3.5	⩾3.5	*P*-value	<150	⩾150	*P*-value	<17	⩾17	*P*-value
Men/women	14/29	53/139	0.549	7/14	41/117	0.473	6/8	41/122	0.150	18/39	49/129	0.514
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Age (years)	79.9 (7.5)	78.3 (7.5)	0.188	82.1 (7.9)	77.9 (7.3)	0.017	77.6 (8.5)	78.4 (7.4)	0.700	80.2 (8.1)	78.1 (7.3)	0.065
BMI (kg/m^2)	16.4 (1.6)	23.2 (3.3)	<0.0001	19.1 (4.8)	22.1 (3.9)	0.002	19.5 (3.9)	22.0 (4.1)	0.035	19.1 (3.6)	22.8 (3.8)	<0.0001
MAC (cm)	20.3 (2.3)	25.4 (3.0)	<0.0001	22.1 (4.7)	24.7 (3.3)	0.002	22.6 (3.9)	24.5 (3.6)	0.053	21.6 (3.4)	25.2 (3.2)	<0.0001
TSF (mm)	8.18 (6.6)	14.3 (8.4)	<0.0001	7.8 (6.3)	13.8 (8.8)	0.003	7.8 (6.4)	13.5 (8.8)	0.018	8.1 (6.1)	14.4 (8.4)	<0.0001
CC (cm)	28.6 (4.7)	31.5 (3.6)	<0.0001	27.1 (4.4)	31.4 (3.9)	<0.0001	26.0 (3.7)	31.3 (4.0)	<0.0001	28.9 (4.5)	31.6 (3.5)	<0.0001
Albumin (g/dl)	3.7 (0.9)	4.1 (0.4)	<0.0001	3.1 (0.3)	4.2 (0.3)	<0.0001	3.1 (0.5)	4.1 (0.4)	<0.0001	3.6 (0.6)	4.2 (0.3)	<0.0001
Total cholesterol (mg/dl)	187 (44)	204 (38)	0.026	152 (32)	207 (36)	<0.0001	129 (19)	206 (35)	<0.0001	175 (42)	208 (36)	<0.0001
MNA score	15.2 (4.8)	21.3 (3.7)	<0.0001	12.0 (5.1)	21.1 (3.7)	<0.0001	12.1 (4.9)	20.8 (4.3)	<0.0001	13.0 (3.4)	21.9 (2.7)	<0.0001
Lymphocyte (count/mm^3)	1620 (577)	1789 (680)	0.244	1890 (692)	1754 (666)	0.513	2016 (742)	1749 (664)	0.273	1829 (630)	1748 (675)	0.557

*Student's, *t* test was conducted except for the gender difference (χ^2-test) and MNA score (Mann–Whitney *U*-test).

except for TSF ($P = 0.001$)), but not with TLC ($P = 0.524$).

Discussion

Although the TLC is one of the most commonly used markers for assessing nutritional status, so far little evidence exists as to whether TLC reflects the nutritional status of the elderly. In the present study, we concluded that TLC is not a suitable marker of malnutrition in the elderly. This conclusion was based on the observation that no correlation was detected between TLC and other well-known nutritional parameters including anthropometric measurements, biochemical markers, and MNA score, a comprehensive nutritional screen tool for the elderly. In addition, MNA score was correlated with all of the nutritional markers used in the present study except for TLC. This result is consistent with the previous observation of Goodwin JS that no significant correlation was observed between lymphocyte count and blood levels of specific nutrients including serum albumin in the independently living healthy elderly.[10]

It has been shown that the serum albumin and total cholesterol levels, both of which are commonly used as nutritional markers, are sometime discordant with clinical assessments of malnutrition, largely because these biomarkers are influenced by factors such as inflammatory activity, hemoconcentration, and various diseases such as liver cirrhosis and nephritic syndrome. However, in the present study, these biochemical markers for malnutrition were well correlated with anthropometric measurements as well as with MNA score.

There is no general agreement of the effect of aging on TLC. Divergent data have been reported concerning age-related changes in total lymphocyte number.[5,11,12] This may be due to the heterogeneity of the aging immune system. The present study suggested that TLC was correlated with aging in subjects between 65 and 90 years old, indicating that TLC appears to be reflective of age rather than of nutritional status. Our results that TLC is not a suitable marker of malnutrition in the elderly does not indicate that malnutrition is not a risk factor for the impairment of immune function. In fact, nutritional status has long been recognized as a major factor in age-related immune impairment, and a number of studies have already demonstrated that malnutrition is associated with decreased lymphocyte proliferation, reduced cytokine release, and lower antibody response to vaccines.[12,13] In addition, an important modification in T lymphocyte subsets is known to occur in aged people.[14] In fact, it has been demonstrated that a low lymphocyte count is associated with an increased mortality risk in older persons.[15]

There are several limitations to this study. First, the study group might have consisted of elderly who had comorbid diseases, given that they were enrolled from clinical settings. Therefore, our results may apply only to the elderly in ill health. The possibility of an association between TLC and nutritional status in the healthy elderly cannot be excluded. Second, the effect of medication on TLC was not considered in this study, due to the fact that medication data were not available.

In conclusion, we found that TLC is not suitable as a marker of nutritional status in the elderly. TLC appears to be reflective of age rather than of nutritional status.

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References

1. Sullivan DH, Sun S, Walls RC. Protein-energy undernutrition among elderly hospitalized patients: a prospective study. *JAMA* 1999;**281**:2013–9.
2. Edington J, Boorman J, Durrant ER, et al. Prevalence of malnutrition on admission to four hospitals in England. The Malnutrition Prevalence Group. *Clin Nutr* 2000;**19**:191–5.
3. Sullivan DH, Walls RC. Protein-energy undernutrition and the risk of mortality within six years of hospital discharge. *J Am Coll Nutr* 1998;**17**:571–8.
4. Keller HH, Ostbye T, Goy R. Nutritional risk predicts quality of life in elderly community-living Canadians. *J Gerontol A Biol Sci Med Sci* 2004;**59**:68–74.
5. Omran ML, Morley JE. Assessment of protein energy malnutrition in older persons, Part II: Laboratory evaluation. *Nutrition* 2000;**16**:131–40.
6. Seiler WO. Clinical pictures of malnutrition in ill elderly subjects. *Nutrition* 2001;**17**:496–8.
7. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition* 1999;**15**:116–22.
8. Kuzuya M, Kanda S, Koike T, Suzuki Y, Satake S, Iguchi A. Evaluation of Mini-Nutritional Assessment for Japanese frail elderly. *Nutrition* 2005 in press.
9. James WP, Francois PJ. The choice of cut-off point for distinguishing normal body weights from underweight or 'chronic energy deficiency' in adults. *Eur J Clin Nutr* 1994;**48**(Suppl. 3):S179–84.
10. Goodwin JS, Garry PJ. Lack of correlation between indices of nutritional status and immunologic function in elderly humans. *J Gerontol* 1988;**43**:M46–9.

11. Diaz-Jouamen E, Strickland RG, Williams RC. Studies of human lymphocytes in the newborn and the aged. *Am J Med* 1975;**58**:620–5.
12. Lesourd BM. Nutrition and immunity in the elderly: modification of immune responses with nutritional treatments. *Am J Clin Nutr* 1997;**66**:478S–84S.
13. Lesourd BM, Mazari L, Ferry M. The role of nutrition in immunity in the aged. *Nutr Rev* 1998;**56**(1 Pt 2):S113–25.
14. Lesourd BM, Meaume S. Cell mediated immunity changes in ageing, relative importance of cell subpopulation switches and of nutritional factors. *Immunol Lett* 1994;**40**: 235–42.
15. Izaks GJ, Remarque EJ, Becker SV, Westendorp RG. Lymphocyte count and mortality risk in older persons. The Leiden 85-Plus Study. *J Am Geriatr Soc* 2003;**51**: 1461–5.

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Evaluation of Mini-Nutritional Assessment for Japanese frail elderly

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Abstract

Objective: We evaluated the Mini-Nutritional Assessment (MNA) test and the short-form MNA as screening tools for malnutrition in the Japanese elderly population.

Methods: A cross-sectional study of 226 elderly Japanese patients (78.6 ± 0.5 y of age, mean ± standard deviation; 67 men and 159 women) in various settings was carried out. Nutritional assessment included MNA, anthropometric measurements, and biochemical markers.

Results: According to the original cutoff point of the full MNA, 19.9% of those assessed were malnourished, 58.0% were at risk of malnutrition, and 22.1% were well nourished. Significant correlations were found between full MNA scores and age ($r = -0.14$), body mass index ($r = 0.59$), serum albumin ($r = 0.60$), total cholesterol ($r = 0.36$), midarm circumference ($r = 0.50$), and triceps skinfold ($r = 0.37$). The sensitivity and specificity of the full MNA score (<17) for hypoalbuminemia were 0.810 and 0.860, respectively. With a cutoff point lower than 18, sensitivity and specificity hypoalbuminemia were 0.857 and 0.815, respectively. Using a short-form MNA score 12 and higher as normal, its sensitivity and specificity for predicting undernutrition were 0.859 and 0.840, respectively.

Conclusions: The full and short forms of the MNA were useful tools to identify elderly Japanese patients with malnutrition or risk of malnutrition. However, the full MNA cutoff point for malnutrition should be modulated for this population.

Keywords: Elderly; Malnutrition; Nutritional assessment; Mini-nutritional assessment; Anthropometric measurements

Introduction

Malnutrition is a frequent and serious problem in geriatric patients. Malnutrition in ill elderly subjects is one of the most common and least-heeded problems in hospitals, nursing homes, and home care [1–4]. Different studies have suggested that malnutrition is an important predictor of morbidity and mortality in the elderly [5,6]. In addition, malnutrition has been shown to prolong hospital stays, thereby imposing enormous costs on health services [7,8]. To identify malnourished elderly or subjects at risk of malnutrition, a conventional malnutrition assessment tool is required [9,10]. Anthropometric measurements such as body mass index (BMI), midarm circumference (MAC), calf circumference (CC), and triceps skinfold (TSF) are essential parts of any nutritional assessment. Biochemical measurements including serum albumin and cholesterol are also frequently used as nutritional parameters, although at present there are no generally accepted criteria for the diagnosis of malnutrition in the elderly. The Mini-Nutritional Assessment (MNA) is a simple clinical scale for the evaluation of the nutritional status of frail elderly subjects. It has been validated in Europe and the United States by comparing its results with a clinical assessment performed by expert geriatric nutritionists [11,12]. Although the MNA was developed specifically for frail older people, it has been validated in a healthy older population [11,12].

The MNA has been demonstrated to be useful in predicting long-term mortality for the institutionalized elderly and acute hospital admission for the elderly living at home [6,13–15]. Recently, the MNA short form (MNA-SF) has been devised as the first step of a two-step process (screen-

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ing with the MNA-SF followed by assessment, if needed, by the full MNA) [16]. The MNA has proved to be a simple, noninvasive, well-validated screening tool for malnutrition in elderly persons in Europe and the United States. Despite the fact that Japan has an aging society and ranks first in the world for life expectancy at birth [17], the MNA has not been validated in the Japanese elderly, and whether the MNA and its established cutoff points for the diagnosis of malnutrition and at-risk status are applicable to the Japanese elderly remain unknown.

In the present study we examined whether the MNA can screen and diagnose for malnutrition and risk for malnutrition in the Japanese elderly.

Materials and methods

Subjects

We enrolled 226 elderly (67 men and 159 women; mean age ± standard deviation = 78.6 ± 0.5 y; age range = 65–95 y) from our geriatric outpatient clinic (n = 68), a nursing home (n = 53), geriatric hospitals (n = 72), and home care patients (n = 33). Sixty-eight consecutive outpatients were living at home independently or with mild decline in activities of daily living. Fifty-three residents and 72 inpatients with mild to severe dependency in activities of daily living were randomly chosen from one private nursing home and two geriatric hospitals, respectively. Thirty-three patients living at home and receiving home care services were also eligible for the study. Subjects diagnosed with infection, inflammation, liver disorders, kidney disorders, cancer, or bone marrow proliferative disorders were excluded by physicians. All participants provided written informed consent.

MNA characteristics

The MNA is a two-step procedure: (1) the MNA-SF is used to screen for malnutrition and risk of malnutrition and (2) the full MNA is used to assess nutritional status [16]. The MNA includes 18 items, including anthropometric measurements: BMI, MAC, CC, weight loss, a global assessment (six questions related to lifestyle, medication, and mobility), a dietary questionnaire (eight questions related to number of meals, food, and fluid intake), and a subjective assessment (self-perception of health and nutrition). The MNA-SF comprises 6 of the 18 items. The maximum possible score of the MNA-SF is 14. Scores 12 and above indicate satisfactory nutritional status. A screening score 11 and below suggests possible malnutrition and a need to proceed to the assessment stage of the MNA [16]. The assessment stage has 12 questions, with a maximum possible score of 16 (total = 30 points). The MNA score distinguishes between elderly patients with adequate nutrition (score ≥ 24), protein-calorie undernutrition (score < 17), and risk of malnutrition (score = 17–23.5) [12].

Anthropometric measurements and biochemical markers

BMI is defined as weight in kilograms divided by height in meters squared. A BMI less than 20 kg/m^2 is widely accepted as underweight [18], particularly in well-developed countries, and 18.5 kg/m^2 is recommended as a practical lower limit for most populations [19]. Therefore, the diagnosis of malnutrition was made when BMI was less than 18.5 kg/m^2. TSF was measured with Harpenden calipers over the triceps muscle at the midway point between the acromion and the olecranon process. MAC and CC were measured on the left arm and calf, respectively, with a tape measure. Three measurements were taken to the nearest 0.5 mm, with the mean taken as the true value. All anthropometric measurements were taken at least twice by two different investigators, and the reported values are the means of the repeated measurements (interrater reliability with Pearson's correlation coefficient, r = 0.923, P < 0.0001). Blood samples were collected after an overnight fast. Serum albumin or total cholesterol levels were determined by kinetic immunonephelometry or enzymatically, respectively. Blood was collected into tubes containing ethylene-diaminetetra-acetic acid, and total lymphocyte count was measured with use of a Coulter counter. Serum albumin and total cholesterol levels were used as biochemical markers for undernutrition: levels lower than 3.5 g/dL of albumin or 150 mg/dL of total cholesterol were taken to indicate malnutrition.

Statistical analysis

Differences between groups (MNA total scores <17, 17–23.5, and ≥24) were determined by analysis of variance or the Kruskal-Wallis test, depending on the distribution of the analyzed variable. Partial rank correlation coefficients adjusted for age were used to measure the relations between MNA total score, MNA-SF, anthropometric measurements, and biochemical markers. To identify optimal threshold values for predicting malnutrition, receiver operating characteristic (ROC) curve analysis was performed by computing the sensitivity and specificity of the different tests at various cutoff levels [20]. The area under the ROC curve was also evaluated. A value of 0.5 under the ROC curve indicates that the variable performs no better than chance, whereas a value of 1.0 indicates perfect discrimination. A larger area under the ROC curve represents a greater reliability and discrimination of the scoring system [21]. Cutoff values can be set depending on the purpose for which the scales are used. For screening purposes, a high sensitivity and a high negative predictive value are required, whereas diagnosis requires a high specificity and a high positive predictive value. Sensitivity, specificity, positive predictive value, and negative predictive value for predicting malnu-

Table 1
MNA score, anthropometric measurements, and clinical chemistry in Japanese elderly

	MNA total score			
	<17	17–23.5	≥24	Analysis of variance (*P*)
n	45	131	50	
Men/women	16/29	40/91	11/39	0.220*
Age (y)†	80.2 (8.0)	78.5 (7.4)	76.9 (7.3)	0.157
BMI (kg/m^2)†	18.5 (3.2)	22.2 (3.8)	24.6 (3.0)	<0.0001
MAC (cm)†	21.6 (3.4)	24.8 (3.2)	26.2 (2.8)	<0.0001
TSF (mm)†	8.1 (6.2)	13.9 (8.2)	15.9 (9.1)	<0.0001
CC (cm)†	27.5 (4.7)	31.2 (3.1)	32.0 (3.3)	<0.0001
Albumin (g/dL)†	3.6 (0.6)	4.1 (0.3)	4.4 (0.3)	<0.0001
Total cholesterol (mg/dL)†	174.0 (42.5)	203.3 (35.4)	217.5 (35.1)	<0.0001
Lymphocyte (/μL)†	1825.0 (641.1)	1750.5 (725.5)	1744.1 (560.6)	0.805

BMI, body mass index; CC, calf circumference; MAC, midarm circumference; MNA, Mini-Nutritional Assessment; TSF, triceps skinfold
* Kruskal-Wallis test.
† Mean (standard deviation).

trition based on the various nutritional markers were also calculated for different cutoff points. The best Youden index (sensitivity + specificity −1) was used to determine the best cutoff point [22]. The Youden index is used to compare the proportion of cases correctly classified. The higher the Youden index, the more accurate the prediction (higher true positive and true negative and fewer false positive and false negative) at the cutoff point. The Kolmogorov-Smirnov test was used to check the normal distribution of variables. The statistical significance level was set at 0.05. Data evaluation was carried out with SPSS software (SPSS Inc., Chicago, IL, USA).

Results

Subjects' average age was 77.8 ± 13.8 y (mean ± standard deviation). MNA total scores averaged 20.2 ± 4.6 and ranged from a minimum of 4.0 to a maximum of 27.5, with a median at 21.0. Table 1 lists the mean results of variables, which are expressed according to the classification of the MNA. According to the original cutoff point of the full MNA, 19.9% (45 of 226) had an MNA score lower than 17, 58.0% (131 of 226) had an MNA score between 17 and 23.5, and 22.1% (50 of 226) had a score of at least 24. There were significant differences between classes with regard to BMI, MAC, TSF, CC, serum albumin, and total cholesterol levels, but not to age ($P = 0.157$) and lymphocyte count ($P = 805$). There was a weak but statistically significant, negative correlation between MNA total score and age (Table 2). There were relations between MNA total score and BMI, MAC, and CC, which are included as anthropometric markers in the MNA. In addition, MNA total score showed good correlation with TSF and serum albumin and total cholesterol, which are not included in the MNA, but no correlation between MNA score and lymphocyte number.

The ROC curves shown in Fig. 1A plot the sensitivity versus 1-specificity for MNA total score in predicting low serum albumin (<3.5 g/dL), total cholesterol (<150 mg/dL), and low BMI (<18.5 kg/m^2) as markers of malnutrition. The area under the ROC curves, which represent the overall accuracy of the MNA total score as a test for malnutrition, was found to be 0.916 (95% confidence interval = 0.846 to 0.985) for albumin ($P < 0.0001$), 0.912 (95% confidence interval = 0.850 to 0.974) for total cholesterol ($P < 0.0001$), and 0.855 (95% confidence interval = 0.801 to 0.908) for BMI ($P < 0.0001$), indicating that the MNA test is relatively accurate. The sensitivity, specificity, Youden index, positive predictive value, and negative predictive value of the MNA total score at the selected threshold MNA score are presented in Table 3. Based on biochemical markers (serum albumin or total cholesterol) or BMI as the indicator of malnutrition, the sensitivity and

Table 2
Correlation between MNA total or MNA-SF score and nutritional parameters in Japanese elderly

	No. of subjects	Correlation with MNA total score*		Correlation with MNA-SF score*	
		r	*P*	*r*	*P*
Age	234	−0.14	0.036†	−0.16	0.012†
BMI	233	0.59	<0.0001	0.57	<0.0001
MAC	227	0.50	<0.0001	0.33	<0.0001
TSF	225	0.37	<0.0001	0.24	0.003
CC	225	0.28	<0.0001	0.31	<0.0001
Albumin	179	0.60	<0.0001	0.56	<0.0001
Total cholesterol	177	0.36	<0.0001	0.30	<0.0001
Lymphocyte	161	0.01	0.930	0.04	0.96
MNA total score	226			0.88	<0.0001

BMI, body mass index; CC, calf circumference; MAC, midarm circumference; MNA, Mini-Nutritional Assessment; MNA-SF, Mini-Nutritional Assessment, Short Form; TSF, triceps skinfold
* Partial rank correlation coefficients adjusted for age were used to measure the association between MNA or MNA-SF score and nutritional parameters except for age.
† Spearman's rank correlation.

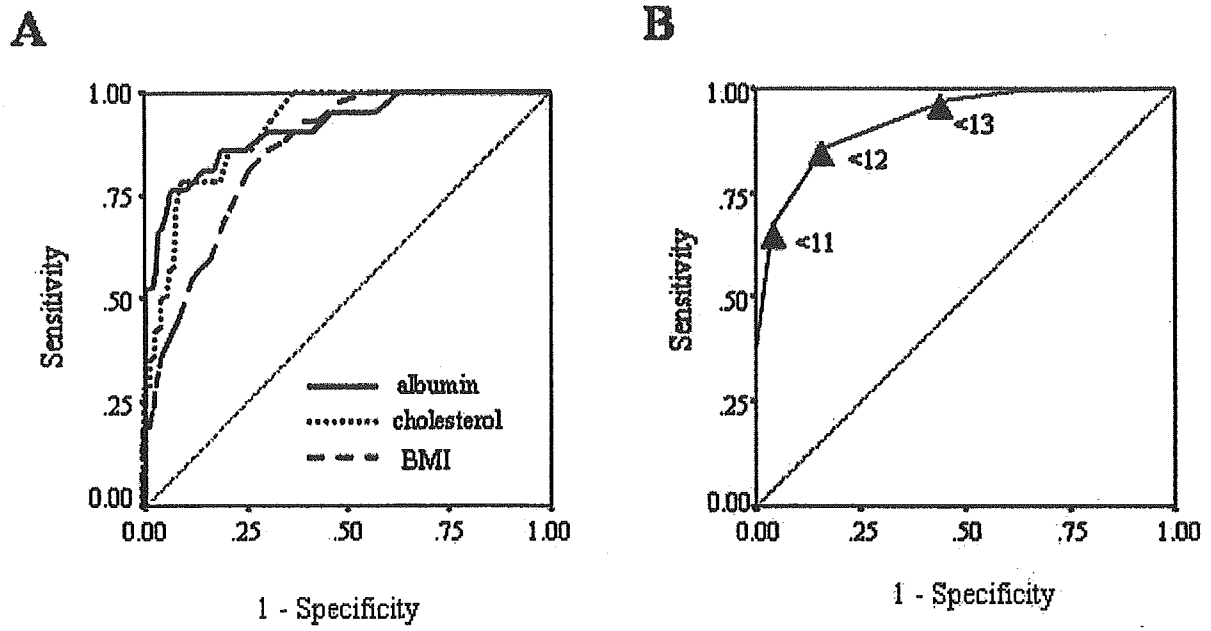

Fig. 1. Receiver operating characteristics (ROC) curve for the (A) full Mini-Nutritional Assessment (MNA) and (B) the MNA short form (MNA-SF) in the Japanese elderly. (A) ROC for MNA as a predictor of albumin levels lower than 3.5 g/dL, total cholesterol levels lower than 150 mg/dL, or BMI lower than 18.5 kg/m^2. (B) ROC for MNA-SF as a predictor of an MNA score below 24. BMI, body mass index.

specificity of the MNA total score were 0.810 and 0.860 for albumin, 0.786 and 0.822 for total cholesterol, and 0.558 and 0.839 for BMI, respectively, with a cutoff point lower than 17 indicating malnutrition. This suggests that 19% of elderly persons with hypoalbuminemia would be missed (sensitivity), and that 14% without hypoalbuminemia would be classified as malnourished (specificity).

Maximal discrimination between malnutrition and risk of malnutrition is by definition reached at the cutoff point that has the highest Youden index (sensitivity + specificity −1). As presented in Table 3, a cutoff point below 15.5 has the highest Youden index, based on hypoalbuminemia and hypocholesterolemia. With a cutoff point below 15.5, the sensitivity and specificity for hypoalbuminemia (<3.5 g/dL) were 0.762 and 0.936, respectively. The figures for hypocholesterolemia and low BMI (<18.5 kg/m^2) showed a

Table 3
Validity values of the MNA total score for malnutritional markers in Japanese elderly

	Threshold for MNA total score							
	<15	<15.5	<16	<16.5	<17	<17.5	<18	<18.5
Albumin (<3.5 g/dL)								
Sensitivity	0.714	0.762	0.762	0.762	0.810	0.810	0.857	0.857
Specificity	0.949	0.936	0.924	0.904	0.860	0.834	0.815	0.777
YI	0.663	0.698	0.686	0.666	0.670	0.644	0.672	0.634
PPV	0.625	0.593	0.552	0.500	0.425	0.386	0.375	0.333
NPV	0.943	0.967	0.967	0.966	0.971	0.970	0.977	0.976
Total cholesterol (<150 mg/dL)								
Sensitivity	0.714	0.786	0.786	0.786	0.786	0.786	0.857	0.857
Specificity	0.914	0.902	0.890	0.871	0.822	0.804	0.785	0.748
YI	0.628	0.688	0.676	0.657	0.608	0.590	0.642	0.605
PPV	0.417	0.407	0.379	0.344	0.275	0.256	0.255	0.226
NPV	0.974	0.980	0.980	0.979	0.978	0.978	0.985	0.984
BMI (<18.5 kg/m^2)								
Sensitivity	0.395	0.419	0.442	0.465	0.558	0.581	0.605	0.674
Specificity	0.902	0.891	0.881	0.870	0.839	0.824	0.798	0.772
YI	0.297	0.310	0.323	0.335	0.397	0.405	0.403	0.446
PPV	0.472	0.462	0.452	0.444	0.436	0.424	0.400	0.397
NPV	0.870	0.873	0.876	0.880	0.895	0.898	0.901	0.914

BMI, body mass index; MNA, Mini-Nutritional Assessment; NPV, negative predictive value; PPV, positive predictive value; YI, Youden index

similar pattern when 15.5 rather than 17 was used as the threshold MNA score; the sensitivities were unchanged or decreased and the specificities increased. With a cutoff point below 18, the sensitivity and specificity for hypoalbuminemia were 0.857 and 0.815, respectively; in this case, the sensitivity of the MNA total score increased but the specificity decreased, as did the positive predictive value.

MNA-SF scores averaged 9.8 ± 0.2 and ranged from a minimum of 1 to a maximum of 14. Although MNA-SF contains only BMI as an anthropometric marker, Table 2 presents the significant correlations between MNA-SF score and age, BMI, MAC, CC, TSF, serum albumin, total cholesterol, or MNA total score. However, the higher degree of correlation existed between these nutritional markers and MNA total score. According to MNA criteria (≥24) used to define "well nourished," only 22.1% of subjects were assessed as such. Thus, 77.9% were malnourished or at risk of malnutrition. The correlation between MNA-SF and MNA total scores was high ($r = 0.88$, $P < 0.0001$). The sensitivity, specificity, Youden index, and positive and negative predictive values for different cutoff points for MNA-SF are presented in Table 4. For MNA-SF, the optimal cutoff point was lower than 12 (sensitivity = 0.861, specificity = 0.840, and Youden index = 0.701). This point can be also determined visually from the ROC curve (Fig. 1B).

Discussion

In the present study, the MNA was validated in the Japanese elderly. We demonstrated that the MNA total score showed a good correlation with anthropometric markers and biochemical markers including serum albumin and total cholesterol. The full MNA contains anthropometric indices including BMI, MAC, and CC. To date, no ethnic-specific anthropometric targets exist; rather, these targets are derived from populations of United States or European origin and are inappropriately applied to men and women of Asian descent. Ethnicity has been recognized as a significant modifier in anthropometric measurements [23]. In addition, MNA contains dietary patterns that may differ across ethnicities [24]. Therefore, the MNA or cutoff point for malnutrition may not be a good fit for the Asian, including Japanese, elderly.

Table 4
Validity values of the MNA-SF score for the risk of malnutrition

	Threshold for MNA-SF score				
	<9	<10	<11	<12	<13
Sensitivity	0.385	0.529	0.679	0.861	0.973
Specificity	1.000	0.980	0.960	0.840	0.540
YI	0.385	0.509	0.639	0.701	0.513
PPV	1.000	0.990	0.984	0.953	0.888
NPV	0.303	0.358	0.444	0.618	0.844

MNA-SF, Mini-Nutritional Assessment, Short Form; NPV, negative predictive value; PPV, positive predictive value; YI, Youden index

Several investigators have dealt with the problem of establishing nutritional parameters for the elderly. In the present study we used anthropometric measurements including BMI, MAC, TSF, and CC and biochemical markers such as serum albumin and total cholesterol as nutritional parameters. Although there are no currently, generally accepted criteria for the diagnosis of malnutrition, these parameters have been widely used to evaluate nutritional status. It should be noted that in the present study cutoff points below 3.5 g/dL for serum albumin and below 150 mg/dL for total cholesterol were considered as undernutrition markers. With aging there may be a small decrease in serum albumin [10]. Total cholesterol levels increase with age in healthy individuals and reach a peak between sixth and ninth decades, only to decrease afterward [10]. The cutoff points used in this study for undernutrition markers are widely accepted even in the elderly [10].

We also showed that the MNA is accurate, based on observation of the ROC curve. These results suggested that the MNA is a useful tool to assess the nutritional status of the Japanese elderly. In the elderly populations in Europe and the United States, an MNA total score cutoff point below 17 as an indicator of protein-calorie undernutrition was found to have a sensitivity of 96%, specificity of 98%, and positive predictive value of 97% [11]. However, the same cutoff point yielded a much lower sensitivity and specificity among the Japanese elderly.

For screening purposes, a malnutrition cutoff point below 18 appears to be better than one below 17 for the Japanese elderly, even though higher cutoff points were associated with lower predictive values. However, if MNA is used as a diagnostic tool, a cutoff point below 15.5 is the best for detecting malnutrition in the Japanese elderly because diagnosis requires a high specificity and a high positive predictive value. MNA is a screening tool mainly for malnutrition. MNA results must be confirmed by other anthropometric, biochemical, and dietary parameters to have a complete nutritional status evaluation and malnutrition diagnosis. Therefore, sensitivity is much more important than specificity, and a cutoff point below 18 appears to be more accurate for the Japanese elderly.

We also demonstrated that there were significant correlations between the MNA-SF score and nutritional parameters in addition to the full MNA score, although these correlations were somewhat stronger in MNA total score than in MNA-SF. When a full MNA score of at least 24 was considered the cutoff point for "normal nutrition" in the Japanese elderly, the optimal MNA-SF cutoff point was at least 12, a finding identical to that in the original report [16]. These results suggest that MNA-SF, which comprises six items, allows a quick screening to determine malnutrition and risk of malnutrition in the Japanese elderly. It has been demonstrated that an MNA score between 17 and 23.5, corresponding to "at risk of malnutrition," can identify older persons with mild malnutrition [25]. In addition, subjects "at risk of malnutrition" had higher mortality rates than did