Table 1. Mean value in diopters of astigmatism by age group

	Age (years)				
	40–49	50–59	60–69	70–79	Total
Number of right eyes (total)	567	559	545	473	2144
Number of right eyes (corneal)	559	552	540	466	2117
Total astigmatism (mean ± SD)	−0.77 ± 0.66	−0.89 ± 0.71	−1.04 ± 0.67	−1.25 ± 0.74	−0.97 ± 0.72
Corneal astigmatism (mean ± SD)	−0.83 ± 0.57	−0.82 ± 0.61	−0.85 ± 0.63	−0.95 ± 0.70	−0.86 ± 0.63

a

b

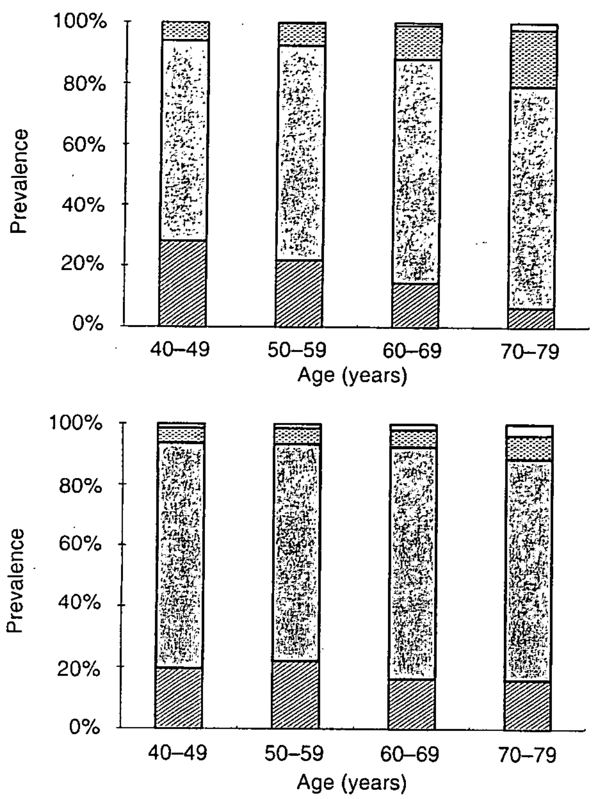

Figure 1. **a** Prevalence of total astigmatism by age group. **b** Prevalence of corneal astigmatism by age group. ▨, <0.5 D; ▤, ≧0.5 D to <2.0 D; ▦, ≧2.0 D; □, not measurable, in ascending order from bottom to top of each column. For total astigmatism, the prevalence of astigmatism ≧0.5 D to <2.0 D was the most frequent in all age groups. The prevalence of astigmatism ≧2.0 D increased, whereas that of astigmatism <0.5 D decreased, with age (**a**). The prevalence of corneal astigmatism tended to be similar to that of total astigmatism in each age group (**b**). As a result, in the eldest age group, the prevalence of astigmatism ≧0.5 D was over 90% for total astigmatism and over 80% for corneal astigmatism. (**a**, **b**).

a

b

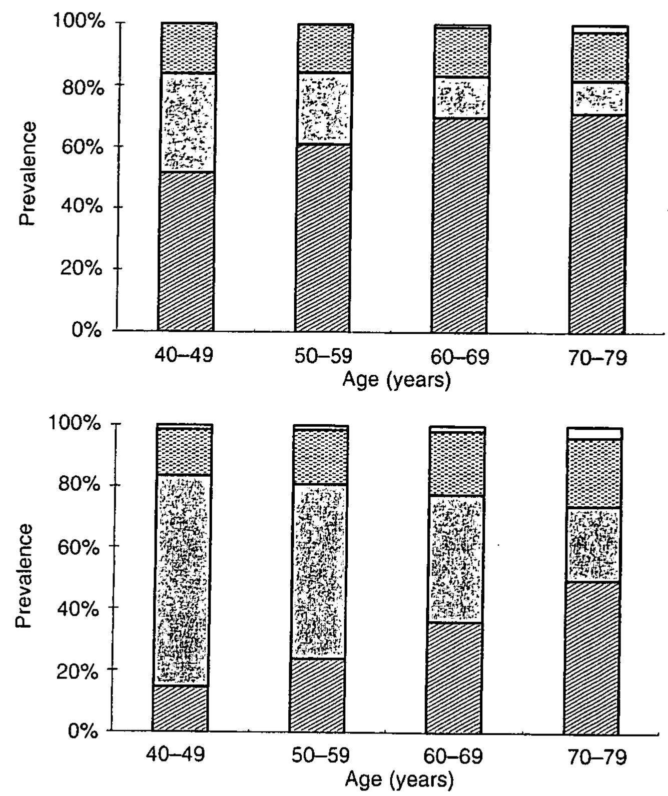

Figure 2. **a** Axis of total astigmatism by age group. **b** Axis of corneal astigmatism by age group. ▨, against-the-rule; ▤, with-the-rule; ▦, oblique; □, not measurable, in ascending order from bottom to top of each column. For total astigmatism, against-the-rule astigmatism was the most frequent in all age groups; the prevalence was over 40% in the 40s age group an increased with age (**a**). For corneal astigmatism, with-the-rule astigmatism was the most frequent in the 40s age group; its prevalence was over 60% in this group and decreased with age. In contrast, the prevalence of against-the-rule astigmatism increased with age (**b**).

lence of astigmatism ≧0.5 D to <2.0 D was the most frequent in all age groups. The prevalence of astigmatism ≧2.0 D increased, whereas that of astigmatism <0.5 D decreased, with age (Cochran-Mantel-Haenzel test, $P < 0.0001$; Fig. 1a). The prevalence of corneal astigmatism tended to be similar to that of total astigmatism in each age group (Cochran-Mantel-Haenzel test, $P < 0.01$; Fig. 1b). As a result, in the oldest age group, the prevalence of astigmatism ≧0.5 D was over 90% for total astigmatism and over 80% for corneal astigmatism. (Fig. 1a, b).

The axis distribution of total and corneal astigmatism by age group is shown in Fig. 2. For total astigmatism, against-the-rule astigmatism was the most frequent in all age groups, and the prevalence was over 40%, which increased with age. On the other hand, the prevalence of with-the-rule astigmatism decreased with age (Cochran-Mantel-Haenzel test, $P < 0.0001$; Fig. 2a). As for corneal astigmatism, with-the-rule astigmatism was the most frequent in the 40s age group; its prevalence was over 60% in this group and decreased with age. In contrast, the prevalence of against-the-rule astigmatism increased with age (Cochran-Mantel-Haenzel test, $P < 0.0001$; Fig. 2b).

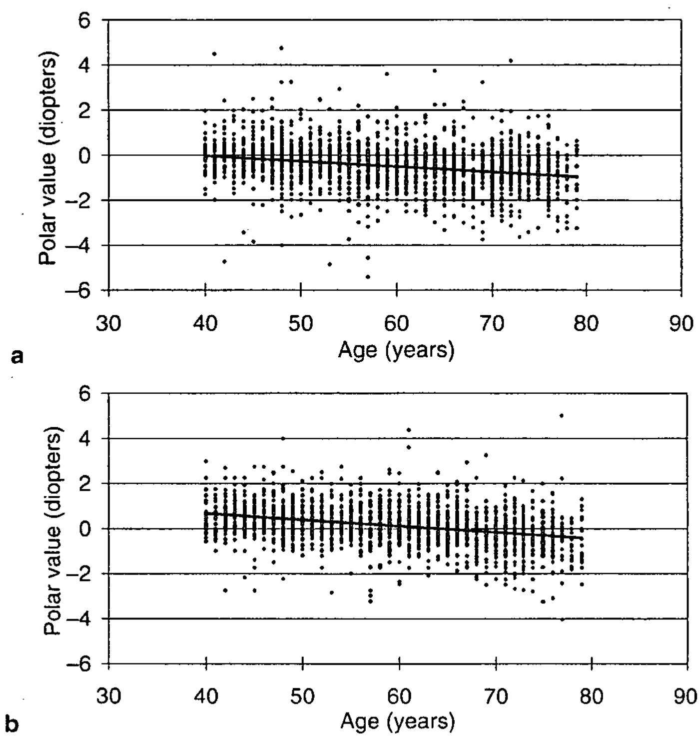

Figure 3. **a** Polar value (dependent variable) of total astigmatism by age (independent variable).

$y = -0.0241x + 0.9375, R^2 = 0.0737$

b Polar value (dependent variable) of corneal astigmatism by age (independent variable).

$y = -0.0277x + 1.7713, R^2 = 0.1145$

Polar value = $M(\sin^2\alpha - \cos^2\alpha)$, where M is the magnitude of net astigmatism in diopters, and α is the meridian of net astigmatism in degrees.

Figure 3 shows the distribution of polar values and the linear regression models for total and corneal astigmatism by age. The regression coefficients (±SE) for total and corneal astigmatism were -0.024 ± 0.002 ($P < 0.0001$) and -0.028 ± 0.002 ($P < 0.0001$), respectively, and there was no statistical difference between them. We confirmed that the prevalence of against-the-rule astigmatism increased with age for both types of astigmatism, because both regression coefficients were negative (Fig. 3a, b).

Discussion

It is well known that visual impairment increases with advancing age[1–4] and that it is associated with decreased physical and psychosocial functioning.[5–9] In addition, visual impairment in the elderly population is related to increased mortality.[37] According to the Salisbury Eye Evaluation (SEE) study, subjective measurements of various visual functions may correlate with motor function and activities of daily living.[12] On the other hand, cataract, one of the structural markers of visual functions, is the most common cause of age-related vision loss and limits the physical activity of the elderly.[4,38] In Japan, there are few comprehensive studies on aging that include eye examinations, such as studies on the relationship between astigmatism and aging. In this study, we investigated the effect of aging on astigmatism in adult Japanese. We used large population-based samples over the age of 40. To the best of our knowledge, the present study is the first population-based study to analyze astigmatic data in Japan.

McKendrick and Brennan[16] have suggested that astigmatism is a bivariate quantity consisting of an astigmatic net value and an axis. Numerous authors have measured the levels of astigmatism exhibited in human populations; however, these studies have focused on the net value only or have grouped the astigmatic axes on some arbitrary basis. Thus, with these approaches researchers have been unable to describe the characteristics of astigmatism accurately and completely. Recently, however, analytical procedures that can evaluate the astigmatic net value and the axis as a complex entity have been developed. For example, McKendrick and Brennan[16] indicated that transformation of the net value from the usual clinical format to a vector format enables a researcher to apply formal multivariate statistical procedures to refractive errors. They have statistically quantified the astigmatic distribution. In their study, vector analysis was used, as it enabled them to apply formal multivariate statistical techniques to astigmatic data, making it possible to simultaneously include both the net value and the axis in the analytical procedure. They applied this method to population data on both total and corneal astigmatism in a sample of 198 adults. There have been other reports using vector analysis to assess astigmatic data.[39–41] Conversely, Toulemont[39] suggested that although vector methods constitute interesting geometrical models, the number of vector methods and the lack of both linearity and explicit expression of results using vector analysis make the methods unsuitable for statistical analysis. He also recommended a reliable, easily programmable method that uses existing software.

Naeser[30] developed the polar value method, which provides a combined index of the net value and axis of the astigmatism. He suggested several advantages of this method: (1) Net astigmatism is characterized by a single number. Thus, a meaningful analysis can be performed with the aid of simple mathematical methods. (2) The defined polar value calculates most accurately the balance between the with- and the against-the-rule components for any given net astigmatism. (3) This model is strictly logical with respect to the with- and against-the-rule concepts, and (4) it provides an exact description of surgically induced with- or against-the-rule astigmatism following cataract extraction. The advantage of this model is that corneal astigmatism can be expressed by a single figure. The system enables each surgeon to evaluate the contribution of the preoperative astigmatism, incision type, suture technique, and postoperative astigmatism treatment to the final astigmatism. This, in turn, allows the surgeon to consider a number of different surgical techniques empirically. By rejecting and choosing from several known techniques, the surgeon may be able to minimize final astigmatism even in cases of significant preoperative astigmatism. Other authors have also suggested this advantage of the polar value method in evaluating astigmatic data.[40–42] Naeser and Hjortdal[41,42] indicated that polar values were specifically developed for analysis of the astigmatic component of refractive surgery. Naeser[30] also reported some disadvantages of the system: (1) loss of specificity, because a number of different combinations of meridians and magnitudes, including mirror-image astigmatisms, may have identical polar values; and (2) discrepancy between the astigmatic numerical magnitude and polar value. Large, oblique types of astigmatism close to the 45° meridian have polar values approximating zero. When a with- and against-the-rule nomenclature is chosen, it is completely logical that a 45° astigmatism with its equal distribution of dioptric components on the 90° and 180° meridians has the polar value of zero. In Japan, a few authors have statistically quantified the astigmatic distribution using vector analysis or the polar value method. Therefore, we used the polar value method[30] to evaluate astigmatic data in this study.

In our study, both the net value and the prevalence of total and corneal astigmatism increased with age. Concerning the axis of total astigmatism, against-the-rule astigmatism was the most frequent in all age groups; the prevalence was over 40% and increased with age. For corneal astigmatism, with-the-rule astigmatism was the most frequent in the 40s age group, in which the prevalence was over 60%, and its prevalence decreased with age. In contrast, the prevalence of against-the-rule astigmatism increased with age in the same group. These results are similar to those of previous studies.[32,35] In the Blue Mountains Eye Study,[35] the sex-adjusted mean cylindrical power for total astigmatism increased with age, from −0.6 D in persons aged 49–59 years to −0.7 D in persons aged 60–69 years, to −1.0 D in persons aged 70–79 years, and to −1.2 D in persons aged 80–97 years ($P < 0.0001$). For corneal astigmatism, Hayashi et al.[32] reported results similar to ours, and the prevalence of with-the-rule astigmatism was 66.6% in their 40s age group. Using the analysis of polar values, we found no statistical difference between the age-related change in total astigmatism and that in corneal astigmatism from with-the-rule to against-the-rule (i.e., the against-the-rule change) in our study. This result indicates that the change in astigmatism is mainly associated with changes in the cornea and confirms the previously described trends.[17] However, the regression coefficients in total and corneal astigmatism were -0.024 ± 0.002 and -0.028 ± 0.002, respectively. In light of these relatively small coefficients, we consider other factors aside from aging to affect the astigmatic status. Thus, in the future it is necessary to investigate the relationship between numerous factors and the astigmatic change.

Previous authors have reported that the most characteristic refractive errors in the elderly are increased hypermetropia and astigmatism.[16–20] It is well known that a change from with-the-rule to against-the-rule astigmatism occurs with increasing age.[17,21–29] Among population-based studies on refractive errors, including astigmatic changes, in elderly white and black adults (Americans, Europeans, etc), Katz et al.[19] reported the prevalence of refractive errors among adult white and black Americans. They indicated that the prevalence of astigmatism increased with age and that the rates of astigmatism were higher for white persons than for black persons at all ages. In Japan, some authors[31,32] have reported astigmatic changes with age, but these results were obtained by clinical-based cross-sectional studies only. Because there have been few comprehensive studies on these changes in Mongoloid adults (Japanese, Chinese, etc), we carried out this population-based study on astigmatic changes with age in adult Japanese.

The shift from with-the-rule to against-the-rule astigmatism in the cornea progresses continuously with aging. The causes of this shift are unknown, though there are many hypotheses for it. Marin-Amat[43] suggested that a combination of two factors may be operative. One factor is the pressure caused by the eyelids in early life, which diminishes with progressive weakness of the orbicularis in old age. Another factor is the action of the extrinsic ocular muscles, particularly the medial rectus muscle. The action of this muscle in convergence flattens the horizontal meridian of the cornea and perhaps also makes the vertical meridian more curved, and thus may increase the with-the-rule astigmatism. This action decreases with aging.

Recently, Mori et al.[44] investigated the relationship between the aging shift in corneal astigmatism and the action of extraocular muscles. They suggested that the progressive axial shift in corneal astigmatism with aging might be correlated with decreased action of the superior rectus muscle. However, it is difficult to conclude that the change is due to these factors, which have such individual variations. Conversely, age-related factors such as intraocular pressure are considered to produce a change in the cornea. Duke-Elder[45] suggested that when an elevated intraocular pressure assumes the preponderant role in the conformation of the globe, as in glaucoma, against-the-rule astigmatism may tend to develop. However, he also indicated that this effect shown in the eyes of experimental animals is not seen regularly in the clinic. Thus, he suggested that the cause is more fundamental, involving a peculiarity of growth, since the corneal curvature forms a part of a similar deformation of the anterior segment of the globe that includes the sclera.

Leighton and Tomlinson[23] found a significant reduction in the axial length of the eyeball with increasing age when one essentially normal eye of each of 72 persons was studied ($P < 0.01$). In 53 of these subjects, the horizontal diameter of the cornea also became less with increasing age ($P < 0.01$). Lens thickness became greater and anterior chamber depth less ($P < 0.001$ for each). Against-the-rule rather than with-the-rule corneal astigmatism was found in old age ($P < 0.001$). Another study reported the influence of genetic factors on corneal astigmatism,[46] and there have been a few reports on the process of astigmatic change from with-the-rule to against-the-rule with aging.[22,28] For example, Saunders[28] followed the changes in the axis of astigmatism of the 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.

Acknowledgment. This study was supported by Health Sciences Research Grants (Research on Eye and Ear Sciences, Immunology, Allergy and Organ Transplantation: H12-kannkakuki-009) from the Ministry of Health, Labour, and Welfare, Japan.

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Nagoya J. Health, Physical Fitness, Sports Vol.28, No.1 (March 2005)

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

site	BMD (g/cm^2) 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. $^*p<0.05$

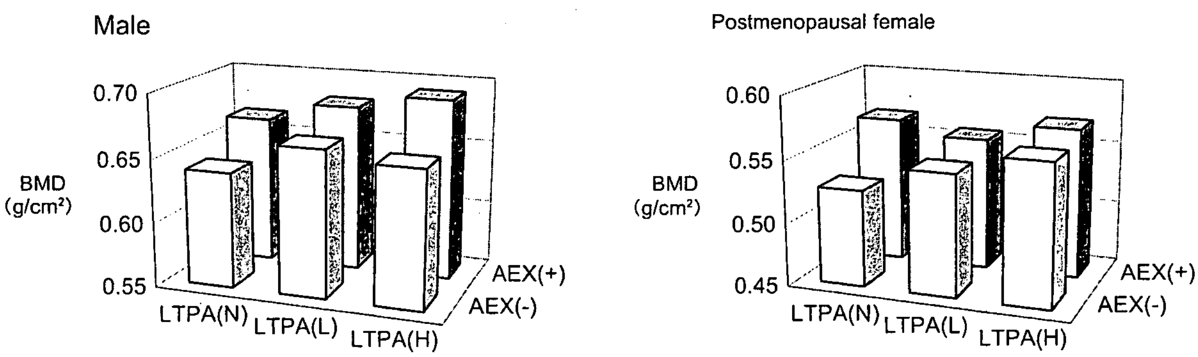

Fig. 1. The relationships of LTPA and AEX with BMD at TR controlled for age, height and weight deviding by gender. LTPA(N), no leisure-time physical activity; LTPA(L), light leisure-time physical activity; LTPA(H), moderate and heavy leisure-time physical activity; AEX(−), without adolescent exercise;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

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(2004年9月21日受付)

Clinical Nutrition (2005) 24, 427–432

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ORIGINAL ARTICLE

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

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Received 30 September 2004; accepted 7 January 2005

KEYWORDS
Malnutrition;
Elderly;
Lymphocyte count;
Mini-nutritional assessment;
Nutritional assessment

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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doi:10.1016/j.clnu.2005.01.003

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/kg²), $n = 235$			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/m²)	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/mm³)	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.

Acknowledgments

This work was supported by a Grant-in Aid for the Comprehensive Research on Aging and Health from the Ministry of Health and Welfare of Japan.

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NUTRITION

Nutrition 21 (2005) 498–503

www.elsevier.com/locate/nut

Applied nutritional investigation

Evaluation of Mini-Nutritional Assessment for Japanese frail elderly

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Manuscript received April 18, 2004; accepted August 6, 2004.

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-

This work was supported by a Grant-in Aid for the Comprehensive Research on Aging and Health from the Ministry of Health and Welfare of Japan.

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0899-9007/05/$ – see front matter
doi:10.1016/j.nut.2004.08.023

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-