副腎皮質ホルモン

副腎皮質ホルモンの比較的高用量(プレドニン換算20mg/日以上)の長期投与で骨格筋萎縮ならびに筋力低下が誘導される．主にタイプⅡ筋線維の萎縮が起こるためである．ステロイドの使用を中止することにより回復する．

核酸系逆転写酵素阻害薬

抗HIV-1薬剤である核酸系逆転写酵素阻害薬を長期間使用することにより筋障害が誘発されることがある．これも可逆性であり，薬剤中止により回復する．

抗精神病薬・ベンゾジアゼピン系薬剤

抗精神病薬やベンゾジアゼピン系の薬剤使用により転倒が増加することが知られる．転倒が多くなる機構としては今まで薬剤副作用として身体バランス障害や錐体外路障害を要因とするものが多いが，これらの薬剤が直接骨格筋に働き，筋肉量減少，筋力低下を誘導するか否かは不明である．

その他多くの薬剤が筋障害を誘導する可能性があり，表4に記載した．

表4　薬剤による筋障害のタイプ

1．壊死性筋障害
スタチン
フィブラート系薬剤
アミノカプロン酸
2．炎症性筋障害
スタチン
D-ペニシラミン
α-インターフェロン
4．Type Ⅱ筋線維萎縮
スタチン
5．ミトコンドリア筋症
核酸系逆転写酵素阻害薬，核酸誘導体
6．ライソゾーム筋障害
クロロキン
7．微小管阻害性筋障害
コルヒチン

(J Neurol Neurosurg Psychiatry 2009：80：832-838. Box1. より改変)

サルコペニアへの薬剤介入の可能性

心不全患者にangiotensin-converting enzyme(ACE)阻害薬を投与することにより，運動能力の向上が報告されたり，平均78.9歳の高血圧の女性を5年間の観察でACE阻害薬を服用していることにより膝関節屈曲力ならびに歩行速度の加齢による低下が抑制されたとの報告がある[6]．しかし，一方で横断研究によりACE阻害薬使用者と未使用者での握力に差がない[4]，カルシウム拮抗薬と筋力や歩行能力に差がなかったとの報告もあり[7]，明確な証拠が確立されているわけではない．一般にACE阻害薬の筋肉への効果を主張する論文ではその効果は筋肉への直接作用のみならず，血流増加，炎症の軽減などの間接的作用によるとしている．一方，現在降圧薬として臨床で盛んに使用されているangiotensin Ⅱ receptor blockers(ARB)の骨格筋への影響を検討した報告はまだほとんどない．

薬剤と虚弱(frailty)

虚弱(frailty)は老年医学の分野でその重要性が強調されており，その存在を放置することにより，身体機能障害が進行し，生命予後にも関連していることが指摘されている[1,8]．虚弱の定義は国際的に定まっているわけではないが，Friedらの5項目の評価(低栄養，疲労感，日常生活活動度の低下，身体能力(歩行速度)の低下，筋力(握力)の低下)のうち3項目以上あてはまれば，診断されることが多い[1,8,9]．詳細は引用文献を参考にされたい．この5項目のうち，2項目はサルコペニアと関連しており，虚弱とサルコペニアは強く関連していることがわかる．

70歳以上を対象とした横断調査ではARB使用者の女性でのみ，虚弱と判定される割合が有意に少ないとする報告があるが[10]，65歳以上の女性を対象とした3年間の前向き調査ではACE阻害薬やスタチン使用者と虚弱の発症率との有意な関係は認められていない[11,12]．

おわりに

サルコペニアの因果関係が明確な薬剤は，特殊なもの以外はきわめて少ない．さらに薬剤によりサルコペニアの予防または治療に結びつきそうなものは残念ながら，今のところ明らかなものはない．今回，ビタミンDなど自然界に存在する栄養素に関連する薬剤は言及しなかったが，それらが今後サルコペニアの予防，治療に貢献する可能性はある．

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Chapter 40
Mid-Upper Arm Anthropometric Measurements as a Mortality Predictor for Community-Dwelling Dependent Elderly

Masafumi Kuzuya and Hiromi Enoki

Abstract It remains controversial whether mid-arm anthropometric measurements are reflected with physical impairment or useful predictors of mortality in the elderly. The inconsistency in terms of the relationship between mid-arm anthropometric measurements and physical function and mortality may be due to the difference in study population, i.e., a healthy younger population vs frail/dependent older people. In this article we overviewed the relationships between mid-arm anthropometric measurements and mortality of elderly based on our studies and previous reports targeting older people. Our cohort study, which was composed of cross-sectional and prospective cohort analyses of 957 community-dwelling dependent elderly, demonstrated that significant higher average triceps skinfold (TSF) levels were observed in participants, compared with age-matched (5-year intervals) those of the standard Japanese population. In contrast, the average arm muscle area (AMA) levels at 5-year intervals were significantly lower than the Japanese norm. The AMA levels of the study participants were correlated with activities of daily living (ADL) score after adjusting for gender and age. Whereas TSF levels were not correlated with ADL function after adjusting for gender, age among study participants. Survival analysis of 2-years mortality was conducted using multivariate Cox proportional hazards models. AMA, TSF, and mid-arm circumference (MAC) were independent risk factors for 2-years mortality in the participants. In conclusion among community-dwelling dependent elderly, mid-arm anthropometric measurements were independent predictors of 2-years mortality.

Abbreviations

ADL	Activities of daily living
AMA	Arm muscle area
BMI	Body mass index
CI	Confidence interval
HR	Hazard ratio
JARD2001	In 2001, Japanese Anthropometric Reference Data
MAC	Mid-upper-arm circumference
NLS-FE	The Nagoya Longitudinal Study of Frail Elderly

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LTCI Long-term care insurance
TSF Triceps skinfold
SPSS Statistical Package for the Social Sciences

40.1 Introduction

Anthropometric indices of weight, height, body mass index (BMI), skinfold thickness, muscle area, and circumference are simple, easily obtainable, and inexpensive measures of assessing nutritional status. Among them, BMI, the most widely used anthropometric index, has been frequently used as an indicator of nutritional status, and is well known as an important predictor of mortality and activities of daily living (ADL) decline among older people (Liu et al. 2002; Flodin et al. 2000). However, it is not uncommon to find dependent older people who cannot be weighed or measured for height. When subjects living at home have severe functional disabilities, it is essential to have special equipment, such as beds or wheelchair scales, to measure their weight. Frequently, it is difficult to measure the height of older people with postural changes, including muscle and arterial contracture and kyphosis. In fact, we have previously shown in a cohort study of community dwelling dependent elderly that 35.9% and 30.7% had missing data for height and weight, respectively (Izawa et al. 2007).

In addition, measuring height reliably in older individuals is one of the most problematic areas of anthropometry. In old age, there is a decline in sitting and standing height due to vertebral compression, change in the height and shape of vertebral disks, loss of muscle tone, and postural changes. When these height measurements are used in the calculation of BMI, it will tend to be artificially inflated. In addition, it can be difficult to measure the standing height of older people with ADL impairment (Hickson and Frost 2003; Zang et al. 1998).

Anthropometric measurements of the mid-upper arm are often taken for measuring body composition, because they are a quick, inexpensive, and non-invasive method of measuring nutritional status. Triceps skinfold (TSF) thickness reflects subcutaneous fat, whereas mid-upper-arm circumference (MAC) takes into account the humeral diameter as well as the skeletal muscles, and fat covering the limb, therefore reflecting changes in lean body mass and fat. Mid-upper-arm muscular circumference and arm muscle area (AMA), which are derived from MAC and TSF, are also useful indicators of muscle mass.

Although these mid-arm anthropometric measurements may be useful indicators of undernutrition in older adults, it remains controversial whether these measurements are useful predictors of mortality in the elderly or whether physical impairment reflects these measurements in the older population. In this article, we overview the mid-arm anthropometric measurements as a predictor of mortality among older people and their relationships with physical functions.

40.2 Mid-Arm Anthropometric Measurements and Mortality of Elderly-Brief Review

In the general population, it has been believed that low muscle mass and high fat mass are associated with higher mortality (Janssen et al. 2002). In fact, Miller and colleagues demonstrated that among 1,396 community dwelling Australian participants aged 70 years and older, those with a low corrected AMA ($\leq$21.4 cm^2 for men and $\leq$21.6 cm^2 for women) had an increased risk of mortality at 8-year follow-up. (Miller et al. 2002), whereas no increased risk in 8-year mortality was identified for those with a high or low BMI (Miller et al. 2002). Another study reported that, in a geriatric assessment unit, it was found that an abnormally low AMA (lower than the fifth percentage of age-matched reference data) is strongly associated with increased mortality at 4.5-year follow-up (Muhlethaler et al. 1995). In contrast, over 24 years of follow-up study of random samples of participants aged 65 years and over living in the community revealed that higher AMA was associated with a significantly reduced risk of mortality from all causes only in men, and not in women (Gale et al. 2007).

The relationship between TSF thickness and mortality in the elderly remains controversial. It has been reported that among 408 elderly long-term-care residents aged 60 years and older, TSF was a significant predictor of mortality during 19 months' follow-up in the univariate analysis, but not in the multivariate analysis (Allard et al. 2004). TSF thickness did not show a statistically significant association, with 4.5-year mortality among 219 geriatric patients in a geriatric assessment unit (Muhlethaler et al. 1995). It has been observed that TSF thickness below the 5th percentile was associated with a significant increase in the relative risk of death during 40–46 months' follow-up in a community sample of 758 older people (Campbell et al. 1990).

Another study showed that, during admission in an acute care geriatric ward, MAC had a more negative trend in patients who died than changes in weight, BMI, and subjective nutritional assessment (Antonelli Incalzi et al. 1996).

40.3 Japanese Cohort Study

40.3.1 Study Design and Aim

We examined whether anthropometric measurements of mid-upper arm may be a good predictor of mortality among disabled community-dwelling older people (Enoki et al. 2007). In the present study targeting dependent community dwelling elderly persons, using the baseline and 2-year follow-up data of the Nagoya Longitudinal Study of Frail Elderly (NLS-FE), the following hypotheses were tested: (1) in community-dwelling elderly persons, who are disabled or dependent and receiving some assistances using the long-term care insurance (LTCI) program, MAC, TSF, and AMA levels are lower than those of not-frail, independent elderly persons living in the community; (2) these lower levels of measurements are associated with physical function impairment and comorbidity status; and (3) lower levels of MAC, TSF, or AMA are independent predictors of relative short-term (2-year) mortality.

40.3.2 Study Participants

This analysis was conducted using a total of 957 subjects (men, 355; women, 602) extracted from the NLS-FE data set. The study population of NLS-FE consisted of 1,875 (men, 632; women, 1,243) community-dwelling elderly (aged 65 years or older) eligible for the LTCI, who lived in Nagoya city (Central Japan) and were provided various home care services from the Nagoya City Health Care Service Foundation for Older People, which is comprised of 17 visiting nursing stations accompanying care-managing centers (Kuzuya et al. 2006, 2008). The LTCI system provides care for the elderly aged 65 years and older. Under the LTCI program, care levels (levels 0–5) are determined according to eligibility criteria (Izawa et al. 2006). The elderly in the community, who are eligible for LTCI, are disabled and chronically ill, have physical and mental problems, and easy to admit to the acute hospital or institute care setting. A total of 957 (men, 355; women, 602) using visiting nurse services under LTCI were enrolled for the anthropometric measurements.

40.3.3 Data Collection

Anthropometric measurements were conducted by trained nurses at the clients' home. Measurement of TSF (to the nearest 2 mm) was made using caliper and MAC (to the nearest 0.1 cm) using a flexible measuring tape, on the right side of the participant's body, unless affected by disability or disease. These measurements were taken at least twice, by one trained nurse, according to the instruction sheet, and reported values were the means of the repeated measurements. Arm muscle circumference (AMC = MAC (cm) − $\pi \times$ TSF (mm)/10) and AMA were calculated using a standard formula: AMA $cm^2 = (AMC\ (cm))^2/4\pi$. BMI was defined as weight in kilogram divided by height squared.

The mean scores of anthropometric measurements of patients grouped by age and gender were compared with the JARD 2001, anthropometric norms for healthy men and women without physical function impairment in each 5-year age bracket, including subjects over age 65 years (Japanese Anthropometric Reference Data 2002). In JARD 2001, a mean value, a central value, standard deviation, maximum value, minimum value, and percentile (5th, 10th, 25th, 75th, 90th, and 95th) were determined according to the age division. Therefore, it was possible to compare the obtained measurement values and these reference values.

40.3.4 Sample Description

Characteristics of subjects in the present study are given in Table 40.1. The mean (SD) age of 957 patients studied was 80.4 (7.9) years, with a range of 65–102 years. Among those, 318 patients (33.2% of total) were 85 years or older. Most were capable of oral food intake (91.5% of total). The physical function of the participants (basic ADL, score range: 0–20) was markedly impaired with a mean (SD) score of 10.3 (6.9). A history of cerebrovascular disease was the most frequent diagnosis observed in this cohort (334 patients, 34.9% of total).

40.3.5 Comparison of Anthropometry Between Study Participants and Japanese Norms

BMI is the anthropometric measurement most widely used for assessing nutrition status. However, it is often difficult for older people with impaired physical function to be measured for height and weight at their homes. In fact, in our cohort, BMI data were not available for 437 out of 957 participants, even though we asked visiting nurses and caregivers to measure weight and height as far as possible. It should be noted that there were no differences in BMI levels between the participants and Japanese norms for any age group in either gender (Enoki et al. 2007) (Tables 40.2 and 40.3).

Table 40.1 Demographic characteristics of patients (Reprinted from Enoki et al. (2007). With permission from Elsevier)

Variables	Categories (year)	Male $N = 355$ N (%), average ± SD	Female $N = 602$ N (%), average ± SD	p-Value
Age (year)		78.50 ± 7.49	81.57 ± 7.97	<0.001
	65–69	47 (13.2)	46 (7.6)	<0.001
	70–74	63 (17.7)	82 (13.6)	
	75–79	100 (28.2)	119 (19.8)	
	80–84	58 (16.3)	124 (20.6)	
	85+	87 (24.5)	231 (38.4)	
Nutrition	Peroral	322 (90.7)	554 (92.0)	0.622
	Enteral feeding	32 (9.0)	45 (7.5)	
	Parenteral nutrition	1 (0.3)	3 (0.5)	
Basic ADL (0–20)		11.0 ± 6.5	9.9 ± 7.1	0.013
Charlson comorbidity index (0–35)		2.5 ± 1.6	2.2 ± 1.6	0.019
Illness	Ischemic heart disease	31 (8.7)	64 (10.6)	0.496
	Congestive heart failure	32 (9.0)	60 (10.0)	0.818
	Liver disease	13 (3.7)	20 (3.3)	0.714
	Cerebrovascular disease	147 (41.4)	187 (31.1)	<0.001
	Diabetes	38 (10.7)	68 (11.3)	0.914
	Dementia	92 (25.9)	221 (36.7)	0.001
	Chronic pulmonary disease	38 (10.7)	42 (7.0)	0.037
	Neoplasia	37 (10.4)	51 (8.5)	0.242
	Hypertension	70 (19.7)	150 (24.9)	0.068
Anthropometric measurements				
Body mass index, kg/m^2		20.8 ± 3.4 ($n = 219$)	20.8 ± 4.4 ($n = 301$)	0.978
Mid-arm circumference, cm		24.3 ± 4.1	23.1 ± 4.5	<0.001
Triceps skinfold thickness, mm		14.3 ± 9.4	15.5 ± 9.5	0.200
Arm muscle area, cm^2		32.4 ± 11.6	28.0 ± 11.5	<0.001

Statistical analysis: unpaired t-test (age, basic ADL, Charlson comorbidity index, and anthrometric measurements) and χ^2 test (age group, nutrition route, and illness)

Table 40.2 Comparison of anthropometry between cohort and Japanese reference data (Male)

Male	Age (Year)	Cohort Average ± SD	JARD Average ± SD	p-value
Mid-arm circumference, cm	65–69	25.3 ± 3.6	27.3 ± 2.7	<0.001
	70–74	25.4 ± 5.5	26.7 ± 2.9	0.078
	75–79	24.0 ± 3.7	25.8 ± 3.0	<0.001
	80–84	24.0 ± 3.4	25.0 ± 3.0	0.046
	85+	23.6 ± 3.5	23.9 ± 3.1	0.351
Triceps skinfold thickness, mm	65–69	14.9 ± 8.6	10.6 ± 4.2	<0.001
	70–74	13.0 ± 10.1	10.8 ± 5.3	0.058
	75–79	14.8 ± 10.1	10.2 ± 4.2	<0.001
	80–84	16.5 ± 9.9	10.3 ± 4.3	<0.001
	85+	12.9 ± 8.1	9.4 ± 4.6	<0.001
Arm muscle area, cm^2	65–69	34.9 ± 13.5	46.1 ± 9.4	<0.001
	70–74	38.0 ± 19.3	43.9 ± 10.2	<0.001
	75–79	30.9 ± 10.9	41.4 ± 9.6	<0.001
	80–84	29.4 ± 10.9	38.2 ± 10.1	<0.001
	85+	31.6 ± 11.9	35.4 ± 8.9	0.004

JARD Japanese Anthropometric Reference Data

Table 40.3 Comparison of anthropometry between cohort and Japanese reference data (female)

Female	Age (Year)	Cohort Average ± SD	JARD Average ± SD	*p*-Value
Mid-arm circumference, cm	65–69	25.6 ± 4.2	26.4 ± 2.7	0.193
	70–74	25.2 ± 4.8	25.6 ± 3.2	0.436
	75–79	24.2 ± 4.8	24.6 ± 3.5	0.381
	80–84	22.5 ± 4.1	23.9 ± 3.3	<0.001
	85+	21.5 ± 3.9	22.9 ± 3.4	<0.001
Triceps skinfold thickness, mm	65–69	18.1 ± 10.4	19.7 ± 7.0	0.068
	70–74	17.9 ± 9.4	17.1± 6.8	0.051
	75–79	17.7 ± 10.0	14.4 ± 6.8	<0.001
	80–84	13.5 ± 9.0	13.0 ± 5.9	0.057
	85+	13.1 ± 8.6	11.7 ± 5.9	<0.001
Arm muscle area, cm^2	65–69	32.5 ± 11.9	32.7 ± 7.6	0.890
	70–74	31.5 ± 12.3	33.2 ± 8.6	0.218
	75–79	29.6 ± 12.6	32.7 ± 8.6	0.011
	80–84	27.4 ± 10.5	31.8 ± 8.1	<0.001
	85+	25.2 ± 10.2	29.4 ± 8.8	<0.001

JARD Japanese Anthropometric Reference Data

Anthropometric measurements of the mid-upper arm including TSF and MAC can be introduced easily in the community-dwelling elderly, as it is a quick, handy, inexpensive and non-invasive method. AMA, as an index for muscle mass, can easily be calculated from TSF and MAC. As shown in Table 40.2, the MAC levels of male participants of the 75–84 years age group were significantly lower than the Japanese norm. In female participants, MAC levels in the 80–84 years and 85 years and older age groups were lower than the Japanese norms (Table 40.3). There were significantly higher TSF levels in male participants of all age groups except for 70–74 years and higher TSF levels in female participants of the 75–79 years and 85 years and older age groups, compared with Japanese norms. The AMA of male participants was significantly lower than the Japanese norm in all age groups. In female participants, lower AMA levels were observed in the 75–79 years, 80–84 years, and 85 years and older age groups. We observed that AMA or TSF levels were lower and higher, respectively, in participants of NLS-FE than those of the standard Japanese population. The lack of differences in BMI levels for each 5-year-interval, gendered age group between our cohorts with some disabilities and the Japanese norm suggested that though there were clear differences in body composition between Japanese subjects with or without physical impairment, total body mass did not reflect those differences.

40.3.6 Anthropometry and ADL

The correlation between anthropometric measurements and ADL function was evaluated using the partial rank correlation coefficients, after adjusting for gender and age. ADL score was significantly correlated with BMI (correlation coefficient (r) = 0.191, $p < 0.01$), MAC ($r = 0.288$, $p < 0.01$), and AMA ($r = 0.298$, $p < 0.01$), but not with TSF ($r = 0.019$, $p = 0.749$). It has been reported in cross-sectional observations that physical disability is associated with increases in percentage body fat as well as a decrease of fat-free mass (Liou et al. 2005; Broadwin et al. 2001; Davison et al. 2002). In cross-sectional analyses from the Rancho Bernardo Cohort Study, a significant positive association was shown between fat mass, which was estimated by bioelectric impedance analysis, and overall functional disability, and a significant negative association was shown between fat-free mass and overall functional disability in both men and women (Broadwin et al. 2001). In agreement with these previous findings, we demonstrated that AMA levels in the study participants were lower than Japanese norms and that AMA levels of the study participants were correlated with ADL score after adjusting for gender and age (i.e., lower AMA levels with lower ADL function). Although recent observation suggested that lower extremity muscle mass is a strong independent predictor of the level of functional impairment in community-dwelling older adults (Reid et al. 2008), our results may also suggest that not only leg muscle mass but also arm muscle mass is an important determinant of physical performance among functionally limited elders.

Our study results were also consistent with previous findings of higher TSF levels in the study participants than those in Japanese subjects without impairment of physical function. However, we observed that TSF levels were not correlated with ADL function after adjusting for gender and age among study participants. When analysis was conducted after adjustment for BMI, ADL score was still correlated with AMA ($r = 0.151$, $p = 0.001$), but not with TSF ($r = -0.081$, $p = 0.072$). These results indicated that TSF levels are influenced by other factors, such as nutritional status, besides only the level of physical function, at least among our participants with ADL disabilities.

40.3.7 Anthropometry of Mid-Arm and 2-Year Mortality

Among the 957 participants, 236 died during the 2-year follow-up period. Tables 40.4 and 40.5 show the univariate and multivariate Cox proportional hazards regression models to identify independent predictors of 2-year mortality. The following baseline data were used in a Cox proportional hazards model to identify independent predictors of 2-year mortality: age, gender, ADL status, comorbidity status, and levels of MAC, TSF, and AMA. The risk of a variable was expressed as a hazard ratio (HR) with a corresponding 95% confidence interval (CI). For the analysis, age was categorized into three groups: 65–74 years, 75–84 years, and 85 years or older. The ADL score (range: 0–20) and the Charlson comorbidity index score, which represents the sum of a weighted index that takes into account the number and seriousness of preexisting comorbid conditions, were categorized into three groups with approximately equal numbers of participants in each group: ADL, high function, ≥18; mild function, 12–17, and low function, ≤11; the Charlson comorbidity index score, <2, 2–3, ≥4. AMA (cm^2) was categorized into three groups by tertile: high, ≥33.4; mild, 23.5–33.3; and low, <23.5. TSF (mm) was categorized into three groups by tertile: high, ≥17; mild, 10–16; and low, <10. MAC (cm) was also categorized into three groups by tertile: high, ≥25.2; mild, 24.5–25.1; and low, <24.5 (Tables 40.4 and 40.5).

Unadjusted univariate analysis suggested that the oldest age category (≥85 years), low ADL function, ≥4 Charlson comorbidity index score, <10 mm TSF thickness, <23.5 cm^2 AMA, and <24.5 cm MAC were associated with 2-year mortality (Tables 40.4 and 40.5). A multivariate Cox proportional hazards regression model based on the all the variables used in univariate analysis showed that low TSF(<10 mm) and low AMA (<23.5 cm^2) were associated with 2-year mortality (Table 40.4). In addition, when MAC was used instead of TSF and AMA, it (mild: 24.5–25.1 cm and low: <24.5 cm) was associated with mortality (Table 40.5) with higher hazard ratio than that of TSF or AMA.

In the general population, it has been demonstrated that fat-free mass and TSF, an indicator of fat mass, have clear negative and positive relationships, respectively, with mortality (lower fat-free mass and higher TSF with higher mortality) (Zhu et al. 2003; Allison et al. 2002). Consistent with those

Table 40.4 Cox proportional hazard models for 2-year mortality (Reprinted from Enoki et al. (2007). With permission from Elsevier)

	Univariate		Multivariate	
Variable	Hazard ratio (95% CI)	*p*-Value	Hazard ratio (95% CI)	*p*-Value
Gender				
Female[a]	1.00		1.00	
Male	1.16 (0.90–1.51)	0.260	1.31 (0.96–1.80)	0.088
Age group				
65–74[a]	1.00		1.00	
75–84	1.31 (0.92–1.87)	0.135	1.01 (0.67–1.51)	0.966
85 year ≤	1.70 (1.19–2.42)	0.004	1.16 (0.76–1.76)	0.486
Basic ADL				
High function (≥18)[a]	1.00		1.00	
Mild function (12–17)	1.26 (0.78–2.03)	0.340	1.03 (0.62–1.69)	0.922
Low function (≤11)	2.36 (1.53–3.63)	<0.001	1.76 (1.09–2.83)	0.020
Charlson comorbidity index				
<2[a]	1.00		1.00	
2–3	1.36 (0.96–1.92)	0.083	1.33 (0.94–1.90)	0.112
≥4	1.70 (1.17–2.46)	0.005	1.35 (0.91–2.02)	0.141
Triceps skinfold thickness (mm)				
High (≥17)[a]	1.00		1.00	
Mild (10–16)	1.14 (0.81–1.59)	0.459	1.26 (0.85–1.88)	0.230
Low (<10)	1.75 (1.26–2.42)	0.001	1.89 (1.30–2.75)	0.001
Arm muscle area (cm^2)				
High (≥33.4)[a]	1.00		1.00	
Mild (23.5–33.3)	1.34 (0.93–1.92)	0.115	1.26 (0.85–1.88)	0.256
Low (<23.5)	2.04 (1.47–2.85)	<0.001	2.03 (1.36–3.02)	<0.001

CI confidence interval
[a]Reference category

Table 40.5 Cox proportional hazard models to examine the association between 2-year mortality and MAC

	Univariate		Multivariate	
Variable	Hazard Ratio (95% CI)	*p*-Value	Hazard Ratio (95% CI)	*p*-Value
Gender				
Female[a]	1.00		1.00	
Male	1.16 (0.90–1.51)	0.26	1.34 (0.98–1.83)	0.061
Age group				
65–74[a]	1.00		1.00	
75–84	1.31 (0.92–1.87)	0.135	0.99 (0.66–1.48)	0.954
85 year ≤	1.70 (1.19–2.42)	0.004	1.16 (0.77–1.76)	0.471
Basic ADL				
High function (≥18)[a]	1.00		1.00	
Mild function (12–17)	1.26 (0.78–2.03)	0.340	1.04 (0.62–1.72)	0.889
Low function (≤11)	2.36 (1.53–3.63)	<0.001	1.71 (1.06–2.76)	0.029
Charlson comorbidity index				
<2[a]	1.00		1.00	
2–3	1.36 (0.96–1.92)	0.083	1.38 (0.97–1.98)	0.075
≥4	1.70 (1.17–2.46)	0.005	1.52 (1.02–2.26)	0.040
Mid-upper-arm circumference (cm)				
High (≥25.2)[a]	1.00		1.00	
Mild (24.5–25.1)	1.81 (0.81–1.59)	0.002	1.63 (1.07–2.47)	<0.001
Low (<24.5)	2.98 (1.26–2.42)	<0.001	2.77 (1.83–4.18)	<0.001

CI confidence interval
[a]Reference category

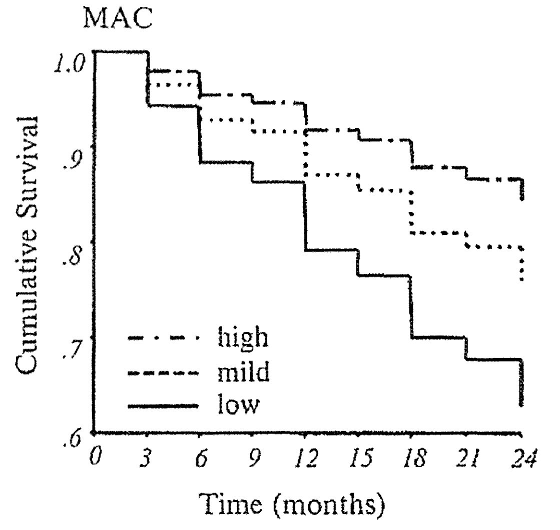

Fig. 40.1 Kaplan–Meier survival curves for elderly subjects with various levels of MAC (cm). MAC (cm) levels were classified as low (<24.5), mild (24.5–251), and high (25.2≤). Survival curves were plotted using the Kaplan–Meier method, adjusting for age, gender, ADL status, and Charlson comorbidity index

findings, a number of studies have demonstrated that AMA or AMC, another indicator of muscle mass, is a predictor of mortality in older people (Miller et al. 2002; Muhlethaler et al. 1995). As described above, controversial results have been reported in terms of the relationships between TSF and mortality in older people. Our prospective observation demonstrated that lower TSF was an independent predictor of 2-year mortality among community-dwelling dependent older people, even after adjusting for possible confounding factors. The inconsistency between our study and previous studies targeting the general population in terms of the relationship between TSF and mortality may be due to the difference in study population, that is, a healthy younger population versus frail older people with some disabilities. A higher TSF seems to reflect obesity and hyperalimentation in the general population, but in our frail elderly participants, a lower TSF seems to reflect undernutrition. However, it may be possible that cultural differences between Japan and other Western countries may affect this inconsistency. Recently, a study demonstrated that fat mass index, measured with a gold standard technique (X-ray absorptiometry) and bioelectrical impedance analysis, is a predictive marker of morbidity and mortality in hospitalized elderly patients (Bouillanne et al. 2009), suggesting that, at least among vulnerable older people, fat mass including TSF has protective role on adverse outcomes of the elderly.

We also observed that MAC was a better predictor of 2-year mortality among community dwelling dependent older people compared with AMA or TSF. This result is not surprising. Because MAC takes into account the humeral diameter as well as the skeletal muscles and fat covering the limb, therefore reflecting both TSF and AMA.

40.3.8 Kaplan–Meier Survival Curves

Figures 40.1 and 40.2 show the multivariate-adjusted Kaplan–Meier survival curves exploring the association between MAC, TSF, or AMA categories and time to death (3-month interval). The lowest category of MAC (<24.5 cm), TSF (<10 mm), and AMA (<23.5 cm^2) showed an increased risk of death during the 2-year follow-up compared with the middle and highest categories (Figs. 40.1 and 40.2a, b).

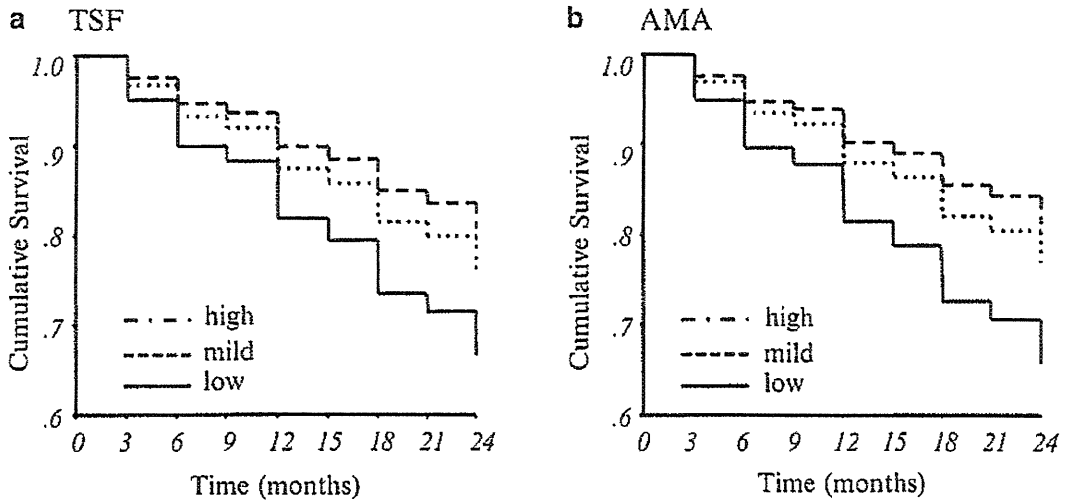

Fig. 40.2 Kaplan–Meier survival curves for elderly subjects with various levels of TSF (A) and AMA (cm²) (b). (a) TSF (mm) levels were classified as low (<10), mild (10–16), and high (17≤). (b) AMA (cm²) levels were classified as low (<23.5), mild (23.5–33.3), and high (33.4≤). Survival curves were plotted using the Kaplan–Meier method, adjusting for age, gender, ADL status, and Charlson comorbidity index (Reprinted from Enoki et al. (2007). With permission from Elsevier)

40.3.9 Combined Evaluation of AMA and TSF

We further characterized study participants using a nine-level measurement that combined AMA levels and TSF levels. Within each level of TSF, risk of mortality rose as levels of AMA decreased. Within each level of AMA, risk of mortality rose as TSF decreased. A striking increase in the risk of 2-year mortality, adjusted for age and gender, was observed in the low TSF with low AMA group (HR: 3.83, 95% CI: 1.97–7.47), versus the high TSF with high AMA (Fig. 40.3). These findings indicate that a combined evaluation of AMA and TSF strengthens the prediction of relative short-term mortality among community-dwelling dependent older people (Fig. 40.3).

40.3.10 Limitations

The current study had several limitations. NLS-FE is a large-scale observational study but does not include the complete spectrum of elderly patients in the Nagoya area, an urban area. In the analysis, baseline data of the anthropometric measurements were included, but changes in the measurements during the follow-up period were not considered. Although recent study suggested that muscle strength is more powerful predictor of mortality than muscle mass (Newman et al. 2006), data of muscle strength were not available in our study. Another limitation is that we enlisted each station to perform evaluation because of a shortage of hands and the large number of settings. This may have biased assessors' evaluations and limited the validity of the results. The results of the present study cannot transfer to the non-frail independent older population, as there should be many differences between the participants of NLS-FE and the standard non-frail older, including ADL levels and comorbidity. In addition, these findings may not be generalizable to other populations given that they may have been influenced by cultural differences, health practices, and a variety of social and economic factors.

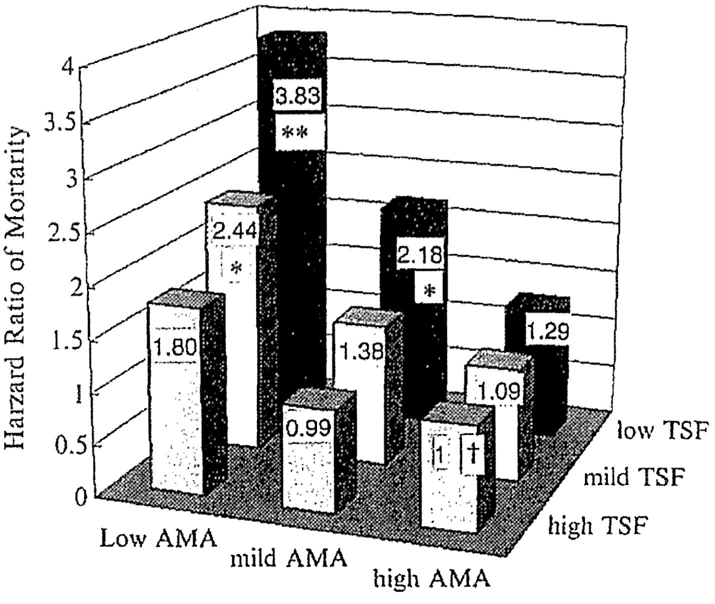

Fig. 40.3 Relative risks for all-cause mortality. Estimations were obtained from Cox regression models adjusting for age and gender. Eight independent variables, created for each level of AMA (low: <23.5 cm^2, mild: 23.5–33.3 cm^2, high: 33.4 cm^2≤) and TSF (low: <10 mm, mild 10–16 mm, high: 17 mm ≤) combined, were used as indicator variables and compared with the reference group (defined as those with high AMA and high TSF). Number on each bar indicates hazard ratio. *: $p < 0.05$, **: $p < 0.01$, †: reference group (Reprinted from Enoki et al. (2007). With permission from Elsevier)

40.4 Conclusion

Anthropometric measurements of the mid-upper arm are performed often in research, but rarely on a clinical basis, even although they are a quick, inexpensive, and non-invasive way of measuring nutritional status. In the present study, we demonstrated a striking picture of increased mortality risk associated with lower AMA levels, lower TSF, and lower MAC. Anthropometric measurements of the mid-arm may be a more practical and suitable index not only for nutritional assessment but also for capturing the vulnerable subset of older people living in the community.

40.4.1 Applications to Other Areas of Health and Disease

In the text, we focused on older people in terms of the mid-upper arm anthropometric measurements as nutritional markers and indicators of mortality risk. However, numbers of researches are using upper arm measurements as nutritional as well as growth markers for the children. The World Health Organization (WHO) introduced the Child Growth Standards, which included MAC and TSF, for assessing the growth and development of children, (WHO Multicentre Growth Reference Study Group 2006). In addition, upper arm measurements were also established as an indicator of mortality risk for children (Lapidus et al. 2009).

Summary Points

- Higher average triceps skinfold (TSF) levels were observed in community-dwelling dependent elderly, compared with age-matched (5-year intervals) individuals of the standard Japanese population.
- Lower average arm muscle area (AMA) levels were observed in community-dwelling dependent elderly, compared with age-matched (5-year intervals) individuals of the standard Japanese population.
- AMA levels of community-dwelling dependent elderly were correlated with their physical function.
- TSF levels of community-dwelling dependent elderly were not correlated with their physical function.
- Lower AMA levels of community-dwelling dependent elderly were associated with 2-year mortality.
- Lower TSF levels of community-dwelling dependent elderly were associated with 2-year mortality.
- Lower mid-arm circumference (MAC) levels of community-dwelling dependent elderly were associated with 2-year mortality.

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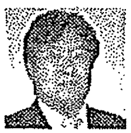
FOOD

その食べかた、間違っています



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メタボは危険、血液ドロドロなど、さんざん脅された中年期。だが、その常識のままで高齢期になると、そこには思わぬ落とし穴が！

高齢者（六十五歳以上）の総人口比率が二一%を超すと超高齢社会と言われる。日本はご存じのように二〇〇七年（平成十九年）にこの基準をクリアし、超高齢社会に突入した。高齢者とは六十五歳以上を指すが、六十代はまだまだ元気であり、医師が関わる疾患も中年と大きく変わるわけではない。しかし、七十五歳の声を聞くと、少しずつ高齢者特有の変化が現われ、健康に関してもいろいろな問題が出はじめてくる。そういった時期に特に注意しなければいけないのが、低栄養（栄養不

足）だ。

実は七十五歳以上のいわゆる後期高齢者は低栄養に陥りやすく、その予防が重要なのである。実際に、自立して生活している後期高齢者のうち低栄養と診断されるのは約一〇％程度だが、要介護認定を受けている人では三〇－四〇％が当てはまると言われており、思ったより高頻度で身近に起こっているのである。

年をとってからのメタボ対策は危険

後期高齢者が低栄養になる要因は多いが、その代表的なものを表1にまとめた。後期高齢者は一人で多くの慢性疾患を抱えていて、これらの病気が原因で栄養障害が起こる場合もある。口腔内の問題は重要で、入れ歯（義歯）が合わないだけでも食事量は落ちる。まして、嚥下障害（ムセやすい）があれば、十分な食事量はまず摂れないと考えた方がよい。

しかし、より深刻なのは、後期高齢者では社会的要因により容易に低栄養に陥ってしまうことである。一人暮らしなどは低栄養になりやすい原因のひとつだ。一人でわざわざ料理をするのも面倒なので適当なものですませる。おまけに一人ぼっち

表1 高齢者が低栄養になってしまう要因

社会的要因
貧困
一人暮らし
介護不足
孤独感

疾病
臓器不全
炎症・悪性腫瘍
薬物副作用
歯科的、咀嚼の問題
嚥下障害
ADL（日常生活動作）障害
疼痛
消化管の問題
（下痢、便秘）

加齢
臭覚、味覚障害
食欲低下
（中枢神経系の関与）

精神的心理的要因
認知機能障害
誤嚥・窒息の恐怖
うつ

その他
食形態の問題
誤った肥満の認識
栄養について誤った認識
（コレステロール、肉に対する恐怖）

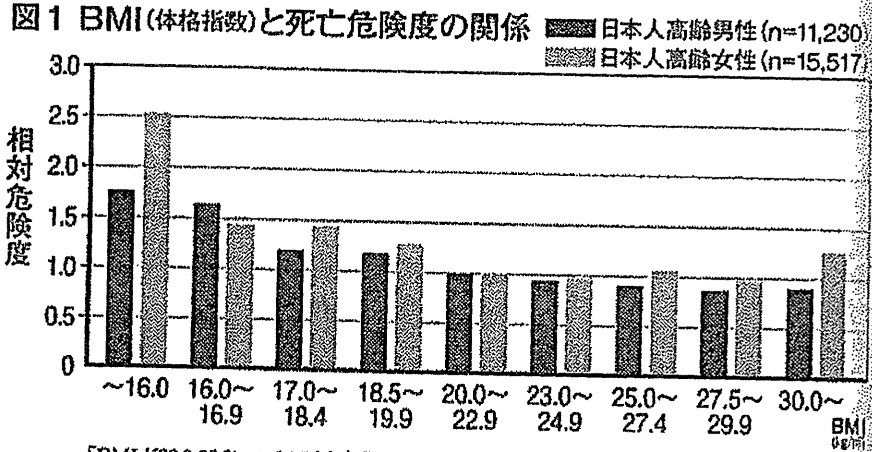
で食事をしても食は進まない。要介護状態にあって適切な介護を受けていない場合には、間違いなく低栄養に陥る。

こういった身体的・社会的要因に加えて近年問題になっているのが、中年期、健康を維持するために得た食生活のスタイルを高齢期になっても実践し続けたために、低栄養に陥るケースだ。中でもメタボリック症候群に関しては、誤解している人が多いので、注意を要する。

メタボリック症候群では肥満、特に腹部（内臓）肥満の危険性が盛んに強調されるが、果たして七十五歳を超えた人に対して同じようにこの考え方を当てはめていいのかどうかは疑問だ。

一般に肥満やヤセは体格指数（body mass index: BMI，体重（kg）÷身長（㎡））を指標として評価され、理想的な体格はBMI22kg／㎡と定められている。しかし、高齢者ではこれよりもBMIが高い方が元気で長生きすることが知られている。図1は最近報告された男女別に日本人高齢者（六十五歳から七十九歳まで）を約十一年間観察して、調査開始時のBMI値（登録時のBMI値）と生命予後（死亡）との関係を見たものである。相対危険度とはBMIが20・0－22・9kg／㎡にある人たちを一・〇〇とした時、何倍死亡しやすいかを表したものだ。図に示すようにB

図1 BMI(体格指数)と死亡危険度の関係



「BMIが20.0-22.9kg/㎡の死亡危険度を1.0とした時の各BMI群の相対リスク(11年間の観察)」
Tamakosi A,et al,Obesity 18:362-369より改編

MIが30kg／㎡を超すような高度肥満者（しかも女性）では死亡の危険度が高くなるようだが、20・0－22・9kg／㎡以上であっても男性、女性とも死亡率が高いわけではない。

一方、BMI値が低いと徐々に相対危険度が高くなり、16・0kg／㎡を切る人は20・0－22・9kg／㎡の人との比較で、男性では一・七八倍、女性では二・五五倍も死亡しやすい。同様な結果はこの報告以外にも多く存在している。このことより、高齢者ではBMIが30kg／㎡を超すような極端なケース以外は、肥満に関してそれほど気にする必要はなく、むしろヤセの方を注意しなければいけないという結論に至る。

ただし、誤解しないでいただきたいのはBMIの値はあくまでも体格の指標であって、この値が低いからと言って必ずしも低栄養とは限らないと

いうことだ。重要なのはＢＭＩの変化、体重の変化である。例えば三カ月で体重が３～４kg以上減ったという時などは要注意だ。

外来で私のところにいらした八十二歳の女性の患者さん（ＢＭＩ27kg／㎡）は自分を高度な肥満と勘違いしていた。

「水を飲んでも太ってしまう。痩せられないので悩んでいる。現在、一日二食にし、野菜を中心とした食事に切り替え、さらには市販のやせ薬を購入して服用している」という。

驚いた私は、「とんでもない、八十歳を超えた方がそんな無理なことを実行したら、かえって体を壊してしまいます。無理な食事制限はせず、三食必ず食べて、これ以上体重が増えないよう気にかける程度にしてください」とお話しした。

実際、私は今まで高齢者が自己流の減量をしてかえって体を壊したケースを多く見てきている。もちろん糖尿病があるとか、脂質異常症、さらには変形性膝関節症など骨関節疾患がある場合は別途考える必要があるが、一般には高齢者の減量は注意が必要であり、勧められない。

ただでさえ、食欲は加齢とともに減退してくる。体重も一般的に男性では六十代、女性では七十代をピークとして徐々に減少する。この体重減少にはさまざまな要因があるが、加齢そのものの影響もあると考えられている。そういった時期に痩せるための食事制限をするなど、とんでもない話だ。

繰り返しになるが、知らない間に体重が減少してくるようなら、健康障害の注意信号と考えたほうがいい。いずれにしろ、一週間に一度は体重計に乗り、自分の体重をチェックしたいものである。

コレステロールや油ものを摂った方がいい場合も

生活習慣病について講演をした時のこと。八十五歳の女性が私のところにいらっしゃって、

「二十年ほど前に、かかりつけの先生からコレステロールや油ものをなるべく避けるように指導され、それ以降、卵や乳製品を摂らないようにしているんです。もちろん肉は鳥のささみしか食べません」

と誇らしげに話された。六十五歳の時と比較すると15kg以上体重が減ったという。

確かにコレステロールは動脈硬化の危険因子である。特に悪玉コレステロール（ＬＤＬコレステロール値）が高いと心筋梗塞などの虚血性心疾患のリスクになる。

そのため血液中の悪玉コレステロールを低下させる目的で食事指導がなされるのが普通だ。一般的に医師は動物性脂肪の摂取をできるだけ避けるように勧める。

しかし、これも中年期までの話。コレステロール摂取によって動脈硬化を引き起こす危険度は高齢者では徐々に低下し、後期高齢者ではその影響は少ない。日本人を対象とした最近の研究では、むしろＬＤＬコレステロール値が低すぎると脳出血のリスクになることが報告されている。ちなみにコレステロールが低すぎると癌になりやすいと言われた時期もあったようだが、近年の研究では否定的である。

さて、件（くだん）の八十五歳の女性は六十代の時に医者から言われたことを二十年間忠実に守り続けた。それで健康で長生きできれば結構なことだ。しかし、極端な話をすると、彼女は動脈硬化になる危険から免れたかもしれないが、脳出血のリスクを抱えたと言うこともできる。実に皮肉なことである。

では、油ものについてはどうだろう。

動物性脂肪は確かに血清コレステロール値を上げるが、後期高齢者にとっては効率のよいエネルギー源でもある。炭水化物、タンパク質が４kcal／gのエネルギーとなるのに比べ、脂肪は９kcal／gを産生でき、極めて効率が良い。私は低栄養の後期高齢者にはなるべく料理に油を使うことを奨励しているくらいである。徐々に痩せてくるような人には油も必要なのである。

ただし、虚血性心疾患などを既に罹患している人はこの限りではなく、動物性脂肪の取り方について主治医と相談する必要があることは言うまでもない。

粗食をやめて、肉を食べよう

最後に「粗食が体にいい」という世間的常識についても考えてみよう。

人間の手足の骨格筋は二十代をピークに加齢とともに萎縮していき、筋肉量としては七十歳で二十代の六〇～七〇％程度になると言われている（193ページ・図２）。

図３（193ページ）は二十五歳と七十五歳の人の大腿のＭＲＩによる断面図だ。七十五歳の骨格筋量が減少し、脂肪に置き換わっているのが明らかにわかる。タンパクの合成よりも分解のほうが上回ると、骨格筋組織を構成する筋細胞数が減少したり、個々の筋細胞が萎縮したりしてしまう。その結果、筋肉量が徐々に低下し、筋力も低下するというわけだ。この現象をサルコペニア（加齢性筋肉減少症〈減弱症〉）と言う。

サルコペニアがあると高齢者はふらついたり、転倒しやすくなったりする。また、

糖尿病の原因となるインスリン抵抗性（インスリンが正常に働かなくなった状態のこと。インスリン抵抗性があると、血糖値が下がらない）とも関係があることがわかっている。

サルコペニアとなる原因については身体活動度の低下、酸化ストレス、ホルモンの変化など諸説あるが、いずれも十分証明されているわけではない。しかし、筋肉タンパクは筋肉へ供給されるアミノ酸からつくられるので、アミノ酸のもとである肉などのタンパク質を十分に摂っているかどうかがポイントになると考えられている。

加齢とともに食事内容は変化し、あっさりしたものに好みが変わりやすい。年をとってから肉より魚を多く食べるようになったという人も多いのではないだろうか。なまじ生活習慣病予防の知識がある高齢者は肉の摂取自体が不健康につながると思いこみ、意識的に避けたりもする。このところの粗食ブームもそれに拍車をかけているようだ。専門家による不必要な食事制限や、誤った食生活の指導も影響があるだろう。

厚生労働省が出している「日本人の食事摂取基準」によると高齢者のタンパク質推定平均必要量は一日あたり0・85g／kg（体重）とされている。例えば60kgの体重の人は51gのタンパク質が一日に必要となる。しかし、実際には高齢者の摂取量は推奨量より二〇－四〇％程度少ないとされる。すなわち、60kgの高齢者では一日につき15g程度タンパク質が足りないことになる。摂取するタンパク質を増やすだけで筋肉量が増加するかどうかは議論があるところだが、減少を予防することはできるだろう。

図2 年をとるにつれて体はこんなに変化する

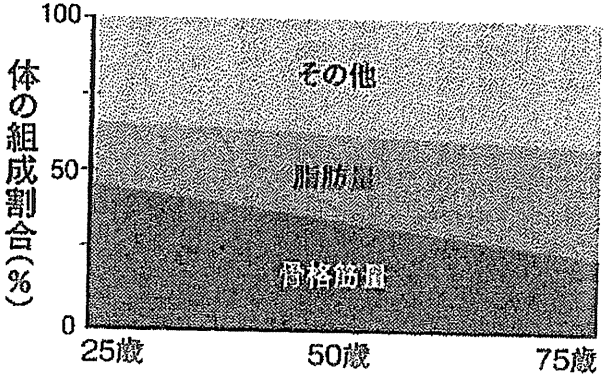
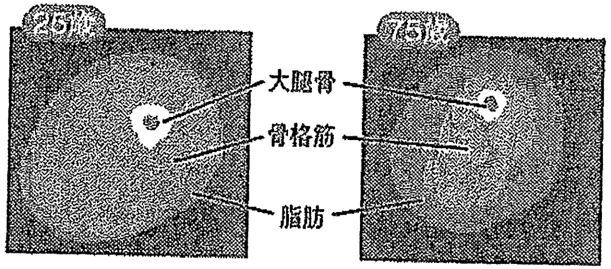


図3 MRIで見ても、これだけ違う



25歳と75歳の大腿のMRIによる断面画像。真ん中の白い円形（中が灰色）は大腿骨で、その周囲の灰色部分が大腿の骨格筋。さらにその外側（やや黒色部分）は脂肪である。明らかに75歳の骨格筋は25歳に比較し減少し、その代わりに脂肪量が増えているのがわかる。

（Roubenoff R.Journal of Gerontology:MEDICAL SCIENCES 2003,Vol.58A,No.11,1012-1017より）