

Table 1. Number of institutions and response rates

Survey year	JOA-authorized hospitals	JCOA hospitals	Total	Response rate (%)
1998 ^a	2270	1529	3799	48.4
1999 ^a	2264	1430	3694	55.1
2000 ^a	2312	1512	3824	47.0
2001	2291	1493	3784	53.0
2002	2276	1466	3742	53.6
2003	2252	1347	3599	52.1
2004	2264	1258	3522	51.3
2005	2229	1224	3453	48.3
2006	2201	1167	3368	48.9
2007	2031	1218	3249	51.8
2008	2016	1104	3120	55.4

JOA, Japanese Orthopaedic Association; JCOA, Japanese Clinical Orthopaedic Association

^aData are from reference 9

by which time steep increases will be observed throughout Asia and Latin America.⁵ Therefore, the medical and socioeconomic burden of hip fractures will be growing rapidly in Asian countries.

Japan is the country with the longest life expectancy in the world. The average life expectancy at birth for Japanese individuals has steadily increased, reaching 78.56 years for men and 85.52 years for women in 2005. As a result, the population structure in Japan has changed dramatically over the past decade. The proportion of the population aged ≥ 65 years increased from 17.5% in 2000 to 22.3% in 2008, and the proportion aged ≥ 75 years grew from 7.1% to 10.5%.⁶ As a result of these changes, Japan's population now contains more elderly individuals than any other developed countries, and the hip fracture burden will therefore be more serious in Japan than in any other country in the near future. In 2005, the life expectancy for 50-year-old men was 29.26 years and that for women was 35.94 years, and the residual lifetime risk of hip fracture for individuals 50 years of age in Japan was estimated to be 5.6% for men and 20.0% for women.³ This compares to 10.7% and 22.9% in Sweden and 3.1% and 11.4% in the United Kingdom, for men and women, respectively.^{7,8} Although the incidence of hip fracture in Japan is lower than that in Sweden,³ the longer average life-span has elevated the residual lifetime fracture risk for individuals 50 years of age.

To elucidate the characteristics of hip fractures and the current status of their treatment in Japan, the Japanese Orthopaedic Association (JOA) conducted a nationwide hip fracture survey from 1998 to the present. We previously reported the survey results obtained between 1998 and 2000.⁹ The aim of the current report was to present additional results from 2001 to 2008, thus describing for a study period of one decade the change in patient distribution by age and fracture type, cause

of fracture, treatment selection, and duration of hospitalization.

Patients and methods

Data collection

A tally of all hip fractures that occurred in patients between 2001 and 2008 was conducted in JOA-authorized hospitals and in Japanese Clinical Orthopaedic Association (JCOA) hospitals. There were 2291 JOA-authorized hospitals and 1493 JCOA hospitals in 2001, and the number decreased thereafter (Table 1).

Inclusion criteria were femoral neck and trochanteric fractures in patients aged ≥ 35 years and treated in JOA-authorized or JCOA hospitals. Pathological fractures due to neoplasm or infection and removal of implants were excluded. Cases of refracture were included, but cases of reoperation due to delayed union or nonunion were excluded. Registration forms were sent to these hospitals by mail each year, and registration was performed by the hospital staff (including orthopedists) based on their hospital records. Registration information included name (initials), sex, date of birth, date of fracture, date of first hospital visit, fracture site, fracture type, fracture location, cause of injury, treatment, and duration of hospitalization. From 2005 onward, the initials and date of birth were omitted from the registration information for the purpose of protecting personal information. Therefore, duplication of cases and refracture were checked based on patient initials, date of birth, and prefecture before 2005 and by fracture date, age, sex, and prefecture from 2005 to 2008.

Causes of injury were divided into six categories: "in bed," "simple fall," "fall on stairs," "traffic accident," "not remembered," and "unknown." The term "in bed"

Table 2. Registered patients ≥ 35 years old with a hip fracture

Survey	No. of patients			Fracture site	
	Male	Female	Total	Right	Left
1998 ^a	7 761	28 275	36 226	17 552	18 379
1999 ^a	8 556	31 253	40 069	19 375	20 253
2000 ^a	7 351	26 889	34 452	16 786	17 458
2001	9 193	35 097	44 469	21 650	22 565
2002	9 547	35 840	45 604	22 185	23 144
2003	9 414	35 189	44 807	21 731	22 790
2004	9 499	36 134	45 835	22 001	23 551
2005	9 644	36 397	46 145	22 287	23 376
2006	10 646	40 087	50 846	24 518	25 738
2007	11 937	44 787	56 816	27 409	28 950
2008	14 334	53 783	68 238	32 795	34 805
Total	84 214	317 314	402 760	194 576	204 919

Values are the number of patients

^aData are from reference 9

indicates a fracture that occurred when lying in bed, “simple fall” describes falling from a standing height or from bed, “not remembered” indicates that the patient did not remember the injury, and “unknown” denotes that the information could not be obtained from patients because of some difficulty, such as dementia. We identified “care fractures” as those that occurred during activities involving care of bed-ridden patients (e.g., during diaper changing and bed baths) and included them in the “in bed” category.

The duration of hospitalization was calculated based on the hospital where the patients were treated just after their injury. Surgical day for the first surgery (e.g., osteosynthesis, arthroplasty) was surveyed from 2003 to 2008, and the duration of hospitalization before surgery was calculated.

Statistical methods

Significant differences between two groups were tested with Wilcoxon tests for paired values (for the number of patients fractured on the right or left side during each year) and Mann-Whitney tests for unpaired values. Patient proportions between groups were compared using the chi-squared test. Seasonal variations were tested with the Friedman test. Approval was obtained from the ethics committees of the JOA, Tottori University, and each participating hospital. Statistical analysis was performed using SPSS (SPSS II for Windows Version 11.0.1J; SPSS Japan, Tokyo, Japan); and $P < 0.05$ was considered statistically significant. Patient data obtained between 1998 and 2000, which we previously reported,⁹ was included in this analysis.

Results

Response rates and number of patients

Response rates ranged from 48.3% to 55.4% (mean 51.8%) (Table 1). The total number of patients aged ≥ 35 years with new hip fractures between 2001 and 2008 was 402 760 (84 214 men, 317 314 women, sex not indicated 1232 cases) (Table 2). The number of women was 3.8 times that of men.

Fractures occurred on the right in 194 576 patients and on the left in 204 919 patients (fracture site was not indicated in 3265 cases) (Table 2). More left hips were fractured than right in all survey years, and the difference was statistically significant ($P < 0.02$, Wilcoxon test).

Age-specific and sex-specific patient totals

Age-specific and sex-specific patient totals were calculated for each survey year. Patient numbers correlated with higher age and peaked in the 85- to 89-year-old group for both sexes (Fig. 1). Patients in the 80- to 89-year-old age group accounted for about half of the total number of patients. However, increases in patient numbers over time (from 1998 to 2008) were more prominent for ages ≥ 90 years for both sexes. The numbers of female patients were 6531, 6241, and 2766 in 1998 for the age groups 80–84, 85–89, and 90–94 years, respectively; they were 12 147, 13 180, and 8358, for these same groups in 2008. The ratios of fracture numbers in 2008 to those in 1998 are 1.90, 2.11, and 3.04, respectively. There were 1413 women and 202 men aged ≥ 100 years with hip fractures during the period 2001–2008.

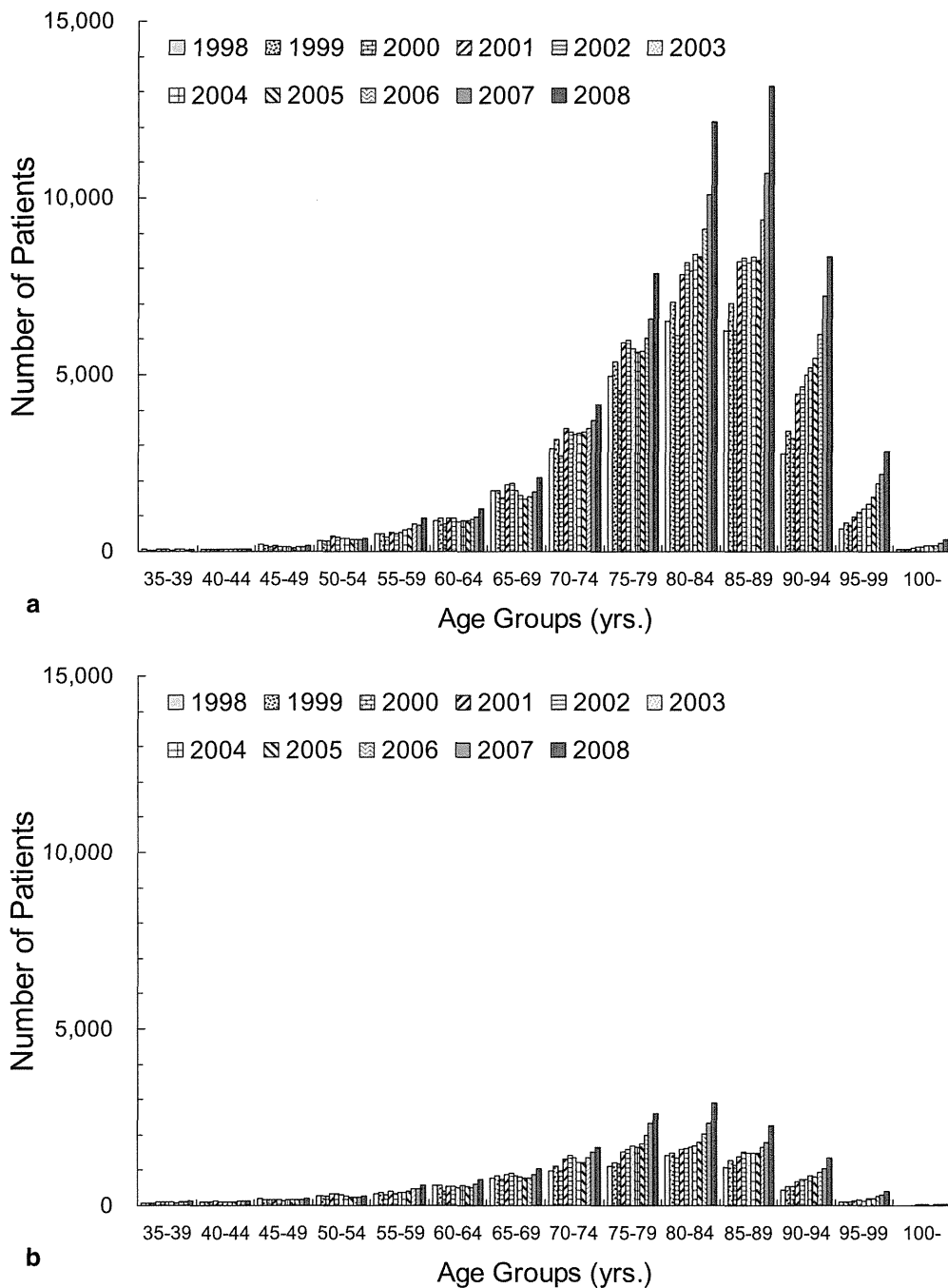


Fig. 1. Age-specific annual numbers of patients with hip fractures. **a** Women. **b** Men. The number increased with age and peaked at age 85–89 years for both sexes. Patients in the 80- to 89-year-old age group accounted for about one-half of the total number of patients; but for both sexes the increases were more prominent for those aged ≥ 90 years

Fracture type

The survey found 182 576 neck fractures and 216 788 trochanteric fractures (3396 unclassified fractures) during the observational period from 2001 to 2008. The change over time in the prevalence of both fracture types is shown in Fig. 2. More trochanteric fractures occurred than neck fractures during the observational period; however, the neck/trochanter ratio increased over time.

Refractures

Patients with refracture at either the opposite or same side of the first fracture side were determined from 2001 to 2004 based on patients' initials and dates of birth (Table 3). During the 1-year observational period 1916 patients (197 men, 1719 women) suffered refracture (Table 3). Initial fractures occurred on the right side in 981 patients and on the left side in 908 patients (fracture side not indicated in 27 cases); 883 of these were neck

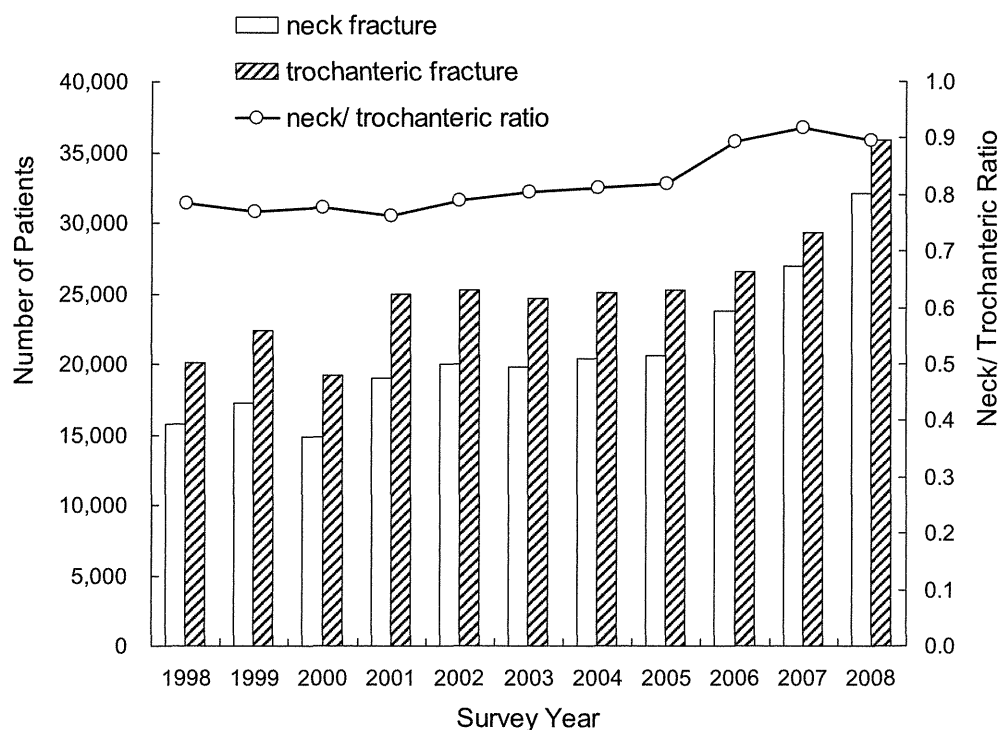


Fig. 2. Fracture type-specific annual numbers of patients with hip fractures. More trochanteric than neck fractures occurred during the observational period, although the neck/trochanter ratio increased over time

Table 3. Patients with refracture

Parameter	2001	2002	2003	2004	Total
Sex (no.)					
Men	49	42	51	55	197
Women	430	431	429	429	1719
First fracture					
Fracture site (no.)					
Right	244	248	244	245	981
Left	228	220	231	229	908
Fracture type					
Neck	239	215	225	204	883
Trochanteric	236	254	244	267	1001
Second fracture of the same type	70.1%	64.1%	66.3%	69.0%	67.4%

fractures, and 1001 were trochanteric fractures (fracture type not indicated in 32 cases). Refractures were of the same type as the initial fractures in 67.4% of cases and on the same side in 2.3% of cases.

Fracture causes

Fractures were due to a simple fall in more than two-thirds of men and four-fifths of women (Table 4). In patients aged ≥ 90 years, a simple fall was the cause in more than 84% of cases. "Care fractures" were identified in 0.2% of the total number of patients.

Altogether, 75% (277 657) of patients sustained fractures indoors, and 25% (93 679) sustained them outdoors (the site of the injury was not indicated in 31 424 cases). Patients aged ≥ 90 years sustained their fractures

indoors 87.9% of the time, whereas this was the case for only 71.8% of patients < 90 years of age, a statistically significant difference ($P < 0.001$, chi-squared test). Comparing sexes, 78.7% of women and 60.3% of men suffered fractured indoors, again a difference that was statistically significant ($P < 0.001$, chi-squared test).

Monthly variation

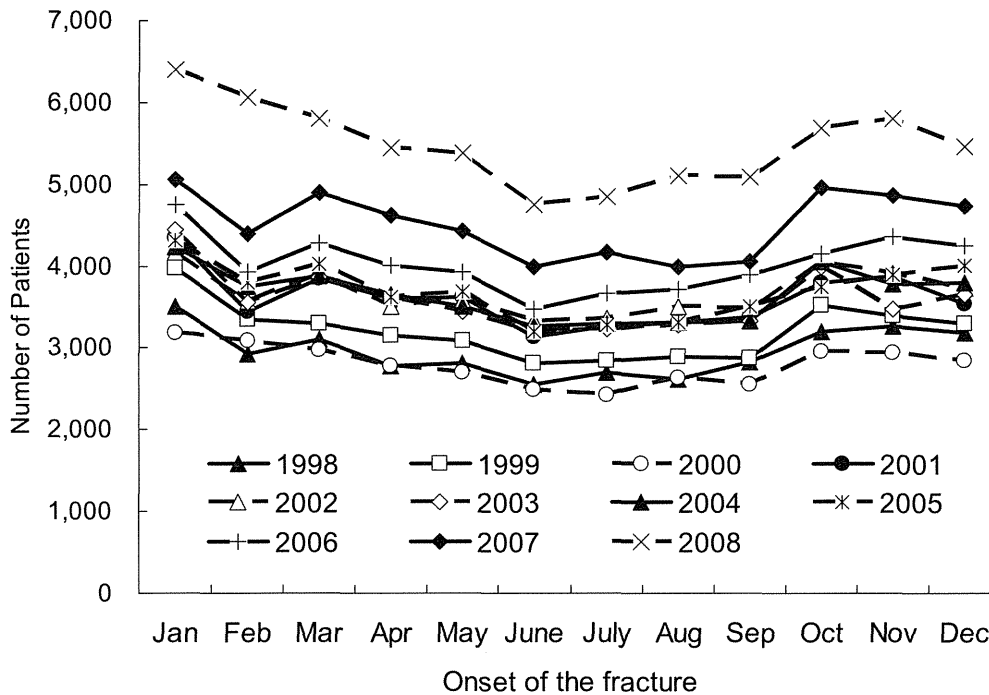
The total number of patients per month was the highest in January in all survey years from 1998 to 2008. It was the lowest in June in all survey years except 2000, when the lowest number was observed in July (Fig. 3). This monthly variation was statistically significant ($P < 0.01$, Friedman test).

Table 4. Cause of hip fractures

Cause	Total	Men	Women	Age < 90 years	Age ≥ 90 years
Simple fall	305 473 (77.7%)	56 950 (69.1%)	248 523 (80.1%)	247 634 (76.4%)	57 839 (84.1%)
Traffic accident	32 754 (8.3%)	15 293 (18.5%)	17 461 (5.6%)	30 688 (9.5%)	2 066 (3.0%)
Fall on stairs	21 994 (5.6%)	4 847 (5.9%)	17 147 (5.5%)	19 776 (6.1%)	2 218 (3.2%)
In bed	5 540 (1.4%)	945 (1.1%)	4 595 (1.5%)	4 292 (1.3%)	1 248 (1.8%)
Not remembered	5 294 (1.3%)	816 (1.0%)	4 478 (1.4%)	4 415 (1.4%)	879 (1.3%)
Unknown	21 843 (5.6%)	3 607 (4.4%)	18 236 (5.9%)	17 317 (5.3%)	4 526 (6.6%)
Care fracture ^a	805 (0.2%)	136 (0.2%)	669 (0.2%)	594 (0.2%)	211 (0.3%)

Values are the total number of patients (years 2001–2008)

^aThose that occurred during the care of bedridden patients, such as when changing a diaper

**Fig. 3.** Monthly variation in the number of patients with hip fractures

Length of stay before surgery or other treatment

More than 90% of patients were treated surgically (Table 5). Among patients with femoral neck fractures, 67.5% were treated with arthroplasty including hemiarthroplasty and total arthroplasty.

The mean length of stay (LOS) before surgery was 5.6 days in 2003, becoming shorter with time over successive observational periods (Table 6). The LOS for neck fractures was longer than that for trochanteric fractures during all survey years ($P < 0.001$ Mann-Whitney). Among patients with neck fractures, the mean LOSs before surgery for patients receiving arthroplasty were 6.5, 6.3, 6.2, 6.1, 6.0, and 5.8 days in 2003, 2004, 2005, 2006, 2007, and 2008, respectively. Those for patients undergoing osteosynthesis were 4.7, 4.6, 4.5, 4.8, 4.2, and 4.3 days, respectively. These differences between fracture types were significant in all survey years ($P < 0.001$ Mann-Whitney). The mean LOSs

before surgery among patients aged ≤ 90 years were 5.7, 5.4, 5.4, 5.2, 5.1, and 4.9 days in 2003, 2004, 2005, 2006, 2007, and 2008, respectively. Those among patients aged ≥ 90 years were 5.2, 5.1, 4.8, 5.0, 4.8, and 4.7 days, respectively. These differences between age groups were significant in all survey years ($P < 0.001$ Mann-Whitney).

Duration of hospitalization

The mean hospitalization period was 53.4 days in 2001, and it became shorter over successive observational periods (Table 6). There was no significant difference in hospitalization duration between patients with neck fractures and those with trochanteric fractures. The hospitalization period was longer in patients < 90 years of age than in those ≥ 90 years in all survey years ($P < 0.001$ Mann-Whitney).

Table 5. Selected treatment for patients with hip fractures

Treatment	Neck	Trochanter	Total
Conservative	11 151 (6.2%)	11 589 (5.4%)	22 740 (5.8%)
Surgery	167 549 (93.8%)	201 715 (94.6%)	369 264 (94.2%)
Arthroplasty	113 130 (67.5%)	2 276 (1.1%)	115 406 (31.3%)
Osteosynthesis	53 450 (31.9%)	198 316 (98.3%)	251 766 (68.2%)
Not indicated	969 (0.6%)	1 123 (0.6%)	2 092 (0.6%)

Values are the total number of patients (years 2001–2008)

Table 6. Preoperative and hospitalization periods

Survey year	Preoperative period (days)			Hospitalization period (days)		
	Neck fracture	Trochanteric fracture	Total	Neck fracture	Trochanteric fracture	Total
2001	—	—	—	53.2, 46 [31–67]	53.5, 46 [29–69]	53.4, 46 [30–68]
2002	—	—	—	50.2, 43 [28–63]	50.6, 43 [27–65]	50.5, 43 [28–64]
2003	5.9, 5 [3–7]	5.3, 4 [2–7]	5.6, 4 [2–7]	48.4, 41 [27–61]	49.6, 42 [26–64]	49.2, 42 [27–63]
2004	5.4, 4 [2–7]	5.0, 4 [2–6]	5.4, 4 [2–7]	47.0, 40 [26–60]	49.0, 41 [26–63]	48.1, 40 [26–61]
2005	5.3, 4 [2–7]	4.9, 4 [2–6]	5.3, 4 [2–7]	47.4, 40 [26–60]	48.6, 41 [25–63]	48.0, 40 [26–62]
2006	5.2, 4 [2–7]	4.8, 4 [2–6]	5.2, 4 [2–7]	44.7, 38 [24–57]	45.2, 38 [23–59]	44.9, 38 [24–58]
2007	5.4, 4 [2–7]	4.7, 4 [2–6]	5.0, 4 [2–6]	42.0, 35 [22–54]	42.7, 35 [22–56]	42.3, 35 [22–55]
2008	5.3, 4 [2–7]	4.6, 4 [2–6]	4.9, 4 [2–6]	40.6, 33 [21–51]	40.7, 33 [21–53]	40.7, 33 [21–52]

Values are the mean, median, and [25%–75% percentiles]

Discussion

This study evaluated the relation of hip fracture incidence to age and fracture type, cause of fracture, treatment selection, length of stay before surgery, and duration of hospitalization. The survey showed a drastic increase in number of patients, especially those aged ≥ 90 years, over the course of one decade. Simple falls were the most common cause of fracture, and about 94% patients were treated surgically with about a 5-day presurgical hospital stay.

Studies in Japan have indicated that hip fracture incidence has been increasing up to the present time.^{3,10} A recent study showed a slight decline in the incidence of hip fracture; however, it is limited in some age groups.¹¹ The current study demonstrated a drastic increase in the number of patients over age 80 years between 1998 and 2008, with numbers in 2008 eclipsing those in 1998 by factors of 1.90, 2.11, and 3.04 for the age ranges 80–84, 85–89, and 90–94 years, respectively. The number of patients ≥ 100 years of age with hip fractures quadrupled from 1998 to 2008. These increases are much higher than those seen in the remainder of the Japanese population from 1998 to 2008, where ratios were 1.64, 1.56, and 1.63 for the age groups 80–84, 85–89, and 90–94 years, respectively.⁶ The registered number of patients per year in each hospital also increased during the observational period. As the 50% response rate demonstrates, this study does not cover all patients with hip

fractures in Japan. Nonetheless, the substantially higher number of patients registered than those expected based on the Japanese population increase is due to the increase in hip fracture incidence in individuals aged ≥ 80 years that we previously reported.³ The overall decrease in physical activity stemming from a Westernized lifestyle may explain the increase in fracture incidence among Japanese patients. Another explanation may be that more seniors with poor health because of other conditions are being treated, which results in people living longer at a time when their risk of falling is quite high.³

The most serious social and economic concern facing our health care system is the rapid rise in the number of patients aged ≥ 90 years. It has been estimated that these patients will account for half of the total number of hip fractures within the next two decades, by which time the total number of hip fractures sustained per year will be about 300 000, approximately double that in 2008. Establishing effective measures to support elderly patients with hip fractures is one of the more urgent issues in our society.

The incidence of femoral neck fractures is higher than that of trochanteric fractures in northern European and African populations, whereas femoral neck fractures are less common than trochanteric fractures in Japanese populations.^{3,12,13} Because trochanteric fractures have a closer relation with low bone mass than do femoral neck fractures, they occur more frequently in the very

elderly.¹⁴ As a result, we had expected that the increase in hip fractures over the last decade would be marked by a relatively higher number of trochanteric fractures than femoral neck fractures—when in fact the opposite was seen. A recent survey in Sweden showed that the neck/trochanteric fracture incidence ratio had leveled off.¹⁵ Although the reason for these trends is uncertain, the neck/trochanteric fracture ratio in Japan might be approaching values observed in northern European populations.

In this study, more left-sided fractures than right-sided fractures were observed. Most patients are right-handed,¹⁶ and it is speculated that falls to the left side exert more impact on the proximal femur than falls to the right owing to poor protection by the nondominant hand.

It is well known that the risk of further hip fractures increases after an initial fracture,¹⁷ so we evaluated second hip fractures occurring during the same year. Although a 1-year observation is insufficient to elucidate the risk of second fracture, about one-fourth of all subsequent fractures occur within 1 year after a first fracture.¹⁸ In this study, the primary hip fractures in patients with a refracture occurred more on the right side than the left, implying that patients with their first hip fracture on the right side have a higher risk of sustaining a second hip fracture than those in whom the primary fracture occurred on the left side.

In this study, a peak in the number of patients with hip fractures was seen in January. A recent study indicated that incidence rates of fragility fractures were highest in winter and lowest in summer.¹⁹ Significant seasonality and an association of monthly hip fracture admission rates with ambient temperature were observed in both sexes.²⁰ Several explanations have been proposed, including low blood pressure, reduced vitamin D production, and heavier clothing during cold weather months. Because the present study found simple falls to be the most common cause of hip fractures and more fractures occurred indoors than outdoors, reducing the risk of indoor falling during the winter is a significant point to be emphasized for the prevention of hip fractures.

This study was the first to report on the length of stay before surgery throughout Japan. The average length was about 5 days, which is substantially longer than the duration reported by other countries.^{21–23} Although it does not seem that high-quality evidence has been established up to this point, early surgery (within 2 days) is recommended to minimize postsurgical hospitalization time and complications.^{24,25} We have to make every endeavor to shorten the length of hospital stays before surgery.

This study showed that over the course of one decade the duration of hospitalization after surgery became shorter with time, although even as of 2008 it remained

much longer than that reported in Europe or North America. The Japanese health care system and insurance programs might contribute to this fact. In a recent study performed in the United States and Japan, shorter lengths of stay after surgery did not predict better survival across the two countries.²³ Another study demonstrated that reducing the length of stay in initial acute care hospitals may be just a method of shifting costs to subsequent care services and is unlikely to bring overall cost saving to the Japanese health care system.²⁶ It is necessary, therefore, to develop strategies that move beyond simple approaches and efficiently and effectively reduce the hospital stay of hip-fractured patients.

There are several limitations to this study. First, the response rate of 50% was somewhat low. Second, although the survey was conducted in hospitals authorized by the JOA and JCOA, surgery for hip fractures is performed not only in these hospitals but also at nonaffiliated hospitals. However, the large number of patients surveyed in this study for more than one decade may compensate for any such bias. Third, the initials and date of birth were omitted from the registration information from 2005 onward; therefore, patients with refracture were not evaluated thereafter. This may have affected the result, although patients moved from other hospitals were checked by each hospital and most patients analyzed for this study were those hospitalized just after the injury.

Conclusion

This one-decade survey studied more than 400 000 patients with hip fractures and demonstrated a drastic increase in the number of patients over the course of the decade, especially in the group aged ≥ 90 years. Appropriate treatment and prevention of hip fractures, including the treatment of osteoporosis and more effective interventions to prevent falls, are important issues to address to reduce the burden of this fracture.

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References

1. Abrahamsen B, Vestergaard P. Declining incidence of hip fractures and the extent of use of anti-osteoporotic therapy in Denmark 1997–2006. *Osteoporos Int* 2010;21:373–80.
2. Leslie WD, O'Donnell S, Jean S, Lagace C, Walsh P, Bancej C, et al. Trends in hip fracture rates in Canada. *JAMA* 2009;302:883–9.

3. Hagino H, Furukawa K, Fujiwara S, Okano T, Katagiri H, Yamamoto K, et al. Recent trends in the incidence and lifetime risk of hip fracture in Tottori, Japan. *Osteoporos Int* 2009;20:543–8.
4. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. *Osteoporos Int* 1997;7:407–13.
5. Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: a world-wide projection. *Osteoporos Int* 1992;2:285–9.
6. Ministry of Health Law, Statistics, & Other Data. 2009.
7. Kanis JA, Johnell O, Oden A, Sembo I, Redlund-Johnell I, Dawson A, et al. Long-term risk of osteoporotic fracture in Malmo. *Osteoporos Int* 2000;11:669–4.
8. Johnell O, Kanis J. Epidemiology of osteoporotic fractures. *Osteoporos Int* 2005;16(suppl 2):S3–7.
9. Committee for Osteoporosis Treatment, The Japanese Orthopaedic Association. Nationwide survey of hip fractures in Japan. *J Orthop Sci* 2004;9:1–5.
10. Morita Y, Endo N, Iga T, Tokunaga K, Ohkawa Y. The incidence of cervical and trochanteric fractures of the proximal femur in 1999 in Niigata Prefecture, Japan. *J Bone Miner Metab* 2002;20:311–8.
11. Orimo H, Yaegashi Y, Onoda T, Fukushima Y, Hosoi T, Sakata K. Hip fracture incidence in Japan: estimates of new patients in 2007 and 20-year trends. *Arch Osteoporos* 2009;4:71–7.
12. Lonnroos E, Kautiainen H, Karppi P, Huusko T, Hartikainen S, Kiviranta I, et al. Increased incidence of hip fractures: a population based-study in Finland. *Bone* 2006;39:623–7.
13. Bjorgul K, Reikeras O. Incidence of hip fracture in southeastern Norway: a study of 1,730 cervical and trochanteric fractures. *Int Orthop* 2007;31:665–9.
14. Mautalen CA, Vega EM, Einhorn TA. Are the etiologies of cervical and trochanteric hip fractures different? *Bone* 1996;18:133S–7S.
15. Lofman O, Berglund K, Larsson L, Toss G. Changes in hip fracture epidemiology: redistribution between ages, genders and fracture types. *Osteoporos Int* 2002;13:18–25.
16. Hagino H, Fujiwara S, Nakashima E, Nanjo Y, Teshima R. Case-control study of risk factors for fractures of the distal radius and proximal humerus among the Japanese population. *Osteoporos Int* 2004;15:226–30.
17. Ryg J, Rejnmark L, Overgaard S, Brixen K, Vestergaard P. Hip fracture patients at risk of second hip fracture: a nationwide population-based cohort study of 169,145 cases during 1977–2001. *J Bone Miner Res* 2009;24:1299–307.
18. Van Geel TA, van Helden S, Geusens PP, Winkens B, Dinant GJ. Clinical subsequent fractures cluster in time after first fractures. *Ann Rheum Dis* 2009;68:99–102.
19. Bischoff-Ferrari HA, Orav JE, Barrett JA, Baron JA. Effect of seasonality and weather on fracture risk in individuals 65 years and older. *Osteoporos Int* 2007;18:1225–33.
20. Lin HC, Xiraxagar S. Seasonality of hip fractures and estimates of season-attributable effects: a multivariate ARIMA analysis of population-based data. *Osteoporos Int* 2006;17:795–806.
21. Vidal EI, Moreira-Filho DC, Coeli CM, Camargo KR Jr, Fukushima FB, Blais R. Hip fracture in the elderly: does counting time from fracture to surgery or from hospital admission to surgery matter when studying in-hospital mortality? *Osteoporos Int* 2009;20:723–9.
22. Verbeek DO, Ponsen KJ, Goslings JC, Heetveld MJ. Effect of surgical delay on outcome in hip fracture patients: a retrospective multivariate analysis of 192 patients. *Int Orthop* 2008;32:13–8.
23. Kondo A, Zierler BK, Isokawa Y, Hagino H, Ito Y, Richerson M. Comparison of lengths of hospital stay after surgery and mortality in elderly hip fracture patients between Japan and the United States: the relationship between the lengths of hospital stay after surgery and mortality. *Disabil Rehabil* 2010;32:826–35.
24. Majumdar SR, Beaupre LA, Johnston DW, Dick DA, Cinats JG, Jiang HX. Lack of association between mortality and timing of surgical fixation in elderly patients with hip fracture: results of a retrospective population-based cohort study. *Med Care* 2006;44:552–9.
25. Rae HC, Harris IA, McEvoy L, Todorova T. Delay to surgery and mortality after hip fracture. *ANZ J Surg* 2007;77:889–91.
26. Kondo A, Zierler BK, Isokawa Y, Hagino H, Ito Y. Comparison of outcomes and costs after hip fracture surgery in three hospitals that have different care systems in Japan. *Health Policy* 2009;91:204–10.

fore, these reasonable components should be integrated into multifactorial fall prevention programs.

It has to be stressed that our study was an effectiveness study and not a randomized clinical trial. The aim of the program was to disseminate and implement fall prevention in the majority of nursing homes in a complete federal state, which means that the program had to be feasible within the daily routine considering limited personal and financial resources. Participating homes committed themselves to offer the strength and balance training at least once a week. There was no funding for hip protectors. There were no direct financial incentives.

The fall prevention liaison nurses were instructed to introduce the program in their nursing homes to all staff members who spend time with residents. Nursing assistants or aides were considered to be major target groups of the in-house teaching sessions.

If nursing homes employed occupational therapists, they were usually involved in the program as exercise instructors and members of the fall prevention team. It was not possible to assign a larger role. A large percentage of German homes do not employ occupational therapists as staff members. Therefore, the program had to respect these limitations.

We absolutely agree that fall prevention measures might have other benefits than fracture reduction. Examples are the reduction of the number of falls and the increase of mobility. Both can contribute to better quality of life.

Since the reported trial, the implementation has been modified in several ways. The exercise is now being delivered twice weekly, a hip protector learning tool has been introduced, nursing staff has played a more active role in the recruiting process, a national guideline on fall prevention in nursing homes was published in 2005, and the intervention has been transferred to other federal states. It remains to be seen whether these changes will be successful at increasing physical activity, reducing falls and fractures in this vulnerable group.

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REFERENCES

1. Rapp K, Lamb SE, Klenk J et al. Effectiveness of a statewide fall prevention program on incidence of femoral fractures in residents of long-term care facilities. *J Am Geriatr Soc* 2010;58:70–75.
2. Cameron ID, Murray GR, Gillespie LD et al. Interventions for preventing falls in older people in nursing care facilities and hospitals. *Cochrane Database Syst Rev* 2010;(1):CD005465.

DOES FALL-RELATED SELF-EFFICACY IN HIP-PROTECTOR USERS AFFECT QUALITY OF LIFE AND PHYSICAL ACTIVITY IN NURSING HOMES IN JAPAN?

To the Editor: Cameron and colleagues¹ reported that supplementary effects of hip protectors in wearers increased fall-related self-efficacy (fall self-efficacy) in community life and led to better physical activity and quality of life (QOL), but whether hip protectors were effective for older adults in care facilities in Japan and in the community was questioned, and the effects of hip protectors on fall self-efficacy, QOL, and physical activity in female nursing home residents in Japan was therefore re-investigated.

METHODS

The subjects of this study were 52 female nursing home residents aged 70 and older who had a score of 20 or higher on the Mini-Mental State Examination (MMSE)² and who were selected through a prospective cluster randomized controlled trial (26 hip protectors, 26 controls). Data were obtained through the Falls Efficacy Scale (FES),³ the Physical Component Summary (PCS) and Mental Component Summary (MCS) of the Medical Outcomes Study 8-Item Short-Form Health Survey (SF-8),⁴ and step count according to a pedometer at the beginning and 6 months after. Adherence to hip protectors and numbers of falls and fracture for 6 months were also investigated.

The FES was designed to assess the degree of perceived efficacy in avoiding a fall during each of 10 activities of daily living (ADLs).³ A question on an activity was scored on a scale of 1 (completely confident) to 10 (no confidence),³ but because the subjects in the present study were residents of a nursing home, the daily activities assessed were modified to fit those in a nursing home situation. It was confirmed that internal consistency and reliability were as significant as those in the original reports.^{3,5}

Two-way (period and groups) repeated analysis of variance (ANOVA) was used for statistical analysis. $P < .05$ was considered significant.

RESULTS

ANOVA revealed that there was no interaction between groups in FES ($P = .99$), PCS ($P = .71$), MCS ($P = .55$), and steps ($P = .23$) (Figure 1). No significant difference was observed in number of falls and fracture between the hip protector and control groups.

DISCUSSION

The present results did not support the results of Cameron and colleagues.¹ The effect of hip protectors on fall

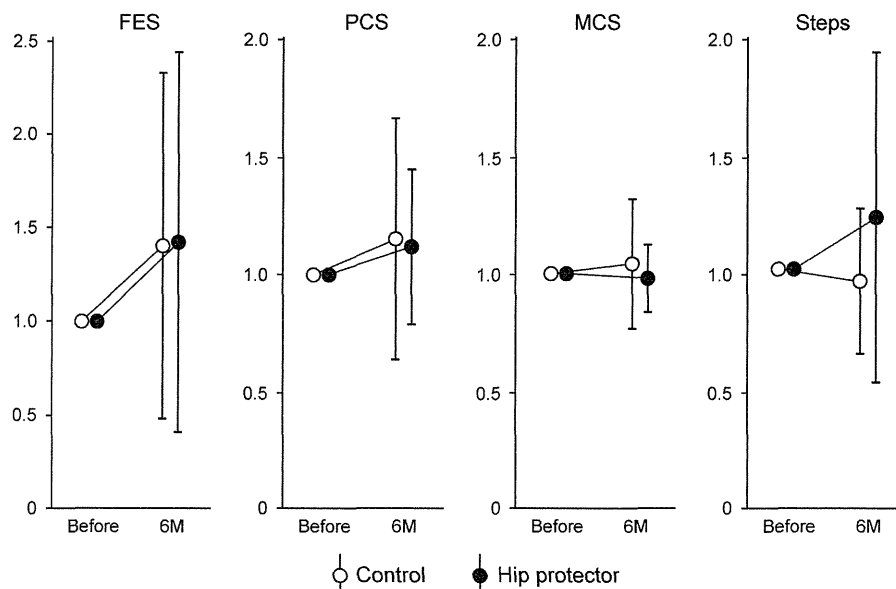


Figure 1. Changes in standardized measured values 6 months (6 M) after the beginning of the study. Values at 6 months were expressed in relation to those at the beginning of the study (before). There was no significant difference between Falls Efficacy Scale (FES), Physical Component Summary (PCS), and Mental Component Summary (MCS) scores and number of steps.

self-efficacy is controversial. A difference in the physical function of subjects between Cameron and colleagues¹ and the present study must be considered. The mean FES score for older adults in nursing homes was also lower (40.6 ± 23.9) than that for older people in the community or in intermediate care facilities (18.6 ± 9.0).³ Because there was a relationship between ADLs and FES,⁶ there remains a possibility that subjects with lower physical function had less fall self-efficacy. Moreover, the wide range in the standard deviation (Figure 1) of FES suggested that the individual difference in fall self-efficacy for institutionalized older adults was large.

Other than FES, no significant differences in interaction between PCS, MCS, and steps were observed between the hip protector and control group, and the number of falls and fractures also showed no significant difference.

Adherence is an important factor in the effects of hip protectors. Average hip protector adherence was 50% in a previous study⁷ and 75% the present study. Cameron and colleagues¹ sought to encourage adherence using adherence nurses' visits to subjects' homes during their trial, whereas no instruction was given during the current study. Education of subjects should affect the result of this study, and without it hip protectors might not be effective.

Regarding the use of the FES for older adults, one study reported that it confirmed the internal consistency or reliability of the FES,⁸ but some older adults in nursing homes may not have engaged in ADLs. If participants were unable to perform an ADL, they were asked to reply "how confident they would be to do so without falling." At such time, the subjects may not have sufficiently reflected their fear of falling. Thus, application of FES might be limited in such subjects.

CONCLUSION

No indirect effects of improvement in fall self-efficacy, QOL, and steps were observed in female nursing home residents using hip protectors.

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REFERENCES

1. Cameron ID, Stafford B, Cumming RG et al. Hip protectors improve falls self-efficacy. *Age Ageing* 2000;29:57–62.
2. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": A practical method for grading the cognitive state for the clinician. *J Psychiatr Res* 1975;12:189–198.
3. Tinetti ME, Richman D, Powell L. Falls efficacy as a measure of fear of falling. *J Gerontol* 1990;45:239–243.
4. Fukuhara S, Suzukamo Y. Manual of the SF-8 Japanese Version. Kyoto: Institute for Health Outcomes & Process Evaluation Research, 2004.
5. Powell LE, Myers AM. The Activities-specific Balance Confidence (ABC) scale. *J Gerontol A Biol Sci Med Sci* 1995;50A:M28–M34.
6. Tinetti ME, Mendes de Leon CF, Doucette JT et al. Fear of falling and fall-related efficacy in relationship to functioning among community-living elders. *J Gerontol* 1994;49:M140–M147.
7. Parker MJ, Gillespie WJ, Gillespie LD. Hip protectors for preventing hip fractures in older people. *Cochrane Database Syst Rev* 2005;20:CD001255.
8. Büla CJ, Martin E, Rochat S et al. Validation of an adapted falls efficacy scale in older rehabilitation patients. *Arch Phys Med Rehabil* 2008;89:291–296.

ONCE-DAILY MEMANTINE: PHARMACOKINETIC AND CLINICAL CONSIDERATIONS

To the Editor: The Food and Drug Administration (FDA) approved memantine in the United States in October 2003 for the treatment of moderate to severe Alzheimer's disease.¹

The relatively long plasma elimination half-life of this drug suggests that once-daily dosing may be comparable with the current twice-daily practice. We offer a pharmacokinetic rationale for once-daily prescribing and suggest that the once-daily strategy may be comparable to traditional twice-daily dosing and improve adherence.

METHODS

The time course and accumulation to steady-state plasma concentration curves were derived for memantine 10 mg every 12 hours and for 20 mg every 24 hours. Peak, trough, and average steady-state concentrations were derived using a one-compartment model for dosing over 21 days using population pharmacokinetic parameters for a 70-kg person (Table 1).^{1–3}

RESULTS

In memantine-naïve subjects, the initiation of 20 mg once daily is predicted to result in an initial peak plasma concentration of 19.5 µg/L, twice that which would occur after an initial dose of 10 mg, 5 hours after ingestion. Because the elimination half-life of memantine is approximately 70 hours, steady state is reached after 2 weeks. As steady state is approached, the difference in peak plasma concentrations between 20 mg once-a-day and 10 mg twice-a-day dosing diminishes (Figure 1). The calculated steady-state peak plasma concentration (92.9 µg/L) after 20 mg once daily is only 6.7% higher than 10 mg twice daily (87.1 µg/L). Similarly, the calculated steady-state trough memantine con-

Table 1. Population Pharmacokinetic Parameters Used to Predict Peak, Trough, and Average Steady-State Concentrations of Memantine

Parameter	Value
Elimination half-life, $T_{1/2}$	70 Hours
Rate of elimination, k_e ($= 0.693/T_{1/2}$)	0.0099 (1/h)
Time of absorption	5 hours
Specific volume of distribution, v_d	10 L/kg
Fraction bound in plasma, b	0.45
Fraction absorbed, f	0.7

centration after 20 mg daily (77.0 µg/L) is only 5.3% lower than with 10 mg twice daily (81.3 µg/L). Furthermore, because of the long elimination half-life, there is only an 8-µg/L variation around the mean for 20 mg once daily, compared with a 3-µg/L variation around the mean for the 10 mg twice daily. As expected, this model is internally consistent because it predicts the same average concentrations at steady state for both regimens (85.0 µg/L for 20 mg once daily, 84.2 µg/L for 10 mg twice daily).

DISCUSSION

This analysis suggests that steady-state memantine therapy can be conveniently administered as a single daily dose. The small peak-to-trough steady-state variation with 10 mg twice- and 20 mg once-daily dosing schemes could be anticipated because of the inherently long half-life of elimination of 60 to 80 hours in subjects with normal renal function. In older adults, reductions in renal function will further increase its elimination half-life.^{1–3} Older adults may have even smaller peak-to-trough fluctuations at steady state than the current analysis predicts.

The peak-to-trough variation derived for the twice-daily regimen assumes 12-hour dosing. In reality, patients are neither instructed nor likely to adhere to 12-hour regimens. A twice-daily dosing regimen, moreover, lends itself to lower adherence than with a single daily dose. The variation between these two drug dosing regimens, therefore, is likely to be even less in favor of 10 mg twice daily than the small differences in plasma levels that the theoretical construct predicts. Validation of the analysis requires blood sampling from patients on these two dosing schemes.

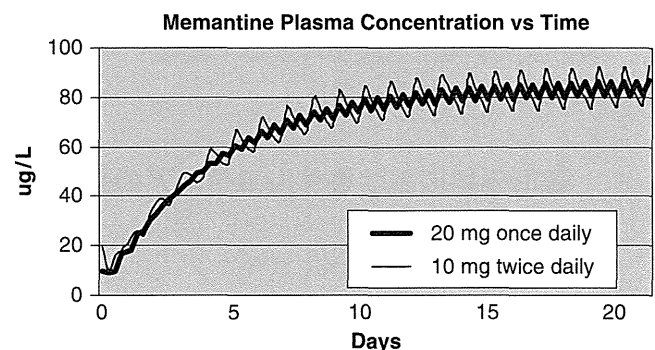


Figure 1. Calculated plasma concentrations of memantine to steady state with dosages of 10 mg every 12 hours and 20 mg every 24 hours.

各論

10. サルコペニアに対する臨床的アプローチ

原田 敦 飛田 哲朗 奥泉 宏康

- サルコペニア
- 運動器不安定症
- ロコモティブシンドローム
- 四肢筋量
- 骨折リスク

整形外科の教科書にはまだサルコペニアは扱われておらず、臨床の場では、運動器不安定症、ロコモティブシンドロームなどの症候群に含めて対処されている。今後、サルコペニア研究がいつそう進んで、高齢になって動きが不自由になる基礎疾患という位置づけが確かなものになることが望まれる。筋肉量の臨床的評価には、全身 DXA 法が有用で、将来的には転倒や骨折のリスクファクターとして使用できることになることが期待される。

はじめに

サルコペニアは、「加齢に伴う筋肉量の減少と筋力の低下」と医学的には定義されるが、初期においては全く無症候であり、かなり進行した段階になって、臨床的には、「力が入らない」「転びやすい」などの主訴を自覚するようになる。しかし、「年齢のせい」と受け入れてしまい、現時点ではサルコペニアだけで受診に至る例は少ない。その姿はかつての骨粗鬆症と非常に似ている。そのようなサルコペニアを診療するためのアプローチに関して、まず整形外科での現状を説明し、次いで臨床で扱っている筋肉量評価法や補正四肢筋肉量と、転倒や骨折との関連性について述べる。

整形外科におけるサルコペニアの認識

1. 教科書におけるサルコペニア

整形外科は、骨・関節・筋から構成される運動器の疾患に対して、長年にわたって診断と治

療を担ってきたが、その歴史の中で、筋肉の扱われ方は、骨および関節に比して量的にも質的にも低いままに留まっている。例えば、代表的な整形外科教科書¹⁾をみると、基礎科学の章では、骨と関節については、構造、生化学、病態生理、損傷修復・再生が50ページ以上を割いて記述されているのに対して、筋は3ページにすぎず、疾患総論の章では、感染症、関節リウマチ、退行性関節疾患、循環障害、先天性骨系統疾患、先天異常症候群、代謝性骨疾患、腫瘍と続き、最後に神経疾患/筋疾患という項があり、筋疾患にはミオパシーとして4ページを当てて、多発性筋炎、皮膚筋炎、進行性筋ジストロフィー、周期性四肢麻痺の4疾患が説明されているだけで終わっている。全体を見渡しても、サルコペニアや筋肉減少症などの病名は全く取り上げられていない。骨粗鬆症が、代謝性骨疾患の項で、成因から、検査として二重エネルギー X 線吸収測定法(dual-energy X-ray absorptiometry, 以下 DXA 法)などによる骨量測定や骨代謝マーカー測定、診断基準、エビデンスのあ

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る薬剤治療までが詳しく説明されているのとは、対照的である。このように教科書にはサルコペニアは扱われていないが、高齢者の増加に伴って転倒をはじめとしたサルコペニアを基礎とした患者は増加の一途であるので、それに対応して、次の2つの症候群が臨床の場で提唱されている。

2. 運動器不安定症

最近、定義を高齢化によりバランス能力および移動・歩行能力の低下が生じ、閉じこもり、転倒リスクが高まった状態として、わが国で日本整形外科学会が提唱して保険収載された症候群に「運動器不安定症」がある。この症候群の基礎疾患である11の運動機能低下を来す疾患には、神経・筋疾患、長期臥床後の運動器廃用、高頻度転倒者が含まれるが、サルコペニアは取り上げられていない²⁾。

3. ロコモティブシンドローム

さらに、日本整形外科学会が提唱する「ロコモティブシンドローム(運動器症候群)」がある。運動器の障害による要介護の状態や要介護リスクの高い状態と定義され、①片脚立ちで靴下がはけない、②家の中でつまずいたり、滑ったりする、③階段を上るのに手すりが必要である、④横断歩道を青信号で渡りきれない、⑤15分くらい続けて歩けない、⑥2kg程度の買い物をして持ち帰るのが困難、⑦家のやや重い仕事が困難である、のうち、1つでも当てはまれば、「ロコモティブシンドローム」の可能性があり、開眼片足立ちやスクワットなどの訓練を行うように勧めるとされている³⁾。これらの病像はサルコペニアそのもののように思われるが、やはりこの病名は見当たらない。

このように、整形外科で繁用されるようになった「運動器不安定症」や「ロコモティブシンドローム」は、サルコペニアの概念と大きく重複すると考えられるが、その説明には、加齢に伴う筋肉量の減少と筋力の低下は指摘せずとも自明の前提であると考えられるためか、サルコペニアという用語は使用されておらず、整形外科の

臨床の場において、その認識は非常に低いままで推移しているのが現状である。今後、研究がいつそう進んで、サルコペニアが高齢になって動きが不自由になる基礎疾患という位置づけが確かなものになることが望まれる。

サルコペニアに対する筋肉量の臨床的評価

筋肉量の評価法は多数報告されており、詳細は他稿に譲るが、大きく分けると、DXA法、生体インピーダンス法、CT、MRI断面積法、四肢周囲径計測がある。

1. DXA法

これは骨密度測定で用いられている方法であり、整形外科領域では馴染み深い方法である。2種類の強さのX線を生体に照射し、それぞれの減衰率から全身身体組織の組成量を、骨塩量、脂肪量、除脂肪量の3種に分け計算することができる。DXA法により測定された組織量と実際に計測された重量とはよく一致し、内臓重量の影響を受けない上下肢においては、除脂肪量と骨格筋量がほぼ一致する。このようにして測定された上下肢の筋量を、BMIと同様の手法により、身長²で割った、補正四肢筋量(appendicular skeletal mass index, 以下ASMI)がサルコペニアの研究において標準的に用いられている。CTやMRIの筋肉の断面積で計測した筋量ともよく相関し⁴⁾、正確性も高い方法であるが⁵⁾、全身骨を測定できるDXAの装置が必要である。ただ、この方法も臨床の場では広く使用されているとはいえない。全身骨は測定時間が長く、骨粗鬆症ガイドラインなどの測定部位となっておらず、筋肉量測定は保険診療の対象ではないことなどのためと思われる。

2. 生体インピーダンス法

これは家庭用体脂肪計の原理と同じで、生体に微弱な交流電気を流し、筋肉と脂肪の電気抵抗が異なる特徴を利用して筋肉量を計算する。簡便で被験者の負担が少ないが、水分量、骨量の影響を受けやすく、合併する疾患の影響を受

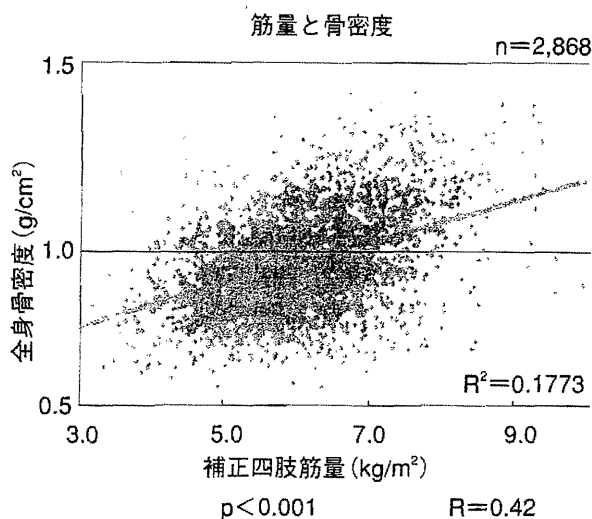


図1 骨密度と補正四肢筋量の関係

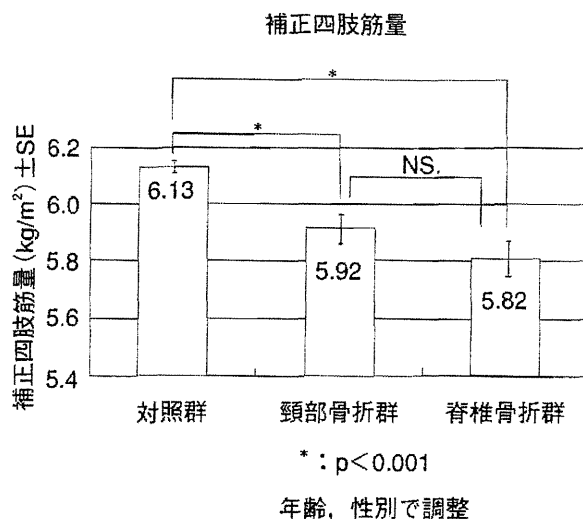


図2 骨折と補正四肢筋量の関係

けやすい⁶⁾。そのため心不全、感染症、脱水などの全身疾患のある患者や骨粗鬆症患者には不向きで、健常者の健診などに有効な方法である。

3. CT, MRI 断面積法

この方法は、大腿などの特定部位においてCTやMRIで筋量の断面積を計測し、筋肉量を求めるものである。検査費用が高額で、計測も自動解析できずに煩雑で、CTでは放射線被曝量が多いため侵襲が大きいことなどが問題点であるが、正確性が期待できる方法である。また、これらの画像による方法では、筋肉中の脂肪変性量も計測できるので質的变化にも迫ることが可能である。

4. 四肢周囲径計測

上腕、前腕、大腿、下腿が主な測定部位で、大腿なら膝蓋骨上縁より10cm頭側にて巻き尺で測り、大腿四頭筋を評価する。下腿なら最大径の部分にて測り、下腿三頭筋を評価する。この方法は簡便であるが、加齢や肥満の影響を受けやすく、皮膚、脂肪などのほかの軟部組織の増減の影響は避けられない。

サルコペニアと転倒や骨折の関連性に関する臨床的検討

筋肉量の減少と筋力の低下は、身体的不安定性を増大させ、転倒リスクを高めると考えられ

ている。メキシコ在住白人およびヒスパニックにおける調査では、DXA法によりASMIを測定した結果、ASMIの低下した人に転倒が多く、身体的不安定性が増すことがわかった⁷⁾。

また、筋肉量は骨量と相関を有しており、われわれの施設で骨粗鬆症を疑い、全身DXA法を施行した患者2,886名における骨密度とASMIの関係を解析すると、両者間には有意な正の相関が認められた(図1)⁸⁾

さらに、われわれの施設に入院した大腿骨近位部骨折および脊椎骨折患者の入院直後にDXA法で測定したASMIを、骨折入院のない骨粗鬆症だけの患者を対照群として比較検討すると(図2)、対照群と比べ、大腿骨近位部骨折、脊椎骨折患者で有意にASMIの低下が認められた。Baumgartnerによるサルコペニアの診断定義(ASMI女性6.45 kg/m²以下、男性7.26 kg/m²以下)を用いると、サルコペニアの合併率は対照群が67%であったのに対して、大腿骨近位部骨折患者が85%、脊椎骨折患者が77%と、骨折患者が対照群に比べ有意に合併率が高く、高齢骨折患者における深刻なサルコペニアの合併の現状が認められた⁹⁾。

さらに最近の2,941名の白人および黒人の男女の縦断研究によれば、大腿部でのCTによる筋肉の脂肪浸潤は、年齢、人種、性、BMI、体脂肪率とは独立しており、脂肪浸潤度が多いほど大腿骨近位部骨折リスクが高く(1SD低下当

たりの相対危険度 1.56), 筋断面積, 筋力で補正後は, この筋肉の脂肪浸潤だけが有意なリスクファクターとして残ったとされており, 筋肉量だけでなく, 脂肪変性などによる質の低下も大腿骨近位部骨折リスクに深く関連することを示している⁹⁾.

おわりに

年を重ねるにつれて筋力が弱くなって, 体が不自由になって困る患者は, サルコペニアを背景としており, 年々増加する一方である. しかしながら, サルコペニア研究の臨床応用はまだ緒についたばかりで, その概念は運動器臨床の場には根付いていない. 日本人のデータ蓄積によるサルコペニアの診断基準や, 新しい治療法の開発が急務である.

文 献

- 1) 標準整形外科学 第10版(国文正一, 鳥巢岳彦監修, 中村利孝ほか編集). 医学書院, 東京, 2008.
- 2) 伊藤博元: 運動器不安定症の診断基準.

CLINICIAN 559: 587-591, 2007.

- 3) <http://www.joa.or.jp/jp/public/locomo/index.html>
- 4) Wang ZM et al: Skeletal muscle mass: evaluation of neutron activation and dual-energy X-ray absorptiometry methods. J Appl Physiol 80: 824-831, 1996.
- 5) Hansen RD et al: Estimation of thigh muscle cross-sectional area by dual-energy X-ray absorptiometry in frail elderly patients. Am J Clin Nutr 86: 952-958, 2007.
- 6) Janssen I et al: Estimation of skeletal muscle mass by bioelectrical impedance analysis. J Appl Physiol 89: 465-471, 2000.
- 7) Rolland Y et al: Sarcopenia, calf circumference, and physical function of elderly women: a cross-sectional study. J Am Geriatr Soc 51: 1120-1124, 2003.
- 8) 飛田哲朗ほか: Dual energy X-ray absorptiometry を用いた大腿骨頸部骨折患者における sarcopenia(筋減少症)の評価. 日本整形外科学会雑誌 83: S96, 2009.
- 9) Lang TF et al: Computed tomography measurements of thigh muscle cross-sectional area and attenuation coefficient predict hip fracture: The Health, Aging and Body Composition Study. J Bone Miner Res, 2009, doi: 10.1359/jbmr.090807

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座談会

サルコペニア

—研究の現状と臨床への応用—



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はじめに

井藤 本日はお忙しいところ、お集まりいただきましてありがとうございます。本日取り上げたテーマは「サルコペニア」で、最近、耳にすることが多くなった問題です。

サルコペニアの概念と定義

井藤 まず、鈴木先生にサルコペニアの研究の流れ、なぜ今、注目されているのかを、お伺いしたいと思います。

鈴木 サルコペニアは一般的に加齢に伴う筋肉量の減少といわれています。筋肉量の減少はこれまでもいろいろな病気に併発することとして知られていましたが、高齢社会になって、病気ではなく、加齢とともに筋肉量が減少するということが注目されています。

しかも、単に筋肉量が減少するだけでなく、それに基づく生活上の不利益、生活機能の障害が生じ、その背景にサルコペニアが間違いなく存在していることが最近の老年医学、高齢者の医療と健康に関わる人たちにとって、急速にクローズアップされてきた問題だと思います。

当然、サルコペニアがあれば、物を握る力、飲み込んだり、噛んだりする力も衰えます。また、転倒も起こしやすくなります。特に下腿三頭筋の筋肉量の著しい減少がいわばしっかりした歩行能力を奪ってしまうのです。

昨今、特に問題になっている要介護の状態にならないようにすることが非常に大事だといわれていますが、その要介護の状態になる原因の1つがサルコペニアであるという点で、サルコペニアが急速にクローズアップされているのです。

運動器と申しますと、これまでは骨や関節に大きな関心が集まっていたのですが、最近は骨や関節と同時に、筋肉の有効な働き、特にサルコペニアによって有効な働きが衰えることをどのように予防するかが大きなポイントになってき

ていると感じています。

井藤 なぜサルコペニアが問題なのかがよくわかりました。次に問題となりますことは、筋肉が減少しているということ、どのような方法、基準で判断するかということでしょう。そこで島田先生にお伺いしたいのですが、サルコペニアの定義、あるいは測定法に関し、最近コンセンサスが得られつつあるのでしょうか。

島田 結論としましては、世界的にコンセンサスの得られているサルコペニアの明確な、操作的な定義は存在しないようです。

とはいいまして、1990年代からサルコペニアの操作的な定義は多くの研究者が行ってきています。ニューメキシコで行われた研究¹⁾が初期で一番有名だと思いますが、その研究ではヒップの周径、握力、姿勢、体重といった簡単な形態測定からDXAで得られた筋量を推計し、サルコペニアの定義を行っています。また、2000年以降から生体インピーダンス法によって筋量を推定し、サルコペニアのカットオフポイントを決めていこうという流れがあります。ただし現時点では従来から行われてきたDXAによる方法で、ある程度のカットオフポイントがみえてきた段階にあります。

サルコペニアを定義する際の問題は、いろいろなスクリーニング方法が提唱され、どの方法も定義は異なるが妥当性があるということで、一体どの方法を使ったらよいのかというので、迷いが生じているといった現状かと思っています。

さらに、わが国の高齢者への適応という観点からいえば、これらの研究はほとんどの母集団がアジア人以外の方々なので、体格が著しく異なり、そのまま日本人の高齢者に外挿していくことは無理があるかと思われま。ですから、わが国においても、大規模調査をベースとしたサルコペニアの定義を作る必要がある段階かと思っています。

井藤 サルコペニアの画像診断では、DXAのほかにCTやMRIも使われていますが、CTやMRIを使った定義もあるのですか。

島田 ラボで少人数では行われていますが、それらの結果を基準として、サルコペニアを診断

していくことは難しいのではないかという気がします。CTやMRIは外的基準として用い、これらを高い水準で予測できる簡便な測定方法と予測式の確立が必要だと思います。

井藤 DXAで測定した筋肉量と対比できている機能としてどのようなものがあるのでしょうか。

島田 筋肉量は多くの身体機能との関係が確認されています。また、ほとんどの研究がIADL機能をアウトカムとして用いています。

井藤 なぜベーシックなADL(基本的ADL)でなく、IADL(手段的ADL)なのですか。

島田 おそらくサルコペニアが大きな問題となる対象が、病気をもっている非常に虚弱な方というよりは、体が弱りかけているがまだ地域に住んでいて、放っておくと危ない高齢者に焦点が当てられるためだと思います。

鈴木 生活機能の障害ですから、一般的に地域在宅の高齢者でみるときは、ベーシックADLよりもIADLのレベルが落ちることを重視していると思います。

井藤 サルコペニアが問題となるのは、虚弱か、虚弱になりかけの人ということですね。

サルコペニア診療の現状

井藤 地域住民を対象にした研究からは虚弱、あるいは虚弱になりかけの人に注目して定義化が進んでいるということなのですが、サルコペニアが臨床でも注目されるようになってきています。そこで原田先生にお伺いしたいのですが、サルコペニアがどのような臨床の問題と関連して注目を集めるようになったのでしょうか。

原田 先ほど鈴木先生がおっしゃいましたように、整形外科では、運動器の障害を、基礎的構造として骨・関節に大別し、それに膝や頸椎などの部位別の特徴を加えて臨床的に扱っています。そこには筋肉を骨・関節と同じレベルの重要性を有する組織として認識するという姿が乏しい状況です。でも、患者さんの運動機能障害には、もちろん骨や関節だけでなく、筋肉の間

すずき たかお
鈴木 隆雄 先生



昭和51年札幌医科大学医学部卒業。同57年東京大学大学院博士課程修了。平成2年東京都老人総合研究所夜学研究室長、同8年部長、同12年副所長、同21年国立長寿医療センター研究所所長、現在に至る。

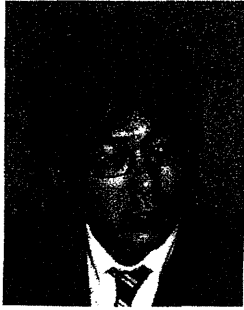
日本老年医学会(評議員)、日本骨粗鬆症学会(理事)など

研究分野:

1. 高齢者の健康と生活機能維持のための総合的な取り組み、特に介護予防の科学的根拠に基づく普及
2. 骨粗鬆症およびその骨折予防、サルコペニアの改善

題が深く関わっていることは少なくありません。これまで、筋肉は、整形外科医にとって十分にあるのが当たり前で、いつの間にか足りなくなって初めてその価値に気づく空気のような存在だったのかもしれませんが。

診療に当たっては、骨粗鬆症の立場からみると、骨に重点が置かれ、関節外科からみると関節に重点が置かれています。ところが運動は関節と骨だけで成立しません。筋肉の機能がそこに付与されて、初めて関節機能、骨の機能が維持、発揮されます。加齢に伴って、その筋肉が量と質の低下、すなわち、サルコペニアによって機能低下に陥ると、骨も関節も含めて、身体全体の運動器の機能低下が起こります。高齢化



しまだ ひろゆき
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ハビリテーション医学博士課程修了、同15～17年東京都老人総合研究所介護予防緊急対策室、同17～18年Prince of Wales Medical Research Institute(シドニー)客員研究員、同18～20年日本学術振興会特別研究員、同20年東京都老人総合研究所自立促進と介護予防研究チーム研究員、現在に至る。

日本理学療法士協会(会員)、日本老年医学会(会員)、日本公衆衛生学会(会員)、理学療法科学会(評議員)、理学療法の医学的基礎研究会(理事)、高齢者健康増進協会(会員)

研究分野：運動生理学、リハビリテーション医学

社会が定着し、サルコペニアのため自立ができなくなる高齢患者(高転倒リスク者など)が増加の一途を辿り、臨床の場にもようやくこの概念に本格的注目が集まるようになったところです。

これまでの整形外科は、運動器に生じた個別の痛みを改善するような治療をした後に、再発予防として筋力訓練を指導するという診療パターンが多かったのですが、上記のような高齢患者を前にして、転倒予防や介護予防を目的に疼痛などの症状とは関係なく、運動機能訓練などを日常診療で行うようになっていきます(運動器不安定症)。開業医の先生たちを中心に、運動器不安定症診断基準のもとに選別された、虚弱か虚弱になりかけの高齢者に運動訓練をするこ

とで診療も成り立ち、患者さんも機能の低下が抑えられたり、向上するということが根づき始めており、寝たきりなどの重い要介護状態になるのを少しでも遅らせたり、軽く済ませるという目的を果たしつつあると思うのですが、その際に病態の中心にサルコペニアが存在すると認識して、その全体像を俯瞰して診療するという意識はまだないようです。

井藤 介護予防ということが個別の臓器、個別の部位のケアだけではなかなか達成できない。全体像を改善していくような視点が必要だということですね。

原田 そう思います。

サルコペニアと関連疾患

1. 転倒・骨折

井藤 実際に臨床の現場で、骨折や膝の関節の痛みを訴える人などいろいろな患者さんを診られると思うのですが、そういう患者さんの症状や骨折の原因として、サルコペニアはどう関わっているのでしょうか。

原田 膝や脊椎の機能を維持し、疼痛などの症状が出にくくするためには、一定以上の筋肉量が必要とされています。例えば、無症状の変形性膝関節症もサルコペニアによって大腿四頭筋の筋肉量減少が進行すれば、立ち上がり時などに痛みを伴うようになり、疼痛による廃用も加わるという悪循環に陥ることが想定されます。

また、高齢者の骨折は、脊椎骨折の一部を除くと、やはり転倒が直接の引き金を引いている場合がほとんどです。そして、転びやすくなる主要な原因に、サルコペニアによる筋力低下があり、サルコペニアは骨粗鬆症と並ぶ骨折の主要要因だと思います。われわれの症例でDXA法で測定した補正四肢筋量の基準値(Baumgartner)で判定したサルコペニア合併率は、対照群に比較して大腿骨近位部と脊椎の部位を問わず、骨折群で高かったという結果を得ています(図1)。

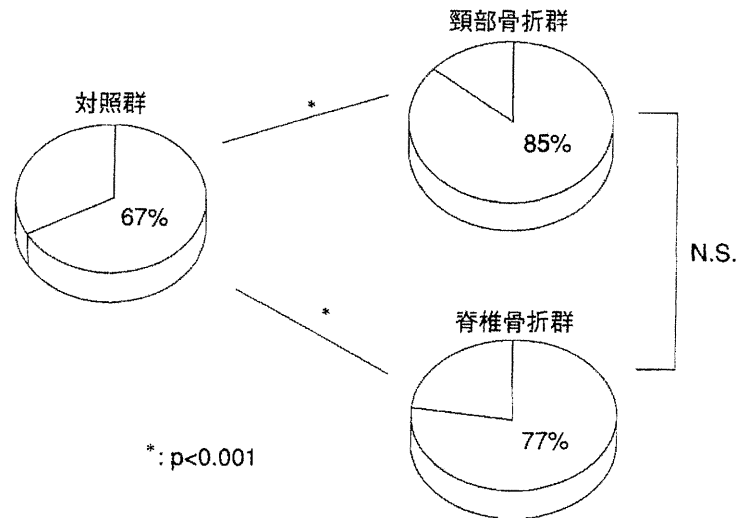


図1 サルコペニアの合併率

2. 老年症候群

井藤 鈴木先生は非常に早くから、サルコペニアと老年症候群に着目されて、研究を進められています。現時点で得られている成果、あるいは今後進めなければいけない研究分野はどういう点になるのでしょうか。

鈴木 高齢者の健康をどう今後維持していくかということは非常に大きな問題です。特に後期高齢者が増えてきますし、後期高齢者は前期高齢者と比べると、明らかに身体機能、運動機能、生活機能が大きく減衰しているのです。今後増えてくる後期高齢者の生活機能をいかに守るかということが非常に重要だと思います。生活機能を守るということは、要介護の状態にしないということですし、要介護の状態にしないということは、転倒・骨折を起こさない、尿失禁で困っている場合には尿失禁を改善する、老人性の肺炎の最大の原因である口腔機能を維持し、低下させないということなのです。いずれの老年症候群も筋力、筋肉のクオリティの問題だということが早くから想定されています。

もう一方で、転倒を予防するという研究は日本では非常に厚みのある研究が行われています。いかに転倒を予防するかという中では、衰えた筋力を筋肉トレーニングによって増強し、転ばせないというやり方が主流だったと思うのです

が、ビタミンD投与によって、転倒を予防できるという研究²⁾が最近注目され、施行されています。しかも、ビタミンDのレセプターは筋肉中に存在しているということが、最近わかってきた³⁾のです。こちら側から「運動して下さい」と言って、応えられる人はよいのですが、後期高齢者で「運動するのもしんどい」という場合は、代替案を考えなければなりません。そういう中でビタミンDは有効な可能性の1つと思います。

また最近では、アミノ酸の中でもロイシンを高負荷すると、筋力が増えるという欧米の研究⁴⁾も報告されています。

サルコペニアには厳密な定義がないものから、われわれは、下腿三頭筋周囲径と膝伸展筋力を測定し、それらをいずれも四分位にしたときに、両方とも四分位(最低位)に含まれてしまうような高齢者を(仮に)サルコペニアと定義しています。このような高齢者を、運動だけを行う群、先ほどのロイシンを高負荷したアミノ酸製剤(市販品)を摂取する群、運動を行いながらアミノ酸を摂取する群、コントロールの4群に分けたRCTを実施しました。

その結果、やはり運動とアミノ酸の両方を負荷している群の機能ははるかによくなっていて、筋力の増加が得られているというデータが得ら