toms, complications, drug contraindications, and previous treatment history. The bone matrix marker, ucOC, reflects vitamin K deficiency, so this information is useful when selecting vitamin K_2 drugs and as an adjunct when evaluating their efficacy (Figs. 2, 3).

Evaluation of drug treatment effects in osteoporosis using bone metabolic markers

Combination of evaluable bone metabolic markers and therapeutic drugs

Using only baseline values of bone metabolic markers it is difficult to predict drug treatment effectiveness. Drug treatment effectiveness can be monitored by repeating the measurement at a given interval after the start of treatment to evaluate changes from baseline values. With drug treatment, only significant changes from baseline values in bone metabolic markers indicate that bone metabolism has changed and the treatment has been effective. In individual patients, the effectiveness of bisphosphonates, SERMs, or estrogen treatment can be assessed using DPD, NTX, CTX, TRACP-5b, BAP, or P1NP. The effectiveness of activated vitamin D_3 (particularly, eldecalcitol) can be assessed using NTX or BAP. The effectiveness of PTH drugs (daily subcutaneous injection) is assessed using P1NP. For other drugs, evaluation by measurement of these bone metabolic markers is not easy. In addition, in treatment using bisphosphonates such as alendronate that have amino groups, changes in urinary free DPD, compared to telopeptides, are known to be smaller [9, 15] (Fig. 4).

One criterion for evaluating treatment effectiveness is whether a change has exceeded the minimum significant change (MSC). The MSC is defined as twice the inter-day variation in the morning in premenopausal women (Table 5). Despite measurement at uniform sample collection times, if no significant changes in bone metabolic markers with drug treatment are observed, patient treatment compliance should first be confirmed. The possibility of another underlying disease causing secondary osteoporosis must also be considered (Table 6). With bisphosphonate therapy, it is also important to check that the time interval between drug administration and meals is sufficient so that there are no problems with drug absorption. If there is no problem with treatment compliance, then the

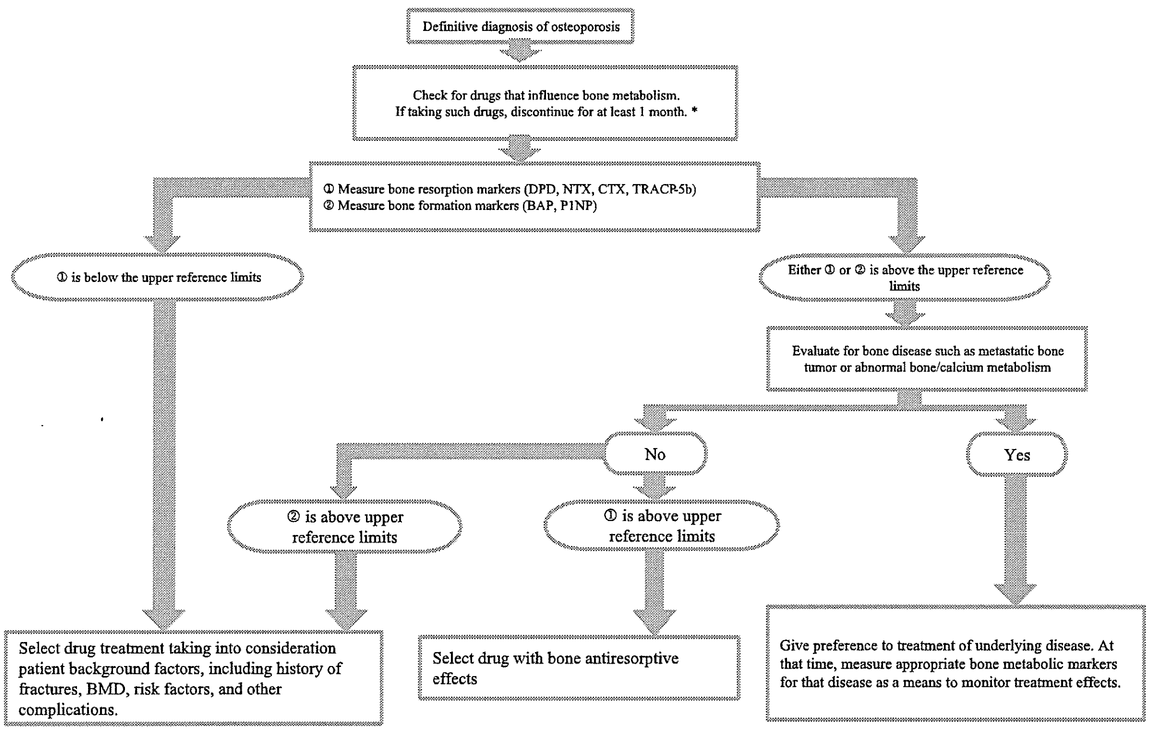

Fig. 2 Measurement of bone resorption markers and bone formation markers when selecting drug treatment for osteoporosis. *Asterisk* for bisphosphonates after stopping for at least 3 months. Bisphosphonates (etidronate disodium, alendronate sodium hydrate, risedronate sodium hydrate, minodronic acid hydrate), SERMs (raloxifene, bazedoxifene), estrogens (estradiol, estriol), calcitonin (elcatonin, salmon calcitonin), and activated vitamin D_3 (eldecalcitol) drugs are known to have bone antiresorptive effects

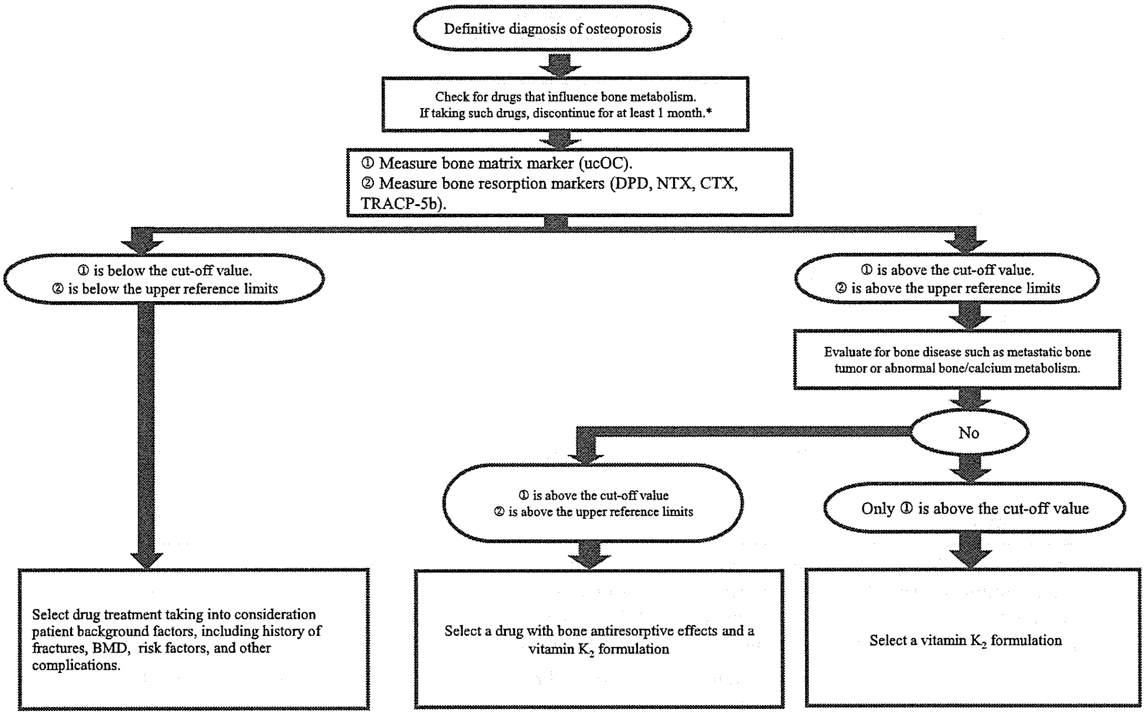

Fig. 3 Measurement of ucOC and bone resorption markers when selecting drug treatment in osteoporosis. *Asterisk* for bisphosphonates after stopping for at least 3 months

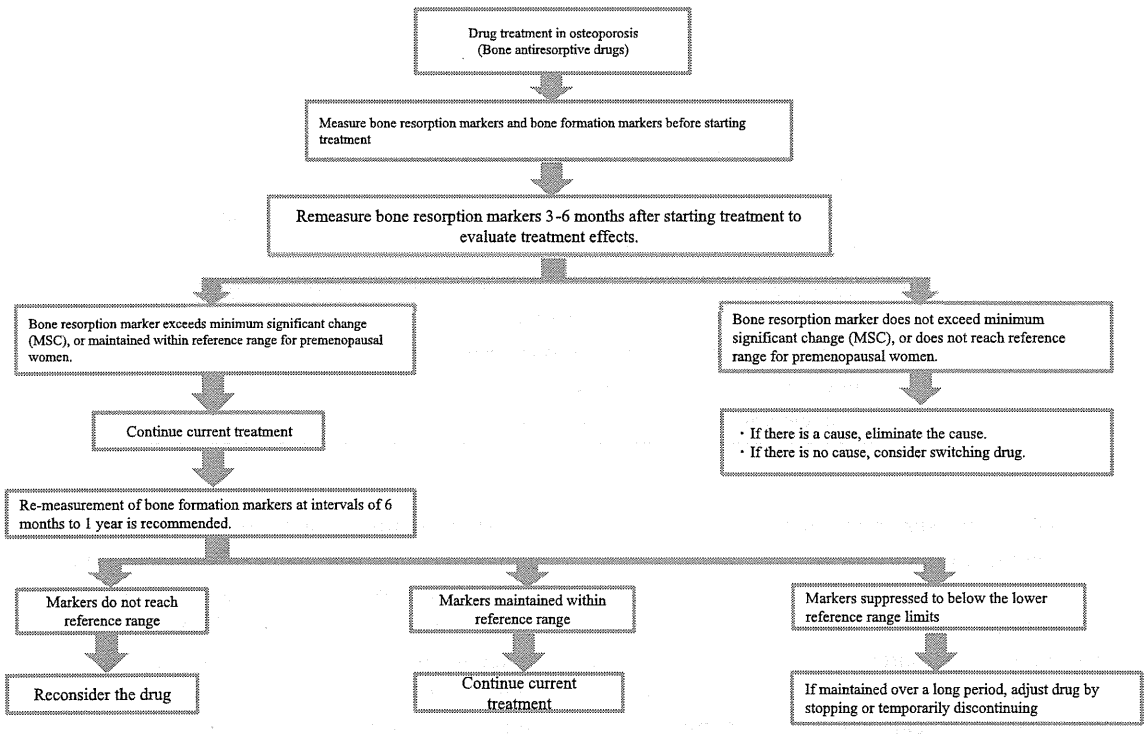

Fig. 4 Evaluation of therapeutic effects of bone antiresorptive drugs using bone resorption markers. Please refer to Table 6

response to drug treatment is inadequate and an increase in dose or switch to another drug is indicated. It should also be kept in mind that depending on the drug administered, there are some drugs for which significant changes in DPD, NTX, CTX, TRACP-5b, BAP, or P1NP are not readily apparent.

Table 5 Minimum significant changes (MSC) in bone turnover markers approved for osteoporosis

Type of marker	Assay method	Units	MSC (%)[a] (twice the mean day-to-day variation)	Reference (%)[b]
Bone formation markers				
BAP	CLEIA	μg/L	9.0	–
BAP	EIA	U/L	–	23.1[c]
P1NP	RIA	μg/L	12.1	–
Bone resorption markers				
DPD[c]	EIA	nmol/mmol Cr	23.5	29.6[c]
sNTX	EIA	Nmol BCE/L	16.3	14.2[c]
uNTX	EIA	nmol BCE/mmol Cr	27.3	35.0 [c]
sCTX	EIA	ng/mL	23.2	–
uCTX	EIA	μg/mmol Cr	23.5	51.1[c]
TRACP-5b	EIA	mU/dL	12.4	16.2[d]
Bone matrix-related marker				
ucOC	ECLIA	ng/mL	32.2	–

BAP bone alkaline phosphatase, *CLEIA* chemiluminescent enzyme immunoassay, *EIA* enzyme immunoassay, *P1NP* Type 1 procollagen-N-propeptide, *RIA* radio immunoassay, *DPD* deoxypyridinoline, *Cr* creatinine, *sNTX* and *uNTX* serum and urinary (respectively) Type 1 collagen cross-linked N-telopeptide, *BCE* bone collagen equivalent, *sCTX* and *uCTX* serum and urinary (respectively) Type 1 collagen cross-linked C-telopeptide, *TRACP-5b* tartrate-resistant acid phosphatase 5b, *ucOC* undercarboxylated osteocalcin

[a] MSC values calculated as twice the day-to-day variations, as requested by committee [basis for establishment: in 10 volunteer premenopausal women, blood and urine samples were collected 5 times during 14 days. These samples were deep-frozen stored until measurement, and measured as batches at a laboratory center (SRL Inc.)]

[b] MSC values are excerpts from the 2004 guidelines and kit package inserts

[c] Described in 2004 guidelines

[d] Described in kit manufacturer's package insert

Table 6 Possible causes for the variation within MSC value in osteoporosis under drug treatment

1. Causes related to various variations
The samples before and after the treatment should be collected at the same time because of the diurnal variation
Measurement errors over a long period of time (e.g., seasonal variation, change in patient status)
Measurement interval is too short
Change in the laboratory performance measurement or change the laboratory site
2. Low compliance of drug and instructions
Inadequate timing with meals (bisphosphonates)
Insufficient medication (low compliance)
3. Current drug for osteoporosis has no effect on bone markers

Appropriate times to measure bone metabolic markers in evaluating treatment effectiveness

The bone resorption markers DPD, NTX, CTX, and TRACP-5b should be measured twice, when treatment is started and 3–6 months after starting treatment, and the percent change should be calculated. With administration of bone antiresorptive drugs, changes in the bone formation markers BAP and P1NP are slightly delayed. For this reason, they should be measured twice—when treatment is started and again at 6 months—and the percent changes should be calculated.

After treatment with bone formation-promoting PTH drugs (recombinant, daily subcutaneous injection), changes in P1NP compared to BAP are more prominent among the bone formation markers. These should be measured twice—when treatment is started and 1–3 months after starting treatment—and the amount/percent of change should be calculated [54, 55]. However, for PTH drugs (weekly subcutaneous injection of teriparatide acetate) administered once a week for 18 months, the bone formation marker osteocalcin (OC) tends to be high throughout the drug administration period, whereas P1NP tends to be high until 3 months, and low from 6 months onwards. In addition, the bone resorption markers DPD and uNTX are reported to be low after starting treatment, so this should also be considered [56].

Displaying the measurement results

The results of bone metabolic marker measurements can be displayed in two ways for easier interpretation of the changes. The percent changes in response to treatment are calculated and plotted as changes from baseline values [57]. The graph may also include threshold values, which indicate the MSC [57]. In addition, the absolute values can be shown together with reference values obtained from premenopausal women. If the data are displayed in this manner, it is easier to explain to patients.

Future issues

This guideline presents the data, as completely as possible, for current NHI-approved bone formation markers (BAP, P1NP), bone resorption markers (DPD, sNTX/uNTX, sCTX/uCTX, TRACP-5b), and a bone matrix marker (ucOC). Drug therapy for which effectiveness has been evaluated is limited to drugs that have been approved in Japan. The proposals in this guideline (based on examined outcomes) assume primary osteoporosis, and in particular, post-menopausal osteoporosis. Accordingly, whether these can be expanded to apply to secondary osteoporosis due to underlying or drug-induced disease is an issue for further investigation.

Meanwhile, bone metabolic marker changes using *T* scores and scoring, fracture risk, and bone loss (categorical data 2 %/3 years) were each examined. No significant relationship between fracture risk and bone metabolic markers was observed. Similarly, based on the examined categorical data, no relationship to the prediction of bone loss rates was observed. No significance was found in scoring of markers for bone loss prediction. With respect to the evaluation of bone metabolic markers using *T* scores, further studies are needed in a larger number of patients, including evaluation by fracture site for each drug, and evaluation of the relationship between percent decrease in markers and fracture reduction.

In examining the issues leading to these guideline proposals, the measurement of bone metabolic markers was performed at a limited number of laboratory test centers. However, in clinical practice, because bone metabolic markers are measured by multiple laboratory test centers, differences and variations among facilities performing measurements should be recognized and kept in mind. For initially approved bone resorption markers, reagent manufacturers voluntarily perform reagent control studies, and efforts to reduce differences among facilities continue in the direction of further improvement. Some issues that must be resolved in the future include how to differentiate and effectively use bone formation markers and bone resorption markers; establishing optimal levels of bone metabolic markers, not only for assessment of effects; and applying these markers in men and in secondary osteoporosis.

These proposed guidelines for the appropriate use of bone metabolic markers take into consideration current health insurance regulations in Japan. However, in order to achieve a more appropriate use of bone metabolic markers it is now recognized that periodic repeated measurement for monitoring after treatment is also effective. In addition, with bone antiresorptive drugs, particularly bisphosphonates containing amino groups, excessive inhibition of bone metabolism has often been observed and may also be a problem. Keeping target values (optimal levels of absolute values) of bone turnover (based on bone metabolic markers) within the physiologic range of reference values in premenopausal women is also considered important in maintaining bone strength [7, 13]. This issue should also be investigated in Japan by further accumulation of clinical data.

Conflict of interest All authors declare that they have no conflict of interest.

References

1. Braithwaite RS, Col NF, Wong JB (2003) Estimating hip fracture morbidity, mortality and costs. J Am Geriatr Soc 51:364–370
2. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy (2001) Osteoporosis prevention, diagnosis, and therapy. JAMA 285:785–795
3. Blake GM, Fogelman I (2007) Role of dual-energy X-ray absorptiometry in the diagnosis and treatment of osteoporosis. J Clin Densitom 10:102–110
4. Orimo H, Hayashi Y, Fukunaga M, Sone T, Fujiwara S, Shiraki M, Kushida K, Miyamoto S, Soen S, Nishimura J, Oh-Hashi Y, Hosoi T, Gorai I, Tanaka H, Igai T, Kishimoto H, Osteoporosis Diagnostic Criteria Review Committee: Japanese Society for Bone and Mineral Research (2001) Diagnostic criteria for primary osteoporosis: year 2000 revision. J Bone Miner Metab 19:331–337
5. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E (2008) FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int 19:385–397
6. Cummings SR, Palermo L, Browner W, Marcus R, Wallace R, Pearson J, Blackwell T, Eckert S, Black D (2000) Monitoring osteoporosis therapy with bone densitometry: misleading changes and regression to the mean. Fracture Intervention Trial Research Group. JAMA 283:1318–1321
7. Weinstein RS (2000) True strength. J Bone Miner Res 15:621–625
8. Chesnut CH III, Rosen CJ, For the Bone Quality Discussion Group (2001) Reconsidering the effects of antiresorptive therapies in reducing osteoporotic fracture. J Bone Miner Res 16:2163–2172

9. Delmas PD, Eastell R, Garnero P, Seibel MJ, Stepan J (2000) The use of biochemical markers of bone turnover in osteoporosis. Osteoporos Int 11:S2–S17
10. Nishizawa Y, Nakamura T, Ohta H, Kushida K, Gorai I, Shiraki M, Fukunaga M, Hosoi T, Miki T, Chaki O, Ichimura S, Nakatsuka K, Miura M, For the Committee on the Guidelines for the Use of Biochemical Markers of Bone Turnover in Osteoporosis, Japan Osteoporosis Society (2004) Guidelines for the use of biochemical makers of bone turnover in osteoporosis. J Bone Miner Metab 23:97–104
11. Orimo H, Hayashi Y, Fukunaga M, Sone T, Fujieara S, Schiraki M, Kushida K, Miyamoto S, Sone S, Nishimura J, Oh-hashi Y, Hosoi T, Gorai I, Tanaka H, Iga T, Kishimoto H (2001) Diagnostic criteria for primary osteoporosis: year 2000 revision. J Bone Miner Metab 19:331–337
12. Cummings SR, Karpf DB, Harris F, Harris F, Genant HK, Ensrud K, LaCroix AZ, Black DM (2002) Improvement of spine bone density and reduction in risk of vertebral fractures during treatment with antiresorptive drugs. Am J Med 112:282–289
13. Heaney RP (2003) Is the paradigm shifting? Bone 33:457–465
14. Garnero P, Hausherr E, Chapuy MC, Marcelli C, Grandjean H, Muller C, Cormier C, Breart G, Meunier PJ, Delmas PD (1996) Markers of bone resorption predict hip fracture in elderly women; EPIDOS prospective study. J Bone Mineral Res 11:1531–1538
15. Garnero P, Sornay-Rendu E, Claustrar B, Claustrat B, Delmas PD (2000) Biochemical markers of bone turnover, endogenous hormones and the risk of fracture in postmenopausal women: the OFELY study. J Bone Miner Res 15:1526–1536
16. Ross PD, Kress BC, Parson RE, Wasnich RD, Armour KA, Mizrahi IA (2000) Serum bone alkaline phosphatase and calcaneus bone density predict fractures; a prospective study. Osteoporos Int 11:76–82
17. Shiraki M, Kushida K, Fukunaga M, For the Alendronate Phase III Osteoporosis Research Group (1999) A double-masked multicenter comparative study between alendronate and alfacalcidol in Japanese patients with osteoporosis. Osteoporos Int 10:183–192
18. Morii H, Ohashi Y, Taketani Y, Fukunaga M, Nakamura T, Itabashi A, Sarkar S, Harper K (2003) Effect of raloxifene on bone mineral density and biochemical markers of bone turnover in Japanese postmenopausal women with osteoporosis: results from a randomized placebo-controlled trial. Osteoporos Int 14:793–800
19. Nishizawa Y (2011) A survey of diagnosis and treatment in Japan (in Japanese). Osteoporos Jpn 19:33–47
20. Committee of Use of Biochemical Markers of Bone Turnover in Osteoporosis, Japan Osteoporosis Society (2001) Guidelines on the use of biochemical markers of bone turnover in osteoporosis (in Japanese). Osteoporos Jpn 9:255–271
21. Committee of Use of Biochemical Markers of Bone Turnover in Osteoporosis, Japan Osteoporosis Society (2002) Guidelines on the use of biochemical markers of bone turnover in osteoporosis (in Japanese). Osteoporos Jpn 10:251–261
22. Bell KJ, Hayen A, Macaskill P, Irwig L, Craig JC, Ensrud K, Bauer DC (2009) Value of routine monitoring of bone mineral density after starting bisphosphonate treatment: secondary analysis of trial data. Br Med J 338:b2266
23. Seeman E, Delmas PD (2006) Bone quality—the material and structural basis of bone strength and fragility. N Engl J Med 354:2250–2261
24. Eriksen EF, Hodgson SF, Eastell R, Cedel SL, O'Fallon WM, Riggs BL (1990) Cancellous bone remodeling in type I (postmenopausal) osteoporosis: quantitative assessment of rates of formation, resorption, and bone loss at tissue and cellular level. J Bone Miner Res 5:311–319
25. Saito M, Marumo K (2010) Collagen-crosslinks as a determinant of bone quality: possible explanation for bone fragility in aging, osteoporosis and diabetes mellitus. Osteoporos Int 21:195–214
26. Saito M, Fujii K, Mori Y, Marumo K (2006) Role of collagen enzymatic and glycation induced cross-links as a determinant of bone quality in spontaneously diabetic WBN/Kob rats. Osteoporos Int 17:1514–1523
27. Nagaoka H, Mochida Y, Atsawasuwan P, Kaku M, Kondoh T, Yamauchi M (2008) 1,25(OH)2D3 regulates collagen quality in an osteoblastic cell culture system. Biochem Biophys Res Commun 377:674–678
28. Raposo B, Rodríguez C, Martínez-González J, Badimon L (2004) High levels of homocysteine inhibit lysyl oxidase (LOX) and down regulate LOX expression in vascular endothelial cells. Atherosclerosis 177:1–8
29. Liu G, Nellaiappan K, Kagan HM (1997) Irreversible inhibition of lysyl oxidase by homocysteine thiolactone and its selenium and oxygen analogues. Implications for homocystinuria. J Biol Chem 272:32370–32377
30. van Meurs JB, Dhonukshe-Rutten RA, Pluijim SM, van der Klift M, de Jonge R, Lindemans J, de Groot LC, Hofman A, Witteman JC, van Leeuwen JP, Breteler MM, Lips P, Pols HA, Uitterlinden AG (2004) Homocysteine levels and the risk of osteoporotic fracture. N Engl J Med 350:2033–2041
31. Shiraki M, Urano T, Kuroda T, Saito M, Tanaka S, Miyao-Koshizuka M, Inoue S (2008) The synergistic effect of bone mineral density and methylenetetrahydrofolate reductase (MTHFR) polymorphism (C677T) on fractures. J Bone Miner Metab 26:595–602
32. Amizuka N, Li M, Hara K, Kobayashi M, de Freitas PH, Ubaidus S, Oda K, Akiyama Y (2009) Warfarin administration disrupts the assembly of mineralized nodules in the osteoid. J Electron Microsc 58:55–65
33. Tsugawa N, Shiraki M, Suhara Y, Kamao M, Tanaka K, Okano T (2006) Vitamin K status of healthy Japanese women: age-related vitamin K requirement for gamma-carboxylation of osteocalcin. Am J Clin Nutr 83:380–386
34. Vergnaud P, Garnero P, Meunier PJ, Bréart G, Kamihagi K, Delmas PD (1997) Undercarboxylated osteocalcin measured with a specific immunoassay predicts hip fracture in elderly women: the EPIDOS study. J Clin Endocrinol Metab 82:719–724
35. Garnero P, Sornay-Rendu E, Claustrat B, Delmas PD (2000) Biochemical markers of bone turnover, endogenous hormones and risk of fractures in postmenopausal women: the OFELY study. J Bone Miner Res 15:1526–1536
36. Okabe R, Nakatsuka K, Inaba M, Miki T, Naka H, Masaki H, Moriguchi A, Nishizawa Y (2001) Clinical evaluation of the Elecsys beta-CrossLaps serum assay, a new assay for degradation products of type I collagen C-telopeptides. Clin Chem 47:1410–1414
37. Nishizawa Y, Inaba M, Ishii M, Yamashita H, Miki T, Goto H, Yamada S, Chaki O, Kurasawa K, Mochizuki Y (2008) Reference intervals of serum tartrate-resistant acid phosphatase type 5b activity measured with a novel assay in Japanese subjects. J Bone Miner Metab 26:265–270
38. Kress BC, Mizrahi IA, Armour KW, Marcus R, Emkey RD, Santora AC 2nd (1999) Use of bone alkaline phosphatase to monitor alendronate therapy in individual postmenopausal osteoporotic women. Clin Chem 45:1009–1017
39. Melkko J, Kauppila S, Niemi S, Risteli L, Haukipuro K, Jukkola A, Risteli J (1996) Immunoassay for intact amino-terminal propeptide of human type I procollagen. Clin Chem 42:947–954
40. Iki M, Akiba T, Matsumoto T, Nishino H, Kagamimori S, Kagawa Y, Yoneshima H, JPOS Study Group (2004) Reference database of biochemical markers of bone turnover for the Japanese female population. Japanese Population-based Osteoporosis (JPOS) Study. Osteoporos Int 15:981–991
41. Bjarnason NH, Sarker S, Duong T, Mitlak B, Delmas PD, Christiansen C (2001) Six and twelve month changes in bone turnover are related to reduction in vertebral fracture risk during

3 years of raloxifene treatment in postmenopausal osteoporosis. Osteoporos Int 12:922–930

42. Eastell R, Barton I, Hannon RA, Chines A, Garnero P, Delmas PD (2003) Relationship of early changes in bone resorption to the reduction in fracture risk with risedronate. J Bone Miner Res 18:1051–1056
43. Delmas PD, Seeman E (2004) Changes in bone mineral density explain little of the reduction in vertebral or nonvertebral fracture risk with anti-resorptive therapy. Bone 34:599–604
44. Delmas PD, Vrigens B, Eastell R, Roux C, Pols HA, Ringe JD, Grauer A, Cahall D, Watts NB (2007) Effect of monitoring bone turnover markers on persistence with risedronate treatment of postmenopausal osteoporosis. J Clin Endocrinol Metab 92:1296–1304
45. Imai E, Horio M, Watanabe T, Iseki K, Yamagata K, Hara S, Ura N, Kiyohara Y, Moriyama T, Ando Y, Fujimoto S, Konta T, Yokoyama H, Makino H, Hishida A, Matsuo S (2009) Prevalence of chronic kidney disease in the Japanese general population. Clin Exp Nephrol 13:621–630
46. Yamada S, Inaba M, Kurajoh M, Shidara K, Imanishi Y, Ishimura E, Nishizawa Y (2008) Utility of serum tartrate-resistant acid phosphatase (TRACP5b) as a bone resorption marker in patients with chronic kidney disease: independence from renal dysfunction. Clin Endocrinol (Oxf) 69:189–196
47. Inaba M, Kurajoh M, Okuno S, Imanishi Y, Yamada S, Mori K, Ishimura E, Yamakawa T, Nishizawa Y (2010) Poor muscle quality rather than reduced lean body mass is responsible for the lower serum creatinine level in hemodialysis patients with diabetes mellitus. Clin Nephrol 74:266–272
48. Delmas PD, Vrijens B, Eastell R, Roux C, Pols HA, Ringe JD, Grauer A, Cahall D, Watts NB (2003) A reinforcement message based on bone turnover marker response influences long-term persistence with risedronate in osteoporosis: IMPACT study. J Bone Miner Res 18:S374
49. Kurasawa K, Chaki O, Hirahara F (2006) Evaluation of serum bone-specific alkaline phosphatase using automated chemiluminescent enzyme immunoassay (in Japanese). Jpn J Med Pharm Sci 55:279–285
50. Shiraki M, Aoki C, Yamazaki N, Ito Y, Tsugawa N, Sunahara Y, Okano T (2007) Clinical assessment of undercarboxylated osteocalcin measurement in serum using and electrochemiluminescence immunoassay: establishment of cut-off values to determine vitamin K insufficiency in bone and to predict fracture leading to clinical use of vitamin K2 (in Japanese). Jpn J Med Pharm Sci 57:537–546
51. Nishizawa Y, Inaba M, Ishi K, Yamashita H, Miki T, Goto H, Yamada S, Chaki O, Karasawa K (2005) Evaluation of newly developed kit for measurement of bone-specific tartrate-resistant acid phosphates in blood (in Japanese). Jpn J Med Pharm Sci 54:709–717
52. Sone T, Yoshikawa K, Tamada T, Takeda N, Fukunaga M (2001) Clinical application of radioimmunoassay for determination of serum intact PINP (procollagen type I amino-terminal propeptide) (in Japanese). Clin Endocrinol 49:1133–1138
53. Greenspan SL, Parker RA, Ferguson L, Rosen HN, Maitland-Ramsey L, Karpf DB (1998) Early changes in biochemical markers of bone turnover predict the long-term response to alendronate therapy in representative elderly women: a randomized clinical trial. J Bone Miner Res 13:1431–1438
54. Miyauchi A, Matsumoto T, Sugimoto T, Tsujimoto M, Warner MR, Nakamura T (2010) Effects of teriparatide on bone mineral density and bone turnover markers in Japanese subjects with osteoporosis at high risk of fracture in a 24-month clinical study: 12-months, randomized, placebo-controlled, double-blind and 12-month open-label phases. Bone 47:493–502
55. Tsujimoto M, Chen P, Miyauchi A, Sowa H, Krege JH (2011) PINP as an aid for monitoring patients treated with teriparatide. Bone 8:798–803
56. Nakamura T, Matsumoto T, Sugimoto T, Shiraki M (2011) Effect of weekly teriparatide in patients with osteoporosis. J Bone Miner Res 26:S1201
57. Eastell R, Brainbridge PR (2003) Bone turnover markers: their place in the investigation of osteoporosis. In: Orwoll ES, Bliziotes M (eds) Osteoporosis: pathophysiology and clinical management. Humana Press, Totowa, pp 185–197

Arch Orthop Trauma Surg (2012) 132:555–563
DOI 10.1007/s00402-011-1418-y

Fall incidence and risk factors in patients after total knee arthroplasty

Hiromi Matsumoto · Makoto Okuno · Tatsuhiko Nakamura · Kichizo Yamamoto · Hiroshi Hagino

Received: 1 June 2011 / Published online: 17 November 2011

Abstract
Purpose To prospectively investigate the relationship between physical function and falls among elderly patients who underwent total knee arthroplasty (TKA) and to determine the incidence of falls as well as their risk factors.
Methods A total of 108 patients (17 male, 91 female) over 60 years of age who underwent TKA were enrolled and who were living independently in community. 75 patients fulfilled our inclusion criteria and 74 (8 male, 66 female) of them agreed to participate. Baseline assessment (physical examination, physical performance tests, and self-administered questionnaire) were conducted between 6 and 12 months after the last arthroplasty and the follow-up assessment was performed 6 months after the baseline assessment. Monthly pre-stamped postcards were sent to assess the incidence of falls.
Results Of the 74 patients enrolled, 70 (94.6%) completed a 6-month prospective observation. 23 of 70 patients (32.9%) fell during the observational period. Postoperative range of knee flexion, ranges of knee flexion and extension and ankle plantar flexion were significantly lower in fallers than in non-fallers ($P = 0.016$, $P = 0.037$, $P = 0.014$, respectively). In the multivariate analysis, postoperative range of knee flexion (OR 0.277, 95%CI 0.088–0.869, $P = 0.028$) and ankle plantar flexion (OR 0.594, 95%CI 0.374–0.945, $P = 0.028$) were determined to be significant risk factors.
Conclusion Elderly people who underwent TKA are considered more likely to fall compared with healthy elderly people. For patients with limited knee flexion and ankle plantar flexion, improvement of ROM by exercise therapy and patient education regarding the prevention of falls and fractures are considered necessary.

Keywords Total knee arthroplasty · Falls · Physical function · Range of motion

H. Matsumoto (✉)
Rehabilitation Division, Hakuai Hospital, Ryomitsuyanagi 1880, Yonago, Tottori 683-0853, Japan
e-mail: spxs7fr9@room.ocn.ne.jp

H. Matsumoto
Graduate School of medical science, Tottori University, Health Science, Yonago, Japan

M. Okuno · T. Nakamura · K. Yamamoto
Department of Orthopedic Surgery, Hakuai Hospital, Yonago, Japan

H. Hagino
School of Health Science, Faculty of Medicine, Tottori University, Yonago, Japan

H. Hagino
Rehabilitation Division, Tottori University Hospital, Yonago, Japan

Introduction

Falls in the elderly have become a social problem. In particular, fragility fractures caused by falls in the elderly reduce their daily activity [1] and may lead to conditions requiring nursing care. Prevention of falls is therefore extremely important in allowing elderly people to continue to live independently.

Among the intrinsic risk factors for falls are deformed or painful joints. Age-related deformities of the knees, feet, or spine impair skeletal alignment and balance, thereby increasing the frequency of falls. Osteoarthritis (OA) in particular causes deformities of the knee joints and pain during walking, and has been reported to increase the risk of falls and fractures [2].

The standard approach to the treatment of deformity and pain in the knee joint is total knee arthroplasty (TKA). TKA is a surgical intervention that eliminates pain and deformity and improves patients' quality of life (QOL). It results in stable outcomes [3] and was performed on approximately 680,000 patients in the USA in 2009 [4]. However, studies have demonstrated persistent deterioration in proprioception of the knee [5] and balance impairment [6] after TKA, and that among the elderly who underwent TKA, quadriceps torque was weaker and walking speed was lower compared with healthy counterparts [7, 8]. These findings suggest that physical functioning in the elderly declines after TKA. Moreover, supracondylar fractures of the femur were shown to occur in 0.3 to 2.5% of patients who underwent TKA [9–11], and delayed union or malunion have been reported after the surgical treatment of these fractures [12, 13]. Fractures around knee joints after TKA are thus a serious problem that impairs patients' activities of daily living (ADL) and QOL.

There are few surveys on falls and fractures after TKA. In 2009, Swinkels et al. [14] used a self-administered questionnaire to conduct a prospective study of the incidence of falls in 99 patients who underwent TKA, and showed that a preoperative history of falls and Geriatric Depression Scale (GDS) scores predicted postoperative occurrence of falls. In addition, Levinger et al. [15] identified impairment of lower limb proprioception and weakened knee extension strength as risk factors for falls during the early post-TKA period (within 4 months). However, there is not yet sufficient evidence on whether physical function after surgery is related to falls among the elderly after TKA.

Falls often occur due to impaired physical function and therefore, assessment of motor function [16] is essential when evaluating elderly patients with respect to their risk of falls for preventive purposes. Other risk factors for falls include changes in lower thoracic slope and knee joint angle [16], weakened lower limb muscles [17], kyphosis [18], and deformity of the foot [19]. Many elderly people who undergo TKA suffered from OA or rheumatoid arthritis (RA) before the surgery and therefore tend to exhibit the impairments mentioned above. For this reason, it is important to evaluate the physical functioning [20] of elderly patients who underwent TKA and clarify the risk factors for falls so as to minimize the postoperative incidence of falls and fractures and maintain QOL and ADL.

The present study was conducted to prospectively investigate the relationship between physical function and falls among elderly patients who underwent TKA and to determine the incidence of falls as well as their risk factors.

Patients and methods

Patients

Subjects included 108 patients (17 male, 91 female) over 60 years of age who underwent TKA at the Hakuai Hospital between January 2008 and December 2010, and who were living independently in community. Both bilateral and unilateral TKA patients were included. Their mean age was 75.8 $\pm$ 6.1 and their operations took place between 6 and 11 months before the enrollment. Patients were ineligible if they had cognitive impairment, mental disease, cerebrovascular disease, or Parkinson's disease. Seven patients were excluded as they did not meet the inclusion criteria. Another four were excluded due to the need for additional surgery and two due to hospital for fracture treatment. An additional 20 patients were excluded because they did not visit our hospital for follow-up. Thus, 75 patients fulfilled the inclusion criteria and 74 (8 male, 66 female) of them agreed to participate. The investigators provided written and verbal explanations of the study and obtained written consent from the subjects. The mean patient age was 75.7 $\pm$ 5.8 years old (range 60–88).

All surgeries were performed with a standard medial parapatellar approach by three orthopedists. The implants used were Scorpio (Stryker, USA) for 70 knees and LCS (DePuy, USA) for 4 knees. Early joint motion and weight bearing were encouraged during hospitalization and patients underwent rehabilitation for about 4 weeks according to the relevant clinical pathway. Postdischarge follow-up was planned for 1, 3, 6 months, and a year after surgery. Table 1 shows patients' preoperative characteristics and surgical information.

We assessed range of motion (ROM) of the knee (flexion, extension, range of flexion and extension) during the preoperative period and conducted the baseline assessment (physical examination, physical performance tests, and self-administered questionnaire) between 6 and 12 months after the last arthroplasty. Follow-up assessment was performed 6 months after the baseline assessment.

Fall assessment

A fall was defined as the subject unintentionally coming to rest on the floor or some lower level and not because of a major intrinsic event. In order to assess the incidence of falls we sent out monthly pre-stamped postcards. The postcard included the following questions: (a) Did you fall during the this month? (b) If you fell, did you fall once, twice, or more than three times? (c) If you fell, did you experience any fractures or injuries? Written reminders were sent if patients did not return their monthly postcard. Patients who completed the postcard incorrectly were contacted by telephone.

Table 1 Preoperative characteristics and surgical information ($n = 74$)

OA grade[a] and deformity type	
Grade 2	3
Grade 3	41
Grade 4	23
Valgus type	3
RA	4
Diagnosis OA:RA	70:4
Femoral tibial angle (degrees)	186.3 ± 6.8 (167–201)
Range of motion of the knee (degrees)	
Flexion	118.3 ± 13.0 (80–145)
Extension	−7.9 ± 6.6 (−30 to 0)
Range of knee flexion and extension	110.9 ± 17.0 (65–135)
TKA type (PS:CR)	65:9
Tibial insert (cm)	11.1 ± 1.4 (10–15)

Data are presented as mean ± SD (range)

OA osteoarthritis, *RA* rheumatoid arthritis, *PS* posterior-stabilized, *CR* cruciate-retaining

[a] Kellgren and Lawrence grade (1–4)

Physical examinations

Preoperative and postoperative (baseline period) ROM of the knee (flexion, extension) and ankle (plantar flexion, dorsal flexion) were measured using a goniometer. All measurements were made with the patients sitting on the chair. All assessments were performed on the side that had been operated on, while for patients who had undergone bilateral TKA, we evaluated the side operated on last.

Anterior–posterior drawer test and varus–valgus stress test were performed to assess the instability of the knee on the TKA-affected side. With the patient lying supine, the examiner sat on the examination table in front of the involved knee and grasped the tibia just below the joint line of the knee. We quantify instability using a 4-point ordinal scale (0: rigid, 1: normal, 2: slightly instable, 3: more than moderately instable).

Muscle strength during knee extension on the TKA-affected side was recorded with a hand-held dynamometry (MUSCULATOR GT-10, OG Giken, Okayama, Japan).Each subject was seated in a chair with the hips flexed 90° and the relevant knee flexed to 75°[21]. The hand-held dynamometry was placed in front of facies anterior cruris and the examiner met the resistance of a 5-s maximal isometric knee extension. The measured value was divided by the subject's body weight (Nm/kg).

Hallux valgus was assessed using the Manchester scale [22]. We defined the hallux valgus on a scale from 1 (no deformity) to 4 (severe deformity).

To assess limitations of ankle mobility we used a modified Niki's method [23, 24]. This method evaluates limitation of mobility in the talocalcaneal joint (inversion and eversion). We defined "limitation" as the restriction of either inversion or eversion, and as with the other examinations, assessed it on the TKA-affected side or the side last operated on (in patients who had undergone bilateral TKA).

Kyphosis was assessed by Milne's method [25]. A 60-cm flexicurve was placed on the patient's back, with one end on the seventh cervical spine and closely applied to the midline of the back. Patients were then asked to stand as erect as possible. The level of the lumbosacral joint was marked on the flexicurve with a grease pencil, and the instrument was then laid on a piece of paper and the spinal curve was copied by running a pencil along the flexicurve. The index of kyphosis was represented by the height of the thoracic curve divided by spinal length. Kyphosis was defined as present if the index was greater than 15% [26].

Physical performance test

One-leg standing test

The one-leg standing test was performed on the leg on the TKA-affected side, and consisted of measuring the length of time a patient was able to stand on one leg. We asked patients to stand on one leg for as long as possible with arms resting by their sides. Patients who underwent bilateral TKA were assessed on the last-operated side.

10-m gait test

Patients were asked to walk 14 m at normal speed, with measurements taken only during the middle 10 m (i.e., between the 2- and 12-m points). The first and last 2 m were used to eliminate periods of acceleration and deceleration. We used a modified version of Tiedemann's method [27]. The time and steps required to walk 10 m at normal speed were assessed, and we used these to calculate gait speed (m/s) and step length (m).

Self-administered questionnaire

Japanese Knee Osteoarthritis Measure (JKOM)

Pain, limitation in mobility related to daily activity, and restriction of participation in social life and health perception were assessed with the JKOM. This measure has sufficient reliability and validity for studying clinical outcomes in Japanese people with knee OA. It consists of a visual analogue scale (VAS) and 25 questions (score range 25–125, with 125 being worst). It has shown good correlation with the Western Ontario and McMaster Universities index (WOMAC) and the Medical Outcome 36-Items Short Form (SF-36) [28].

Geriatric Depression Scale (GDS)

The GDS was administered and scored according to published procedures [29, 30]. GDS scores were interpreted as indicating no depression (GDS score $\leq$5), probable depression (GDS score >5 and $\leq$10), or definite depression (GDS score >10).

Modified Fall Efficacy Scale (MFES)

The MFES is a 14-item "balance efficacy" questionnaire that measures a person's confidence in their ability to avoid a fall during each of 14 essential, non-hazardous activities of daily living (ADLs) [31]. A higher score indicates greater independence or ability to balance (score range, 14–140, with 14 being worst). Full score means the patient has no fear of falling [32]. The MFES has been found to be internally consistent and demonstrates good test–retest reliability [33, 34].

Statistical analysis

All data are expressed as mean ± SD. Patients were classified as either "non-fallers" or "fallers" (one or more falls) based on data gathered during the prospective 6-month observation.

Differences between groups were determined using Pearson's chi-square test. The non-paired *t* test and Mann–Whitney U test were conducted to compare grading scales between non-fallers and fallers.

Both multivariate and univariate analyses were performed. Variables with a significance level of $P < 0.05$ as determined by univariate analysis were selected for multivariate analysis. Multivariate logistic regression was used to provide adjusted odds ratio estimates for associations with falls.

All data were analyzed using PASW statistical software (version 18 for Windows; SPSS Inc., Japan). For all analyses, a P value <0.05 was considered significant.

This study was approved by the local ethics committees of the Faculty of Medicine, Tottori University (No1264), and Hakuai Hospital.

Results

Of the 74 patients enrolled, 70 (94.6%) completed a 6-month prospective observation. One patient was unable to follow-up. Three patients were withdrawn from the study because contralateral TKA was performed during the study period.

Incidence of falls

Twenty-three of 70 patients (32.9%) fell during the observational period; 6 subjects fell twice each, while 4 subjects fell 3 times each. One patient sustained a dislocated shoulder and two patients had bruises and slight injuries due to falling. There were no fall-related fractures during the 6-month observational period.

Patient characteristics

Characteristics of non-fallers and fallers are presented in Table 2. There was no significant difference between the two groups except for the number of patients with eye problems, cardiac disease, and diabetes, which tended to be higher in fallers than non-fallers ($P = 0.051$, $P = 0.065$, $P = 0.058$, respectively).

Physical examinations and performance tests

Physical examination and performance test variables are presented in Table 3. Postoperative range of knee flexion (range 80–140°) was significantly lower in fallers than in non-fallers ($P = 0.016$). Six of 70 patients (8.6%) had less than 100° of knee flexion, 23 of 70 patients (32.9%) had less than 120° and more than 100° of knee flexion. 41 of 70 patients (58.6%) had more than 120° of knee flexion.

Postoperative ranges of knee flexion and extension (range 60–135°) and ankle plantar flexion (range 40–70°) were significantly lower in fallers than in non-fallers ($P = 0.037$, $P = 0.014$, respectively). Preoperative knee flexion (range 80–145°) and ankle dorsal flexion (range 5–30°) tended to be lower in fallers than non-fallers ($P = 0.055$, $P = 0.070$, respectively).

Two of 70 patients (2.9%) had more than moderate instability of the knee that had undergone TKA. 27 of 70 patients (38.6%) had hallux valgus (scale of 2–4) and 18 of 70 patients (25.7%) had limited ankle mobility. Mean index of kyphosis was 8.3 ± 3.6% (range 2–20%). There were no significant differences between the two groups in terms of preoperative range of knee extension, preoperative range of knee flexion and extension, postoperative range of knee extension, knee instability, muscle strength during knee extension, hallux valgus, degree of limitation of ankle mobility, and degree of kyphosis.

One-leg standing time (range 0–32.5 s), mean gait speed (range 0.3–1.53 s/m) and step length (0.2–0.71 m) showed no significant differences between the two groups.

Self-administered questionnaires

The results of the self-administered questionnaires (JKOM, GDS, and MFES) are presented in Table 4. 44 of 70 patients (62.9%) scored less than 50 on the JKOM (range 29–95). Based on GDS score, 21 of 70 patients (30.0%) had probable depression (GDS score >5 and $\leq$10) while 6

Table 2 Characteristics of non-fallers and fallers

	Total (n = 70)	Non-fallers (n = 47)	Fallers (n = 23)	P value
Age (years)	75.5 ± 6.0	76.2 ± 5.4	74.1 ± 6.9	0.156
Sex ratio (M:F)	(8:62)	(5:42)	(3:20)	0.766
Height (cm)	152.0 ± 7.5	152.5 ± 7.2	151.0 ± 8.3	0.435
Weight (kg)	57.4 ± 9.1	56.9 ± 8.9	58.5 ± 9.5	0.494
BMI (kg/m^2)	24.8 ± 3.2	24.4 ± 3.0	25.6 ± 3.3	0.142
TKA side				
Right (%)	31.4	31.9	30.4	0.969
Left (%)	22.9	23.4	21.7	
Bilateral (%)	45.7	44.7	47.8	
Diagnosis OA:RA	(66:4)	(44:3)	(22:1)	0.730
Mean time since surgery (month)	8.2 ± 2.7	8.1 ± 2.7	8.6 ± 2.7	0.444
Prior hip surgery (%)	4.3	2.1	8.7	0.986
Total no. of prescribed regular medications (number)	3.3 ± 2.6	3.3 ± 2.8	3.4 ± 2.5	0.843
Hearing problems (%)[a]	40.0	42.5	34.8	0.533
Eye problems (%)[a]	48.6	40.4	65.2	0.051
Complications				
Cardiac disease (%)	5.7	2.1	13.0	0.065
Diabetes (%)	11.4	6.3	21.7	0.058
Hypertension (%)	34.3	36.1	30.4	0.422
Ambulation				
Walking without device (%)	68.6	70.2	65.2	0.466
One cane (%)	30.0	29.8	30.4	
Walker (%)	1.4	0.0	4.3	

Data are mean ± SD (range)

[a] Self reported

of 70 patients (8.6%) had definite depression (GDS score >10). 45 of 70 patients (64.3%) did not achieve full scores on the MFES (range 22–140). There were no significant differences between the two groups in terms of JKOM, GDS, or MFES scores.

Multivariate logistic regression analysis

Postoperative range of knee flexion was divided into 6 groups of 10 degrees each (range 80–140°). Postoperative range of knee flexion and extension was similarly divided into 8 groups of 10 degrees each (range 60–135), and range of ankle plantar flexion was divided into 6 groups of 5 degrees each (range 40–70°).

In the multivariate analysis, postoperative range of knee flexion and ankle plantar flexion were determined to be significant risk factors (Table 5). Patients with a higher postoperative range of knee flexion were less likely to fall; a 10-degree increase significantly reduced the odds of falling during the observation period by 72.3%. Similarly, patients with a higher range of ankle plantar flexion were less likely to fall; a 5-degree increase significantly reduced the odds of falling by 40.6%.

Discussion

The present study examined for the first time the relationship between falls and physical function among elderly persons who had undergone TKA. Our prospective investigation demonstrated that 23 out of 70 elderly TKA patients fell at least once during the 6-month observation period. The incidence of falls was 32.9%, which was higher than one study's previously reported incidence range of 10–20%[35] among elderly in Japan, and another study's annual incidence of 29.3% among people between the ages of 75 and 79 [36], similar ages to the subjects in this study.

Swinkels et al. [14] examined whether or not the incidence of falls changed before and after TKA in patients with OA or RA. They found an incidence of 24.2% both before and after TKA. The authors speculated that TKA lowers fall incidence because the estimated incidence for community-dwelling elderly people was 33% and the number of falls was reduced after TKA. The annual incidence of falls among patients with RA was reported to be 50% [37], indicating that these patients are at risk. The incidence of falls among patients with OA is also speculated to be high. Levinger et al. [15] reported that 48% of

Table 3 Physical examinations and performance tests in fallers and non-fallers

	Total (*n* = 70)	Non-fallers (*n* = 47)	Fallers (*n* = 23)	*P* value
ROM of the knee (°)				
Preoperative				
Flexion	118.4 ± 13.0	120.3 ± 12.2	113.2 ± 14.0	0.055
Extension	−7.7 ± 6.6	−7.6 ± 7.3	−8.5 ± 4.6	0.561
Range of flexion and extension	110.5 ± 17.3	112.7 ± 16.9	104.7 ± 17.3	0.105
Postoperative				
Flexion	116.4 ± 15.3	119.5 ± 14.1	110.2 ± 16.1	0.016
Extension	−9.7 ± 4.6	−9.8 ± 4.4	−9.6 ± 5.0	0.850
Range of flexion and extension	106.7 ± 17.1	109.7 ± 15.9	100.6 ± 18.4	0.037
ROM of the ankle (°)				
Dorsal flexion	16.6 ± 5.1	17.3 ± 5.1	15.0 ± 4.8	0.070
Plantar flexion	57.9 ± 6.3	59.1 ± 6.1	55.2 ± 6.1	0.014
Instability (0−3; 3 = most unstable)[a]	0.9 ± 0.7	1.0 ± 0.8	0.8 ± 0.7	0.384
Muscles strengths of knee extension (Nm/kg)	2.1 ± 0.5	2.1 ± 0.5	2.1 ± 0.5	0.816
Hallux valgus (1−4; 4 = most severe)[b]	1.9 ± 1.0	2.0 ± 1.1	1.9 ± 0.9	0.867
Limitation of ankle mobility (%)[c]	25.7	25.5	26.1	0.960
Kyphosis (%)[d]	8.6	6.8	15.0	0.350
One-leg standing (s)	8.6 ± 7.7	8.9 ± 7.9	7.8 ± 7.6	0.578
10-m gait test				
Speed (m/s)	0.97 ± 0.2	0.98 ± 0.2	0.95 ± 0.2	0.612
Step length (m)	0.49 ± 0.1	0.50 ± 0.1	0.49 ± 0.1	0.686

Data are mean ± SD (range)

[a] Used 4-point ordinal scale (0 = rigid,1 = normal, 2 = slightly instable, 3 = more than moderately instable)

[b] Manchester scale (1 = no deformity, to 4 = severe deformity)

[c] ROM of talocalcaneal joint (inversion and eversion)

[d] Milne's method was used ("kyphosis" defined as an index greater than 15%)

Table 4 Self-administered questionnaires in non-fallers and fallers

	Total (*n* = 70)	Non-fallers (*n* = 47)	Fallers (*n* = 23)	*P* value
JKOM				
Total score (25–125; 125 = worst)	46.1 ± 15.9	45.5 ± 16.7	47.6 ± 14.5	0.601
VAS (0−10; 10 = worst)	1.9 ± 2.4	1.7 ± 2.4	2.2 ± 2.4	0.342
Pain (8−40; 40 = worst)	13.8 ± 5.3	13.8 ± 5.9	13.8 ± 4.1	0.985
Limitations of activity (10−50; 50 = worst)	18.6 ± 6.7	18.3 ± 6.9	19.6 ± 6.3	0.449
Restriction of participation (7−35; 35 = worst)	13.9 ± 5.6	13.7 ± 5.7	14.3 ± 5.6	0.679
GDS (0−15; 15 = worst)	4.2 ± 4.0	4.0 ± 4.2	4.8 ± 3.6	0.459
MFES (14−140; 14 = worst)	122.9 ± 24.4	123.3 ± 23.3	122.2 ± 27.1	0.874

Data are means ± SD (range)

JKOM Japanese Knee Osteoarthritis Measure, *VAS* Visual Analogue Scale, *GDS* Geriatric Depression Scale, *MFES* Modified Fall Efficacy Scale

patients fell during the year prior to TKA and another study showed that the annual incidence among elderly women with musculoskeletal pain in lower extremities was 39% [38]. Thus, although TKA may reduce the incidence of falls in patients with OA or RA, elderly people who underwent TKA are considered more likely to fall compared with healthy elderly people.

In the study by Swinkels et al. [14], subjects were surveyed using self-administered questionnaires that included the WOMAC and Activities-specific Balance Confidence (ABC) Scale before and after TKA. However, the results of these questionnaires did not demonstrate any risk factors for postoperative falls. Similarly, the results of the self-administered questionnaires in the present study, including

Table5 Selected risk factors for falls by multivariate analysis

	Odds ratio	95% IC	*P* value
Range of knee flexion (postoperative)[a]	0.277	0.088–0.869	0.028
Range of knee flexion and extension (postoperative)[b]	2.308	0.847–6.289	0.102
Range of ankle plantar flexion[c]	0.594	0.374–0.945	0.028

Variables for multivariate analysis were selected by univariate analysis using a significance level of $P < 0.05$

[a] Knee flexion categorized into 10-degree groups (80−140)

[b] Knee flexion and extension categorized into 10-degree groups (60−135)

[c] Ankle plantar flexion categorized into 5-degree groups (40−70)

the JKOM regarding ADLs, did not show any difference between fallers and non-fallers. The JKOM examines respondents' level of difficulty with daily activities due to pain at the time of the survey, while MFES measures the confidence of respondents in their ability to avoid a fall during ADLs. Nevertheless, considering the results of past studies which demonstrated inaccurate perceptions of postural stability borders among elderly people [39] and greater errors in estimated reach distance in the elderly who fell compared with those who did not fall [40], it is possible that our subjects who fell overestimated their ability to perform activities and selected the answers "no difficulty" or "I can do it" in self-administered questionnaires. Swinkels et al. [14] found that the preoperative GDS score was a risk factor for falls. In our study, although approximately 40% of subjects had either probable or definite depression, there was no difference between fallers and non-fallers. Therefore, no particular relationship between depression and falls was identified in this study.

In the present study, the occurrence of falls was prospectively examined after objectively evaluating the physical function of elderly individuals who underwent TKA. Our results showed significant differences in postoperative range of knee flexion, postoperative range of knee flexion and extension and range of ankle plantar flexion between fallers and non-fallers. Fallers demonstrated lower values in all three parameters. In addition, multivariate analysis showed that postoperative ranges of knee flexion and ankle plantar flexion were risk factors for falls among the elderly who underwent TKA.

Among activities of daily living, the motion in which limited knee flexion is most likely to cause falls is rising from a chair. Itokazu et al. [41] conducted biomechanical analyses of patients who underwent TKA to examine the relationship between knee flexion angle and the motion of rising from a chair, and showed that patients whose range of knee flexion was limited (100° or less) required higher angular velocity of the hip and higher swing velocity to lift the trunk forward than patients whose range of motion was larger. When individuals whose knee flexion is limited attempt to force themselves to rise from chairs by increasing the flexing action of the trunk and hip in order to compensate for limited knee flexion, they may fall forward or, if the center of gravity of their upper bodies does not sufficiently shift forward, lose their balance and fall backwards. These individuals may trip while ascending steps or experience difficulty in lowering their center of gravity while descending steps, leading to loss of balance and falls.

Limited knee flexion also frequently causes falls while walking. In normal walking, it is speculated that people repeat flexion and extension of their knees twice in a gait cycle with a maximum flexion angle of approximately 65° [42], while gait analysis after TKA [43] has revealed that the knee flexion angle of the swing phase is smaller than that of healthy elderly people. Therefore, patients who cannot sufficiently flex their knees while walking may trip over obstacles and fall. Moreover, crouching requires 130° or greater knee flexion [44]. Thus, these motions are difficult for elderly who have undergone TKA and have limited knee flexion, again potentially leading to loss of balance and falls.

Range of ankle plantar flexion is the most important ROM of joints during the push-off phase of the gait cycle and in ensuring the toe-off. Barak et al. [45] conducted a gait analysis of healthy elderly people in their seventies who fell during the past 6 months, and reported that their range of ankle plantar flexion during the push-off phase of the gait cycle was smaller than that of those who did not fall. Furthermore, another study showed that smaller range of ankle plantar flexion during the push-off phase leads to delayed heel-off, which is compensated for by movements including excessive ankle dorsal flexion of the foot and anteversion of the trunk in order to move forward [42]. Such compensation may disturb balance, pushing the body forward and causing falls. The small ranges of both knee flexion and ankle plantar flexion in the fallers in our study suggests that they may have joints with limited ROM throughout their bodies. We speculated that the decrease in ROM of the joints in the lower limbs, in particular, coupled with impaired motor skills, can cause falls.

One of the limitations of this study is its small sample size. However, as a result of the detailed physical examinations and performance tests we conducted on all subjects, sufficient objective data for various indices were obtained and significant risk factors for falls that are characteristic of elderly people who underwent TKA were obtained despite the small number of subjects. Another limitation is that the incidence of falls and physical function were not compared with those of any control group. Direct comparison of many of our examined variables could not be performed in this study, and we therefore compared our results with those of similar previous studies and characterized the incidence of falls among elderly individuals who had undergone TKA. In the future, this incidence should be compared with that of healthy elderly people or patients with OA or RA who have equivalent levels of physical function. In addition, comparison of physical function and studies on changes in the incidence of falls before and after TKA should also be performed.

In conclusion, this 6-month prospective study of elderly subjects who underwent TKA revealed a fall incidence of 32.9%, higher than that in elderly population in general. Reduced postoperative ranges of knee flexion and ankle plantar flexion were determined to be risk factors for falls among the elderly who underwent TKA. For patients with limited knee flexion, improvement of ROM by exercise therapy and patient education regarding the prevention of falls and fractures are considered necessary.

Acknowledgments The authors thank Sakura Kida, Yuki Kitsuda, Ryuji Kuwamura, Tatsuhiko Konishi, and Ayumi Tanabe, their help and support.

References

1. Theander E, Jarnlo GB, Ornstein E, Karlsson M (2004) Activities of daily living decrease similarly in hospital-treated patients with a hip fracture or a vertebral fracture: a one-year prospective study in 151 patients. Scand J Public Health 32(5):356–360. doi:10.1080/14034940410026912
2. Arden NK, Crozier S, Smith H, Anderson F, Edwards C, Raphael H, Cooper C (2006) Knee pain, knee osteoarthritis, and the risk of fracture. Arthritis Rheum 55(4):610–615. doi:10.1002/art.22088
3. Jones DL, Westby MD, Greidanus N, Johanson NA, Krebs DE, Robbins L, Rooks DS, Brander V (2005) Update on hip and knee arthroplasty: current state of evidence. Arthritis Rheum 53(5):772–780. doi:10.1002/art.21465
4. Agency for Healthcare Research and Quality HCUPnet. National statistics on all stays:2009 outcomes by patient and hospital characteristics for ICD-9-CM principal procedure code 81.54 total knee replacement. http://hcupnet.ahrq.gov/HCUPnet.jsp. Accessed 27 April 2011
5. Sawada Y, Akagi M, Hamanishi C, Aasada S, Mori S, Maruo Y, Fukuda K (2008) Perioperative changes in proprioception after total knee arthroplasty and identification of factors affecting it. Rigakuryohokagaku 23(2):279–283 in Japanese
6. Gage WH, Frank JS, Prentice SD, Stevenson P (2008) Postural responses following a rotational support surface perturbation, following knee joint replacement: frontal plane rotations. Gait Posture 27(2):286–293. doi:10.1016/j.gaitpost.2007.04.006
7. Bade MJ, Kohrt WM, Stevens-Lapsley JE (2010) Outcomes before and after total knee arthroplasty compared to healthy adults. J Orthop Sports Phys Ther 40(9):559–567. doi:10.2519/jospt.2010.3317
8. Ouellet D, Moffet H (2002) Locomotor deficits before and two months after knee arthroplasty. Arthritis Rheum 47(5):484–493. doi:10.1002/art.10652
9. Figgie MP, Goldberg VM, Figgie HE 3rd, Sobel M (1990) The results of treatment of supracondylar fracture above total knee arthroplasty. J Arthroplasty 5(3):267–276
10. Merkel KD, Johnson EW Jr (1986) Supracondylar fracture of the femur after total knee arthroplasty. J Bone Joint Surg Am 68(1):29–43
11. Ritter MA, Faris PM, Keating EM (1988) Anterior femoral notching and ipsilateral supracondylar femur fracture in total knee arthroplasty. J Arthroplasty 3(2):185–187
12. Matsumori H, Takahashi S, Onozawa T, Shiraiwa Y (2009) A six case of periprosthetic fractures in this hospital. J Hokkaido Orthop Traumatol Assoc 25:10–14 in Japanese
13. Kadowaki T, Kin M, Ishikawa T, Ishiyama S (2005) Periprosthetic fracture after THA and TKA. Seikei Saigai Geka 48(13):1523–1530 in Japanese
14. Swinkels A, Newman JH, Allain TJ (2009) A prospective observational study of falling before and after knee replacement surgery. Age Ageing 38(2):175–181. doi:10.1093/ageing/afn229
15. Levinger P, Menz HB, Wee E, Feller JA, Bartlett JR, Bergman NR (2010) Physiological risk factors for falls in people with knee osteoarthritis before and early after knee replacement surgery. Knee Surg Sports Traumatol Arthrosc. doi:10.1007/s00167-010-1325-8
16. O'Brien K, Culham E, Pickles B (1997) Balance and skeletal alignment in a group of elderly female fallers and nonfallers. J Gerontol A Biol Sci Med Sci 52(4):B221–B226
17. Oya Y, Nakamura M, Tabata E, Morizono R, Mori S, Kimuro Y, Horikawa E (2008) Fall risk assessment and knee extensor muscle activity in elderly people. Nippon Ronen Igakkai Zasshi 45(3):308–314. doi:JST.JSTAGE/geriatrics/45.308 in Japanese
18. Kado DM, Huang MH, Nguyen CB, Barrett-Connor E, Greendale GA (2007) Hyperkyphotic posture and risk of injurious falls in older persons: the Rancho Bernardo Study. J Gerontol A Biol Sci Med Sci 62(6):652–657. doi:62/6/652
19. Menz HB, Morris ME, Lord SR (2006) Foot and ankle risk factors for falls in older people: a prospective study. J Gerontol A Biol Sci Med Sci 61(8):866–870. doi:61/8/866
20. Nevitt MC, Cummings SR, Kidd S, Black D (1989) Risk factors for recurrent nonsyncopal falls. A prospective study. JAMA 261(18):2663–2668
21. Roy MA, Doherty TJ (2004) Reliability of hand-held dynamometry in assessment of knee extensor strength after hip fracture. Am J Phys Med Rehabil 83(11):813–818. doi:00002060-200411000-00001
22. Garrow AP, Papageorgiou A, Silman AJ, Thomas E, Jayson MI, Macfarlane GJ (2001) The grading of hallux valgus. The Manchester Scale. J Am Pediatr Med Assoc 91(2):74–78
23. Niki H, Aoki H, Inokuchi S, Ozeki S, Kinoshita M, Kura H, Tanaka Y, Noguchi M, Nomura S, Hatori M, Tatsunami S (2005) Development and reliability of a standard rating system for outcome measurement of foot and ankle disorders II: interclinician and intraclinician reliability and validity of the newly established standard rating scales and Japanese Orthopaedic Association rating scale. J Orthop Sci 10(5):466–474. doi:10.1007/s00776-005-0937-1
24. Niki H, Aoki H, Inokuchi S, Ozeki S, Kinoshita M, Kura H, Tanaka Y, Noguchi M, Nomura S, Hatori M, Tatsunami S (2005) Development and reliability of a standard rating system for outcome measurement of foot and ankle disorders I: development of standard rating system. J Orthop Sci 10(5):457–465. doi:10.1007/s00776-005-0936-2
25. Milne JS, Lauder IJ (1974) Age effects in kyphosis and lordosis in adults. Ann Hum Biol 1(3):327–337
26. Teragaki Y, Araya K, Sueki K, Iriuchijima K, Yamauchi J, Usuda S (2004) Reliability validity of the index kyphosis on sitting Rigakuryouhou Kagaku 19(2):137–140 in Japanese
27. Tiedemann A, Shimada H, Sherrington C, Murray S, Lord S (2008) The comparative ability of eight functional mobility tests for predicting falls in community-dwelling older people. Age Ageing 37(4):430–435. doi:10.1093/ageing/afn100

28. Akai M, Doi T, Fujino K, Iwaya T, Kurosawa H, Nasu T (2005) An outcome measure for Japanese people with knee osteoarthritis. J Rheumatol 32(8):1524–1532. doi:0315162X-32-1524
29. D'Ath P, Katona P, Mullan E, Evans S, Katona C (1994) Screening, detection and management of depression in elderly primary care attenders. I: the acceptability and performance of the 15 item Geriatric Depression Scale (GDS15) and the development of short versions. Fam Pract 11(3):260–266
30. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, Leirer VO (1982) Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 17(1):37–49
31. Hill KD, Schwarz JA, Kalogeropoulos AJ, Gibson SJ (1996) Fear of falling revisited. Arch Phys Med Rehabil 77(10):1025–1029. doi:S0003-9993(96)90063-5
32. Murakami Y, Shiba Y, Watanabe S, Obuchi S, Inaba Y (2008) Factors of Fear of Falling among the Community Dwelling Elderly. Rigakuryoho Kagaku 23(3):413–418 in Japanese
33. Cumming RG, Salkeld G, Thomas M, Szonyi G (2000) Prospective study of the impact of fear of falling on activities of daily living, SF-36 scores, and nursing home admission. J Gerontol A Biol Sci Med Sci 55(5):M299–M305
34. Salkeld G, Cameron ID, Cumming RG, Easter S, Seymour J, Kurrle SE, Quine S (2000) Quality of life related to fear of falling and hip fracture in older women: a time trade off study. BMJ 320(7231):341–346
35. Hasegawa M, Yasumura S (2008) Fall incidence of a Japanese elderly and fracture and injury with falling [fall and osteoporosis]. J Osteoporos Med 7(3):180–185 in Japanese
36. Yasumura S, Haga H, Nagai H, Suzuki T, Amano H, Shibata H (1994) Rate of falls and the correlates among elderly people living in an urban community in Japan. Age Ageing 23(4):323–327
37. Hayashibara M, Hagino H, Katagiri H, Okano T, Okada J, Teshima R (2010) Incidence and risk factors of falling in ambulatory patients with rheumatoid arthritis: a prospective 1-year study. Osteoporos Int 21(11):1825–1833. doi:10.1007/s00198-009-1150-4
38. Leveille SG, Bean J, Bandeen-Roche K, Jones R, Hochberg M, Guralnik JM (2002) Musculoskeletal pain and risk for falls in older disabled women living in the community. J Am Geriatr Soc 50(4):671–678. doi:50161
39. Robinovitch SN, Cronin T (1999) Perception of postural limits in elderly nursing home and day care participants. J Gerontol A Biol Sci Med Sci 54(3):B124–B130 discussion B131
40. Okada Y, Takatori K, Nagano K, Tokuhisa K, Ikuno K, Tsuruta K, Shomoto K (2008) Relationship between error in estimated reach distance and falls in community-dwelling elderly people. Rigakuryohogaku 35(6):279–284 in Japanese
41. Itokazu M, Uemura S, Aoki T, Takatsu T (1998) Analysis of rising from a chair after total knee arthroplasty. Bull Hosp Jt Dis 57(2):88–92
42. Götz-Neuman K (2005) Gait analysis in a physical therapy (trans: Tsukishiro K, Yamamoto S, Ehara Y, Bonkohara S). Igaku syoin, tokyo, pp 120 in Japanese
43. Benedetti MG, Catani F, Bilotta TW, Marcacci M, Mariani E, Giannini S (2003) Muscle activation pattern and gait biomechanics after total knee replacement. Clin Biomech 18(9):871–876. doi:10.1016/S0268-0033(03)00146-3
44. Yoshimoto Y (1988) Hip and knee motion measurements for selected activities of daily living. Rigakuryohogaku 15(3):247–250 in Japanese
45. Barak Y, Wagenaar RC, Holt KG (2006) Gait characteristics of elderly people with a history of falls: a dynamic approach. Phys Ther 86(11):1501–1510. doi:10.2522/ptj.20050387

Calcif Tissue Int (2012) 90:14–21
DOI 10.1007/s00223-011-9545-6

ORIGINAL RESEARCH

The Risk of a Second Hip Fracture in Patients after Their First Hip Fracture

Hiroshi Hagino · Takeshi Sawaguchi · Naoto Endo · Yasuyo Ito · Tetsuo Nakano · Yoshinobu Watanabe

Received: 4 May 2011 / Accepted: 14 October 2011 / Published online: 12 November 2011

Abstract We investigated the incidence of additional fractures and the rate of prescription of osteoporotic pharmacotherapy after an initial hip fracture. We surveyed female patients aged 65 and over who sustained their first hip fracture between January 1, 2006, and December 31, 2007, treated at 25 hospitals in five geographic areas in Japan. Data for 1 year after the first hip fracture were collected from medical records, and questionnaires were mailed to all patients. In total, 2,663 patients were enrolled, and 335 patients were excluded based on exclusion criteria. The analysis was performed on 2,328 patients. During the 1-year follow-up period 160 fractures occurred in 153 patients and 77 subsequent hip fractures occurred in 77 patients. The incidence of all additional fractures among patients who sustained their first hip fracture was 70 (per 1,000 person-year) and that for second hip fracture was 34. In comparison to the general population, women ≥65 years of age who sustained an initial hip fracture were four times as likely to sustain an additional hip fracture. Antiosteoporosis pharmacotherapy was prescribed for 436 patients (18.7%), while 1,240 patients (53.3%) did not receive any treatment during the 1-year period. Patients who have sustained one hip fracture have a higher risk of a second hip fracture compared to the general population, and most of these women receive no pharmaceutical treatment for osteoporosis.

Keywords Hip fracture · Second hip fracture · Treatment of osteoporosis

The authors have stated that they have no conflict of interest.

H. Hagino (✉) · Y. Ito
School of Health Science, Tottori University,
86 Nishi-Cho, Yonago, Tottori 683-8503, Japan
e-mail: hagino@med.tottori-u.ac.jp

T. Sawaguchi
Department of Orthopedic Surgery, Toyama City Hospital,
Toyama City, Japan

N. Endo
Department of Orthopedic Surgery, Niigata University,
Niigata, Japan

T. Nakano
Department of Orthopedic Surgery, Tamana Central Hospital,
Tamana, Japan

Y. Watanabe
Department of Orthopedic Surgery, Teikyo University,
Tokyo, Japan

Introduction

Hip fractures are a common cause of morbidity and mortality in the elderly and are associated with considerable health expenditures in most industrialized countries. Several studies have suggested a worldwide geographic variation in the incidence of hip fractures, with the highest rates reported for northern European countries and the United States and the lowest rates reported in Africa and some Asian populations [1]. However, epidemiological information regarding the risk of sustaining subsequent hip fractures is limited compared to that of sustaining the first hip fracture as fewer studies have addressed this issue. Overall 1- and 5-year mortality rates after the first hip fracture are 15.9 and 45.4%, while rates after a second hip fracture are 24.1 and 66.5%, respectively [2].

The incidence of hip fractures had been increasing in Europe and the United States until about 10 years ago, when this rate plateaued or decreased [3–5]. Contrast this to Japan and other Asian countries, where the incidence of hip fractures has increased steadily from 1986 to 2006 [1, 6]. However, only a few epidemiological studies have been conducted to determine the incidence of sustaining a second hip fracture within the Asian population.

Because of the high risk of sustaining a second hip fracture in patients after their initial hip fracture, pharmacologic intervention is essential. However, reports suggest that pharmacotherapy is not necessarily prescribed adequately in these populations. Cadarette et al. [7] reported an increased proportion of hip-fracture patients treated with osteoporosis drugs; however, the overall proportion remains low, with fewer than one-third of these patients receiving pharmacotherapy. In another report, 9.2% of women and 4.1% of men began therapy after a hip fracture in 2004 [8]. Currently, no data are available concerning the rates of prescription for osteoporosis treatment after a first hip fracture based on an investigation of Asian patients.

The aim of this study was to elucidate the incidence of additional fractures in patients within 1 year after they sustained their first hip fracture. An additional aim was to investigate the frequency of prescription of antiosteoporotic pharmaceuticals in these patients.

Patients and Methods

Study Design and Overview

The present study was designed as a historical, register-based, uncontrolled, follow-up study. This study was approved by the local ethics committee at the Faculty of Medicine, Tottori University (no. 1096), and by each participating hospital. Data on demographics, treatments, and health outcomes during each patient's hospital stay were collected from medical records. Data on patients who were followed after the treatment for 1 year following the fracture were also collected from medical records at each hospital. A voluntary and confidential questionnaire was mailed to patients and/or their family members regarding the patients' health outcomes in the 1-year period after the initial hip fracture. The letter included an informed consent explaining the study purpose, with instructions on how to complete and return the survey.

Five geographic areas in Japan were selected for this study: Niigata, Toyama, Tokyo, Tottori, and Kumamoto. Within each area, four, five, two, nine, and five hospitals (total of 25) participated in the study, respectively. A tally of all female patients who sustained a hip fracture, 65 years or older, injured during the 2-year period from January 1, 2006, to December 31, 2007, and treated in these hospitals was conducted. All hospital data, registered anonymously by number, were sent to Tottori University and compiled.

Data Collection

Medical Record Review

Hip fractures were identified by hospital records with radiographs. Inclusion criteria were female patients 65 years or older who had experienced a hip fracture due to minor trauma for the first time and had been admitted to one of the 25 study hospitals during the study period (January 2006 to December 2007). Patients with pathological fractures or high-impact trauma, such as traffic accidents, were excluded from the enrollment. During the medical records review, all patients were selected according to the above inclusion and exclusion criteria by orthopedists.

Data collected from medical records were patient's age at the time of the first hip fracture, fracture site (right or left), fracture type (neck or trochanter), date of birth, body height, body weight, residence before the fracture, bone mineral density (BMD, percent of young adult mean, YAM), and if osteoporosis medications were taken. The patients' ambulatory ability before the first hip fracture was also recorded, divided into the following six categories: ability to walk without difficulty, ability to walk outside with a walking aid, ability to walk only inside with an aid, inability to walk without support, complete inability to walk, and unknown.

Comorbidities were defined as conditions that patients had before hip-fracture surgery. Main comorbidities included hypertension, heart failure, arrhythmia, diabetes mellitus, respiratory disease, a history of stroke, Parkinson disease, osteoarthritis, rheumatoid arthritis, and dementia. Dementia was defined as patients having fewer than 21 points on the revised version of Hasegawa's Dementia Scale. The presence of cognitive dysfunction was ascertained by a medical records review.

Treatment data included admission and discharge dates, type of surgery (osteosynthesis or arthroplasty), implants used for surgery, rehabilitation protocol, and if osteoporosis treatment was prescribed during the hospital stay. Medical record reviews at the treating hospitals confirmed whether follow-up data were available in the hospital, if the patient was currently alive or dead, the occurrence of new fractures within 1 year after the first hip fracture and treatment for those fractures, and if osteoporosis was treated. Fractures were verified by radiographs.

Questionnaire

A letter was sent from coinvestigators at each hospital to the patients who met the study inclusion criteria. The informed consent and surveys were sent to the billing addresses used at their last hospitalization. Patients and/or their family members were asked to sign the consent form and complete and return the questionnaire in a self-addressed, stamped envelope if they agreed to participate in the study. The questionnaire inquired if osteoporosis treatment had been prescribed and the occurrence of any new fractures. If the latter was present, the details about the new fracture site, the cause of the fracture, and treatment details were also asked.

Statistical Analysis

Age-specific incidence was calculated based on the number of fractures and observational year. Age- and gender-specific incidences (per 1,000 person-years), reported previously for the general population in Japan, were adopted to compare the risk of hip fracture among patients with a prior hip fracture. Age- and gender-specific incidences (per 1,000 person-years) of hip fracture for the general population in women are 1.9, 8.6, 24.5, and 25.4 in the age groups of 65–74, 75–84, 85–94, and ≥95 years, respectively, and the risk for all women 65 years old or older is 8.3 (data were analyzed based on the study by Hagino et al. [1]).

Continuous variables, including age, body height, body weight, and body mass index (BMI) before surgery, were compared using *t*-tests. Pearson's chi-squared tests or Fisher's exact tests were used to compare the categories/ratios of variables.

A multivariate analysis was performed in addition to a univariate analysis. Variables determined during the hospitalization with a significance level of $P < 0.05$, as determined by univariate analysis, were selected for multivariate analysis. Multivariate logistic regression analysis was used to provide adjusted odds ratio (OR) estimates for associations with subsequent fractures.

Statistical analysis was performed using SPSS software (SPSS II for Windows, version 11.0.1J; SPSS, Inc., Tokyo, Japan).

Results

Enrolled Patients and Response Rates for Questionnaires

Two hundred thirty-five patients from the Niigata area, 605 patients from the Toyama area, 216 patients from the Tokyo area, 892 patients from the Tottori area, and 715 patients from the Kumamoto area (in total 2,663 patients) were enrolled. Three hundred thirty-five patients were excluded according to the exclusion criteria: 213 had a fracture before or after the study period, 96 were under 65 years old, and 26 were lacking detailed data regarding the cause of the fracture including a suspicion of pathological fracture. The analysis was then conducted for 2,328 patients (Fig. 1). Fractures occurred on the right side in 1,200 patients and on the left side in 1,128 patients; 1,025 were neck fractures and 1,303 were trochanteric fractures. One thousand eighty-five (46.6%) of 2,328 patients returned their questionnaires. Sixty-one patients died during the follow-up period. Among the remaining patients, 1,076 were followed based on both medical records and patient questionnaires and 887 patients who did not return the patient questionnaires were followed by a medical record review. As a result, 304 were lost to follow-up.

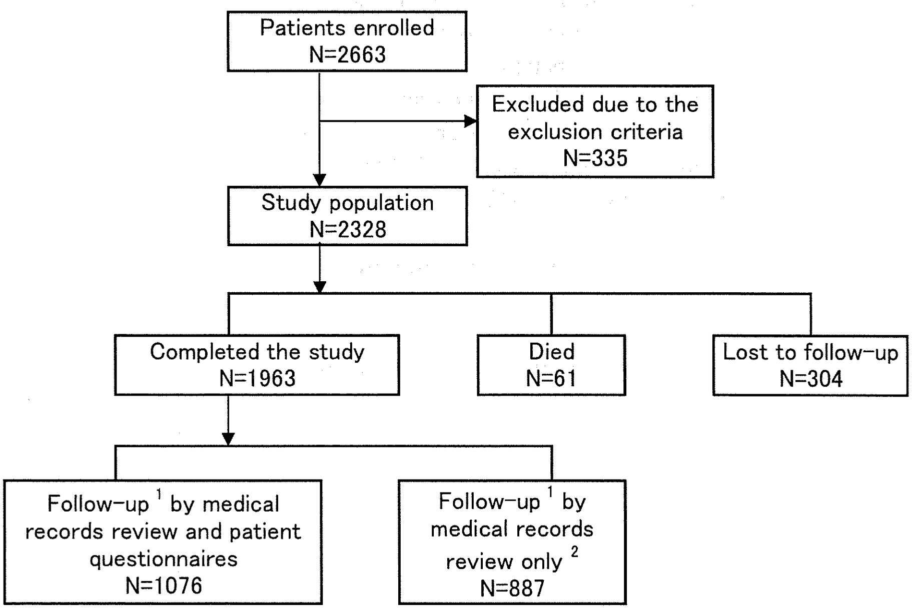

Fig. 1 Patient disposition. *1*, Duration of follow-up 1 year; *2*, patient questionnaires were not returned

Demographics of the Patients

The average age at the time of the initial fracture was 83.6 years (range 65–104). The place of residence, investigated by medical chart records, was the patient's own home in 1,550 patients, a nursing home in 482 patients, a hospital in 190 patients, other in 9 patients, and unknown in 97 patients.

Ambulatory abilities before the first hip fracture according to the medical charts were "Able to walk without difficulty" in 881 patients (37.8%), "Able to walk outside with a walking aid" in 670 patients (28.8%), "Able to walk only inside with aid" in 132 patients (5.7%), "Unable to walk without support" in 329 patients (14.1%), "Unable to walk" in 171 patients (7.3%), and unknown in 145 patients (6.3%).

Regarding comorbidities, hypertension was diagnosed in 1,030 patients, heart failure in 297 patients, arrhythmias in 123 patients, diabetes mellitus in 317 patients, respiratory disease in 148 patients, a history of stroke in 320 patients, Parkinson disease in 87 patients, osteoarthritis in 236 patients, and rheumatoid arthritis in 60 patients. Dementia was diagnosed in 500 patients (21.5%), was not diagnosed in 666 patients (28.6%), and was not examined in 1,139 patients (48.9%). Among those not examined, cognitive dysfunction was present in 472 patients (20.3%).

Osteoporosis was diagnosed before the first hip fracture in 274 patients (11.8%), was not diagnosed in 1,587 patients (68.2%), and status was unknown in 467 patients (20.1%). Antiosteoporosis medication was administered in 185 patients (7.9%). Importantly, no information regarding medications was available in 2,038 patients (87.5%).

BMD was measured in 365 patients (15.7%) before the first hip fracture or during the hospitalization for treatment of the first hip fracture. BMD measurements were performed using dual-energy X-ray absorptiometry of the lumbar spine and hip in 241 patients (66.0%) and of the forearm in 117 patients (32.1%). Radiographic absorptiometry of the metacarpal bone was measured in one patient (0.27%). The mean BMD value (YAM%) was 60.1 ± 15.2%, with a range of 27–127%.

Treatment during Hospitalization for First Hip Fracture

Among 2,328 patients, 2,192 (94.2%) were treated surgically. Among patients with femoral neck fractures treated surgically ($n = 951$), 630 (66.2%) were treated with arthroplasty, including hemiarthroplasty and total arthroplasty. Among patients with trochanteric fractures treated surgically ($n = 1,241$), 1,232 (99.3%) were treated with osteosynthesis (cannulated screw or pin 10, sliding hip screw 484, short femoral nail 726, other 12) and 8 (0.6%) were treated with arthroplasty (unknown 1). Postoperative rehabilitation was prescribed for 2,196 patients (94.3%), was not performed in 109 patients (4.7%), and status was unknown in 23 patients (1.0%). Antiosteoporotic pharmacotherapy was administered to 456 patients (19.6%) during their hospitalization. The mean duration of hospitalization was 48.6 ± 53.4 days for neck fractures and 48.0 ± 41.1 days for trochanteric fractures.

Treatment after Discharge from First Hospital Stay

Data regarding treatment after discharge from the first hospital stay were collected from the patient questionnaires and follow-up data, if available, and confirmed by hospital records. During this 1-year period, antiosteoporosis pharmacotherapy was given in 436 patients (18.7%) and 1,240 patients (53.3%) received no treatment. In 24.8% of patients the treatment status was unknown. Only 166 patients (36.4 %) among the 456 receiving antiosteoporosis pharmacotherapy during hospitalization continued treatment during the 1-year follow-up.

Fractures after the First Hip Fracture

During the 1-year follow-up period, 160 fractures occurred in 153 patients (Table 1). Among them, 129 were verified by radiography and confirmed by orthopedic doctors and 24 were self-reported in questionnaires. The average age in this subset of patients at the time of the first fracture was 84.0 years (range 68–98). Sixty-six (43.1%) fractures occurred within 6 months after the first hip fracture and 88 (57.5%) within 8 months (Fig. 2). Among these, 77 hip fractures occurred in 77 patients, 25 clinical vertebral fractures occurred in 25 patients, and 9 forearm fractures occurred in 9 patients within 1 year after the first hip fracture. Among the 77 hip fractures, 67 were verified by radiography and confirmed by orthopedic doctors and 10 were self-reported in questionnaires. Forty (51.9%) hip fractures occurred within 6 months after the first hip fracture and 48 (62.3%) within 8 months (Fig. 2). Subsequent hip fractures occurred on the opposite side in 58 patients (75.3%) and 63.3% were similar in fracture type to the first fracture.

The incidence of all fractures among patients with a first hip fracture was 70 (per 1,000 person-years), and that for hip fractures was 34. Age-specific incidences for subsequent fractures were highest in the ≥95 year age group; however, the differences between the age groups were small (Table 2). In comparison to the general population, women ≥65 years of age who sustained an initial hip fracture were four times as likely to sustain an additional hip fracture. The rate ratio among those with one hip fracture was as high as 18.6 times in the age group 65–74 years compared to that in the general population (Table 2).

Table 1 Characteristics of patients with subsequent fractures

	All fracture		*P*	Hip fracture		*P*
	(+) $n = 153$	(–) $n = 2,175$		(+) $n = 77$	(–) $n = 2,251$	
Age (years)	84.2 ± 7.0	83.6 ± 7.1	n.s.	84.4 ± 7.3	83.6 ± 7.1	n.s.
Body height (cm)	145.3 ± 7.2	146.7 ± 7.0	n.s.	144.8 ± 7.6	146.6 ± 7.0	n.s.
Body weight (kg)	42.8 ± 8.3	44.3 ± 8.6	0.038	42.2 ± 7.9	44.3 ± 8.6	0.046
Body mass index (kg/m^2)	20.1 ± 3.1	20.6 ± 3.4	n.s.	20.0 ± 3.0	20.6 ± 3.4	n.s.
Comorbid disease						
+	135	1,964		66	2,033	
–	17	159	n.s.	10	166	n.s.
Cognitive dysfunction						
+	70	902		35	937	
–	74	1,117	n.s.	39	1,152	n.s.
Ambulatory abilities before the first hip fracture						
No aid	24	476		12	488	
Dependent	123	1,560	0.049	61	1,622	n.s.
Fracture site (1st hip fracture)						
Right	80	1,120		41	1,159	
Left	73	1,055	n.s.	36	1,092	n.s.
Fracture type						
Neck	69	956		40	985	
Trochanteric	84	1,219	n.s.	37	1,266	n.s.
Surgical procedure						
Osteosynthesis	105	1,446		53	1,498	
Arthroplasty	43	595	n.s.	22	616	n.s.
Pharmacotherapy						
During hospitalization						
+	38	418		13	443	
–	107	1,717	n.s.	58	1,766	n.s.
Posthospitalization						
+	48	388		19	417	
–	103	1,715	<0.001	57	1,761	n.s.

n.s. Nonsignificant

Among patients with subsequent fractures, antiosteoporosis drugs were administered in 24 (15.7%, unknown 123 [80.4%]) before the first hip fracture, 38 (24.8%, unknown 8 [5.2%]) during the hospitalization, and 48 (31.4%, unknown 29 [19.0%]) during the 1-year follow-up period. Among 77 patients with a second hip fracture, antiosteoporosis drugs were administered in 11 (14.3%, unknown 64 [83.1%]) before the first hip fracture, 13 (16.9 %, unknown 6 [7.8%]) during the hospitalization, and 19 (24.7%, unknown 18 [23.4%]) during the 1-year follow-up period.

There were significant differences in body weight between patients with and without subsequent fractures (Table 1). Ambulatory abilities were divided into two categories of "no aid" and "dependent": "no aid" was "to

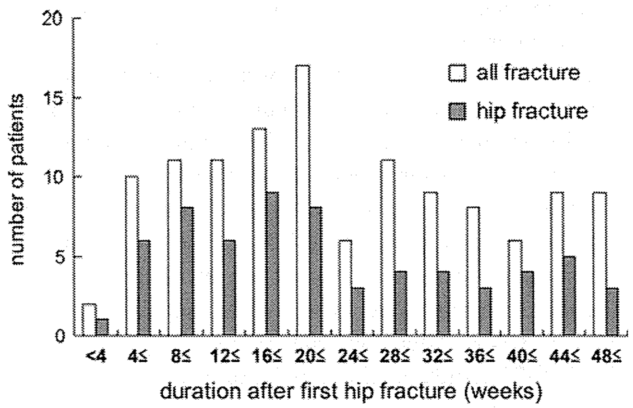

Fig. 2 Number of patients with subsequent fractures in selected time intervals after the first hip fracture