Surgical treatment reduces in-hospital mortality after hip fracture: retrospective analysis using the Japanese Diagnosis Procedure Combination database

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2011-000416
Article Type:	Research
Date Submitted by the Author:	16-Jan-2012
Complete List of Authors:	Shoda, Naoko; The University of Tokyo, Department of Orthpaedic Surgery Yasunaga, Hideo; Graduate School of Medicine University of Tokyo, Department of Health Management and Policy Horiguchi, Hiromasa; Graduate School of Medicine University of Tokyo, Department of Health Management and Policy Matsuda, Shinya; University of Occupational and Environmental Health, Department of Preventive Medicine and Community Health Kadono, Yuho; The University of Tokyo, Department of Orthpaedic Surgery Tanaka, Sakae; The University of Tokyo, Department of Orthopaedic Surgery
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Dentistry and oral medicine
Keywords:	ALTITUDE MEDICINE, Anaesthesia in cardiology < ANAESTHETICS, Anaesthesia in oncology < ANAESTHETICS

SCHOLARONE™
Manuscripts

Shoda et al.

Surgical treatment reduces in-hospital mortality after hip fracture: retrospective analysis using the Japanese Diagnosis Procedure Combination database

Naoko Shoda, researcher[1] Hideo Yasunaga, associate professor[2] Hiromasa Horiguchi, lecturer[2] Yuho Kadono, assistant professor[1] Shinya Matsuda, professor[3] Sakae Tanaka, associate professor[1]

[1] Department of Orthopaedic Surgery, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

[2] Department of Health Management and Policy, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

[3] Department of Preventive Medicine and Community Health, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, Japan

Correspondence to: S Tanaka, Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Tel: +81-3-3815-5415 ext 33376; Fax: +81-3-3818-4082

TANAKAS-ORT@h.u-tokyo.ac.jp

Abstract

Objective: To identify risk factors for in-hospital mortality in patients with hip fractures using the Japanese Diagnosis Procedure Combination (DPC) nationwide administrative claims database.

Design: Retrospective observational study.

Setting: Hospitals adopting the DPC system during 2007–2009.

Participants: We extracted a total of 80,800 eligible patients aged ≥60 years old with a single hip fracture (ICD-10 codes: S72.0 and S72.1). The DPC database includes patients treated between July and December each year.

Main outcome measures: In-hospital mortality after hip fracture.

Results: The overall in-hospital mortality rate after hip fractures was 3.3%. Multivariate analysis indicated that in-hospital mortality was significantly associated with male gender (odds ratio [OR] 2.12; 95% confidence interval [CI] 1.94 to 2.31), advancing age and number of comorbidities. Significantly higher mortality was observed in those treated conservatively (OR 4.25; 95% CI 3.92 to 4.61). Surgical delays of 5 days or more were significantly associated with higher rates of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50).

Conclusions: In patients with hip fractures, surgical treatment was associated with

lower rates of in-hospital mortality.

What is already known on this topic

Hip fracture is a serious problem in an aging society and associated with high mortality. Previous studies have shown several factors that may be associated with the increased mortality after hip fracture.

What this study adds

In-hospital mortality was significantly associated with male gender, advancing age and number of comorbidities. Significantly higher mortality was observed in those treated conservatively. Surgical delays of 5 days or more were significantly associated with higher rates of in-hospital mortality.

BMJ Open

Shoda et al.

INTRODUCTION

Hip fracture is a serious injury related to bone fragility caused by osteoporosis, and it has emerged as a public health burden in an aging society such as that of Japan.[1-5] It is estimated that the number of hip fractures worldwide will rise from 1.7 million in 1990 to 6.3 million in 2050.[6] Recent studies have reported an increased incidence of hip fractures in Japan[3 5] although the incidence is decreasing in some Western countries.[7 8] Hip fracture leads to impaired function, loss of independence and increased mortality of the patients. It has been reported that the increased mortality after hip fracture is associated with many factors such as increasing age, comorbidity and pre-fracture functional disability of the patients.[9-12] Hip fractures are usually treated by orthopaedic surgical procedures such as hemiarthroplasty or internal fixation, and several studies have shown that early surgery is associated with lower rates of mortality,[13-16] while other studies exhibited no benefit of early surgery in reducing mortality or improving functional recovery.[17 18] Conservative treatment is often chosen for patients with severe comorbidities. However, it is not clear whether conservative treatment is actually superior in reducing mortality compared with surgical treatment in high risk patients. In this study, we investigated the in-hospital mortality rate of hip fracture patients using data from the Japanese Diagnosis Procedure Combination (DPC) nationwide

administrative claims database, and compared mortality following hip fractures between groups treated surgically or conservatively.

METHODS

DPC database

The DPC database is a diagnosis-dominant case-mix system administered by the Ministry of Health, Labour and Welfare of Japan, and linked with a lump-sum payment system.[19] All 82 university teaching hospitals in Japan are obliged to adopt the DPC system, while adoption by community hospitals is voluntary. A comprehensive survey of the DPC hospitals is conducted between July 1 and December 31 each year by the DPC Research Group, funded by the Japanese government. Detailed patient data, as well as administrative claims data, are collected for all the inpatients discharged from the participating hospitals between July 1 and December 31 each year. The number of participating hospitals increased to 818 with 2.57 million patients in 2009, which represented approximately 40% of all the in-patient admissions to acute care hospitals in Japan. Hospitals send all the anonymised data for each month to the DPC Research Group for compilation in the database server in the Department of Health Management and Policy, The University of Tokyo.

The database includes the following data: hospital location; patients' age and sex; diagnoses, comorbidities at admission, and complications after admission, recorded in accordance with the International Classification of Diseases, 10th Revision (ICD-10) codes and text data in the Japanese language; procedures coded with the Japanese original K codes; comorbidities at admission; complications after admission coded with the ICD-10 codes; in-hospital mortality; length of stay; and hospital charges.

This study was based on a secondary analysis of the administrative claims data. The requirement for informed consent was waived because of the anonymous nature of the data. Study approval was obtained from the Institutional Review Board at the University of Occupational and Environmental Health.

Data compilation

We retrospectively collected data of patients coded S72.0 (fracture of the neck of the femur) and S72.1 (pertrochanteric fracture) between 2007 and 2009 from the DPC database. Exclusion criteria were as follows: age < 60 years; patients with open fractures or multiple fractures; and incomplete data. We extracted data on age, sex, method of treatment (surgical or conservative), number of acute beds and in-hospital mortality. From the comorbidities at admission, we collected data on seven factors:

BMJ Open

malignancy, diabetes mellitus, cardiovascular disease, cerebrovascular disease, lung disease, renal failure, hepatic failure.

Statistical analysis

The Chi-squared test was used for univariate comparisons of the surgical and conservative treatment groups. Multivariate logistic regression analysis was performed to analyse the confounding effects of various factors on in-hospital mortality. Odds ratios (OR) and 95% confidence intervals (CI) were determined. The OR of in-hospital mortality in conservatively treated patients was analysed in subgroups of patients stratified according to number of comorbidities or age. In addition, the effect of surgical delays in surgically treated patients was analysed. A p-value <0.05 was considered significant. All the statistical analyses were performed using SPSS Statistics ver. 19.0 (IBM SPSS Inc.; Chicago, IL, US).

RESULTS

Patient background

Data of 94,139 patients with hip fractures were extracted based on ICD-10 codes. We excluded 8,956 patients with open fractures or multiple fractures, 496 patients with

BMJ Open

incomplete data and 3887 patients aged <60 years. Finally, 80,800 eligible patients were included in the analysis.

Table1 presents the patient characteristics. Overall, 79.1% were females. The mean (standard deviation) age was 82.8 (8.3) years. The patients were categorised into the following four age groups: 60–69 (n=5,523), 70–79 (n=18,618), 80–89 (n=37,362), and ≥90 (n=19,297). Approximately 83% (n=66,893) of patients underwent surgical treatment, while 17% (n=13,907) were treated conservatively. Hospital size was categorised into four groups according to the number of acute beds: ≤199 (13.9%), 200–399 (40.4%), 400–599 (28.6%), and ≥600 (15.0%). The proportion of patients with comorbidities at admission was as follows: malignancy (5.7%), diabetes mellitus (13.4%), cardiovascular disease (7.6%), cerebrovascular disease (8.0%), lung disease (6.4%), renal failure (4.4%) and hepatic failure (0.8%).

Univariate analysis of in-hospital mortality

Table 2 shows the factors associated with in-hospital mortality according to the univariate analysis. The overall in-hospital mortality rate was 3.3% (n=2,681) with the average length of stay of 38 days. Male gender, advancing age, conservative treatment and smaller hospital size were significantly associated with higher mortality. As for

http://mc.manuscriptcentral.com/bmj

BMJ

comorbidities, patients with malignancy, lung disease, renal failure and hepatic failure at admission exhibited higher mortality rates. In contrast, diabetes mellitus, cardiovascular disease or cerebrovascular disease did not significantly affect the mortality of the patients. The number of comorbidities at admission was positively related to the mortality rate.

Multivariate analysis of in-hospital mortality

Table 3 shows the adjusted OR and 95% CI for in-hospital mortality as determined by multivariate analysis. Consistent with the univariate analysis, the in-hospital mortality was significantly associated with male gender (OR 2.12 compared with female gender; $p<0.001$), advancing age (OR 1.57 in the 70–79 years age group, 2.28 in the 80–89 years group and 3.51 in the ≥90 years group compared with the 60–69 years age group, $p<0.001$), conservative treatment (OR 4.25 compared with the surgical treatment group, $p<0.001$), and number of comorbidities (OR 2.50 in patients with one comorbidity and 3.79 in those with two or more comorbidities as compared with no comorbidity, $p<0.001$). There was no association with hospital size. We then stratified the patients into the following three groups according to the number of comorbidities: no comorbidity (n=51,544), one comorbidity (n=22,170), and two or more comorbidities

http://mc.manuscriptcentral.com/bmj

(n=7,086). Regardless of the number of comorbidities, conservative treatment was significantly associated with higher mortality compared with surgical treatment (fig 1A). In addition, patients with conservative treatment exhibited higher mortality even the patients were stratified according to age (fig 1B).

We finally analysed the effect of surgical delays on in-hospital mortality in patients treated surgically. Delays to surgery of 5 days or longer after admission were significantly associated with a higher rate of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50), while there was no significant difference in mortality among patients undergoing surgery within 4 days.

DISCUSSION

Previous studies have reported that 3.6% to 6.0% of patients with hip fractures die during hospitalisation,[9 20] and that the 1-year mortality rate is between 10.1% and 27.3%.[12 21] The reasons for the high mortality rate after hip fracture have been extensively studied. Frost et al. recently reported that men had a 2.4 times higher risk of in-hospital death compared with women, and advancing age increased the risk by 2.06 times for every 10-year increase in age.[9] Maggi et al. reported that 6-month mortality was positively associated with increasing age, comorbidity, pre-fracture functional disability and having surgery more than 48 hours after admission.[22] Hu et al. identified the following 12 preoperative predictors of postoperative mortality in hip fracture patients through systematic review: advanced age, male gender, nursing home or facility residence, poor preoperative walking capacity, poor activities of daily living, higher ASA (American Society of Anesthesiologists) grading, poor mental state, multiple comorbidities, dementia or cognitive impairment, diabetes, cancer and cardiac disease.[10]

In this study, we investigated the in-hospital mortality rate after hip fractures using the Japanese DPC administrative claims database. The DPC database is equivalent in several ways to the Nationwide Inpatient Sample database in the United States, but there is an advantage of the DPC database whereby complications occurring after admission are clearly differentiated with comorbidities that were already present at admission.

In our study, 83% of the patients underwent surgery and 17% were treated conservatively, which were similar rates to previous studies. Among them, 3.3% of patients died during the hospitalisation. The overall mortality rate was slightly lower than that in previous reports. In multivariate analysis, we found that male gender, advancing age and number of comorbidities were positively and independently associated with the mortality, which is consistent with previous studies. The size of hospital as determined by the number of acute beds had no significant relationship with in-hospital mortality in our study. This result may suggest that high risk patients are not necessarily treated at large hospitals. Schilling et al. reported that decreased hospital-wide nurse staffing levels are associated with increased in-hospital mortality among patients with hip fracture.[20] In contrast, Browne et al. reported that hospital volume is not associated with decreased mortality in the treatment of hip fractures.[23] There are various scales to represent hospital quality, so more studies may be needed to clarify the relationship between hospital quality and hip fracture mortality.

Interestingly, conservative treatment was an independent risk factor for in-hospital mortality. The analysis indicated that this did not arise because of patients with higher risks being more likely to undergo conservative treatment, because patients treated conservatively exhibited more than four times higher risk for mortality even after stratification according to the number of comorbidities or age. The exact reason for the higher mortality in conservatively treated patients is unclear, but the patients treated surgically can start rehabilitation earlier, and therefore avoid the complications caused by long-term bed rest such as bedsores, venous thromboembolism, atelectasis and hypostatic pneumonia.

We found that surgical delays of 5 days or more were significantly associated with higher rates of in-hospital mortality, which was consistent with the recent prospective cohort study by Vidan et al., showing that surgical delays longer than 5 days were associated with higher mortality and medical complication rates.[15]

Our study has several limitations. First, this is a retrospective observational study. Thus, patient allocation was non-randomised and the cohort of patients we used did not constitute random sampling. Consequently, our results are potentially biased due to unmeasured confounders. Second, the DPC adopting hospitals are generally of large size although the DPC database covered more than 40% of all inpatient admissions in Japan. Third, this database is for administrative claims, so recorded diagnoses may be less well validated than in planned prospective surveys. Finally, this database includes information only during the hospitalisation, and we were unable to determine the condition of patients before admission or after discharge. Despite these limitations, our study provides helpful information about the risk factors of in-hospital mortality for treatment decision-making in patients with hip fractures.

CONCLUSION

This study has shown that timely surgical treatment in patients with hip fractures was associated with lower rates of in-hospital mortality.

BMJ Open

Shoda et al.

Acknowledgement

Contributors: NS, HY, HH and ST designed the study, analysed and interpreted the data, and drafted the manuscript. YK contributed to the study design, analysis and interpretation of the data. SM interpreted the data and made significant contributions to drafts of the manuscript. All authors had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. SN, HY and ST are guarantors.

Funding: This study was supported in part by Grants-in-Aid for Research on Policy Planning and Evaluation from the Ministry of Health, Labour and Welfare, Japan; the Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST program) from the Council for Science and Technology Policy, Japan; and a research grant from Japan Osteoporosis Foundation. The funding source was not involved in the design, conduct or interpretation of the study, or in the writing of the submitted work.

Competing interests: None declared.

Ethical approval: Not needed

References

1. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 1997;7(5):407-13.
2. 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. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2009;20(4):543-8.
3. Hagino H, Sakamoto K, Harada A, Nakamura T, Mutoh Y, Mori S, et al. Nationwide one-decade survey of hip fractures in Japan. Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association 2010;15(6):737-45.
4. Johnell O, Kanis JA. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2004;15(11):897-902.
5. 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(1-2):71-77.
6. Sambrook P, Cooper C. Osteoporosis. Lancet 2006;367(9527):2010-8.
7. Abrahamsen B, Vestergaard P. Declining incidence of hip fractures and the extent of use of anti-osteoporotic therapy in Denmark 1997-2006. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2010;21(3):373-80.
8. Leslie WD, O'Donnell S, Jean S, Lagace C, Walsh P, Bancej C, et al. Trends in hip fracture rates in Canada. JAMA : the journal of the American Medical Association 2009;302(8):883-9.
9. Frost SA, Nguyen ND, Black DA, Eisman JA, Nguyen TV. Risk factors for in-hospital post-hip fracture mortality. Bone 2011;49(3):553-8.
10. Hu F, Jiang C, Shen J, Tang P, Wang Y. Preoperative predictors for mortality following hip fracture surgery: A systematic review and meta-analysis. Injury 2011.
11. Meyer HE, Tverdal A, Falch JA, Pedersen JI. Factors associated with mortality after hip fracture. Osteoporosis international : a journal established as result of cooperation

Shoda et al.

between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2000;11(3):228-32.

12. Panula J, Pihlajamaki H, Mattila VM, Jaatinen P, Vahlberg T, Aarnio P, et al. Mortality and cause of death in hip fracture patients aged 65 or older: a population-based study. BMC Musculoskelet Disord 2011;12:105.
13. Bottle A, Aylin P. Mortality associated with delay in operation after hip fracture: observational study. BMJ 2006;332(7547):947-51.
14. Gdalevich M, Cohen D, Yosef D, Tauber C. Morbidity and mortality after hip fracture: the impact of operative delay. Archives of orthopaedic and trauma surgery 2004;124(5):334-40.
15. Vidan MT, Sanchez E, Gracia Y, Maranon E, Vaquero J, Serra JA. Causes and effects of surgical delay in patients with hip fracture: a cohort study. Annals of internal medicine 2011;155(4):226-33.
16. Simunovic N, Devereaux PJ, Sprague S, Guyatt GH, Schemitsch E, Debeer J, et al. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2010;182(15):1609-16.
17. Orosz GM, Magaziner J, Hannan EL, Morrison RS, Koval K, Gilbert M, et al. Association of timing of surgery for hip fracture and patient outcomes. JAMA : the journal of the American Medical Association 2004;291(14):1738-43.
18. Siegmeth AW, Gurusamy K, Parker MJ. Delay to surgery prolongs hospital stay in patients with fractures of the proximal femur. The Journal of bone and joint surgery. British volume 2005;87(8):1123-6.
19. Matsuda S, Ishikawa KB, Kuwabara K, Fujimori K, Fushimi K, Hashimoto H. Development and use of the Japanese case-mix system. . Eurohealth 2009;14(3):25-30.
20. Schilling P, Goulet JA, Dougherty PJ. Do Higher Hospital-wide Nurse Staffing Levels Reduce In-hospital Mortality in Elderly Patients with Hip Fractures: A Pilot Study. Clin Orthop Relat Res 2011.
21. Sakamoto K, Nakamura T, Hagino H, Endo N, Mori S, Muto Y, et al. Report on the Japanese Orthopaedic Association's 3-year project observing hip fractures at fixed-point hospitals. Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association 2006;11(2):127-34.
22. Maggi S, Siviero P, Wetle T, Besdine RW, Saugo M, Crepaldi G. A multicenter survey on profile of care for hip fracture: predictors of mortality and disability. Osteoporosis international : a journal established as result of cooperation between the European

Shoda et al.

Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2010;21(2):223-31.

23. Browne JA, Pietrobon R, Olson SA. Hip fracture outcomes: does surgeon or hospital volume really matter? The Journal of trauma 2009;66(3):809-14.

Figure legends

Table 1 Patient characteristics

Table 2 Risk factors for in-hospital mortality (univariate analysis)

Table 3 Risk factors for in-hospital mortality (multivariate analysis)

Fig 1 Odds ratios of in-hospital mortality and 95% confidence intervals in hip fracture patients treated conservatively. **A.** Patients were stratified into three groups according to the number of comorbidities. **B.** Patients were stratified into four groups according to age.

Table 1 Patient characteristics

		n	(%)
Gender			
	Females	63,920	(79.1)
	Males	16,880	(20.9)
Age			
	60–69	5,523	(6.8)
	70–79	18,618	(23.0)
	80–89	37,362	(46.2)
	≥90	19,297	(23.9)
Treatment			
	Surgical	66,893	(82.8)
	Conservative	13,907	(17.2)
Hospital size (number of acute beds)			
	≤199	11,243	(13.9)
	200–399	32,613	(40.4)
	400–599	23,125	(28.6)
	≥600	12,099	(15.0)
Comorbidities			
	Malignancy	4,753	(5.7)
	Diabetes mellitus	10,795	(13.4)
	Cardiovascular disease	6,147	(7.6)
	Cerebrovascular disease	6,438	(8.0)
	Lung disease	5,179	(6.4)
	Renal failure	3,554	(4.4)
	Hepatic failure	646	(0.8)
Number of comorbidities			
	0	51,544	(63.8)
	1	22,170	(27.4)
	≥2	7,086	(8.8)

Shoda et al.

Table 2 Risk factors for in-hospital mortality (univariate analysis)

		n	(%)	p-value
Total		2681	(3.3)	
Gender				
	Females	1677	(2.6)	<0.001
	Males	1004	(5.9)	
Age				
	60–69	97	(1.8)	<0.001
	70–79	488	(2.6)	
	80–89	1223	(3.3)	
	≥90	873	(4.5)	
Treatment				
	Surgical	1372	(2.1)	<0.001
	Conservative	1309	(9.4)	
Hospital size (number of acute beds)				
	≤199	454	(4.0)	<0.001
	200–399	1080	(3.3)	
	400–599	672	(2.9)	
	≥600	412	(3.4)	
Comorbidities				
	Malignancy	669	(14.6)	<0.001
	Diabetes mellitus	365	(3.4)	0.694
	Cardiovascular disease	198	(3.2)	0.659
	Cerebrovascular disease	215	(3.3)	0.920
	Lung disease	516	(10.0)	<0.001
	Renal failure	305	(8.6)	<0.001
	Hepatic failure	126	(19.5)	<0.001
Number of comorbidities				
	0	968	(1.9)	<0.001
	1	1139	(5.1)	
	≥2	574	(8.1)	

Table 3 Risk factors for in-hospital mortality (multivariate analysis)

		Odds ratio	95% confidence interval	p-value
Gender				
	Females	reference		
	Males	2.12	1.94 to 2.31	<0.001
Age				
	60–69	reference		
	70–79	1.57	1.25 to 1.96	<0.001
	80–89	2.28	1.84 to 2.82	<0.001
	≥90	3.51	2.83 to 4.37	<0.001
Treatment				
	Surgical	reference		
	Conservative	4.25	3.92 to 4.61	<0.001
Hospital size (number of acute beds)				
	≤199	reference		
	200–399	0.99	0.88 to 1.11	0.814
	400–599	0.88	0.77 to 1.00	0.043
	≥600	0.93	0.81 to 1.07	0.304
Number of comorbidities				
	0	reference		
	1	2.50	2.28 to 2.74	<0.001
	≥2	3.79	3.38 to 4.24	<0.001

Shoda et al.

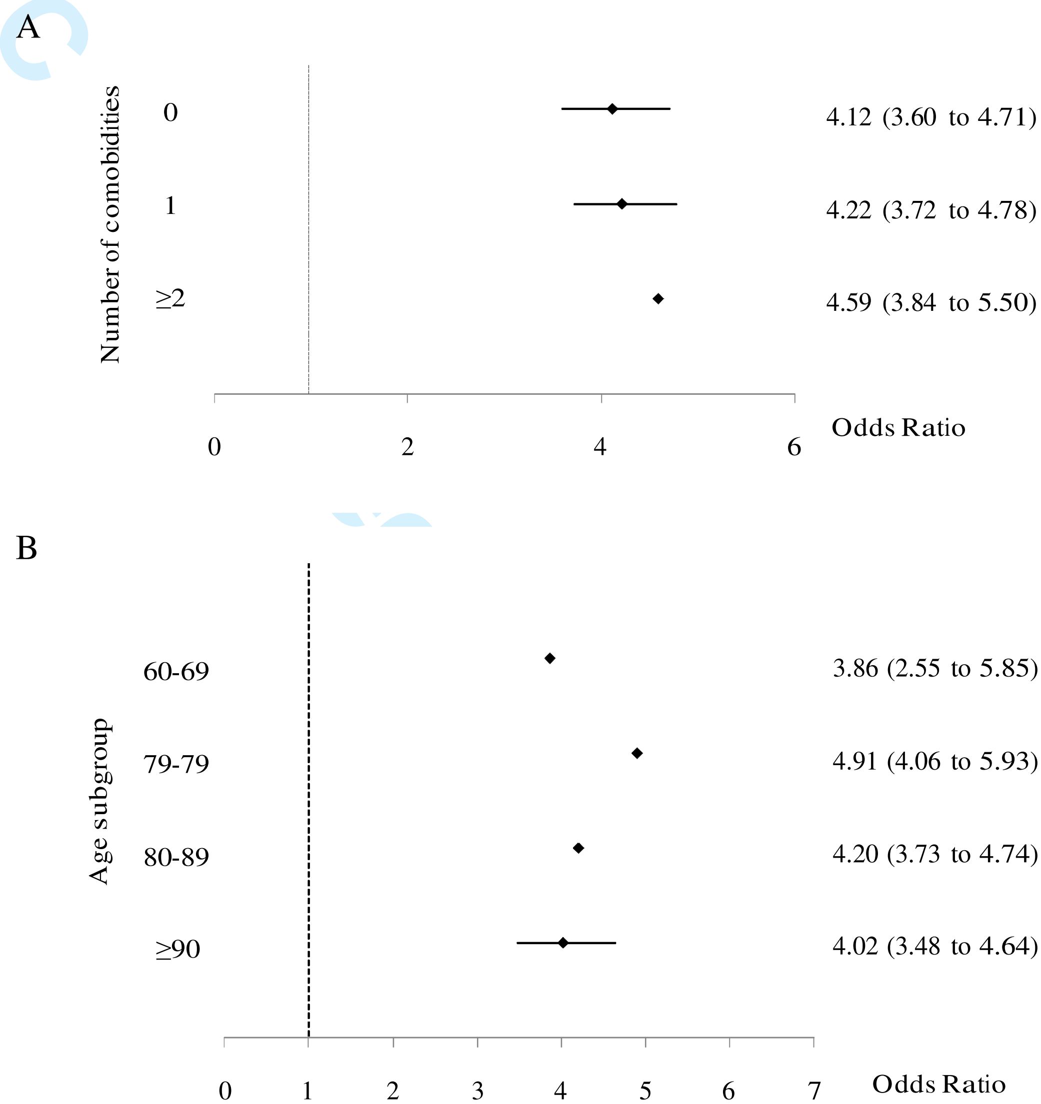


Fig 1

http://mc.manuscriptcentral.com/bmj

Risk factors affecting in-hospital mortality after hip fracture: retrospective analysis using the Japanese Diagnosis Procedure Combination database

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2011-000416.R1
Article Type:	Research
Date Submitted by the Author:	19-Mar-2012
Complete List of Authors:	Shoda, Naoko; The University of Tokyo, Department of Orthpaedic Surgery Yasunaga, Hideo; Graduate School of Medicine University of Tokyo, Department of Health Management and Policy Horiguchi, Hiromasa; Graduate School of Medicine University of Tokyo, Department of Health Management and Policy Matsuda, Shinya; University of Occupational and Environmental Health, Department of Preventive Medicine and Community Health Ohe, Kazuhiko; University of Tokyo, Department of Medical Informatics and Economics, Graduate School of Medicine Kadono, Yuho; The University of Tokyo, Department of Orthpaedic Surgery Tanaka, Sakae; The University of Tokyo, Department of Orthopaedic Surgery
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Epidemiology, Surgery
Keywords:	Trauma management < ORTHOPAEDIC & TRAUMA SURGERY, Bone diseases < ORTHOPAEDIC & TRAUMA SURGERY, Hip < ORTHOPAEDIC & TRAUMA SURGERY, TRAUMA MANAGEMENT

SCHOLARONE™
Manuscripts

Risk factors affecting in-hospital mortality after hip fracture: retrospective analysis using the Japanese Diagnosis Procedure Combination database

Naoko Shoda, researcher[1] Hideo Yasunaga, associate professor[2] Hiromasa Horiguchi, lecturer[2] Shinya Matsuda, professor[3] Kazuhiko Ohe, professor[4] Yuho Kadono, assistant professor[1] Sakae Tanaka, professor[1]

[1] Department of Orthopaedic Surgery, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

[2] Department of Health Management and Policy, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

[3] Department of Preventive Medicine and Community Health, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, Japan

[4] Department of Medical Informatics and Economics, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Correspondence to: S Tanaka, Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Tel: +81-3-3815-5415 ext 33376; Fax: +81-3-3818-4082

TANAKAS-ORT@h.u-tokyo.ac.jp

Article Summary

Article focus

- Hip fracture leads to impaired function, loss of independence and increased mortality of the patients.
- The aim of this study is to identify risk factors for in-hospital mortality in patients with hip fractures

Key messages

- Using the Japanese Diagnosis Procedure Combination (DPC) nationwide administrative claims database, we analysed 80,800 hip fracture patients in total.
- The overall in-hospital mortality rate was 3.3%, and the in-hospital mortality was significantly associated with male gender (OR 2.12 compared with female gender; p<0.001), advancing age (OR 1.57 in the 70–79 years age group, 2.28 in the 80–89 years group and 3.51 in the ≥90 years group compared with the 60–69 years age group, p<0.001), conservative treatment (OR 4.25 compared with the surgical treatment group, p<0.001), and number of comorbidities (OR 2.50 in patients with one comorbidity and 3.79 in those with two or more comorbidities as compared with no comorbidity, p<0.001). W
- The proportion of patients with delay to surgery of 5 days or longer was 53.6%, and

the delay was significantly associated with a higher rate of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50), while there was no significant difference in mortality among patients undergoing surgery within 4 days.

Strengths and limitations of this study

- We analysed a large number of patients using the Japanese DPC administrative claims database, which included approximately 40% of all the in-patient admissions to acute care hospitals in Japan.
- Complications occurring after admission are clearly differentiated with comorbidities that were already present at admission.
- This is a retrospective observational study, and the database includes information only during the hospitalisation.

Abstract

Objective: To identify risk factors for in-hospital mortality in patients with hip fractures using the Japanese Diagnosis Procedure Combination (DPC) nationwide administrative claims database.

Design: Retrospective observational study.

Setting: Hospitals adopting the DPC system during 2007–2009.

Participants: We extracted a total of 80,800 eligible patients aged ≥60 years old with a single hip fracture (ICD-10 codes: S72.0 and S72.1). The DPC database includes patients treated between July and December each year.

Main outcome measures: In-hospital mortality after hip fracture.

Results: The overall in-hospital mortality rate after hip fractures was 3.3%. Multivariate analysis indicated that in-hospital mortality was significantly associated with male gender (odds ratio [OR] 2.12; 95% confidence interval [CI] 1.94 to 2.31), advancing age and number of comorbidities. Significantly higher mortality was observed in those treated conservatively (OR 4.25; 95% CI 3.92 to 4.61). Surgical delays of 5 days or more were significantly associated with higher rates of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50).

Conclusions: In patients with hip fractures, male gender, advancing age, high number

of comorbidities and the surgical delay of 5 days or more were associated with higher rates of in-hospital mortality.

INTRODUCTION

Hip fracture is a serious injury related to bone fragility caused by osteoporosis, and it has emerged as a public health burden in an aging society such as that of Japan.[1-5] It is estimated that the number of hip fractures worldwide will rise from 1.7 million in 1990 to 6.3 million in 2050.[6] Recent studies have reported an increased incidence of hip fractures in Japan[3 5] although the incidence is decreasing in some Western countries.[7 8] Hip fracture leads to impaired function, loss of independence and increased mortality of the patients. It has been reported that the increased mortality after hip fracture is associated with many factors such as increasing age, comorbidity and pre-fracture functional disability of the patients.[9-12] Hip fractures are usually treated by orthopaedic surgical procedures such as hemiarthroplasty or internal fixation, and several studies have shown that early surgery is associated with lower rates of mortality,[13-16] while other studies exhibited no benefit of early surgery in reducing mortality or improving functional recovery.[17 18] Conservative treatment is often chosen for patients with severe comorbidities. However, it is not clear whether conservative treatment is actually superior in reducing mortality compared with surgical treatment in high risk patients. In this study, we investigated the in-hospital mortality rate of hip fracture patients using data from the Japanese Diagnosis Procedure Combination (DPC) nationwide

administrative claims database, and compared mortality following hip fractures between groups treated surgically or conservatively.

METHODS

DPC database

The DPC database is a diagnosis-dominant case-mix system administered by the Ministry of Health, Labour and Welfare of Japan, and linked with a lump-sum payment system.[19] All 82 university teaching hospitals in Japan are obliged to adopt the DPC system, while adoption by community hospitals is voluntary. A comprehensive survey of the DPC hospitals is conducted between July 1 and December 31 each year by the DPC Research Group, funded by the Japanese government. Detailed patient data, as well as administrative claims data, are collected for all the inpatients discharged from the participating hospitals between July 1 and December 31 each year. The number of participating hospitals increased to 818 with 2.57 million patients in 2009, which represented approximately 40% of all the in-patient admissions to acute care hospitals in Japan. Hospitals send all the anonymised data for each month to the DPC Research Group for compilation in the database server in the Department of Health Management and Policy, The University of Tokyo.

The database includes the following data: hospital location; patients' age and sex; diagnoses, comorbidities at admission, and complications after admission, recorded in accordance with the International Classification of Diseases, 10th Revision (ICD-10) codes and text data in the Japanese language; procedures coded with the Japanese original K codes; comorbidities at admission; complications after admission coded with the ICD-10 codes; in-hospital mortality; length of stay; and hospital charges.

This study was based on a secondary analysis of the administrative claims data. The requirement for informed consent was waived because of the anonymous nature of the data. Study approval was obtained from the Institutional Review Board at the University of Occupational and Environmental Health.

Data compilation

We retrospectively collected data of patients coded S72.0 (fracture of the neck of the femur) and S72.1 (pertrochanteric fracture) between 2007 and 2009 from the DPC database. Exclusion criteria were as follows: age < 60 years; patients with open fractures or multiple fractures; and incomplete data. We extracted data on age, sex, method of treatment (surgical or conservative), number of acute beds and in-hospital mortality. From the comorbidities at admission, we collected data on seven factors:

malignancy, diabetes mellitus, cardiovascular disease, cerebrovascular disease, lung disease, renal failure, hepatic failure.

Statistical analysis

The Chi-squared test was used for univariate comparisons of the surgical and conservative treatment groups. Multivariate logistic regression analysis was performed to analyse the confounding effects of various factors on in-hospital mortality. Odds ratios (OR) and 95% confidence intervals (CI) were determined. The OR of in-hospital mortality in conservatively treated patients was analysed in subgroups of patients stratified according to number of comorbidities or age. In addition, the effect of surgical delays in surgically treated patients was analysed. A p-value <0.05 was considered significant. All the statistical analyses were performed using SPSS Statistics ver. 19.0 (IBM SPSS Inc.; Chicago, IL, US).

Data sharing statement: No additional data are available.

RESULTS

Patient background

Data of 94,139 patients with hip fractures were extracted based on ICD-10 codes. We excluded 8,956 patients with open fractures or multiple fractures, 496 patients with incomplete data and 3887 patients aged <60 years. Finally, 80,800 eligible patients were included in the analysis.

Table1 presents the patient characteristics. Overall, 79.1% were females. The mean (standard deviation) age was 82.8 (8.3) years. The patients were categorised into the following four age groups: 60–69 (n=5,523), 70–79 (n=18,618), 80–89 (n=37,362), and ≥90 (n=19,297). Approximately 83% (n=66,893) of patients underwent surgical treatment, while 17% (n=13,907) were treated conservatively. Hospital size was categorised into four groups according to the number of acute beds: ≤199 (13.9%), 200–399 (40.4%), 400–599 (28.6%), and ≥600 (15.0%). The proportion of patients with comorbidities at admission was as follows: malignancy (5.7%), diabetes mellitus (13.4%), cardiovascular disease (7.6%), cerebrovascular disease (8.0%), lung disease (6.4%), renal failure (4.4%) and hepatic failure (0.8%).

Univariate analysis of in-hospital mortality

Table 2 shows the factors associated with in-hospital mortality according to the univariate analysis. The overall in-hospital mortality rate was 3.3% (n=2,681) with the average length of stay of 38 days. Male gender, advancing age, conservative treatment and smaller hospital size were significantly associated with higher mortality. As for comorbidities, patients with malignancy, lung disease, renal failure and hepatic failure at admission exhibited higher mortality rates. In contrast, diabetes mellitus, cardiovascular disease or cerebrovascular disease did not significantly affect the mortality of the patients. The number of comorbidities at admission was positively related to the mortality rate.

Multivariate analysis of in-hospital mortality

Table 3 shows the adjusted OR and 95% CI for in-hospital mortality as determined by multivariate analysis. Consistent with the univariate analysis, the in-hospital mortality was significantly associated with male gender (OR 2.12 compared with female gender; $p<0.001$), advancing age (OR 1.57 in the 70–79 years age group, 2.28 in the 80–89 years group and 3.51 in the ≥90 years group compared with the 60–69 years age group, $p<0.001$), conservative treatment (OR 4.25 compared with the surgical treatment group, $p<0.001$), and number of comorbidities (OR 2.50 in patients with one comorbidity and 3.79 in those with two or more comorbidities as compared with no comorbidity, $p<0.001$). There was no association with hospital size. We then stratified the patients into the following three groups according to the number of comorbidities: no comorbidity (n=51,544), one comorbidity (n=22,170), and two or more comorbidities (n=7,086). Regardless of the number of comorbidities, conservative treatment was significantly associated with higher mortality compared with surgical treatment (fig 1A). In addition, patients with conservative treatment exhibited higher mortality even the patients were stratified according to age (fig 1B).

We finally analysed the effect of surgical delays on in-hospital mortality in patients treated surgically. The proportion of patients with delay to surgery of 5 days or longer was 53.6%, and the delay was significantly associated with a higher rate of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50), while there was no significant difference in mortality among patients undergoing surgery within 4 days.

DISCUSSION

Previous studies have reported that 3.6% to 6.0% of patients with hip fractures die during hospitalisation,[9 20] and that the 1-year mortality rate is between 10.1% and 27.3%.[12 21] The reasons for the high mortality rate after hip fracture have been extensively studied. Frost et al. recently reported that men had a 2.4 times higher risk of in-hospital death compared with women, and advancing age increased the risk by 2.06

times for every 10-year increase in age.[9] Maggi et al. reported that 6-month mortality was positively associated with increasing age, comorbidity, pre-fracture functional disability and having surgery more than 48 hours after admission.[22] Hu et al. identified the following 12 preoperative predictors of postoperative mortality in hip fracture patients through systematic review: advanced age, male gender, nursing home or facility residence, poor preoperative walking capacity, poor activities of daily living, higher ASA (American Society of Anesthesiologists) grading, poor mental state, multiple comorbidities, dementia or cognitive impairment, diabetes, cancer and cardiac disease.[10]

In this study, we investigated the in-hospital mortality rate after hip fractures using the Japanese DPC administrative claims database. The DPC database is equivalent in several ways to the Nationwide Inpatient Sample database in the United States, but there is an advantage of the DPC database whereby complications occurring after admission are clearly differentiated with comorbidities that were already present at admission.

In our study, 83% of the patients underwent surgery and 17% were treated conservatively, which were similar rates to previous studies[21]. The proportion of conservative treatment was higher than that in the Western countries, which may be due to the insurance system in Japan, which allows patients a longer hospital stay.

Overall, 3.3% of patients died during the hospitalisation. The mortality rate was slightly lower than that in previous reports. In multivariate analysis, we found that male gender, advancing age and number of comorbidities were positively and independently associated with the mortality, which is consistent with previous studies. The size of hospital as determined by the number of acute beds had no significant relationship with in-hospital mortality in our study. This result may suggest that high risk patients are not necessarily treated at large hospitals. Schilling et al. reported that decreased hospital-wide nurse staffing levels are associated with increased in-hospital mortality among patients with hip fracture.[20] In contrast, Browne et al. reported that hospital volume is not associated with decreased mortality in the treatment of hip fractures.[23] There are various scales to represent hospital quality, so more studies may be needed to clarify the relationship between hospital quality and hip fracture mortality.

Interestingly, conservative treatment was an independent risk factor for in-hospital mortality. The analysis indicated that this did not arise because of patients with higher risks being more likely to undergo conservative treatment, because patients treated conservatively exhibited more than four times higher risk for mortality even after stratification according to the number of comorbidities or age. The exact reason for the higher mortality in conservatively treated patients is unclear, but the patients treated surgically can start rehabilitation earlier, and therefore avoid the complications caused by long-term bed rest such as bedsores, venous thromboembolism, atelectasis and hypostatic pneumonia.

We found that surgical delays of 5 days or more were significantly associated with higher rates of in-hospital mortality, which was consistent with the recent prospective cohort study by Vidan et al., showing that surgical delays longer than 5 days were associated with higher mortality and medical complication rates.[15]

Our study has several limitations. First, this is a retrospective observational study. Thus, patient allocation was non-randomised and the cohort of patients we used did not constitute random sampling. Consequently, our results are potentially biased due to unmeasured confounders. Second, the DPC adopting hospitals are generally of large size although the DPC database covered more than 40% of all inpatient admissions in Japan. Third, this database is for administrative claims, so recorded diagnoses may be less well validated than in planned prospective surveys. Finally, this database includes information only during the hospitalisation, and we were unable to determine the condition of patients before admission or after discharge. Despite these limitations, our study provides helpful information about the risk factors of in-hospital mortality for treatment decision-making in patients with hip fractures.

CONCLUSION

This study has shown that male gender, advancing age, high number of comorbidities and surgical delay were associated with higher rates of in-hospital mortality in patients with hip fractures.

Acknowledgement

Contributors: NS, HY, HH and ST designed the study, analysed and interpreted the data, and drafted the manuscript. YK contributed to the study design, analysis and interpretation of the data. SM interpreted the data and made significant contributions to drafts of the manuscript. All authors had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. SN, HY and ST are guarantors.

Funding: This study was supported in part by Grants-in-Aid for Research on Policy Planning and Evaluation from the Ministry of Health, Labour and Welfare, Japan; the Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST program) from the Council for Science and Technology Policy, Japan; and a research grant from Japan Osteoporosis Foundation. The funding source was not involved in the design, conduct or interpretation of the study, or in the writing of the

submitted work.

Competing interests: None declared.

Ethical approval: Not needed

References

1. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 1997;7(5):407-13.

2. Hagino H, Furukawa K, Fujiwara S, *et al.* Recent trends in the incidence and lifetime risk of hip fracture in Tottori, Japan. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2009;20(4):543-8.

3. Hagino H, Sakamoto K, Harada A, *et al.* Nationwide one-decade survey of hip fractures in Japan. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association* 2010;15(6):737-45.

4. Johnell O, Kanis JA. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2004;15(11):897-902.

5. Orimo H, Yaegashi Y, Onoda T, *et al.* Hip fracture incidence in Japan: estimates of new patients in 2007 and 20-year trends. *Arch Osteoporos* 2009;4(1-2):71-77.

6. Sambrook P, Cooper C. Osteoporosis. *Lancet* 2006;367(9527):2010-8.

7. Abrahamsen B, Vestergaard P. Declining incidence of hip fractures and the extent of use of anti-osteoporotic therapy in Denmark 1997-2006. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2010;21(3):373-80.

8. Leslie WD, O'Donnell S, Jean S, *et al.* Trends in hip fracture rates in Canada. *JAMA : the journal of the American Medical Association* 2009;302(8):883-9.

9. Frost SA, Nguyen ND, Black DA, *et al.* Risk factors for in-hospital post-hip fracture mortality. *Bone* 2011;49(3):553-8.

10. Hu F, Jiang C, Shen J, *et al.* Preoperative predictors for mortality following hip fracture surgery: A systematic review and meta-analysis. *Injury* 2011.

11. Meyer HE, Tverdal A, Falch JA, *et al.* Factors associated with mortality after hip fracture. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2000;11(3):228-32.

12. Panula J, Pihlajamaki H, Mattila VM, *et al.* Mortality and cause of death in hip fracture

patients aged 65 or older: a population-based study. *BMC Musculoskelet Disord* 2011;12:105.

13. Bottle A, Aylin P. Mortality associated with delay in operation after hip fracture: observational study. *BMJ* 2006;332(7547):947-51.
14. Gdalevich M, Cohen D, Yosef D*, et al.* Morbidity and mortality after hip fracture: the impact of operative delay. *Archives of orthopaedic and trauma surgery* 2004;124(5):334-40.
15. Vidan MT, Sanchez E, Gracia Y*, et al.* Causes and effects of surgical delay in patients with hip fracture: a cohort study. *Annals of internal medicine* 2011;155(4):226-33.
16. Simunovic N, Devereaux PJ, Sprague S*, et al.* Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne* 2010;182(15):1609-16.
17. Orosz GM, Magaziner J, Hannan EL*, et al.* Association of timing of surgery for hip fracture and patient outcomes. *JAMA : the journal of the American Medical Association* 2004;291(14):1738-43.
18. Siegmeth AW, Gurusamy K, Parker MJ. Delay to surgery prolongs hospital stay in patients with fractures of the proximal femur. *The Journal of bone and joint surgery. British volume* 2005;87(8):1123-6.
19. Matsuda S, Ishikawa KB, Kuwabara K*, et al.* Development and use of the Japanese case-mix system. . *Eurohealth* 2009;14(3):25-30.
20. Schilling P, Goulet JA, Dougherty PJ. Do Higher Hospital-wide Nurse Staffing Levels Reduce In-hospital Mortality in Elderly Patients with Hip Fractures: A Pilot Study. *Clin Orthop Relat Res* 2011.
21. Sakamoto K, Nakamura T, Hagino H*, et al.* Report on the Japanese Orthopaedic Association's 3-year project observing hip fractures at fixed-point hospitals. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association* 2006;11(2):127-34.
22. Maggi S, Siviero P, Wetle T*, et al.* A multicenter survey on profile of care for hip fracture: predictors of mortality and disability. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2010;21(2):223-31.
23. Browne JA, Pietrobon R, Olson SA. Hip fracture outcomes: does surgeon or hospital volume really matter? *The Journal of trauma* 2009;66(3):809-14.

Figure legends

Fig 1 Odds ratios of in-hospital mortality and 95% confidence intervals in hip fracture patients treated conservatively. **A.** Patients were stratified into three groups according to the number of comorbidities. **B.** Patients were stratified into four groups according to age.

Table 1 Patient characteristics

		n	(%)
Gender			
	Females	63,920	(79.1)
	Males	16,880	(20.9)
Age			
	60–69	5,523	(6.8)
	70–79	18,618	(23.0)
	80–89	37,362	(46.2)
	≥90	19,297	(23.9)
Treatment			
	Surgical	66,893	(82.8)
	Conservative	13,907	(17.2)
Hospital size (number of acute beds)			
	≤199	11,243	(13.9)
	200–399	32,613	(40.4)
	400–599	23,125	(28.6)
	≥600	12,099	(15.0)
Comorbidities			
	Malignancy	4,753	(5.7)
	Diabetes mellitus	10,795	(13.4)
	Cardiovascular disease	6,147	(7.6)
	Cerebrovascular disease	6,438	(8.0)
	Lung disease	5,179	(6.4)
	Renal failure	3,554	(4.4)
	Hepatic failure	646	(0.8)
Number of comorbidities			
	0	51,544	(63.8)
	1	22,170	(27.4)
	≥2	7,086	(8.8)

Shoda et al.

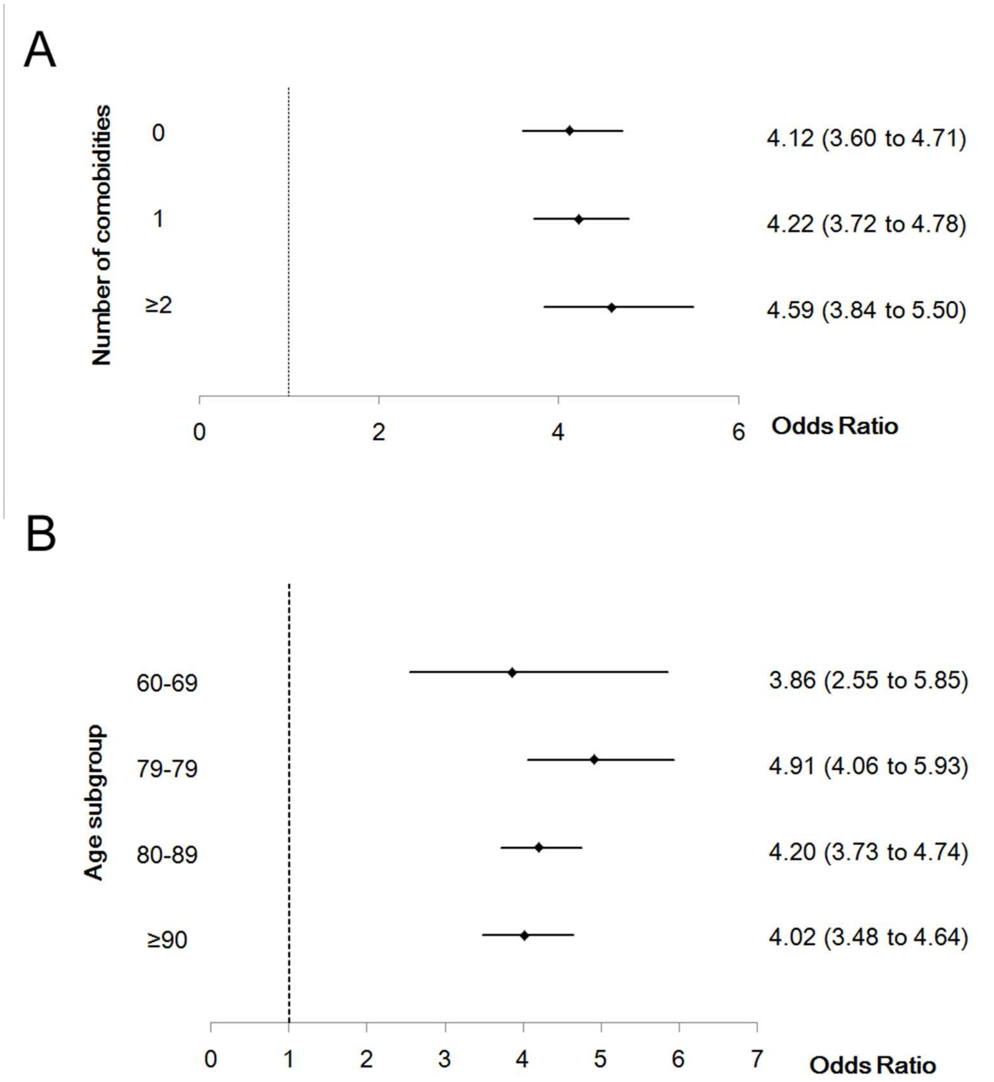
Table 2 Risk factors for in-hospital mortality (univariate analysis)

	In-hospital mortality		
	n	(%)	p-value
Total	2681	(3.3)	
Gender			
Females	1677	(2.6)	<0.001
Males	1004	(5.9)	
Age			
60–69	97	(1.8)	<0.001
70–79	488	(2.6)	
80–89	1223	(3.3)	
≥90	873	(4.5)	
Treatment			
Surgical	1372	(2.1)	<0.001
Conservative	1309	(9.4)	
Hospital size (number of acute beds)			
≤199	454	(4.0)	<0.001
200–399	1080	(3.3)	
400–599	672	(2.9)	
≥600	412	(3.4)	
Comorbidities			
Malignancy	669	(14.6)	<0.001
Diabetes mellitus	365	(3.4)	0.694
Cardiovascular disease	198	(3.2)	0.659
Cerebrovascular disease	215	(3.3)	0.920
Lung disease	516	(10.0)	<0.001
Renal failure	305	(8.6)	<0.001
Hepatic failure	126	(19.5)	<0.001
Number of comorbidities			
0	968	(1.9)	<0.001
1	1139	(5.1)	
≥2	574	(8.1)	

Shoda et al.

Table 3 Risk factors for in-hospital mortality (multivariate analysis)

		Odds ratio	95% confidence interval	p-value
Gender				
	Females	reference		
	Males	2.12	1.94 to 2.31	<0.001
Age				
	60–69	reference		
	70–79	1.57	1.25 to 1.96	<0.001
	80–89	2.28	1.84 to 2.82	<0.001
	≥90	3.51	2.83 to 4.37	<0.001
Treatment				
	Surgical	reference		
	Conservative	4.25	3.92 to 4.61	<0.001
Hospital size (number of acute beds)				
	≤199	reference		
	200–399	0.99	0.88 to 1.11	0.814
	400–599	0.88	0.77 to 1.00	0.043
	≥600	0.93	0.81 to 1.07	0.304
Number of comorbidities				
	0	reference		
	1	2.50	2.28 to 2.74	<0.001
	≥2	3.79	3.38 to 4.24	<0.001



344x377mm (72 x 72 DPI)

Shoda et al., Supplementary file

Risk factors affecting in-hospital mortality after hip fracture: retrospective analysis using the Japanese Diagnosis Procedure Combination database

Naoko Shoda, researcher[1] Hideo Yasunaga, associate professor[2] Hiromasa Horiguchi, lecturer[2] Shinya Matsuda, professor[3] Kazuhiko Ohe, professor[4] Yuho Kadono, assistant professor[1] Sakae Tanaka, professor[1]

[1] Department of Orthopaedic Surgery, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

[2] Department of Health Management and Policy, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

[3] Department of Preventive Medicine and Community Health, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, Japan

[4] Department of Medical Informatics and Economics, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Correspondence to: S Tanaka, Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Tel: +81-3-3815-5415 ext 33376; Fax: +81-3-3818-4082

TANAKAS-ORT@h.u-tokyo.ac.jp

Article Summary

Article focus

- Hip fracture leads to impaired function, loss of independence and increased mortality of the patients.
- The aim of this study is to identify risk factors for in-hospital mortality in patients with hip fractures

Key messages

- Using the Japanese Diagnosis Procedure Combination (DPC) nationwide administrative claims database, we analysed 80,800 hip fracture patients in total.
- The overall in-hospital mortality rate was 3.3%, and the in-hospital mortality was significantly associated with male gender (OR 2.12 compared with female gender; p<0.001), advancing age (OR 1.57 in the 70–79 years age group, 2.28 in the 80–89 years group and 3.51 in the ≥90 years group compared with the 60–69 years age group, p<0.001), conservative treatment (OR 4.25 compared with the surgical treatment group, p<0.001), and number of comorbidities (OR 2.50 in patients with one comorbidity and 3.79 in those with two or more comorbidities as compared with no comorbidity, p<0.001). W
- The proportion of patients with delay to surgery of 5 days or longer was 53.6%, and

the delay was significantly associated with a higher rate of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50), while there was no significant difference in mortality among patients undergoing surgery within 4 days.

Strengths and limitations of this study

- We analysed a large number of patients using the Japanese DPC administrative claims database, which included approximately 40% of all the in-patient admissions to acute care hospitals in Japan.
- Complications occurring after admission are clearly differentiated with comorbidities that were already present at admission.
- This is a retrospective observational study, and the database includes information only during the hospitalisation.

Abstract

Objective: To identify risk factors for in-hospital mortality in patients with hip fractures using the Japanese Diagnosis Procedure Combination (DPC) nationwide administrative claims database.

Design: Retrospective observational study.

Setting: Hospitals adopting the DPC system during 2007–2009.

Participants: We extracted a total of 80,800 eligible patients aged ≥60 years old with a single hip fracture (ICD-10 codes: S72.0 and S72.1). The DPC database includes patients treated between July and December each year.

Main outcome measures: In-hospital mortality after hip fracture.

Results: The overall in-hospital mortality rate after hip fractures was 3.3%. Multivariate analysis indicated that in-hospital mortality was significantly associated with male gender (odds ratio [OR] 2.12; 95% confidence interval [CI] 1.94 to 2.31), advancing age and number of comorbidities. Significantly higher mortality was observed in those treated conservatively (OR 4.25; 95% CI 3.92 to 4.61). Surgical delays of 5 days or more were significantly associated with higher rates of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50).

Conclusions: In patients with hip fractures, male gender, advancing age, high number

of comorbidities and the surgical delay of 5 days or more were associated with higher rates of in-hospital mortality.

INTRODUCTION

Hip fracture is a serious injury related to bone fragility caused by osteoporosis, and it has emerged as a public health burden in an aging society such as that of Japan.[1-5] It is estimated that the number of hip fractures worldwide will rise from 1.7 million in 1990 to 6.3 million in 2050.[6] Recent studies have reported an increased incidence of hip fractures in Japan[3 5] although the incidence is decreasing in some Western countries.[7 8] Hip fracture leads to impaired function, loss of independence and increased mortality of the patients. It has been reported that the increased mortality after hip fracture is associated with many factors such as increasing age, comorbidity and pre-fracture functional disability of the patients.[9-12] Hip fractures are usually treated by orthopaedic surgical procedures such as hemiarthroplasty or internal fixation, and several studies have shown that early surgery is associated with lower rates of mortality,[13-16] while other studies exhibited no benefit of early surgery in reducing mortality or improving functional recovery.[17 18] Conservative treatment is often chosen for patients with severe comorbidities. However, it is not clear whether conservative treatment is actually superior in reducing mortality compared with surgical treatment in high risk patients. In this study, we investigated the in-hospital mortality rate of hip fracture patients using data from the Japanese Diagnosis Procedure Combination (DPC) nationwide

administrative claims database, and compared mortality following hip fractures between groups treated surgically or conservatively.

METHODS

DPC database

The DPC database is a diagnosis-dominant case-mix system administered by the Ministry of Health, Labour and Welfare of Japan, and linked with a lump-sum payment system.[19] All 82 university teaching hospitals in Japan are obliged to adopt the DPC system, while adoption by community hospitals is voluntary. A comprehensive survey of the DPC hospitals is conducted between July 1 and December 31 each year by the DPC Research Group, funded by the Japanese government. Detailed patient data, as well as administrative claims data, are collected for all the inpatients discharged from the participating hospitals between July 1 and December 31 each year. The number of participating hospitals increased to 818 with 2.57 million patients in 2009, which represented approximately 40% of all the in-patient admissions to acute care hospitals in Japan. Hospitals send all the anonymised data for each month to the DPC Research Group for compilation in the database server in the Department of Health Management and Policy, The University of Tokyo.

The database includes the following data: hospital location; patients' age and sex; diagnoses, comorbidities at admission, and complications after admission, recorded in accordance with the International Classification of Diseases, 10th Revision (ICD-10) codes and text data in the Japanese language; procedures coded with the Japanese original K codes; comorbidities at admission; complications after admission coded with the ICD-10 codes; in-hospital mortality; length of stay; and hospital charges.

This study was based on a secondary analysis of the administrative claims data. The requirement for informed consent was waived because of the anonymous nature of the data. Study approval was obtained from the Institutional Review Board at the University of Occupational and Environmental Health.

Data compilation

We retrospectively collected data of patients coded S72.0 (fracture of the neck of the femur) and S72.1 (pertrochanteric fracture) between 2007 and 2009 from the DPC database. Exclusion criteria were as follows: age < 60 years; patients with open fractures or multiple fractures; and incomplete data. We extracted data on age, sex, method of treatment (surgical or conservative), number of acute beds and in-hospital mortality. From the comorbidities at admission, we collected data on seven factors:

malignancy, diabetes mellitus, cardiovascular disease, cerebrovascular disease, lung disease, renal failure, hepatic failure.

Statistical analysis

The Chi-squared test was used for univariate comparisons of the surgical and conservative treatment groups. Multivariate logistic regression analysis was performed to analyse the confounding effects of various factors on in-hospital mortality. Odds ratios (OR) and 95% confidence intervals (CI) were determined. The OR of in-hospital mortality in conservatively treated patients was analysed in subgroups of patients stratified according to number of comorbidities or age. In addition, the effect of surgical delays in surgically treated patients was analysed. A p-value <0.05 was considered significant. All the statistical analyses were performed using SPSS Statistics ver. 19.0 (IBM SPSS Inc.; Chicago, IL, US).

Data sharing statement: No additional data are available.

RESULTS

Patient background

Data of 94,139 patients with hip fractures were extracted based on ICD-10 codes. We excluded 8,956 patients with open fractures or multiple fractures, 496 patients with incomplete data and 3887 patients aged <60 years. Finally, 80,800 eligible patients were included in the analysis.

Table1 presents the patient characteristics. Overall, 79.1% were females. The mean (standard deviation) age was 82.8 (8.3) years. The patients were categorised into the following four age groups: 60–69 (n=5,523), 70–79 (n=18,618), 80–89 (n=37,362), and ≥90 (n=19,297). Approximately 83% (n=66,893) of patients underwent surgical treatment, while 17% (n=13,907) were treated conservatively. Hospital size was categorised into four groups according to the number of acute beds: ≤199 (13.9%), 200–399 (40.4%), 400–599 (28.6%), and ≥600 (15.0%). The proportion of patients with comorbidities at admission was as follows: malignancy (5.7%), diabetes mellitus (13.4%), cardiovascular disease (7.6%), cerebrovascular disease (8.0%), lung disease (6.4%), renal failure (4.4%) and hepatic failure (0.8%).

Univariate analysis of in-hospital mortality

Table 2 shows the factors associated with in-hospital mortality according to the univariate analysis. The overall in-hospital mortality rate was 3.3% (n=2,681) with the

Shoda et al., Supplementary file

average length of stay of 38 days. Male gender, advancing age, conservative treatment and smaller hospital size were significantly associated with higher mortality. As for comorbidities, patients with malignancy, lung disease, renal failure and hepatic failure at admission exhibited higher mortality rates. In contrast, diabetes mellitus, cardiovascular disease or cerebrovascular disease did not significantly affect the mortality of the patients. The number of comorbidities at admission was positively related to the mortality rate.

Multivariate analysis of in-hospital mortality

Table 3 shows the adjusted OR and 95% CI for in-hospital mortality as determined by multivariate analysis. Consistent with the univariate analysis, the in-hospital mortality was significantly associated with male gender (OR 2.12 compared with female gender; $p<0.001$), advancing age (OR 1.57 in the 70–79 years age group, 2.28 in the 80–89 years group and 3.51 in the ≥90 years group compared with the 60–69 years age group, $p<0.001$), conservative treatment (OR 4.25 compared with the surgical treatment group, $p<0.001$), and number of comorbidities (OR 2.50 in patients with one comorbidity and 3.79 in those with two or more comorbidities as compared with no comorbidity, $p<0.001$). There was no association with hospital size. We then stratified the patients into the following three groups according to the number of comorbidities: no comorbidity (n=51,544), one comorbidity (n=22,170), and two or more comorbidities (n=7,086). Regardless of the number of comorbidities, conservative treatment was significantly associated with higher mortality compared with surgical treatment (fig 1A). In addition, patients with conservative treatment exhibited higher mortality even the patients were stratified according to age (fig 1B).

We finally analysed the effect of surgical delays on in-hospital mortality in patients treated surgically. The proportion of patients with delay to surgery of 5 days or longer was 53.6%, and the delay was significantly associated with a higher rate of in-hospital mortality (OR 1.34; 95% CI 1.20 to 1.50), while there was no significant difference in mortality among patients undergoing surgery within 4 days.

DISCUSSION

Previous studies have reported that 3.6% to 6.0% of patients with hip fractures die during hospitalisation,[9 20] and that the 1-year mortality rate is between 10.1% and 27.3%.[12 21] The reasons for the high mortality rate after hip fracture have been extensively studied. Frost et al. recently reported that men had a 2.4 times higher risk of in-hospital death compared with women, and advancing age increased the risk by 2.06

times for every 10-year increase in age.[9] Maggi et al. reported that 6-month mortality was positively associated with increasing age, comorbidity, pre-fracture functional disability and having surgery more than 48 hours after admission.[22] Hu et al. identified the following 12 preoperative predictors of postoperative mortality in hip fracture patients through systematic review: advanced age, male gender, nursing home or facility residence, poor preoperative walking capacity, poor activities of daily living, higher ASA (American Society of Anesthesiologists) grading, poor mental state, multiple comorbidities, dementia or cognitive impairment, diabetes, cancer and cardiac disease.[10]

In this study, we investigated the in-hospital mortality rate after hip fractures using the Japanese DPC administrative claims database. The DPC database is equivalent in several ways to the Nationwide Inpatient Sample database in the United States, but there is an advantage of the DPC database whereby complications occurring after admission are clearly differentiated with comorbidities that were already present at admission.

In our study, 83% of the patients underwent surgery and 17% were treated conservatively, which were similar rates to previous studies[21]. The proportion of conservative treatment was higher than that in the Western countries, which may be due to the insurance system in Japan, which allows patients a longer hospital stay.

Overall, 3.3% of patients died during the hospitalisation. The mortality rate was slightly lower than that in previous reports. In multivariate analysis, we found that male gender, advancing age and number of comorbidities were positively and independently associated with the mortality, which is consistent with previous studies. The size of hospital as determined by the number of acute beds had no significant relationship with in-hospital mortality in our study. This result may suggest that high risk patients are not necessarily treated at large hospitals. Schilling et al. reported that decreased hospital-wide nurse staffing levels are associated with increased in-hospital mortality among patients with hip fracture.[20] In contrast, Browne et al. reported that hospital volume is not associated with decreased mortality in the treatment of hip fractures.[23] There are various scales to represent hospital quality, so more studies may be needed to clarify the relationship between hospital quality and hip fracture mortality.

Interestingly, conservative treatment was an independent risk factor for in-hospital mortality. The analysis indicated that this did not arise because of patients with higher risks being more likely to undergo conservative treatment, because patients treated conservatively exhibited more than four times higher risk for mortality even after stratification according to the number of comorbidities or age. The exact reason for the higher mortality in conservatively treated patients is unclear, but the patients treated surgically can start rehabilitation earlier, and therefore avoid the complications caused by long-term bed rest such as bedsores, venous thromboembolism, atelectasis and hypostatic pneumonia.

We found that surgical delays of 5 days or more were significantly associated with higher rates of in-hospital mortality, which was consistent with the recent prospective cohort study by Vidan et al., showing that surgical delays longer than 5 days were associated with higher mortality and medical complication rates.[15]

Our study has several limitations. First, this is a retrospective observational study. Thus, patient allocation was non-randomised and the cohort of patients we used did not constitute random sampling. Consequently, our results are potentially biased due to unmeasured confounders. Second, the DPC adopting hospitals are generally of large size although the DPC database covered more than 40% of all inpatient admissions in Japan. Third, this database is for administrative claims, so recorded diagnoses may be less well validated than in planned prospective surveys. Finally, this database includes information only during the hospitalisation, and we were unable to determine the condition of patients before admission or after discharge. Despite these limitations, our study provides helpful information about the risk factors of in-hospital mortality for treatment decision-making in patients with hip fractures.

Shoda et al., Supplementary file

CONCLUSION

This study has shown that male gender, advancing age, high number of comorbidities and surgical delay were associated with higher rates of in-hospital mortality in patients with hip fractures.

Acknowledgement

Contributors: NS, HY, HH and ST designed the study, analysed and interpreted the data, and drafted the manuscript. YK contributed to the study design, analysis and interpretation of the data. SM interpreted the data and made significant contributions to drafts of the manuscript. All authors had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. SN, HY and ST are guarantors.

Funding: This study was supported in part by Grants-in-Aid for Research on Policy Planning and Evaluation from the Ministry of Health, Labour and Welfare, Japan; the Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST program) from the Council for Science and Technology Policy, Japan; and a research grant from Japan Osteoporosis Foundation. The funding source was not involved in the design, conduct or interpretation of the study, or in the writing of the

submitted work.

Competing interests: None declared.

Ethical approval: Not needed

References

1. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 1997;7(5):407-13.
2. Hagino H, Furukawa K, Fujiwara S, *et al.* Recent trends in the incidence and lifetime risk of hip fracture in Tottori, Japan. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2009;20(4):543-8.
3. Hagino H, Sakamoto K, Harada A, *et al.* Nationwide one-decade survey of hip fractures in Japan. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association* 2010;15(6):737-45.
4. Johnell O, Kanis JA. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2004;15(11):897-902.
5. Orimo H, Yaegashi Y, Onoda T, *et al.* Hip fracture incidence in Japan: estimates of new patients in 2007 and 20-year trends. *Arch Osteoporos* 2009;4(1-2):71-77.
6. Sambrook P, Cooper C. Osteoporosis. *Lancet* 2006;367(9527):2010-8.
7. Abrahamsen B, Vestergaard P. Declining incidence of hip fractures and the extent of use of anti-osteoporotic therapy in Denmark 1997-2006. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2010;21(3):373-80.
8. Leslie WD, O'Donnell S, Jean S, *et al.* Trends in hip fracture rates in Canada. *JAMA : the journal of the American Medical Association* 2009;302(8):883-9.
9. Frost SA, Nguyen ND, Black DA, *et al.* Risk factors for in-hospital post-hip fracture mortality. *Bone* 2011;49(3):553-8.
10. Hu F, Jiang C, Shen J, *et al.* Preoperative predictors for mortality following hip fracture surgery: A systematic review and meta-analysis. *Injury* 2011.
11. Meyer HE, Tverdal A, Falch JA, *et al.* Factors associated with mortality after hip fracture. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2000;11(3):228-32.
12. Panula J, Pihlajamaki H, Mattila VM, *et al.* Mortality and cause of death in hip fracture

patients aged 65 or older: a population-based study. *BMC Musculoskelet Disord* 2011;12:105.

13. Bottle A, Aylin P. Mortality associated with delay in operation after hip fracture: observational study. *BMJ* 2006;332(7547):947-51.
14. Gdalevich M, Cohen D, Yosef D*, et al.* Morbidity and mortality after hip fracture: the impact of operative delay. *Archives of orthopaedic and trauma surgery* 2004;124(5):334-40.
15. Vidan MT, Sanchez E, Gracia Y*, et al.* Causes and effects of surgical delay in patients with hip fracture: a cohort study. *Annals of internal medicine* 2011;155(4):226-33.
16. Simunovic N, Devereaux PJ, Sprague S*, et al.* Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne* 2010;182(15):1609-16.
17. Orosz GM, Magaziner J, Hannan EL*, et al.* Association of timing of surgery for hip fracture and patient outcomes. *JAMA : the journal of the American Medical Association* 2004;291(14):1738-43.
18. Siegmeth AW, Gurusamy K, Parker MJ. Delay to surgery prolongs hospital stay in patients with fractures of the proximal femur. *The Journal of bone and joint surgery. British volume* 2005;87(8):1123-6.
19. Matsuda S, Ishikawa KB, Kuwabara K*, et al.* Development and use of the Japanese case-mix system. . *Eurohealth* 2009;14(3):25-30.
20. Schilling P, Goulet JA, Dougherty PJ. Do Higher Hospital-wide Nurse Staffing Levels Reduce In-hospital Mortality in Elderly Patients with Hip Fractures: A Pilot Study. *Clin Orthop Relat Res* 2011.
21. Sakamoto K, Nakamura T, Hagino H*, et al.* Report on the Japanese Orthopaedic Association's 3-year project observing hip fractures at fixed-point hospitals. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association* 2006;11(2):127-34.
22. Maggi S, Siviero P, Wetle T*, et al.* A multicenter survey on profile of care for hip fracture: predictors of mortality and disability. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2010;21(2):223-31.
23. Browne JA, Pietrobon R, Olson SA. Hip fracture outcomes: does surgeon or hospital volume really matter? *The Journal of trauma* 2009;66(3):809-14.

Shoda et al., Supplementary file

Figure legends

Fig 1 Odds ratios of in-hospital mortality and 95% confidence intervals in hip fracture patients treated conservatively. **A.** Patients were stratified into three groups according to the number of comorbidities. **B.** Patients were stratified into four groups according to age.

Table 1 Patient characteristics

		n	(%)
Gender			
	Females	63,920	(79.1)
	Males	16,880	(20.9)
Age			
	60–69	5,523	(6.8)
	70–79	18,618	(23.0)
	80–89	37,362	(46.2)
	≥90	19,297	(23.9)
Treatment			
	Surgical	66,893	(82.8)
	Conservative	13,907	(17.2)
Hospital size (number of acute beds)			
	≤199	11,243	(13.9)
	200–399	32,613	(40.4)
	400–599	23,125	(28.6)
	≥600	12,099	(15.0)
Comorbidities			
	Malignancy	4,753	(5.7)
	Diabetes mellitus	10,795	(13.4)
	Cardiovascular disease	6,147	(7.6)
	Cerebrovascular disease	6,438	(8.0)
	Lung disease	5,179	(6.4)
	Renal failure	3,554	(4.4)
	Hepatic failure	646	(0.8)
Number of comorbidities			
	0	51,544	(63.8)
	1	22,170	(27.4)
	≥2	7,086	(8.8)

Shoda et al., Supplementary file

Table 2 Risk factors for in-hospital mortality (univariate analysis)

		In-hospital mortality		
		n	(%)	p-value
Total		2681	(3.3)	
Gender				
	Females	1677	(2.6)	<0.001
	Males	1004	(5.9)	
Age				
	60–69	97	(1.8)	<0.001
	70–79	488	(2.6)	
	80–89	1223	(3.3)	
	≥90	873	(4.5)	
Treatment				
	Surgical	1372	(2.1)	<0.001
	Conservative	1309	(9.4)	
Hospital size (number of acute beds)				
	≤199	454	(4.0)	<0.001
	200–399	1080	(3.3)	
	400–599	672	(2.9)	
	≥600	412	(3.4)	
Comorbidities				
	Malignancy	669	(14.6)	<0.001
	Diabetes mellitus	365	(3.4)	0.694
	Cardiovascular disease	198	(3.2)	0.659
	Cerebrovascular disease	215	(3.3)	0.920
	Lung disease	516	(10.0)	<0.001
	Renal failure	305	(8.6)	<0.001
	Hepatic failure	126	(19.5)	<0.001
Number of comorbidities				
	0	968	(1.9)	<0.001
	1	1139	(5.1)	
	≥2	574	(8.1)	

Shoda et al., Supplementary file

Table 3 Risk factors for in-hospital mortality (multivariate analysis)

		Odds ratio	95% confidence interval	p-value
Gender				
	Females	reference		
	Males	2.12	1.94 to 2.31	<0.001
Age				
	60–69	reference		
	70–79	1.57	1.25 to 1.96	<0.001
	80–89	2.28	1.84 to 2.82	<0.001
	≥90	3.51	2.83 to 4.37	<0.001
Treatment				
	Surgical	reference		
	Conservative	4.25	3.92 to 4.61	<0.001
Hospital size (number of acute beds)				
	≤199	reference		
	200–399	0.99	0.88 to 1.11	0.814
	400–599	0.88	0.77 to 1.00	0.043
	≥600	0.93	0.81 to 1.07	0.304
Number of comorbidities				
	0	reference		
	1	2.50	2.28 to 2.74	<0.001
	≥2	3.79	3.38 to 4.24	<0.001