Beneficial effects of bipolar hemiarthroplasty replacement and fosamax in the retrospective cohort study of refracture and mortality of hip fractured patients

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Abstract: The epidemiological hip fracture leads to a high death rate in the elderly with osteoporosis worldwide. However, the appropriate surgical styles or anti-osteoporotic therapy could prevent these patients with hip fractures from suffering refracture, but the efficacy of such treatment remains elusive for first hip fractured patients. Our retrospective analysis was conducted on 508 hip fracture patients who were enrolled from Show Chwan Memorial Hospital from January 2005 through December 2011 and followed up until the end of 2012. However, bipolar hemiarthroplasty replacement and open reduction internal fixation (ORIF) are treatment options for femoral neck and intertrochanic hip fracture in our study population. Among these patients, 82 suffered 2nd hip fracture (refracture) with femoral neck or intertrochanteric fracture and 39 died after surgical intervention accompanied complications. Kaplan-Meier analysis revealed a better outcome in patients with bipolar hemiarthroplasty replacement or fosamax therapy of hip fractured patients than those with femoral neck/ ORIF and intertrochanteric/ ORIF or without fosamax therapy. Multivariate cox regression analysis revealed the lowest incidence of refracture and mortality in hip fracture patients with received bipolar hemiarthroplasty replacement surgical intervention (OR=0.732, CI=0.587-0.912; P=0.006). It is therefore concluded that fosamax therapy may improve bone density and increase bone tissue repair to prevent patients with hip fracture from refracture, and bipolar hemiarthroplasty replacement may promote patients who undertake outdoor activities to produce more vitamin D than those who have received ORIF.

Keywords: hip fracture, bipolar hemiarthroplasty replacement and fosamax

INTRODUCTION

The common cause of disability and mortality among the elderly is due to hip fracture (Sattui and Saag, 2014). A review has been shown that industrialized countries have a higher incidence of hip fracture than developing countries with geographic features and extensive statistics throughout the world (Dhanwal *et al*., 2011). The highest hip fracture incidence rates are seen in north Europe and the United States and lowest in Latin America and Africa (Dhanwal *et al*., 2011). However, in Asia countries, including Taiwan, have an intermediate frequency of hip fracture (Dhanwal *et al*., 2011). Particularly, from a nationwide study in Taiwan, the excess mortality is in short-term, not long-term hip fractured patients (Wang *et al*., 2013). Usually, the second fracture increases the excess mortality among patients (Sobolev *et al*., 2015).

The osteoporosis-mediated metabolic bone aberrance in females is twice that of males (Sugerman, 2014), especially in postmenopausal women and those older than 50 years, and they have thinning bones, which then can fracture easily (Sugerman, 2014). However, osteoporosis with fracture frequently goes unrecognized in a clinical setting (Unnanuntana *et al*., 2010). Additionally, fosamax (bisphosphonates) is wildly used to increase bone density, and further decrease spin and hip fracture, especially in postmenopausal women that usually reveal osteoporotic symptoms (Black *et al*., 1996; Cummings *et al*., 1998; Tonino *et al*., 2000).

Although the antifracture efficacy of fosamax in those with osteoporosis is known, the effect of fosamax remains elusive after treatment of a femoral neck fracture. Therefore, further analysis of the refracture and mortality of 508 hip fractured patients with or without fosamax was undertaken. On the other hand, surgical types which included intertrochanteric/ ORIF group, femoral neck/ ORIF group and femoral neck/ bipolar group were also estimated as to frequencies of refracture and mortality rates in these groups. The aim of this study is to investigate the relasionship of hip refractures and mortality, surgical types and anti-osteoporotic therapy by cox regression, in order to inform initiatives for improvements of their health.

MATERIALS AND METHODS

Study subjects

Five hundred and eight patients had first hip fracture after surgery and two hundred and sixteen of these patients who had weekly received fosamax were enrolled in this study. The following first hip fractured patients who

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underwent one of the three procedures (femoral neck/ORIF, intertrochanteric/ORIF and femoral neck/bipolar) and excluded osteoarthritis of the hip and previous fracture involving the lower extremities. Informed consents were obtained from all sample donors in accordance with the Declaration of Helsinki and were obtained at the time of their donation. All of the patients were treated at the Department of Orthopedic Surgery, Changhua Show Chwan Hospital, between 2005 and 2011. Our study is supervised by the Institutional Review Board, Changhua Show Chwan Hospital (number: 1011006).

STATISTICAL ANALYSIS

Chi-square analysis was calculated by using Version 18.0 SPSS software (Chicago, IL, USA) for statistical analysis. Cumulative incidence of refracture and mortality curves were plotted using the Kaplan–Meier method and variables related to cumulative incidence of refracture and mortality were analyzed by using Cox's proportional hazards regression model. A value of $P<0.05$ was considered to be statistically significant.

RESULTS

The elderly, those over sixty-five years old, are more susceptible to mortality than those under sixty-five years, but not refracture

In our data sets for 2005-2011, 261 (63.78%) patients had intertrochanteric fracture and underwent ORIF, 63 (12.40 %) patients had femoral neck fracture and underwent ORIF and 184 (36.22%) patients had femoral neck fracture and underwent bipolar hemiarthroplasty replacement. The frequencies of the elderly's (>65 years old), tumbles and Intertrochanteric/ ORIF group were higher than others, respectively (table 1). Among the mortality of 39 patients, causes included sepsis/septic shock, respiratory complication and cardiovascular complication (table 2). We therefore examined whether the elderly (>65) were more frequent participants with higher refracture and mortality than in the young. As expected, the elderly had a significantly higher mortality rate than the young. Conversely, the young had significantly higher refracture rates than the elderly ($P=0.001$ and $P<0.001$, respectively, table 3). The results indicate that age had a different effect on the refracture and mortality of patients. However, the refracture incidence was not fully ascribed to those over sixty-five years of age in hip fractured patients.

Association of Intertrochanteric/ ORIF patients in which refracture and mortality occurred frequently

It was next investigated whether surgical types could be correlated with refracture and mortality. Interestingly, intertrochanteric/ ORIF and femoral neck / ORIF groups had significantly higher refracture rates than the femoral neck / bipolar group and the intertrochanteric/ ORIF and femoral neck/ ORIF groups had significantly higher death rates than the femoral neck/ bipolar group ($P=0.001$ and $P=0.029$, respectively, table 4). Overall, intertrochanteric/ ORIF and femoral neck / ORIF groups had significantly higher refracture and/or death rates than the femoral neck/ bipolar group ($P=0.001$, table 4). These results show that the ORIF group of surgical types could increase the risk of refracture and death. Additionally, as the above results show, refracture and death of ORIF of surgical types could be correlated with osteoporosis, and without receipt of fosamax therapy ($P=0.019$, table 4).

Table 1: Characteristics of hip fractured patients (intertrochanteric and femoral neck fracture) who underwent open reduction internal fixation (ORIF) and bipolar hemiarthroplasty replacement.

Hip fractured patients (N=508) (%)	
Age (y/o)	
65	119 (23.43)
>65	389 (76.57)
Gender	
Female	294 (57.87)
Male	214 (42.13)
Cause	
Tumble	399(76.25)
Falling	10 (1.91)
Traffic accident	93 (21.84)
Unknown	6 (0)
Style of hip fracture/surgical types	
Intertrochanteric/ORIF group	261 (63.78)
Femoral neck/ORIF group	63 (12.40)
Femoral neck/bipolar group	184 (36.22)

Table 2: The properties of complications in the 39 postoperative deaths.

Complications	Postoperative deaths N=39 (%)
Sepsis/septic shock	13 (33.33)
Respiratory complication	7 (17.95)
Cardiovascular complication	9 (23.08)
Others	10 (25.64)

The hip fractured patients without bipolar hemiarthroplasty replacement or receipt of fosamax therapy had a higher cumulative incidence of refracture and mortality

We next examined whether fosamax therapy and surgery could be associated with incidence of refracture and mortality in hip fractured patients. Kaplan-Meier analysis showed that the cumulative incidence of refracture and mortality were higher for patients who received open reduction internal fixation than patients who received bipolar hemiarthroplasty replacement ($P<0.001$, fig. 1A). Interestingly, cumulative incidence of refracture and

mortality was higher for those without fosamax therapy than those with fosamax therapy (P=0.038, fig. 1B). A multivariate cox regression model was used to examine whether therapy and surgical types could be associated with cumulative incidence of refracture and mortality in hip fractured patients. As shown in table 5, a marginal significance of highly cumulative incidence of refracture and mortality were seen in without therapy patients. (HR: 0.710, 95% CI: 0.455-1.108, P=0.131, table 5). More importantly, patients who received bipolar hemiarthroplasty replacement had the lowest cumulative incidence of refracture and mortality (HR: 0.732, 95% CI: 0.587-0.912, P=0.006, table 5). These results clearly show that fosamax-mediated therapy and bipolar hemiarthroplasty replacement-mediated surgery could be beneficial in decreasing the cumulative incidence of refracture and mortality.

Table 3: The relationship of age, re-fracture and mortality.

	Age (y/o)		p-value
	65 (N=119)	>65 (N=389)	
Re-fracture			
No	85 (71.43)	341 (87.66)	0.001
Yes	34 (28.57)	48 (12.34)	
Death			
No	118 (99.12)	351 (90.23)	<0.001
Yes	1 (0.88)	38 (9.77)	

P value was obtained from x2 test.

DISCUSSION

Based on the Longitudinal National Health Insurance (NIH) database released by the Taiwan National Health Research Institute (NHRI) and covering the years from 1997 to 2011, the results indicate those over the age of 60 years with hip fractures have a significantly increased occurrence of mortality (Wang *et al*., 2013). Interestingly, a review study of the National Surgical Quality Improvement Program database has shown that no differences were found in the mortality rates among the ORIF and HA groups (Fisher *et al*., 2013). But a recent study found hip fractured patients who choose an artificial total hip replacement reveals they have better hip activity and less refracture occurrence than those with internal fixation over a period of seventeen years (Chammout *et al*., 2012). Our results agreed with previous clinical observations, that patients with a bipolar hemiarthroplasty replacement of the femoral neck was faster in their ability to undertake normal activities than open reduction internal fixation that makes hip fractured patients produce more vitamin D when the sun shines on their skin for the health of their bones (Malhotra *et al*., 1995; Schneppendahl *et al*., 2012; Maeda *et al*., 2013; Sakai *et al*., 2015). Interestingly, combining fosamax and vitamin D3 in a single once-weekly tablet has the advantage efficacy for osteoporosis management (Epstein, 2006).

However, osteoporosis is involved in skeletal disorders including low bone density and micro-architectural collapse that cause the increase of fracture; and osteoclast function is critical role for bone graft incorporation after surgical treatment (Goodship *et al*., 1994). For repairing the fractured bone, an anti-osteoporotic agent (such as bisphosphonates) has to be applied to regulate the remodeling phase of the bone. (Goodship *et al*., 1994). In an animal model, it was shown that an anti-osteoporotic agent retrieves glucocorticoid-mediated osteoporosis of an adult zebrafish. (Pasqualetti *et al*., 2015) and also promoted fracture healing in the Brtl/+ mouse model of osteogenesis imperfecta (Meganck *et al*., 2013). These observations in two animal models were consistent with our study, which showed that fosamax will help hip fractured patients in preventing refracture and mortality.

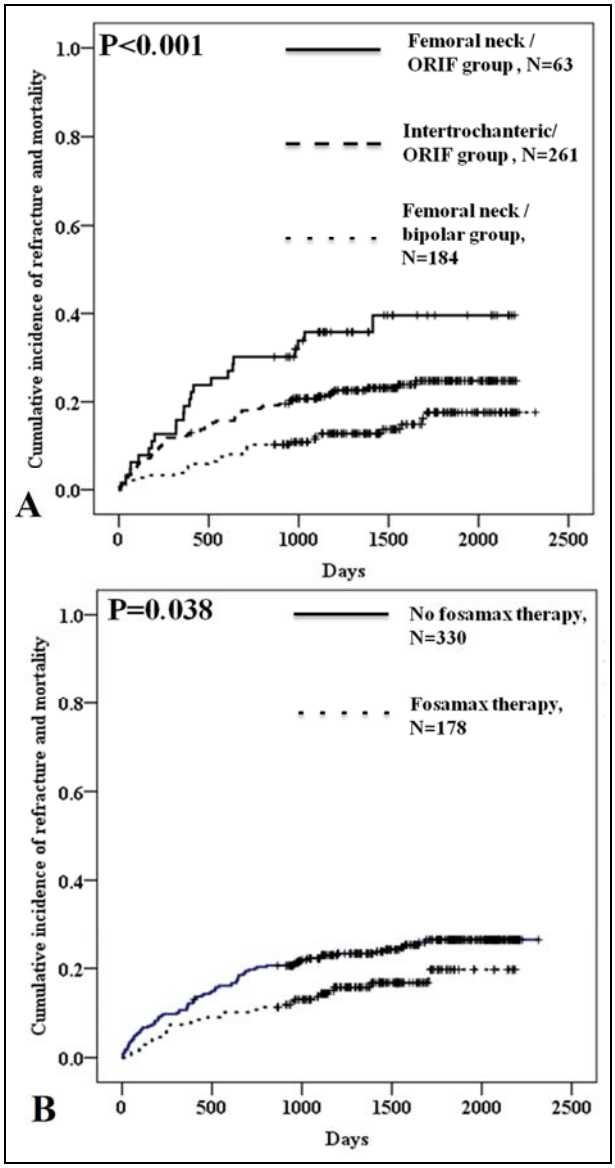

Fig. 1: Kaplan–Meier survival analysis of fosamax therapy and surgical types influence on incidence of refracture and mortality in hip fractured patients.

Table 4: The relationship of hip fracture, refracture and mortality and fosamax therapy.

	Styles of first hip fracture/ surgical types			p-value
	Intertrochanteric/ ORIF group (N=261)	Femoral neck / ORIF group (N=63)	Femoral neck / bipolar group (N=184)	
Refracture				
No	222 (54.02)	42 (41.27)	162 (69.02)	0.001
Yes	39 (45.98)	21 (58.73)	22 (30.98)	
Death				
No	233 (89.27)	60 (95.24)	176 (95.65)	0.029
Yes	28 (10.73)	3 (4.76)	8 (4.35)	
Re-fracture and/or Death				0.001
No	200 (76.66)	40 (63.49)	157 (85.33)	
Yes	61 (23.34)	23 (36.51)	27 (14.67)	0.019
Fosamax therapy (after first hip fracture)				
No	173 (66.28)	49 (77.77)	108 (58.70)	
Yes	88 (33.72)	14 (22.23)	76 (41.30)	

P value was obtained from x^2 test.

Table 5: Multivariate cox regression analysis for potential influence of fosamax therapy and surgical types in refracture or mortality of hip fractured patients.

Variables	Incidence of refracture and/or death				p-value
	Case No.	Median (days)	Incidence (%)	HR (95%CI)	
Fosamax therapy					
No	330	1449	24.8	1	0.131
Yes	178	1325	16.3	0.710 (0.455-1.108)	
Styles of first hip fracture/surgical types					
Femoral neck/ORIF group	63	1111	36.5	1	
Intertrochanteric/ORIF group	261	1412	23.6	0.645 (0.385-1.080)	0.095
Femoral neck/bipolar group	184	1450	14.7	0.732 (0.587-0.912)	0.006

HR: adjusted for the parameters of age and gender.

It's worth noting that fractured surgery that leads to many complications is unusually common, and these complications often depend on whether the fracture is extra capsular or intracapsular. Additionally, osteoporosis treatment, advancement of early mobilization and vitamin D supplementation of the modes in order to avoid falls are recommendations for an optimal rehabilitation of hip fractured patients (Carpintero *et al*., 2014).

In summary, we provide evidence to demonstrate lower refracture and mortality rates due to fosamax therapy or alteration of surgical treatment that occurs among hip fractured patients. We suggest that hip fractured patients should have to undergo the bipolar hemiarthroplasty treatment and also receive fosamax therapy and open reduction internal fixation could be a harmful treatment for osteoporotic patients.

CONCLUSION

The present analysis found differences in the refracture and mortality rates among femoral neck/ORIF, intertrochanteric/ORIF and femoral neck/bipolar in patients. Femoral neck/bipolar demonstrated a lower likelihood of developing respiratory complications compared with intertrochanteric/ORIF and femoral neck/ORIF. Patients who does not meet the criteria undergo ORIF with either cannulated screws or Knowles pins have the poorer mechanical strenght of this implants potentially due to osteoporosis, and these patients tend to have longer period of immobilization and poorer gait function.

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