Different Risk Magnitudes of Femoral Neck and Intertrochanteric Fractures in Thai Women

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Objective: To study the risk factors associated of femoral neck and intertrochanteric fractures in Thai women
Material and Method: A case-control study was conducted in Bangkok and its vicinity between 1997 and 1998 to compare factors related to each type of hip fracture in Thai women. Cases, aged $\geq$ 51 years old, were diagnosed as intertrochanteric or femoral neck fracture and were matched with controls by age and sex. Multinomial logistic regression was performed for significant associated factors.
Results: Recent physical activity and steroid-containing traditional medicine were strongly associated with intertrochanteric fractures (adjusted odds ratio (OR) 0.17 (95% CI: 0.07, 0.42) and 6.50 (95% CI: 1.93,21.82), respectively) when compared to femoral neck fractures. Cerebrovascular accident (CVA) was more related to femoral neck fractures when compared to intertrochanteric fractures (adjusted OR 8.63 (95% CI: 2.28,32.66), and 4.79 (95% CI: 1.19,19.29), respectively).
Conclusion: Intertrochanteric fracture could be minimized more by encouraging physical activities and avoidance of steroid use while the reduction of femoral neck fracture should be achieved more by CVA prevention.

Keywords: Hip Fracture, risk factors, femoral neck, intertrochanter, Thai.

Osteoporotic hip fractures have been increasing worldwide especially in women[1-7]. Most epidemiologic studies combined femoral neck (cervical), intertrochanteric (trochanteric), and subtrochanteric fractures into hip fractures[1-10]. However, these types of fractures differ in many aspects such as incidence of fractures, age of onset, geometry of bone trabeculae, mechanism of injury, treatment, and prognosis[5,11-16].

The studies compared intertrochanteric and femoral neck fractures showed that the ratio of trochanteric fractures to fractures of the femoral neck increased linearly with age in white women[16,17] but not in black women and men[17]. A study of factors related to hip fractures revealed that the patients with intertrochanteric fractures are thinner and older compared to patients with femoral neck fractures because osteoporosis affected largely on trabecular bone[18]. While patients with femoral neck fractures have higher steroid use and impaired functional ability. Hip axis length and decreased bone mineral density in upper part of the femoral neck was also a predictor of femoral neck fractures. Other risk factors such as walking exercise, surgical menopause, current calcium use, alcoholic consumption, and health status are controversial[17].

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The incidence and risks of hip fractures in Thailand have been explored with remaining gap of knowledge on how much differences of the factors related to each type of hip fractures in the country, and pertinent limitation of generalizability to use data from other reports according to racial difference, setting, and risk factors[2,15-19]. Therefore, this study was aimed to determine and compare the factors related to femoral neck and intertrochanteric fractures in Thai women.

Material and Method

This case control study was a sub-study of factors related to hip fractures in Thai women, which had been launched from June 1, 1997 to May 31, 1998 in Bangkok and its vicinity[19]. All participants provided verbal informed consent and the study were approved by The Committee on Human Rights Related to Researches involving Human Subjects, Faculty of Medicine Ramathibodi Hospital and all included trauma centers.

Cases consisted of female patients, aged ≥ 51 years old, who were diagnosed as intertrochanteric or femoral neck fracture, and were admitted in orthopedic wards of 14 hospitals. Subtrochanteric fractures were not included in the study since it accounted for only 2-4% of hip fractures and were highly suspected to have pathological fractures from tumor. The diagnosis was confirmed by orthopaedists and x-ray reports at the time of the study according to ICD-9 code 820.0-820.9. Patients who had pathological hip fracture from tumor, sufficient trauma defined as an accident that forces more than fall from standing, inability to cooperate and no proxy respondents to interview were excluded.

Community controls were neighborhoods of cases, age ≥ 51 years, matched to the cases according to sex, age $\pm$ 5 years, and not being direct relatives of cases. The exclusion criteria of controls were hip fractures, inability to cooperate and no proxy respondents to interview.

The major exposure variable was physical activity which has been shown as having a significant protective effect in previous literatures[19-22]. Physical activities were categorized into recent and past activities in order to represent the production of peak bone mass in the past, and maintenance of peak bone mass at present. The recent activities included walking, walking upstairs, walking on slope, walking with load, performing housework, and laborious work. Each activity was categorized into 4 levels; 0, 1, 2, ≥ 3

times per week. Recent activity scores were calculated from the summation of scores from all activities and were divided into thirtile groups; inactive, active, and very active. For the past physical activity, scores were calculated from levels of performing housework (1-2 scores), doing laborious work (1-4 scores), and sporting (1-2 scores) at age of 18-24, 25-50, and more than age of 50 years. Then the scores were categorized into 3 groups as mentioned in recent activity categories.

Other potential factors related to hip fractures such as age, race, body mass index (BMI), mental status using 10-item Mental test score from the information/orientation section of the Clifton Assessment Procedure (MST score), pre-fracture status, history of falls in a previous year, calcium intake in 1 week period prior to fracture (milligram per day), substance use, alcohol, smoking, underlying diseases, and reproductive history were collected. BMI was categorized into thirtile groups: low, medium, and high. Pre-fracture status was determined by walking ability before hip fractures: independent (subjects could walk by themselves without any help), partially dependent (subjects could walk by themselves with some helps, gait aid or assistants), and totally dependent (subjects could not walk even with any help).

Data collection was composed of interviewer's information, medical records (diagnosis, operation, x-ray, weight and height), and questionnaires. The questionnaires were sent to the central center, Ramathibodi Hospital, where two investigators (PS, PW) checked for completeness and coded data before data entry.

Statistical analysis

The comparative analyses were performed for femoral neck fractures versus controls, and intertrochanteric fractures versus controls. Continuous variables were described using mean $\pm$ standard deviation (SD), and categorical variables were described using frequency and percentage. T-test and Chi-square test were used to compare baseline characteristics between groups for continuous and categorical variables, respectively.

Univariate analysis was performed by using multinomial logit models in order to decrease type I error. Odds ratio (OR) and its 95% confidence interval (CI) of each variable were estimated. Variables that had p-value of less than 0.20 were considered as potential factors and were included in multivariate analysis.

Multivariate analysis was performed by using multinomial logit models. The main exposure variables (physical activity, age, race, and BMI) were forced into the model. The likelihood ratio (LR) test was then used to select other variables to be included in the model. The goodness of fit was checked in the parsimonious model using Hosmer-Lemeshow goodness of fit test. All analyses were performed using STATA version 7.0. P-value less than 0.05 was considered as statistically significant.

Sample size

We set up alpha error = 0.05, the power of the study = 0.8, and ratio of case versus control was 1:1. The proportion of having active physical activity among femoral neck fractures was 0.4, among inter-trochanteric fractures was 0.3, and among controls was 0.6[20]. The sample size estimation was performed using Power and Sample Size Program version 3.0 (Vanderbilt) were 97, and 42, respectively. Therefore, the estimated sample size was 97 in each group.

Results

Sixty hundred and eighty-one women were recruited from Bangkok and its vicinity. There were 231 cases, and 224 community controls matched by age $\pm$ 5 years and sex. One-hundred and fifty-five cases were intertrochanteric fractures and 116 cases were femoral neck fractures. Mean age was about 74 years old. All women were menopause, except one in controls. Nearly 79% were Thai and the rest of them were Chinese. For fracture groups, 97% of intertrochanteric

group, and 94% of femoral neck group fell down on the ground before hip fracture. Eighty-two percent of intertrochanteric fracture and 85% of femoral neck fracture were performed the operation for treatment. Hip fractures occurred in the left side more than the right in femoral neck fracture group (55%) and occurred equally in sides in intertrochanteric group.

The demographic baseline characteristics of women were shown in Table 1. Intertrochanteric fracture group had mean BMI at 22.5 ± 4.1 kg/m^2 compared to 21.9 ± 4.0 kg/m^2 in femoral neck fracture group. Eighty-six percent of intertrochanteric fracture had good mental status compared to 90% in femoral neck fractures.

Regarding walking ability before hip fracture, more independency was found in femoral neck fracture (66.4%) compared to intertrochanteric group (62.6%). Intertrochanteric fracture had lower physical activity scores and lower proportion of active activity in comparison with femoral neck fracture. However, both types of fracture were inactive compared to controls as shown in Table 2. Although the history of fractures at other parts of body and number of falls in a previous year were lower, the proportion of falling was higher in intertrochanteric fracture group than femoral neck fracture.

Drugs and substances used in both types of hip fracture in women were shown in Table 3. Femoral neck fracture group had higher proportion of alcoholic intake, and sedative drug use while intertrochanteric fracture group had higher proportion of smoking, calcium intake, and sedative drug use when compared with each other.

Table 1. Demographic baseline characteristics of cases and controls

Characteristics	Fracture cases		Controls (n = 224)
	Femoral neck (n = 116)	Intertrochanter (n = 115)	
Age (year), mean $\pm$ SD	74.7 $\pm$ 9.6	76.0 $\pm$ 8.5	73.9 $\pm$ 8.4
Race, %			
Thai	72 (62.1)	69 (60.0)	176 (78.6)
Chinese	44 (37.9)	46 (40.0)	48 (21.4)
BMI (kg/m^2), mean $\pm$ SD	21.9 $\pm$ 4.0	22.5 $\pm$ 4.1	23.5 $\pm$ 4.6
Low	44 (37.9)	39 (33.9)	76 (33.9)
Medium	30 (25.9)	32 (27.8)	75 (33.5)
High	42 (36.2)	44 (38.3)	73 (33.6)
Mental status (score), %			
≥ 7	104 (89.7)	99 (86.1)	220 (98.2)
< 7	12 (10.3)	16 (13.9)	4 (1.8)

Table 2. Physical activities and falls in each group

Characteristics	Fracture cases		Controls (n = 224)
	Femoral neck (n = 116)	Intertrochanter (n = 115)	
Activity before fracture, %			
Independent	77 (66.4)	72 (62.6)	178 (79.5)
Partially dependent	38 (32.8)	38 (33.0)	40 (17.9)
Totally dependent	1 (0.9)	5 (4.3)	6 (2.7)
Recent activity, %			
Inactive	69 (59.5)	84 (73.0)	77 (34.4)
Active	29 (25.0)	20 (17.4)	77 (34.4)
Very active	18 (15.5)	11 (9.6)	70 (31.2)
Past activity, %			
Inactive	62 (54.5)	83 (72.1)	85 (37.9)
Active	42 (36.2)	24 (20.9)	66 (29.5)
Very active	12 (10.3)	8 (7.0)	73 (32.6)
Falls in a previous year, %	46 (39.7)	54 (47.0)	67 (29.9)
History of fractures, %	10 (8.6)	9 (7.8)	6 (2.7)

Table 3. Substances and drug uses in case and control groups

Characteristics	Fracture cases		Controls (n = 224)
	Femoral neck (n = 116)	Intertrochanter (n = 115)	
Smoking, %			
Non-smoker	101 (87.1)	98 (85.2)	194 (86.6)
Ex-smoker	14 (12.1)	13 (11.3)	18 (8.0)
Current smoker	1 (0.9)	4 (3.5)	12 (5.4)
Alcohol intake, %			
Non-drinker	98 (84.5)	105 (91.3)	207 (92.4)
Drinker	18 (15.5)	10 (8.7)	17 (7.6)
Calcium intake, %			
Low	44 (37.9)	39 (33.9)	75 (33.5)
Medium	30 (25.9)	32 (27.8)	75 (33.5)
High	42 (36.2)	44 (38.3)	74 (33.0)
Diuretics (%)	8 (7.1)	8 (7.3)	6 (2.7)
Sedatives (%)	6 (5.3)	10 (8.9)	6 (2.7)
Steroid (%)	0	1 (1.1)	1 (0.5)
Antihypertensive (%)	34 (29.3)	32 (28.1)	51 (23.2)
Thyroid (%)	2 (1.7)	2 (1.8)	3 (1.4)
Hormone (estrogen) (%)	0	2 (1.8)	1 (0.5)
Anticonvulsant (%)	0	1 (0.9)	0
Antihistamine (%)	8 (7.0)	7 (6.2)	1 (0.4)
Steroid-containing traditional medicine (%)	9 (7.8)	11 (9.6)	8 (3.6)

Table 4 showed the distribution of underlying diseases and reproductive history. Both types of hip fracture had the same distribution of underlying diseases but intertrochanteric fracture had hypertension and diabetes mellitus more than femoral neck fracture.

Table 4. Underlying diseases and reproductive history according to groups

Characteristics	Fracture cases		Controls (n = 224)
	Femoral neck (n = 116)	Intertrochanter (n = 115)	
Hypertension (%)	47 (40.5)	54 (47.0)	66 (29.5)
Cerebrovascular disease (%)	18 (15.5)	13 (11.3)	5 (2.2)
Diabetes (%)	25 (21.5)	35 (30.4)	38 (17.0)
Thyroid (%)	8 (6.9)	5 (4.3)	4 (1.8)
Kidney disease (%)	8 (6.9)	10 (8.7)	10 (4.5)
Parkinsonism (%)	3 (2.6)	1 (0.9)	1 (0.4)
Cancer (%)	2 (1.7)	5 (4.3)	4 (1.8)
Malabsorption (%)	8 (6.9)	3 (2.6)	7 (3.1)
Cardiovascular disease (%)	10 (8.6)	5 (4.3)	10 (4.5)
Age at menarche (year), mean $\pm$ SD	15.4 $\pm$ 1.7	15.6 $\pm$ 1.9	15.5 $\pm$ 1.8
No. of pregnancy, median (range)	5 (0-14)	4 (0-14)	5 (0-16)
No. of liveborn, median (range)	5 (0-11)	4 (0-13)	5 (0-16)
No. of breast feeding, median(range)	4 (0-11)	4 (0-13)	5 (0-16)
Surgical menopause, %	5 (4.3)	3 (2.6)	8 (3.6)
Age at menopause (year), mean $\pm$ SD	48.2 $\pm$ 4.7	48.1 $\pm$ 4.9	47.5 $\pm$ 5.1
Hormonal replacement therapy, %	1 (0.9)	1 (0.9)	7 (3.1)
Oophorectomy, %	3 (2.6)	4 (3.5)	12 (5.4)

For the reproductive history, average age at menarche was around 15.5 years old in every group, and average age at menopause was 48 years. Median livebirths, children, and breast-feeding were approximately 4-5 in all groups. However, both fractures had lower range of these reproductive histories than controls. After taking age of menarche, menopause, children and breast-feeding into account, the estimate duration of exposure to estrogen was about 20-30 years. Three percent of hip fracture and 5% of controls were performed oophorectomy, but there was only 1-3% receiving hormonal replacement therapy.

The results from univariate analysis were analyzed by comparing each type of fracture with controls. Significant factors related to intertrochanteric fractures were age, race, BMI, mental status, physical activity, history of fracture, calcium intake, sedatives, antihistamine, steroid-containing traditional medicine, hypertension, and cerebrovascular accident (CVA). Most of the factors related to intertrochanteric fracture were associated with femoral neck fracture, except diuretics.

The multivariate analysis was performed by using multinomial logistic regression to compare each type of fracture with controls. After controlling for age, past activity, calcium intake, and age at menarche, the factors related to femoral neck fracture were Chinese race, recent and past physical activity, calcium intake, history of fracture, CVA, diuretics, antihistamine, and low mental status score as shown in Table 5. Factors related to femoral neck fracture were the same as those of intertrochanteric fracture, except diuretics.

Chinese race, history of fracture, CVA, antihistamine, steroid-containing traditional medicine, and low mental status score increased the risk of having both types of hip fracture. The strength of these associations was around 2-4 times compared to reference group, except stronger association for CVA and antihistamine. According to femoral neck fracture, CVA increased risk with adjusted OR 8.63 (95% CI 2.28-32.66) and antihistamine increased risk with adjusted OR 13.87 (95% CI 1.44-133.67) when compared to the reference group. For intertrochanteric fracture, CVA increased risk less than that of femoral neck fracture (adjusted OR 4.79, 95% CI (1.19-19.29)). However, antihistamine produced the same risk of having both types of hip fracture. Diuretic use was significantly related to only femoral neck fracture with adjusted OR 3.95, 95% CI (1.14-13.66). For steroid-containing traditional medicine, the adjusted OR was higher in intertrochanteric group than the other.

Significant preventive factors for hip fracture were recent and past physical activity and calcium

Table 5. Multivariate analysis of factors associated with each type of hip fracture

Factors	Femoral neck vs. controls		Intertrochanter vs. controls	
	OR[a] (95% CI)	p-value	OR[a] (95% CI)	p-value
Race				
Thai*				
Chinese	2.41 (1.32-4.38)	0.004[#]	2.43 (1.13-4.51)	0.005[#]
Recent activity				
Inactive*				
Active	0.44 (0.22-0.86)	0.016[#]	0.21 (0.10-0.44)	<0.001[#]
Very active	0.36 (0.17-0.77)	0.008[#]	0.17 (0.07-0.42)	<0.001[#]
Past activity				
Inactive*				
Active	1.00 (0.55-1.82)	0.982	0.51 (0.26-0.98)	0.044[#]
Very active	0.26 (0.12-0.58)	0.001[#]	0.12 (0.04-0.31)	<0.001[#]
Calcium intake				
Low*				
Medium	0.43 (0.21-0.85)	0.017[#]	0.35 (0.17-0.74)	0.006[#]
High	0.67 (0.35-1.27)	0.223	0.64 (0.33-1.25)	0.199
History of fracture	4.42 (1.32-14.77)	0.016[#]	4.09 (1.12-14.98)	0.033[#]
CVA	8.63 (2.28-32.66)	0.001[#]	4.79 (1.19-19.29)	0.027[#]
Diuretics	3.95 (1.14-13.66)	0.030[#]	3.09 (0.82-11.56)	0.093
Sedatives	1.27 (0.31-5.07)	0.733	2.54 (0.71-9.10)	0.151
Antihistamine	13.87 (1.44-133.67)	0.023[#]	11.63 (1.19-113.12)	0.034[#]
Steroid-containing traditional medicine	3.77 (1.14-12.43)	0.029[#]	6.50 (1.93-21.82)	0.002[#]
Mental status				
Normal*				
Low	8.90 (2.12-37.20)	0.003[#]	11.76(2.83-49.76)	0.001[#]

[a] Multivariate model included age and BMI
* Reference group, [#] p-value < 0.05

intake after controlling for age, BMI, and other factors. Recent physical activity showed dose-response relationship in reducing risk of hip fracture and it had more preventive effect in intertrochanteric fracture than in femoral neck fracture (Table 5). Active recent physical activity decreased the risk of femoral neck fracture by 56% and decreased the risk of intertrochanteric fracture by 79%. Very high recent physical activity reduced the risk of femoral neck fracture by 64% and 83% for intertrochanteric fracture. Past physical activity also significantly reduced the risk of intertrochanteric fracture with dose-response relationship; 49% for active past activity, and 88% for very high past activity. Past physical activity was a significant preventive factor for femoral neck fracture only if it was very high activity by 74% compared to the reference group.

    Calcium intake at medium level significantly reduced the risk of femoral neck and intertrochanteric fracture with adjusted OR 0.43 (95% CI 0.21-0.85), and OR 1.08 (95% CI 0.55-2.10), respectively. High calcium intake did not show any significant relationship.

    After taking the proxy respondents into account, there was no any significant different result.

Discussion

    The factors related to both types of fracture were Chinese race, physical activity, calcium, and history of fracture, CVA, antihistamine, steroid-containing traditional medicine, and mental status. Diuretic use was associated only with femoral fracture. Intertrochanteric fractures were about 2 times more related to physical activity, and steroid-containing traditional medicine. On the other hand, femoral neck fractures were highly associated with diuretic use and CVA when compared to intertrochanteric fractures. There was non-significant relationship between each type of hip fracture and age, BMI, reproductive

history, smoking, and alcohol use. This study was matched by age and most of participants were not obese when compared to the reference group. Our results differ from previous report that intertrochanteric fractures were thinner and older compared to patients with femoral neck fractures, while the patients with femoral neck fractures have higher steroid use and impaired functional ability[17]. Non-significant association of reproductive history, smoking, and alcohol use and each type of hip fracture were consistent with our results[17,20].

Chinese race increased the risk of having each type of hip fractures about 2.4 times. Genetic factors, bone geometry and quality might play important roles as predisposing factors of hip fractures. Chinese race may have longer hip axis length; higher neck shaft angle, wider femoral neck diameter, and lower bone mineral density of femoral neck, intertrochanter, and Ward's triangle when compared to Thai race since these factors were different among race[15,23,24].

Physical activity has been shown that it increased bone mineral density in young age[25], improved muscle strength, and trunk balance especially in postmenopausal women[21]. Some studies have found that the patients who had intertrochanteric fractures were more osteoporotic and had higher incidence of previous fracture[14,18]. Therefore, the effect of physical activity on bone mineral density may substantially influence on intertrochanteric fracture more than femoral neck fracture[20].

Calcium intake was slightly more associated with intertrochanteric fracture than femoral neck fracture. Low calcium level and decreased bone mass effect cancellous bone in postmenopausal and may lead to more intertrochanteric fractures. However, only medium level of calcium intake had significant relationship. High calcium supplement in cases may preclude the effect of high calcium and hip fractures. Fox KM, et al found that calcium intake was not significantly associated with types of hip fracture[17]. Therefore, calcium intake was still a controversial factor related among types of fracture.

CVA affected femoral neck fracture more than intertrochanteric fracture about 2 times, which is consistent with the other study[17].

Diuretic drugs may affect the calcium balance in body and influence both types of hip fracture in the same magnitude. However, after controlling for confounding factor, it was not significantly associated with intertrochanteric fracture. Antihistamine had psychotropic effect and may induce falling leading to hip fractures. Higher number of previous falls may explain higher strength of the association between antihistamine and femoral neck fracture when compared to intertrochanteric fracture. The steroid use affected bone mass by inhibiting osteoblastic activity and osteoclast apoptosis. It may affect cancellous bone more than cortical bone and may not increase the accumulation of unrepaired micro-damage in the femoral neck[17]. Impaired mental status increased the risk of intertrochanteric fracture more than the other. It may reduce functional ability and then decreased bone mass[17].

Although this study tried to find out various factors associated with each type of hip fracture by using a case-control study, it still has some limitations. It is not possible to demonstrate the relationship between age and fractures since it was matched. According to the retrospective design, it confronted with recall bias, measurement bias, and ascertainment bias. However, most of the exposure variables were identified by objective manners such as using portion in milligram of calcium-containing food as pictures, and validating data between patients and proxy respondents. Bone mineral density was not routinely investigated in Thailand at the time of study. It might be the important confounder.

Conclusion

Factor related to femoral neck and intertrochanteric fracture has different magnitude of risk. Femoral neck fracture can be reduced more by prevention of CVA, and prevention of diuretic use. Intertrochanteric fracture can be reduced more if women actively perform recent and past physical activity, and do not use steroid-containing traditional medicine. Further studies on genetics, bone geometry in Thailand may reveal complex association between multi-factorial exposures and each type of hip fractures.

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ความแตกต่างระหว่างปัจจัยเสี่ยงของการเกิดภาวะกระดูกคอสะโพกและกระดูกสะโพกส่วนต้นหักในหญิงไทย

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วัตถุประสงค์: เพื่อเปรียบเทียบปัจจัยเสี่ยงของการเกิดกระดูกสะโพกหักแต่ละชนิดในหญิงไทย

วัสดุและวิธีการ: การศึกษา case-control ในกรุงเทพมหานครและปริมณฑลระหว่าง พ.ศ. 2540-2541 รวบรวมผู้ป่วยอายุ ≥ 51 ปี ที่มีกระดูกคอสะโพกหรือกระดูกสะโพกส่วนต้นหักจับคู่กับกลุ่มควบคุมตามอายุและเพศ วิเคราะห์ข้อมูลแบบ multinomial logistic regression

ผลการศึกษา: พบว่าการออกกำลังกายและการใช้สารสเตียรอยด์มีความสัมพันธ์ กับภาวะกระดูกสะโพกส่วนต้นหักมากกว่า (adjusted OR = 0.17 (95% CI: 0.07,0.42), และ 6.50 (95% CI: 1.93,21.82), ตามลำดับ) การเกิด cerebrovascular accident (CVA) สัมพันธ์กับกระดูกคอสะโพกมากกว่ากระดูกสะโพกส่วนต้นหัก (adjusted OR 8.63 (95% CI: 2.28,32.66), และ 4.79 (95% CI: 1.19,19.29), ตามลำดับ)

สรุป: การออกกำลังกายและการหลีกเลี่ยงการใช้สารสเตียรอยด์ น่าจะสามารถป้องกันกระดูกสะโพกส่วนต้นหักได้มากกว่า และการป้องกัน CVA สามารถลดการเกิดกระดูกคอสะโพกหักได้มากกว่า