Ten years change in post fracture care for hip fracture patients

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Abstract

Purpose

This multi-center, retrospective study aimed to clarify the changes in postoperative care provided by orthopaedic surgeons after hip fractures and clarify the incidence of secondary fractures requiring surgery.

Methods

Subjects were patients with hip fracture treated surgically in seven hospitals during the 10-year period from January 2008 to December 2017. Data on patient demographics, comorbidities, preoperative and postoperative osteoporosis treatments, and secondary fractures were collected from the medical records.

Results

In total, 4764 new hip fractures in 982 men and 3782 women (mean age: 81.3±10.0 years) were identified. Approximately 10% of patients had a history of osteoporosis drug treatment and 35% of patients received postoperative drug treatment. The proportion of patients receiving postoperative drug therapy increased by approximately 10% between 2009 and 2010, 10% between 2010 and 2011, and 10% between 2011 and 2013. Although the rate of secondary fractures during the entire period and within 3 years decreased from 2011, the rate of secondary fracture within 1 year remained at around 2% every year.

Conclusions

The approval of new osteoporosis drugs and the establishment of osteoporosis liaison services have had a positive effect on the use of postoperative drug therapy in the orthopedic field. Our finding that the rate of secondary fracture within 1 year of the initial fracture remained around 2% every year, despite improvements in postoperative drug therapy, suggests that both rehabilitation for preventing falls and early postoperative drug therapy are essential to prevent secondary fractures.

Keywords: hip fracture, secondary fracture, anti-osteoporosis therapy, osteoporosis liaison service

Introduction

Hip fractures are associated with increased morbidity, functional decline, and death in older adults, as well as increased use of health care services in most industrialized countries [1,2]. It is estimated that the number of hip fractures worldwide will rise from 1.7 million in 1990 to 6.3 million in 2050 [3]. In particular, given that three-quarters of the world's population lives in Asia, it is projected that Asian countries will contribute more to the pool of hip fractures in the coming years. By 2050, more than 50% of all osteoporotic fractures will occur in Asia [4,5]. According to a nationwide survey of hip fractures in Japan, the total number of patients who experienced a hip fracture in 2012 was 175,700 (men, 37,600; women, 138,100), which represents an increase from 2007 (total, 148,100; men, 31,300; women, 116,800) [6,7]. The annual costs of medical and nursing care associated with osteoporotic fractures have been estimated to be JPY 797.4 to 989.5 billion (US$7.974 to 9.895 billion; US$1=JPY100) in Japan [8] and are expected to rise in parallel with the increase in the incidence of osteoporotic fractures.

Patients with hip fractures have a 2.5-fold increased risk of secondary fractures compared to age-matched persons without previous fractures [9]. More specifically, patients who have sustained one hip fracture have a higher risk of a contralateral hip fracture compared to the general populations [10], and second hip fractures often occur within 1 year of initial fractures [11,12]. Treatment with anti-osteoporosis drugs is essential for patients after their initial fracture, as a first fracture is the highest risk factor for a second fracture [13,14]. Nevertheless, data suggest that few patients with hip fracture actually received pharmacologic therapy for osteoporosis [15-18]. Therefore, poor persistence with osteoporosis treatments is a global public health problem.

Recently, various anti-osteoporosis drugs have been developed and are available on the market. In Japan, teriparatide (TPD), recombinant human parathyroid hormone (1–34),

and denosumab (DSMAB), a fully human monoclonal antibody that binds the cytokine receptor activator of NFκB ligand (RANKL), were approved in 2010 and 2013, respectively. Additionally, based on the fracture liaison services (FLS) [19,20], a coordinator-based secondary fracture prevention service developed in the United Kingdom, the osteoporosis liaison service (OLS) was established in Japan in 2012 as a comprehensive care system for osteoporosis. On the contrary, in Japan, hip fractures are usually treated by orthopedic surgical procedures and followed with postoperative therapy by the same orthopedic surgeon, not a physician specializing in osteoporosis treatment. Therefore, it is of great importance to assess how postoperative care after hip fracture that is provided by an orthopedic surgeon has changed now that various anti-osteoporosis drugs have been approved and the OLS has been established.

The objectives of this multi-center retrospective study were to investigate the rate of postoperative care change after hip fracture and the incidence of secondary fractures requiring surgery. The hypothesis of this study is that development of anti-osteoporosis drugs and dissemination of knowledge about treatment for osteoporosis among surgeons has improved the treatment rate for bone fragility and the prevention of secondary fractures.

Methods

This study was designed as a retrospective, registry-based, uncontrolled, follow-up study. This study was approved by the local ethics committee at the Hokkaido University Hospital (017-0448) and by each participating hospital. A total of 4803 hip fracture patients treated with surgery at seven hospitals that function as base hospitals in regional cities in Hokkaido prefecture in Japan during the 10-year period from January 2008 to December 2017 were included. Data were collected from medical records. Thirty-nine patients who were younger than 50 years were exclude. Finally, 4764 patients (male, 982; female, 3782)

were included in this current study. Three of the seven hospitals carried out OLS.

Data on patient demographics including age, sex, and body mass index (BMI), comorbidities including diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), malignant tumor, and rheumatoid arthritis, and glucocorticoid use, preoperative medical history for osteoporosis drugs including bisphosphonate (BP), selective estrogen receptor modulator (SERM), TPD and DSMAB, and calcium (Ca) or active vitamin D3 preparation at surgery were collected from their medical records. Data on postoperative osteoporosis treatment, osteoporosis inspection (dual energy x-ray absorptiometry), outpatient visits after discharge, the occurrence of a secondary fracture (contralateral hip fracture, distal radial fracture and proximal humerus fracture) requiring surgery, and follow-up period after the initial surgery were also collected from medical records.

Chi-squared or independent t-tests were used to compare differences in subject demographics. The incidence of secondary fracture was estimated by the Kaplan-Meier method, and differences were investigated by the log-rank test among the patients who could be followed. All statistical analyses were performed using SPSS Statistics version 23.0 (IBM Corporation, Armonk, NY) with a significance level set at 0.05.

Results

Patient demographics and osteoporosis care during the whole period

In this study, the number of the hip fractures treated with the surgery in this study gradually increased during the entire period (Fig.1). Table 1 shows a summary of patient demographics. Male patients with hip fracture were significantly younger than the female patients ($P<0.001$). A significantly higher proportion of male patients experienced COPD and malignant tumors compared to female patients ($P<0.001$). In contrast, a significantly higher proportion of female patients experienced rheumatoid arthritis (RA) compared to male

patients (P=0.024). Preoperatively, 8.4% of patients underwent osteoporosis drug therapy and 6.3% took active vitamin D3 or Ca preparations. Postoperatively, 13.0 % of patients underwent osteoporosis inspection, 34.2% underwent osteoporosis drug therapy, and 12.6% took active vitamin D3 or Ca preparations. A significantly lower proportion of male patients underwent preoperative and postoperative inspection and therapy compared to female patients (P<0.001). Postoperatively, 35.7% of patients attended outpatient visits after discharge, 4.1% sustained a secondary fracture, and 2.0% had a secondary fracture within 1 year of the initial fracture. The mean follow-up period was 25.8 months. There were no significant differences in these parameters between male and female patients.

Patients who underwent preoperative drug therapy were older than those who did not (P<0.001) (Table 2). Significantly more patients who underwent preoperative osteoporosis drug therapy experienced RA and used glucocorticoid steroids (GCs) compared to those who did not (P<0.001). The proportion of patients who underwent postoperative osteoporosis inspection, took active vitamin D3 or Ca preparations, and attended outpatient visits after discharge was higher in patients who received preoperative drug therapy compared to those who did not (P<0.001). Although 1278 patients of 4360 patients (29.3%) who did not receive preoperative therapy started drug therapy postoperatively, 51 patients of 404 patients (12.2%) who received preoperative therapy did not continue drug therapy. No differences in the incidence of secondary fracture and secondary fracture within 1 year and 3 years, or the duration between the initial and secondary fractures were found in patients who underwent preoperative drug therapy and those who did not.

Changes in postoperative osteoporosis care over time (2008-2017)

The proportion of patients who received postoperative osteoporosis drug therapy increased by approximately 10% from 2010 (when TPD was approved), 2011 and 2013 (when DSMAB was approved) compared with their proportion in the preceding (Fig. 2). The

proportion of patients who received preoperative osteoporosis drug therapy was around 5%. The majority of the postoperative drug therapy involved BP (over 80%) (Fig. 3). The proportion of TPD and DSMAB administration increased slowly after approval. On the conntrary, the proportion of postoperative osteoporosis inspection and outpatient visits after discharge increased gradually from 2014 (Fig. 2). The proportion of patients who took Ca or active vitamin D3 was 5%-10% until 2012, increased gradually and reached around 20% in 2017. One hospital started OLS from 2012 and the other two hospitals stared it from 2015. There were totally 1295 patients who received OLS. The hospitals operating OLS exhibited higher proportion of postoperative therapy compared to those without OLS (Fig. 4).

Efficacy of postoperative osteoporosis drug therapy

Patients who received postoperative drug therapy were significantly more likely to have received preoperative drug therapy and take Ca or active vitamin D3 preparations compared to those who did not receive postoperative drug therapy (Table 3). Of the 1631 patients who received postoperative osteoporosis drug therapy, 509 patients (31.2%) underwent postoperative inspection, and 728 patients (44.6 %) attended outpatient appointments after discharge. These proportions were significantly higher compared to patients who did not receive postoperative drug therapy. On the contrary, no significant differences in the occurrence of secondary fractures, occurrence of secondary fractures within 1 year of the initial fracture, or duration between initial and secondary fractures were noted in patients who had received postoperative drug therapy and those who had not.

The 120-month cumulative incidence of secondary fracture was estimated to be 23.9% in patients with postoperative therapy and 32.5% in those without postoperative therapy, with a difference between the two groups, albeit not statistically significant (P=0.057, log-rank test) (Fig. 5). Although the prevalence of secondary fractures during the whole period and within 3 years of initial surgery decreased from 2011, the prevalence of

secondary fractures occurring within 1 year was around 2% every year (Fig. 6). No significant differences in the occurrence of secondary fractures, occurrence of secondary fractures within 1 year of the initial fracture, or duration between initial and secondary fractures were found in patients who had received postoperative Ca or active vitamin D3 preparations and those who had not.

Discussion

This multicenter retrospective study addressed the changes in approaches to postoperative osteoporosis treatment. The finding of this current study that the total number of hip fractures increased over 10 years is consistent with the overall trend of increase due to the aging population in Japan [21]. Although the majority of the postoperative drug therapy involved bisphosphonate over the whole period, the proportion of patients undergoing postoperative drug therapy and inspection and the number of patients attending outpatient visits after discharge increased gradually. Considering that the proportion of the secondary fracture within 3 years clearly decreased from 2011, when the proportion of the postoperative drug therapy got increased, the improvement of the postoperative therapy could be considered to have a positive effect for preventing the secondary fracture.

The increase in the proportion of drug therapy demonstrated in this study is consistent with the recent Japanese report [22], suggesting that orthopedic surgeons are promoting awareness of osteoporosis interventions after the first fragility fractures much better. In North America, several studies have recommended that the orthopedic surgeon directly treating the fracture should perform a BMD examination and forward the results to the primary care physician following the course of osteoporosis treatment [23-25]. Additionally, Miki et al. showed improved rates of early osteoporosis drug treatment following hip fractures when osteoporosis education was initiated by the treating orthopedic

surgeon while the patient is still in the hospital and the treatment is initiated in an orthopedic osteoporosis clinic [25]. The main limitation of this multicenter retrospective therapy was that the time of starting OLS and insurance medical treatment system, such as on diagnosis procedure combination system, vary with each hospital. The finding of this study that almost all postoperative therapy in the entire period was BP and TPD and DSMAB might not contribute directly to the increase in postoperative therapy as expected might be affected by the medical care system in Japan. However, considering that the rates of postoperative osteoporosis drug therapy increased by approximately 10% in 2010, 2011, and 2013 and the differences in the proportions of postoperative therapy between hospitals with and without OLS, the approval of new osteoporosis drugs and the establishment of OLS programs could have a further positive effect on the administration of postoperative drug therapy in patients with the hip fracture. The finding of this study that the proportion of the postoperative osteoporosis inspection has risen since 2014 could also be considered to be the effect of OLS.

Our finding that postoperative drug therapy showed a trend to reduce the secondary fracture is consistent to the previous prospective cohort studies about the efficacy of bisphosphonate for preventing a secondary hip fracture [26,27]. Because less than half of the patients who received postoperative drug therapy attended outpatient visits after discharge in this study, the discrepancy of efficacy for preventing the secondary fracture between this study and these previous prospective cohort studies might be explained by the differences in follow-up rate, as well as the study design. More specifically, the proportion of patients undergoing postoperative drug therapy was higher than the proportion of patients who attended outpatient appointments after discharge between 2011 and 2013, suggesting that the continuation of postoperative drug therapy might be more difficult in Japan compared to in the immediate postoperative period. Because the prescription of anti-osteoporosis therapy medications in rehabilitation hospitals is limited in Japan, modification of the care system as

well as osteoporosis education for orthopedic surgeons might be necessary for prevention of secondary fractures.

Our finding that half of patients with a secondary fracture experienced that fracture within 1 year of the initial hip fracture is consistent with the previous reports about the incidence of secondary hip fracture [28-30]. The reason for the transient marked increase in risk is not known, but immobilization and impaired coordination are potential factors [31,32]. In contrast, our finding that the rate of secondary fracture within 1 year after the initial fracture remained around 2% every year, regardless of improvements in postoperative drug therapy, is contrary to the conclusion of the recent large cohort studies that reported immediate treatment after initial fracture can prevent a higher number of new fractures compared to when treatment is delayed [33,34]. The discrepancy between this current study and other reports might be explained by a limitation of this study that we did not include all secondary fractures, but only those treated surgically. Considering Lyles's report that there was no difference in new hip fracture occurrence within 1 year of the surgery [26], rehabilitation for preventing fall in addition to early postoperative drug therapy after surgery is essential for secondary fracture prevention.

Several other limitations need to be considered when interpreting the results of this study. First, in this study, patients who received BP therapy were not divided according to alendronate, risedronate, minodronate, ibandronate, and zoledronate therapy. Given the possibility of differences in adherence and absorptivity of each drug, future studies should address the efficacy and adherence of each individual drug. Second, because all data were collected retrospectively from medical records, adherence to therapy could not be investigated. Third, other secondary fragility fractures such as distal radius, proximal humerus, and lumbar vertebrae fractures that do not require surgery were not investigated. Therefore, future prospective studies that focused on specific therapies might be necessary.

Fourth, this study did not include dementia as a comorbidity. Dementia has reported to be a strong risk factor for hip fracture. In addition, the presence of dementia is expected to disturb the follow-up, nutritional instruction, and treatment compliance in osteoporotic patients. Fifth, although the participating hospitals were main hospitals in their cities, patients who received therapy from other hospitals in the same area may have been included.

Conclusion

Over the study period, the proportion of patients receiving postoperative drug therapy and inspection, and attending outpatient visits after discharge increased gradually in the north side of Japan. The approval of new osteoporosis drugs and establishment of OLS programs could have a further positive effect on postoperative drug therapy in the orthopedic field. Our finding that the proportion of secondary fractures within 1 year of the initial fracture remained around 2% every year, despite improvements in postoperative osteoporosis drug therapy, suggests that rehabilitation for preventing falls as well as early postoperative drug therapy after surgery, are essential for secondary fracture prevention.

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Table 1 Summary of patient demographics, comorbidities, and preoperative and postoperative treatment according to sex

	Total (N=4764)	Male (N=982)	Female (N=3782)	P-value
Age (years)	81.3 (10.0)	78.0 (10.6)	82.2 (9.6)	<0.001
BMI (kg/m^2)	21.1 (3.9)	21.2 (3.5)	21.1 (4.0)	0.486
Comorbidities				
DM	981 (20.6%)	210 (21.4%)	771 (20.4%)	0.490
CKD	1094 (23.0%)	232 (23.6%)	862 (22.8%)	0.580
COPD	213 (4.5%)	71 (7.2%)	142 (3.7%)	<0.001
Malignant tumor	585 (12.3%)	171 (17.4%)	414 (10.9%)	<0.001
RA	133 (2.8%)	17 (1.7%)	116 (3.1%)	0.024
GC use	136 (2.8%)	20 (2.5%)	116 (3.1%)	0.084
Preoperative				
Osteoporosis drug therapy	404 (8.4%)	26 (2.6%)	378 (10.0%)	<0.001
Ca or active Vit.D3 preparations	301 (6.3%)	29 (3.7%)	272 (7.2%)	<0.001
Postoperative				
Osteoporosis inspection	617 (13.0%)	96 (9.8%)	521 (13.8%)	0.001
Osteoporosis drug therapy	1631 (34.2%)	241 (24.5%)	1390 (36.8%)	<0.001
Ca or active Vit.D3 preparations	599 (12.6%)	79 (8.0%)	520 (13.7%)	<0.001
Outpatient visits after discharge	1701 (35.7%)	330 (33.6%)	1371 (36.3%)	0.123
Secondary fx	194 (4.1%)	37 (3.8%)	157 (4.1%)	0.585
Secondary fx within 3 years	145 (3.0%)	30 (3.1%)	115 (3.0%)	0.981
Secondary fx within 1 year	97 (2.0%)	23 (2.3%)	74 (2.0%)	0.516
Duration between fxs, (months)	21.1 (22.3)	14.9 (23.3)	22.6 (16.2)	0.061

BMI, body mass index; Ca, calcium; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; RA, rheumatoid arthritis; GC, glucocorticoid steroid; Vit.D3, vitamin D3; fx, fracture.

Table 2 Summary of patient demographics, comorbidities, and preoperative and postoperative treatment according to use of preoperative osteoporosis drug therapy

	Preoperative (+) (N=404)	Preoperative (-) (N=4360)	P-value
Age (years)	83.3 (8.1)	81.2 (10.1)	<0.001
BMI (kg/m^2)	20.9 (4.1)	21.2 (3.3)	0.214
Comorbidities			
DM	64 (15.8%)	917 (21.0%)	0.014
CKD	90 (22.3%)	1004 (23.2%)	0.732
COPD	23 (5.7%)	190 (4.4%)	0.214
Malignant tumor	53 (13.1%)	532 (12.2%)	0.591
RA	27 (6.7%)	106 (2.4%)	<0.001
GC use	27 (6.7%)	109 (2.5%)	<0.001
Postoperative			
Osteoporosis inspection	87 (21.5%)	530 (12.2%)	<0.001
Osteoporosis drug therapy	353 (87.8%)	1278 (29.3%)	<0.001
Ca or active Vit.D3 preparations	120 (29.7%)	479 (11.0%)	<0.001
Follow-up	180 (44.6%)	1521 (34.9%)	<0.001
Secondary fx	19 (4.7%)	175 (4.0%)	0.504
Secondary fx within 3 years	18 (4.5%)	127 (2.9%)	0.084
Secondary fx within 1 year	13 (2.3%)	84 (2.0%)	0.338
Duration between fxs (months)	13.0 (11.9)	22.0 (23.0)	0.098

BMI, body mass index; Ca, calcium; DM, diabetes mellitus; CKD; chronic kidney disease, COPD, chronic obstructive pulmonary disease; RA, rheumatoid arthritis; GCs, glucocorticoid steroid; Vit.D3, vitamin D3; fx, fracture.

Table 3 Summary of patient demographics, comorbidities, and preoperative and postoperative treatment according to use of postoperative osteoporosis drug therapy

	Postoperative (+) (N=1631)	Postoperative (-) (N=3133)	P-value
Preoperative			
Osteoporosis treatment	353 (21.6%)	51 (1.6%)	<0.001
Ca or active Vit.D3 preparations	168 (10.3%)	133 (4.2%)	<0.001
Postoperative			
Osteoporosis inspection	509 (31.2%)	108 (3.4%)	<0.001
Outpatient visits after discharge	728 (44.6%)	973 (31.1%)	<0.001
Secondary fx.	58 (3.6%)	136 (4.3%)	0.191
Secondary fx within 3 years	49 (3.0%)	96 (3.1%)	0.909
Secondary fx within 1 year	31 (1.9%)	66 (2.1%)	0.687
Duration for secondary fx, month	17.5 (18.9)	22.9 (23.5)	0.135

BMI, body mass index; Ca, calcium; DM, diabetes mellitus; CKD; chronic kidney disease, COPD, chronic obstructive pulmonary disease; RA, rheumatoid arthritis; GCs, glucocorticoid steroid; Vit.D3, vitamin D3; fx, fracture.

Figure legends

Fig. 1 Longitudinal numbers of the hip fracture cases during the whole period

White circle, total patient number; black square, male patient number; black circle, female patient number.

Fig. 2 Longitudinal trends in postoperative osteoporosis care during the whole period

Black circle, proportion of patients who received preoperative drug therapy; white circle, proportion of patients who received postoperative drug therapy; square, proportion of patients who received postoperative inspection; triangle, proportion of patients who attended outpatient appointments after discharge.

TPD; teriparatide, OLS; osteoporosis liaison service.

Fig. 3 Longitudinal trends in postoperative osteoporosis drug therapy during the whole period

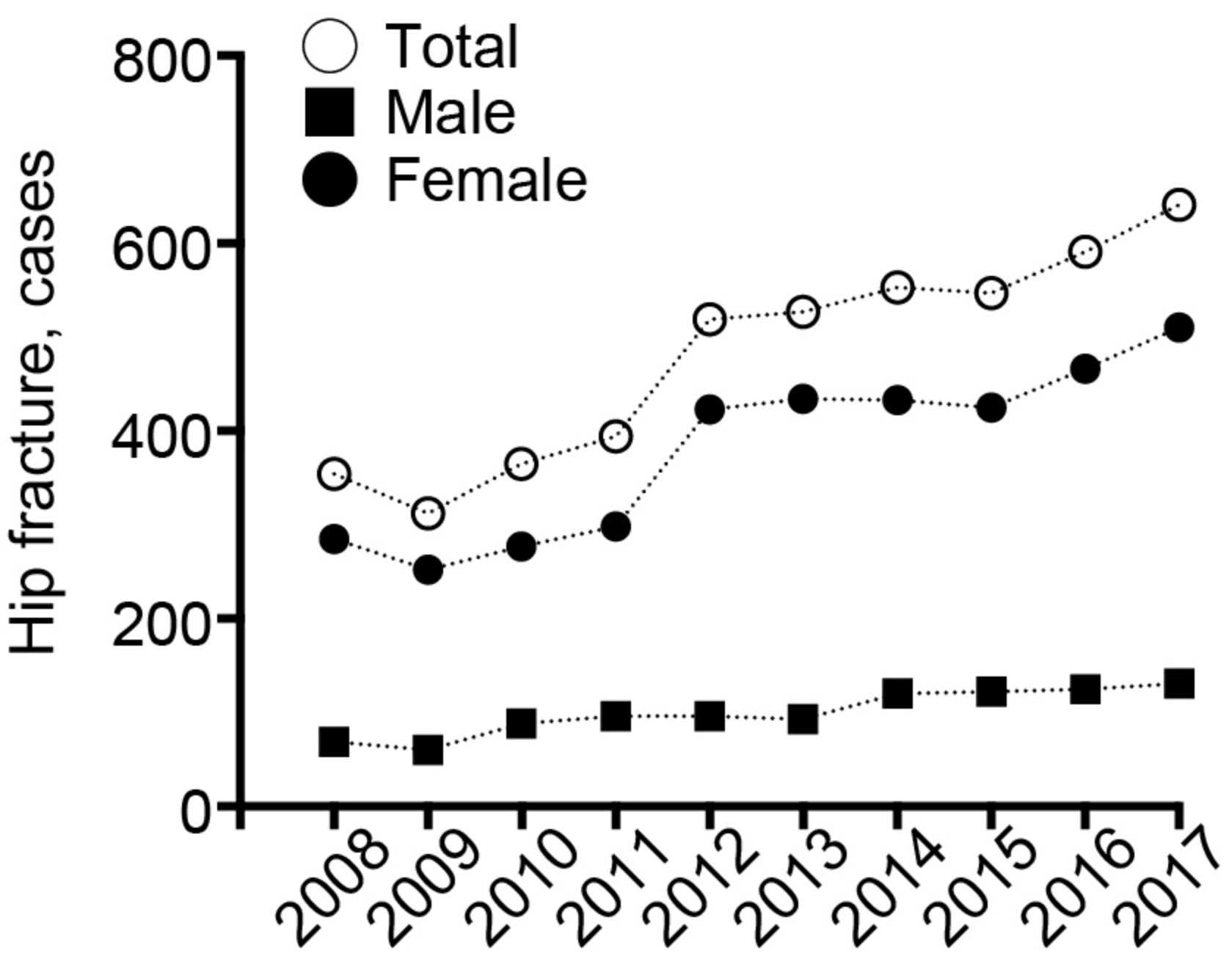
Black circle, proportion of patients who received postoperative bisphosphonate (BP) therapy; white circle, proportion of patients who received postoperative selective estrogen receptor modulator (SERM) therapy; square, proportion of patients who received postoperative teriparatide (TPD) therapy; triangle, proportion of patients who received postoperative denosumab (DSMAB) therapy.

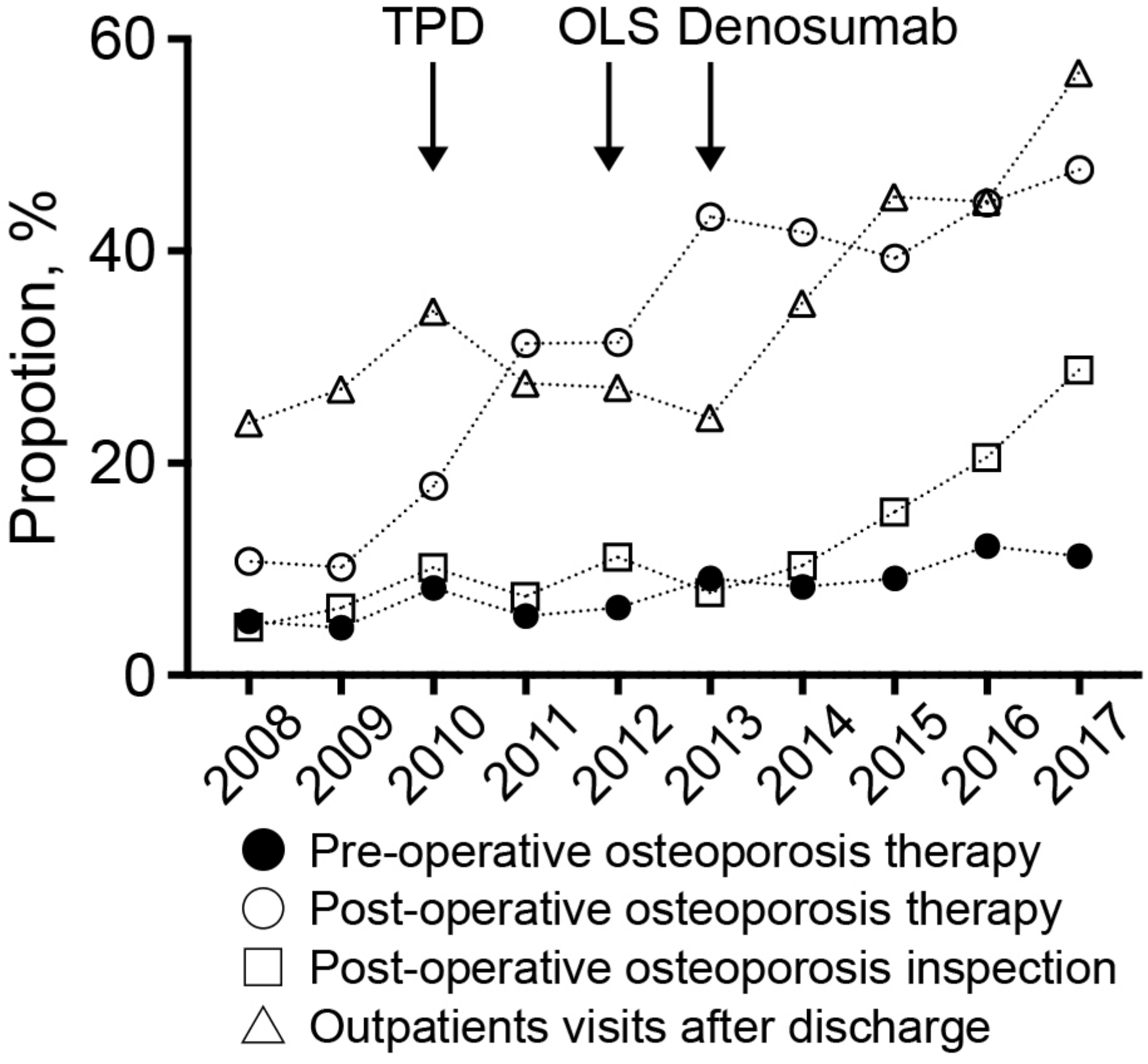
Fig. 4 Longitudinal trends in the proportion of the postoperative therapy between hospitals with and without OLS. OLS; osteoporosis liaison service

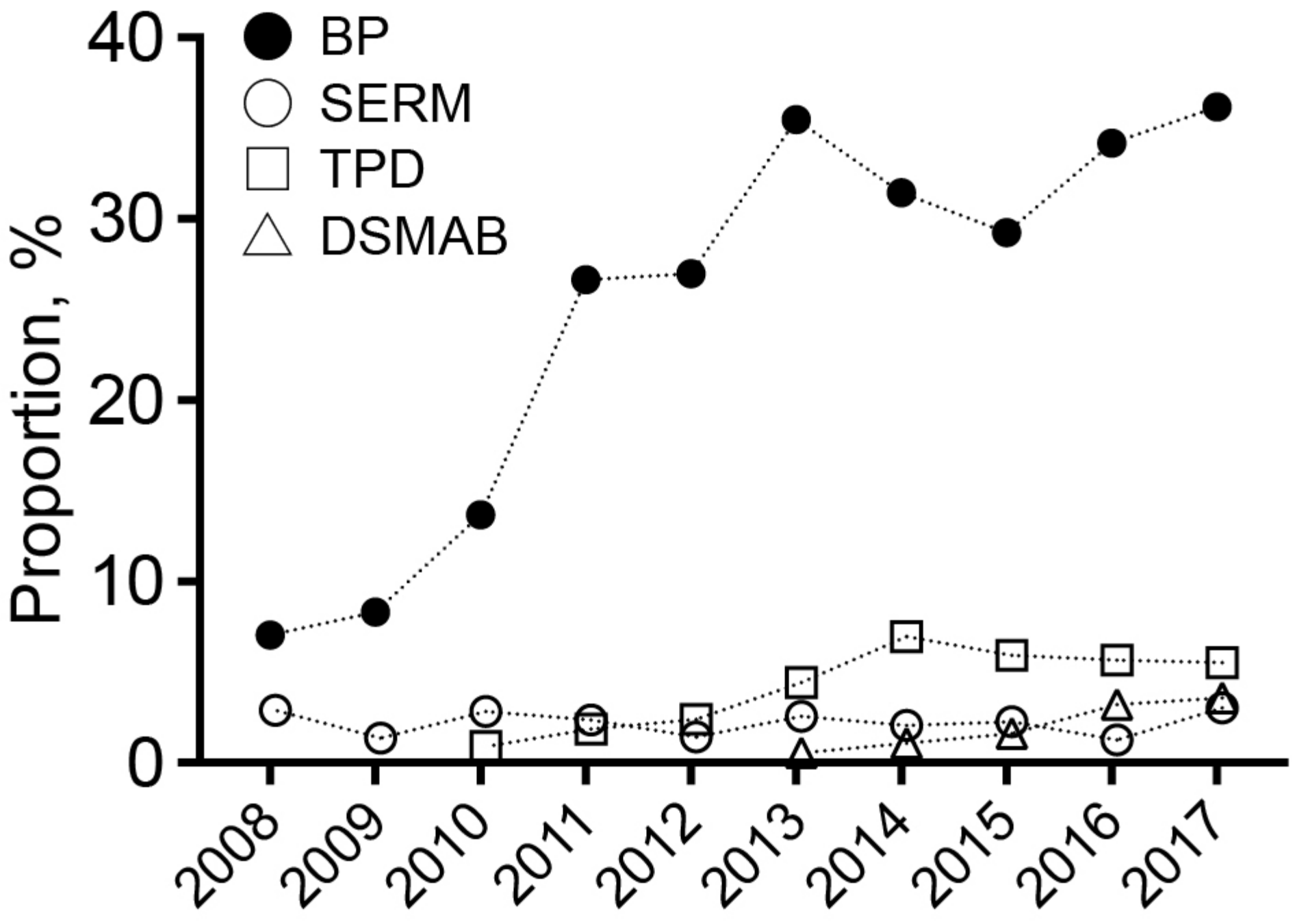
Fig. 5 Kaplan–Meier curves for the occurrence of secondary fracture between patients with and without postoperative therapy

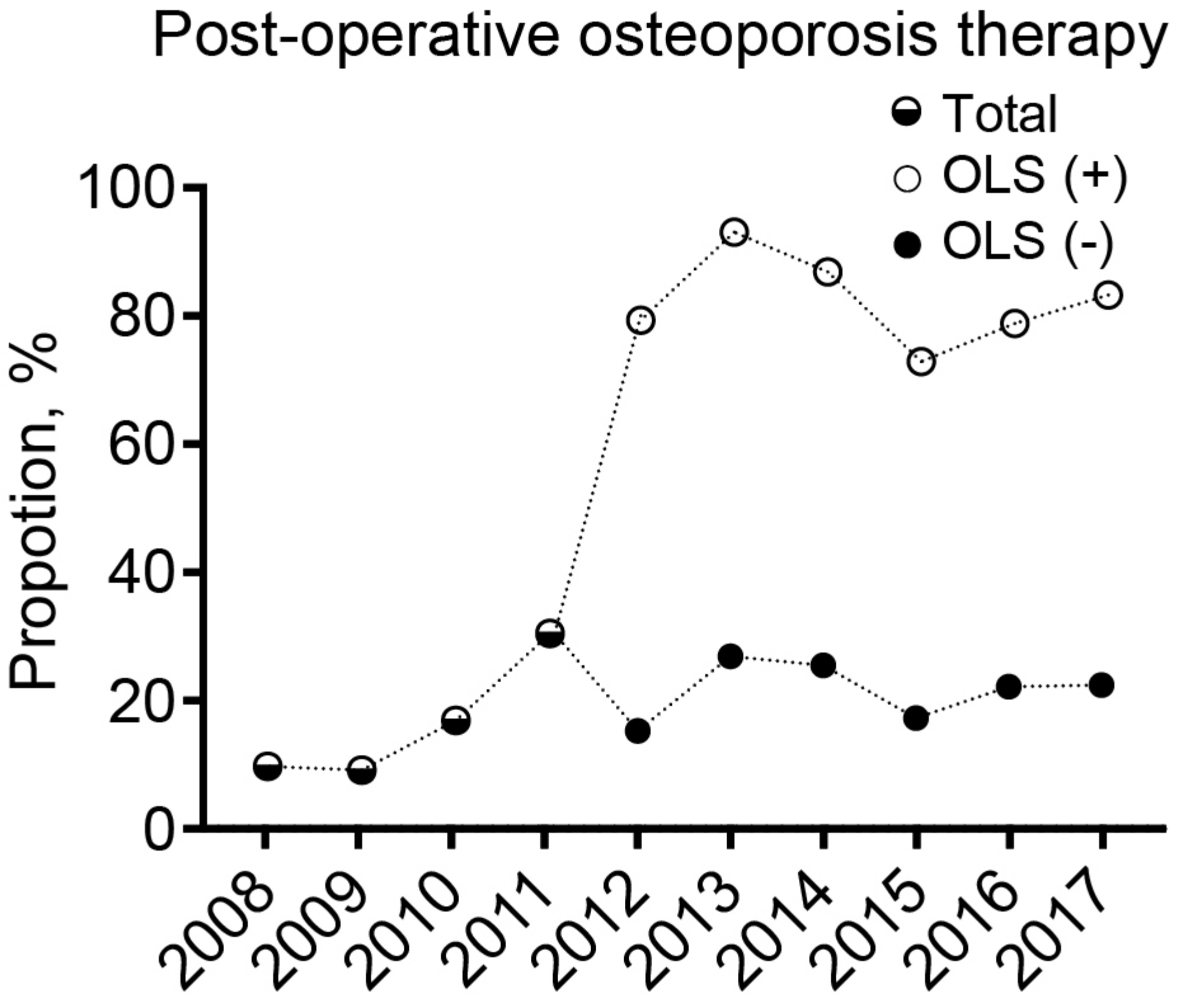
Fig. 6 Longitudinal trends in secondary fractures during the whole period

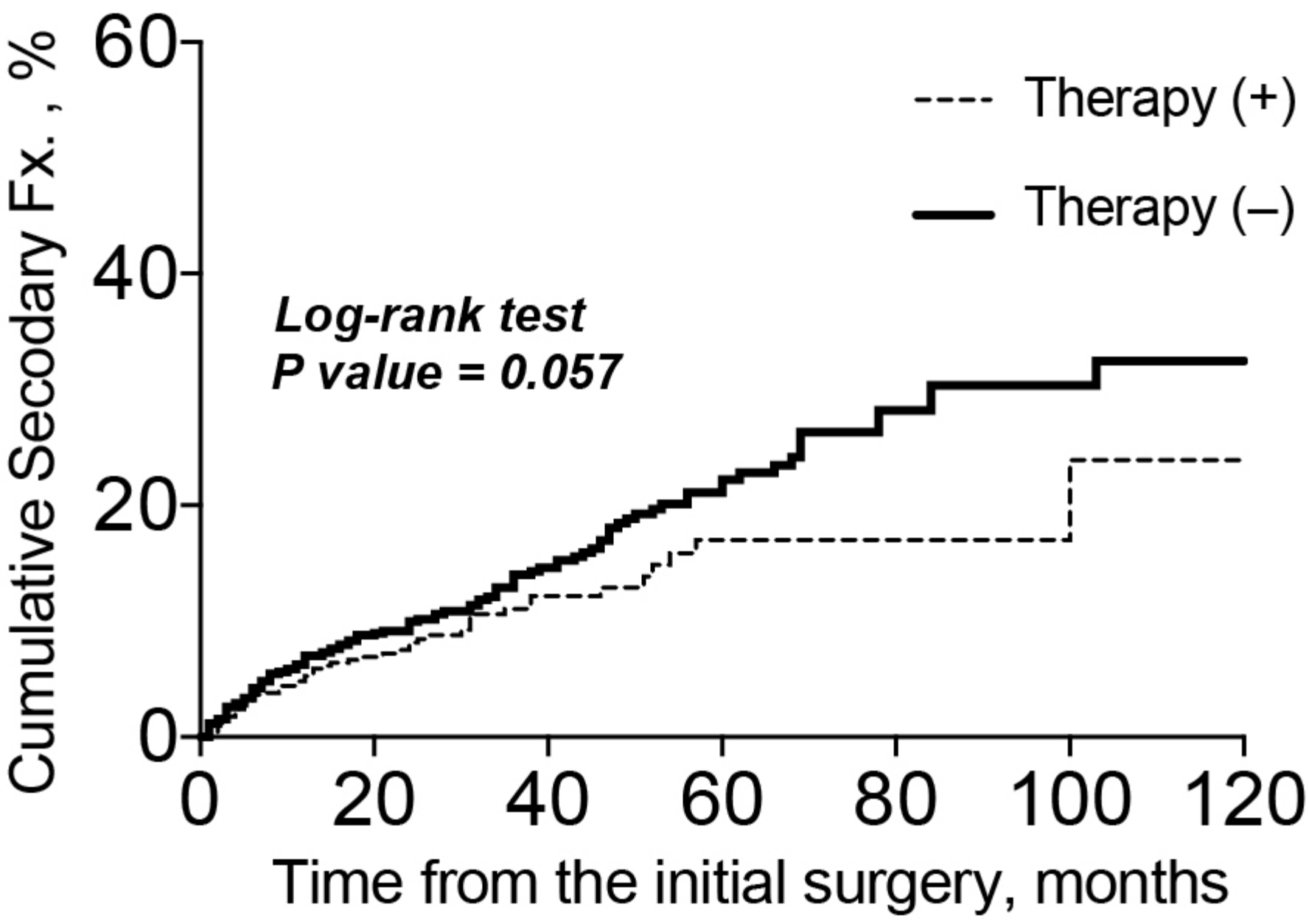
White circle, proportion of patients who sustained a secondary fracture; white square proportion of patients who had a secondary fracture within 3 years of the initial hip fracture; black circle, proportion of patients who suffered a secondary fracture within 1 year of the initial hip fracture. Fx, fracture

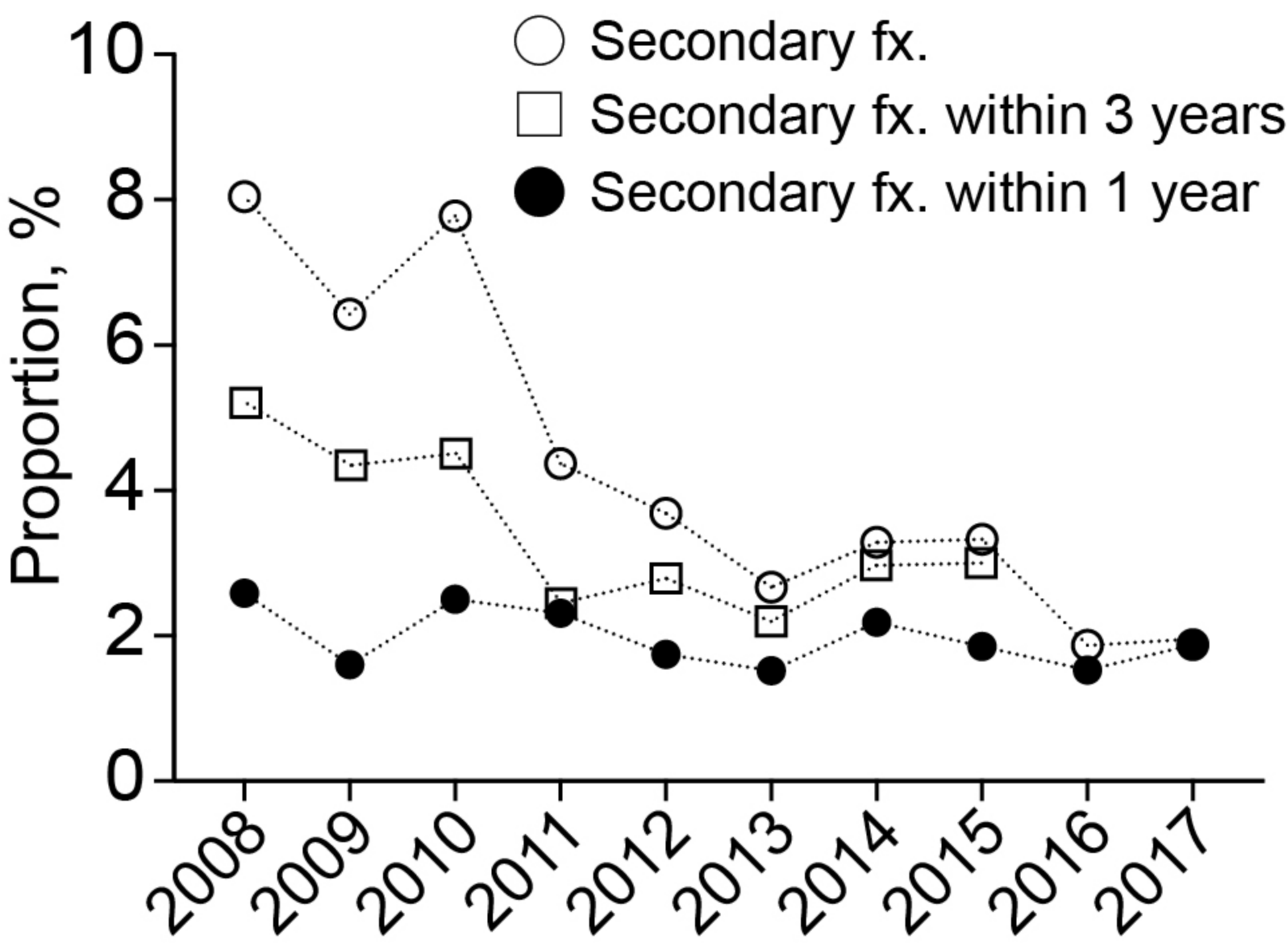

Total
Male
Female
Hip fracture, cases
800
600
400
200
0
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017


TPD
OLS
Denosumab
60
40
20
0
Propotion, %
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Pre-operative osteoporosis therapy
Post-operative osteoporosis therapy
Post-operative osteoporosis inspection
Outpatients visits after discharge


BP
SERM
TPD
DSMAB
Proportion, %
40
30
20
10
0
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017


Post-operative osteoporosis therapy
Total
OLS (+)
OLS (-)
Propotion, %
100
80
60
40
20
0
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017


Cumulative Secodary Fx. , %
60
40
20
0
Therapy (+)
Therapy (–)
Log-rank test
P value = 0.057
0
20
40
60
80
100
120
Time from the initial surgery, months


Secondary fx.
Secondary fx. within 3 years
Secondary fx. within 1 year
Proportion, %
0
2
4
6
8
10
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017