Treatment pattern of osteoporosis in postmenopausal women using OMOP CDM

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Background

Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture (1). It is more likely to occur in postmenopausal women. Osteoporosis treatment is classified into antiresorptive, osteoanabolic and dual-action drugs (2). Antiresorptive agents include selective estrogen receptor modulators (SERMs), bisphosphonates (BPs), and denosumab. Osteoanabolic agents contained recombinant human parathyroid hormone 1-34 (rhPTH). The dual-action agent is romosozumab.

Denosumab, a novel anti-osteoporosis drug, is known to provide better adherence than BPs (3). However, changes in routine clinical practice remains elusive. To provide further evidence to support the scheme in clinical practice, it is crucial to identify patterns of sequential therapy for osteoporosis in the real world.

In this study, we aim to evaluate changes in the treatment patterns of osteoporosis treatment in postmenopausal women over the past decade following the approval (2017) and insurance coverage (2019) of denosumab, a novel anti-osteoporosis drug. To compare the effectiveness of denosumab and BPs, we estimate osteoporotic fracture risk according to treatment change.

Methods

This was a retrospective, observational cohort study across 3 tertiary hospitals in South Korea. Two analyses were conducted: 1) Treatment pathways to evaluate the changes in the treatment pattern of osteoporosis and 2) Comparative effectiveness analysis to estimate osteoporotic fracture risk.

For treatment pathway analysis, the osteoporosis cohort comprised women 50 years or older with osteoporosis. Given that denosumab was approved in 2017 and covered by national insurance since 2019 in South Korea, we divided the cohorts into years of diagnosis (before 2017, from 2017 to 2018, after 2019). We defined patients receiving SERM, BPs (dose type, PO or IV), denosumab, rhPTH and romosozumab after the first diagnosis of osteoporosis as each medication cohort. Maximum duration of 180 days between medication prescription was allowed to verify persistence of drug exposure.

The sequence of medicine taken by each patient was extracted from the database during the post index time window, ordering them by exposure to the medicine as events. We aggregated the sequences for patients into summary statistics and visualized them as sunburst plots.

For comparative effect estimation, patient with osteoporosis aged over 50 years women who were first-

line users of denosumab and BPs were divided into target and comparator cohorts, respectively. The index date was defined as the date of osteoporosis treatment initiation. A 210-day gap between consecutive prescriptions was allowed at the end of the treatment duration. The primary outcome was the 2-year risk of osteoporotic fractures. For the sensitivity analysis, we set up the on-treatment times of risk.

We performed 1:1 propensity score (PS) matching to reduce potential confounding between the target and comparator cohorts. The covariates were used including age, race, ethnicity, year of cohort entry, all recorded medications, medical history, procedures performed, measurement values, devices, the Charlson Comorbidity Index score, and Diabetes Comorbidity Severity Index (DCSI) in the year and a month prior to the index date. PSs were estimated using L1 regularized logistic regression tuned by 10-fold cross-validation. After Matching, cox proportional hazard models were fitted to estimate the hazard ratios (HRs) and 95% CIs. The subgroup analysis was performed by dose type of BPs (PO or IV).

Results

Among 46,170 postmenopausal women with osteoporosis, 25,551 (55.3%) patients were enrolled in treatment pathways. Based on diagnosis year, 20,502 patients were included before 2017, 11,206 between 2017-2018, and 14,462 after 2019; 12,549 (61.2%), 5,464 (48.8%), and 7,538 (52.1%) of patients were enrolled, respectively.

Figure 1 shows the treatment pathways for the four osteoporosis medication combinations of all cohorts. BPs) were the most used medication (68.3%) in 2012-2016 but with gradual increase of denosumab use and decrease of BPs use, denosumab became the most common medication (44%) in 2019-2021. The most common second-line medication after BPs was denosumab, while the most common second-line medication after denosumab was BPs.

A total of 3,737 user of denosumab and 14,792 users of BPs. After PS matching, 1,133 patients were included from each cohort in primary analysis. The risk of osteoporotic fracture in denosumab was no significant difference than BPs (HR, 1.12; 95% CI, 0.91-1.76). The results were consistent across on-treatment analyses (Table1).

Subgroup analyses were performed according to dose type of BPs (Table2). After 1:1 PS matching, there was no significant difference in the HRs for osteoporotic fracture between the target and comparative groups in both PO BPs and IV BPs (PO BPs: HR 1.77; 95% CI, 0.98-3.34; IV BPs: HR 0.77; 95% CI, 0.43-1.36).
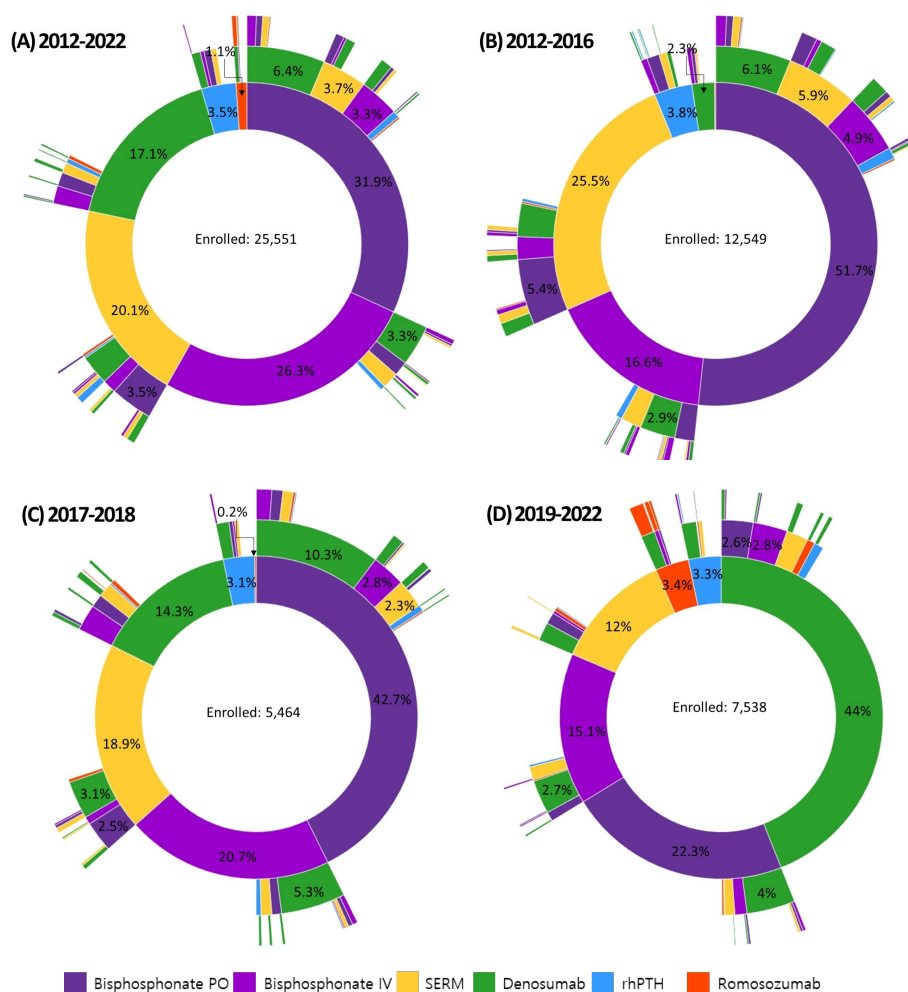
Figure 1. Treatment pathways for all cohorts. For each cohort, (A) Patients diagnosed with osteoporosis before 2017, (B) Patients diagnosed with osteoporosis between 2017 and 2018, (C) Patients diagnosed with osteoporosis after 2019, and (D) the overall treatment pathway. The inner circle shows the first medication the patient was prescribed, the second circle shows the second medication, and so on.

Table 1. Comparative risk of osteoporotic fracture between first line user of denosumab vs bisphosphonate

	Denosumab			Bisphosphonate			
	Patients	**Events**	**IR (1,000 PY)**	**Patients**	**Events**	**IR (1,000 PY)**	**HR (95% CI)**
2-year risk	1,166	40	24.53	1,166	35	22.19	1.12 (0.91-1.76)
On-treatment	849	20	17.78	849	17	20.81	0.90 (0.47-1.74)

Table 2. Subgroup analyses for 2-year risk of osteoporotic fracture events by dose type of bisphosphonate

	Denosumab, No. of events/total No.	Bisphosphonate, No. of events/total No.	HR (95% CI)

Dose type of BPs			
PO BPs	29/958	16/958	1.77 (0.98-3.34)
IV BPs	21/448	27/448	0.77 (0.43-1.36)

Conclusion

In our study of postmenopausal women with osteoporosis, we observed a shift in the sequential use of medications. Starting from 2019, denosumab has become the predominant choice, replacing BPs as the most prescribed in both first line and second line.

To compare the effectiveness of denosumab and BPs, we estimated comparative osteoporotic fracture risk between the first-line users of denosumab and BPs. There was no difference in risk of osteoporotic fracture between denosumab compared with BPs (overall drug type, PO, IV).

In future research, we aim to investigate the global trends in the use of anti-osteoporosis medications.

Reference

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