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Association between teriparatide adherence and healthcare utilization and costs among hip fracture patients in the United States

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ABSTRACT

Purpose: This study examined the association between teriparatide (TPTD) adherence, and healthcare utilization and costs among hip fracture (HFx) patients.
Methods: Individuals aged 50 years and older with an HFx between 1/1/2002-12/31/2010 were identified from a large US administrative claims database. The first HFx date during this period was designated as the index. Selected patients had at least 6 months of pre-index continuous enrollment (baseline) and no baseline TPTD use, cancer, or Paget's disease. Patients initiating TPTD post-index were followed until censoring at switch to bisphosphonates, disenrollment, 36 months post-index, or diagnosis of cancer or Paget's disease. Teriparatide adherence was measured as the proportion of days covered (PDC) by TPTD prescriptions, during the follow-up period, to construct three adherence groups: low (PDC $\leq$ 0.5), medium (0.5 < PDC $\leq$ 0.8), and high (PDC > 0.8) adherence. Outcome measures were repeated HFx, number of inpatient admissions, and per-patient-per-month (PPPM) healthcare costs. Multivariable generalized linear models examined the association between the TPTD adherence groups and the outcomes, adjusting for cross-group differences in patient characteristics.
Results: A total of 824 patients (mean age 75 years, 90% female) were included: 30% low, 27% medium, and 44% high adherence. In multivariable analyses, high adherence was significantly (all $p < 0.05$) directly associated with increased PPPM pharmacy costs ($621 low, $1093 medium, and $1572 high), but also with the lowest inpatient ($963 low, $960 medium, and $629 high) and outpatient ($1087 low, $1068 medium, and $776 high) costs, leading to the highest total costs in the medium adherence group but similar costs in the high and low adherence groups ($2599 low, $3163 medium, and $2869 high). The high adherence group also had the lowest number of inpatient admissions.
Conclusions: Significantly increased pharmacy costs associated with the high TPTD adherence group were offset by significantly fewer inpatient admissions, fewer repeated HFx, and lower inpatient and outpatient costs.

Introduction

Osteoporosis is a major health threat for more than half of the United States (US) population over the age of 50, or approximately 44 million people [1], and is characterized by reduced bone mineral density (BMD), deterioration in bone microstructure, and increased risk of fracture [2]. Osteoporosis is the primary underlying cause of fractures in the elderly, and it contributes to more than 1.5 million fractures each year in the affected US population [3]. Estimated to exceed $25 billion by 2025, direct medical costs associated with osteoporosis have been estimated between $13.7 and $20.3 billion in the US in 2005 [4]. Hip fractures (HFx), one of the three most common fractures associated with osteoporosis [5], are a major health problem because of their high frequency and associated costs [5,6]. Approximately 330,000 HFx occur annually in the US [7].

The 2013 National Osteoporosis Foundation (NOF) guidelines recommend that postmenopausal women and men over the age of 50 with a fracture undergo BMD testing, spine imaging, and evaluation for pharmacologic osteoporosis treatment to decrease future fracture risk [2]. Currently, in the US, the treatment of osteoporosis includes raloxifene, oral and intravenous bisphosphonates, teriparatide (TPTD), denosumab, estrogen, and calcitonin [8]. According to NOF guidelines, to reduce the risk of fracture, physicians should encourage patients to practice compliance with their osteoporosis therapies [2]. Several studies have examined the roles of adherence (which has been defined as the extent to which patients take their medication as prescribed [9,10]) and persistence (which has been defined as the duration of

Abbreviations: AIR, adjusted incidence ratio; BMD, bone mineral density; COBRA, Consolidated Omnibus Budget Reconciliation Act; Deyo-CCI, Deyo-Charlson Comorbidity Index; DXA, dual X-ray absorptiometry; GLM, generalized linear model; HFx, hip fracture(s); HIPAA, Health Insurance Portability and Accountability Act; IRB, Institutional Review Board; NOF, National Osteoporosis Foundation; PDC, proportion of days covered; PPPM, per-patient-per-month; TPTD, teriparatide; US, United States.

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time for which patients continue on their treatment as indicated [9,10]) in the treatment of osteoporosis and have established that optimal adherence and persistence with osteoporosis medication is associated with decreases in the risk of fractures, rate of hospitalizations, and general healthcare utilization and costs [11–20]; however, there is very limited evidence on the association between TPTD adherence, persistence, and outcomes. A recent study demonstrated that the risk of any clinical, vertebral, and non-vertebral fractures decreased as TPTD adherence and persistence increased [21]. Yet, the association between TPTD adherence and persistence, and healthcare utilization and costs has not been examined. Additionally, no known study of TPTD adherence and outcomes has focused on HFx patients.

Using a large US administrative claims database capturing HFx patients who were newly initiating TPTD, this study examined the association between TPTD adherence and healthcare utilization and costs. Healthcare utilization included repeated HFx, number of inpatient admissions, and per-patient-per-month (PPPM) healthcare costs. Multivariable regressions were employed to examine the association between TPTD adherence and healthcare utilization and costs.

Materials and methods

Data source

Administrative claims data from the 2002–2010 Truven Health MarketScan® Commercial and Medicare Supplemental Databases were used in this study. The Truven Health MarketScan® databases have been used in many published retrospective studies of osteoporosis and fractures [21–30]. These databases represent the largest convenience sample available in proprietary and administrative claims databases (over 30 million unique individuals, each year), drawing administrative claims data from employers and health plans from across the US. Data from active non-Medicare eligible employees, early retirees, and Consolidated Omnibus Budget Reconciliation Act (COBRA) continuees and their dependents insured by employer-sponsored plans are included in the Commercial Database. Data from Medicare-eligible retirees with employer-sponsored Medicare Supplemental insurance are included in the Medicare Supplemental Database, where both the Medicare-paid amount and the employer-paid supplemental insurance amounts are included.

Both databases contain individual-level inpatient medical, outpatient medical, and outpatient prescription claims data, as well as individual-level insurance enrollment information. Available from these claims are gross covered payments for the healthcare services or products provided (i.e., the amount eligible for payment after applying pricing guidelines such as fee schedules and discounts but including deductibles, copayments, and coordination of benefits).

All database records are de-identified and fully compliant with US patient confidentiality requirements, including the Health Insurance Portability and Accountability Act (HIPAA) of 1996. This study used only de-identified patient records and did not involve the collection, use, or transmittal of individually identifiable data; therefore, Institutional Review Board (IRB) approval to conduct this study was not necessary.

Patient selection criteria

Patients with any HFx (see details in Supplementary Table 1) occurring between January 1, 2002 and December 31, 2010 were selected. The first HFx service date was denoted as the HFx index. To be included, patients must have initiated TPTD within a 36-month period after the HFx index. The dispense date of the first TPTD prescription was defined as the TPTD index. All selected patients were 50 years and older as of the HFx index; had no claims for cancer (excluding non-melanoma skin cancer) or Paget's disease of the bone in the 6 months prior to HFx index or on/before TPTD index; had continuous 6-month enrollment prior to the HFx index; had continuous enrollment from HFx index to TPTD index; and did not have a TPTD prescription filled for the 6 months prior to HFx index.

Study period

The baseline period of this study corresponded to the 6-month period prior to TPTD index. The follow-up period corresponded to the time from the TPTD index until censoring at 36 months after the HFx index date, switching to bisphosphonates, disenrollment from health insurance, reaching the end date of December 31, 2010, or being diagnosed with cancer (excluding non-melanoma skin cancer) or Paget's disease of the bone.

Measures

The primary measure of interest in this study was TPTD adherence. Adherence was measured as the proportion of days covered (PDC) by TPTD prescriptions during the follow-up period. Patients were classified into three TPTD adherence groups: low ($PDC \leq 0.5$), medium ($0.5 < PDC \leq 0.8$), and high ($PDC > 0.8$) adherence. These adherence groups were chosen based on a prior study which used the same thresholds [21].

Demographic characteristics were measured from insurance enrollment data and included age, sex, geographic region, urbanicity, health plan type, and TPTD index year. Clinical characteristics were measured from the medical and prescription claims data and included baseline fractures, baseline use of dual X-ray absorptiometry (DXA) scan, Deyo–Charlson Comorbidity Index (Deyo-CCI) [31], duration of the follow-up period, and days from HFx index to TPTD index. Also included among the clinical characteristics was the use of the following medications: anticonvulsants, calcitonin, glucocorticoids (systemic), hormone deprivation therapy, hormone replacement therapy, immunosuppressants, non-opioid analgesics, strong opioids (alfentanil, buprenorphine, fentanyl, hydromorphone, levorphanol tartrate, meperidine, methadone, morphine sulfate, oxycodone, oxymorphone, and remifentanil), weak opioids (butorphanol, codeine, dihydrocodeine, hydrocodone, nalbuphine, pentazocine, propoxyphene, and tramadol), raloxifene, and thiazolidinediones.

Outcome measures included any repeated HFx, any inpatient admissions and number of inpatient admissions, PPPM total costs as well as costs by place of service (inpatient costs, outpatient costs, and pharmacy costs). Healthcare costs in 2010 US dollars were examined after being adjusted by using the Medical Care component of the Consumer Price Index [32].

Statistical analyses

Patient demographics, clinical characteristics, and the study outcomes were compared between the TPTD adherence groups. Chi-square tests were used to evaluate the statistical significance of differences among categorical variables, and t-tests were used to evaluate continuous variables. Multivariable generalized linear models (GLMs) were used to examine the association between the TPTD adherence groups and the outcomes, after adjusting for the differences in demographic and clinical characteristics. Specifically, GLM regressions with a log link and gamma error distribution were used to estimate PPPM total, outpatient, and pharmacy costs. Two-part models were employed for inpatient costs, as relatively few patients incurred inpatient admissions. The first part of the model was a logistic regression (a GLM with logit link and binomial error distribution) that predicted any inpatient admissions, and the second part was a GLM regression with a log link and gamma error distribution on inpatient costs for the subset of patients with positive costs. The predicted costs were calculated based on the probability estimated from the logistic regression described above in the first part of the model and the cost estimate from GLM