



Lower Total Knee Arthroplasty Revision Risk Associated With Bisphosphonate Use, Even in Patients With Normal Bone Density



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ABSTRACT

Background: Bisphosphonates (BPs) are associated with lower total knee arthroplasty (TKA) revision risk, but the effect of bone mineral density has not been evaluated.

Methods: A cohort of 34,116 primary TKA patients was evaluated with revision surgery and periprosthetic fractures as end points. BP usage was the exposure of interest. Bone quality (normal, osteopenia, and osteoporosis) and patient age (<65 vs ≥65 years) were evaluated as effect modifiers of risk estimates.

Results: Of the patients, 19.6% were BP users. In BP users, 0.5% underwent an aseptic revision; and 0.6%, a periprosthetic fracture. In non-BP users, 1.6% underwent aseptic revision; and 0.1%, a periprosthetic fracture.

Conclusion: Bisphosphonate use was associated with lower risk of revision in all bone quality categories in those older than 65 years. The risk of periprosthetic fractures was higher for patients on BP.

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More than 10 million individuals in the United States have osteoporosis, and bisphosphonates (BPs) are the most widely used medication for treatment [1]. Many patients undergoing total knee arthroplasty (TKA) have osteoporosis and may be taking BPs. The interaction of this medication with the implantation of an artificial knee is not well understood, and few studies have evaluated outcomes of these patients. Recently, BPs were reported to reduce the risk of aseptic revisions in TKA [2,3]. Decreased implant migration was observed in randomized controlled trials of oral and topical clodronate, using radiostereometric measurements [2]. A nearly 2-fold increase in TKA survivorship has been observed [4] with BPs in a population-based study [3]. The reasons for this observation are not fully understood, but reduction in periprosthetic bone loss has been implicated [5].

Prior studies have not evaluated whether bone quality might affect the interaction of BPs and TKA outcomes. It has not been determined

whether the decreased revision TKA risk is observed only in patients with osteopenic bone or in patients with lesser degrees of bone mineral loss.

In addition, previous investigations have not evaluated the efficacy of BPs in individuals younger than 65 years, an increasing proportion of TKA patients in contemporary orthopedic practices. The current study was conducted to evaluate the effect of BPs on TKA stratified by bone density and age while adjusting for other patient, implant, and surgical factors. In addition, the potential effect of BPs on periprosthetic fractures was a focus of the current study.

Methods

Study Design, Sample, and Data Sources

A retrospective study of a prospectively followed cohort was conducted. All primary elective TKA patients diagnosed with osteoarthritis treated between April 2001 and December 2011 at Kaiser Permanente Southern California (KPSC) were included in the study (n = 34,166). During the course of the study, the membership of this integrated health care system was approximately 3 million people. Patients younger than 40 years were not included in this study [3].

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Three data sources from KPSC were used to conduct the study:

- (1) A large, US integrated health system's total joint replacement registry (TJRR) was used to identify the study sample, implant longevity (all-cause and aseptic revisions), and whether other procedures such as a total hip arthroplasty (THA) were performed [6]. The data collection procedures, coverage, participation rate, and data and tools available from the TJRR have already been published [5–7]. Briefly, the TJRR collect intraoperative information on all arthroplasty surgeries from the surgeon using a paper and computer entry form that is sent to a data repository for data entry and quality control. In addition to this information, patient-, surgeon-, and medical center-specific information is also collected using other data sources within Kaiser Permanente (eg, electronic medical records [EMR], diabetes registry, geographically enriched member sociodemographics, institutional membership and mortality, and administrative claims data). Arthroplasty outcomes (ie, surgical site infections, revision procedures, and venous thrombotic events) are prospectively identified using electronic screening algorithms of the EMR and administrative claims data, in combination with a chart review of cases to confirm the event. The registry reported a 95% participation rate for TKA in 2011 [8].
- (2) The integrated health care system's EMR. The pharmacy module was accessed to determine the BP use of patients within the cohort. We identified all medication orders for risedronate sodium, alendronate sodium, ibandronate sodium, alendronate-sodium-cholecalciferol, etidronate disodium, and zoledronic acid written and dispensed during the study period. The inpatient and

outpatient modules of the EMR were used to identify diagnostic codes associated with periprosthetic fractures using the following *International Classification of Diseases, Ninth Revision*, codes: 820-821, 823, 996.44, and 733.10, 733.14, 733.15, 733.19, 733.96, 733.9.

- (3) The KPSC “Healthy Bones Database” that tracks periprosthetic fractures and dual-energy x-ray absorptiometry (DEXA) scan results of members of the KPSC health care system was used to obtain bone mineral density results and verify periprosthetic fractures. Details on this data source and its processes have been published elsewhere [9–11].

Outcomes of Interest

The main end point of this study was revision for any reason after TKA. A revision procedure was defined as any procedure where a component is replaced. Secondary outcomes of this study were aseptic revision and periprosthetic fracture. *Aseptic revision* was defined as a revision of at least 1 component for any reason other than infection. *Periprosthetic fracture* was defined as an ipsilateral femur (distal to the lesser trochanter) or tibia fracture, which may have been treated operatively or nonoperatively. Periprosthetic fracture information was available from 2005 to 2011 for the study, and therefore, the denominator of this sub analysis is slightly smaller than the full cohort (n = 26,520).

Exposure of Interest

The main exposure of interest in this study was the use of BP medication. Bisphosphonate usage was determined similarly to the criteria reported by Prieto-Alhambra et al [3]. In brief, patients were considered BP users if they (1) had not had a revision procedure and had filled at least 2

Table 1
Study Sample Characteristics by BP User Status.

		Total Sample		BP User			
		n	%	No		Yes	
				n	%	n	%
Age category, y	All	34,116	100.0	27,424	100.0	6692	100.0
	<65	13,332	39.1	12,190	44.5	1142	17.1
	≥65	20,784	60.9	15,234	55.6	5550	82.9
Sex	Female	21,500	63.0	15,857	57.8	5643	84.3
	Male	12,616	37.0	11,567	42.2	1049	15.7
Race	White	20,313	59.5	16,118	58.8	4195	62.7
	Hispanic	6546	19.2	5251	19.2	1295	19.4
	Black	3320	9.7	2872	10.5	448	6.7
	Asian	1561	4.6	1080	3.9	481	7.2
	Other/multi	482	1.4	396	1.4	86	1.3
	Unknown	1894	5.6	1707	6.2	187	2.8
BMI category, kg/m ²	<30	14,353	42.1	10,468	38.2	3885	58.1
	≥30 and <35	10,117	29.7	8459	30.9	1658	24.8
	≥35	9027	26.5	7923	28.9	1104	16.5
	Unknown	619	1.8	574	2.1	45	0.7
ASA category	1 and 2	20,123	59.0	16,326	59.5	3797	56.7
	≥3	13,186	38.7	10,417	38.0	2769	41.4
	Unknown	807	2.4	681	2.5	126	1.9
Diabetes		10,420	30.5	8679	31.7	1741	26.0
TJA fellowship training		18,485	54.2	14,919	54.4	3566	53.3
Bilateral		3592	10.5	3084	11.3	508	7.6
THA		945	2.8	728	2.7	217	3.2
Cement	Cemented	30,738	90.1	24,561	89.6	6177	92.3
	Cementless	490	1.4	459	1.7	31	0.5
	Hybrid	1569	4.6	1306	4.8	263	3.9
	Missing	1319	3.9	1098	4.0	221	3.3
	DEXA scan within 5 y	No scan	11,620	34.1	10,894	39.7	726
	Normal	8933	26.2	8404	30.6	529	7.9
	Osteopenia	10,415	30.5	7316	26.7	3099	46.3
	Osteoporosis	3148	9.2	810	3.0	2338	34.9
	Mean		SD	Mean	SD	Mean	SD
Age, continuous, y		67.3	9.1	66.1	9.0	72.1	7.8
BMI, continuous, kg/m ²		31.7	6.2	32.3	6.2	29.6	5.8

Abbreviation: TJA, total joint arthroplasty.

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