SHORT REPORT

Positive predictive values of the coding for bisphosphonate therapy among cancer patients in the Danish National Patient Registry

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Background: The purpose of this study was to estimate the positive predictive value (PPV) of the coding for bisphosphonate treatment in selected cancer patients from the Danish National Patient Registry (DNPR).

Methods: Through the DNPR, we identified all patients with recorded cancer of the breast, prostate, lung, kidney, and with multiple myeloma. We restricted the study sample to patients with bisphosphonate treatment recorded during an admission to Aalborg Hospital, Denmark, from 2005 through 2009. We retrieved and reviewed medical records of these patients from the initial cancer diagnosis onwards to confirm or rule out bisphosphonate therapy. We calculated the PPV of the treatment coding as the proportion of patients with confirmed bisphosphonate treatment.

Results: We retrieved and reviewed the medical records of 60 cancer patients with treatment codes corresponding to bisphosphonate therapy. Recorded code corresponded to treatment administered intravenously for 59 of 60 patients, corresponding to a PPV of 98.3% (95% confidence interval 92.5–99.8). In the remaining patient, bisphosphonate treatment was also confirmed but was an orally administered bisphosphonate; thus, the treatment for any bisphosphonate regardless of administration was confirmed for all 60 patients (PPV of 100%, 95% confidence interval 95.9–100.0).

Conclusion: The PPV of bisphosphonate treatment coding among cancer patients in the DNPR is very high and the recorded treatment nearly always corresponds to intravenous administration.

Keywords: bisphosphonate, neoplasm metastases, predictive value of tests, validation studies

Introduction

Skeletal related events (SRE) are relatively common and severe consequences of cancers that have metastasized to bone, in particular for solid cancers of the prostate, breast, or lung.[1] Jensen et al reported a cumulative 5-year incidence of SREs among breast cancer patients with bone metastases of 51.7% (95% confidence interval [CI] 48.9–54.4).[2] Intravenous bisphosphonates, usually administered during hospitalization, are one of the cornerstone methods of SRE prevention.[3] Bisphosphonates inhibit osteoclast activity and reduce skeletal morbidity by 30%–60% in patients with metastatic bone disease.[3] In addition, bisphosphonates are also used for treatment of hypercalcemia in cancer patients. Nonetheless, concern has been raised that treatment with bisphosphonates may be associated with adverse events, such as atrial fibrillation,[4] osteonecrosis of the jaw,[5] and renal impairment.[6] Cancer patients, who receive bisphosphonates in doses approximately 10 times higher than doses used to treat osteoporosis, may be

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at comparatively higher risk of bisphosphonate-induced adverse events. Therefore, pharmacovigilance studies are of major importance, but require readily available, updated, and high-quality data. Inability to identify hospital-administered medications is a limitation of many observational studies of drug effects relying on automated databases, particularly in situations, in which drugs are primarily administered in a hospital setting. The Danish National Patient Registry (DNPR) is an electronic population-based medical registry which tracks hospital-based visits nationwide.[7] In addition, the DNPR is one of the few automated databases in which certain hospital-administered medications are identifiable on an individual level, potentially offering a cost-effective way of identifying patients receiving in-hospital treatment with intravenous bisphosphonates. In order to monitor patients treated with intravenous bisphosphonates, the validity of the coding is of utmost importance. While several studies have measured the validity of diagnostic coding in the DNPR,[8–10] the validity of most coding of treatments, including bisphosphonate therapy, has not been evaluated. Therefore, we conducted a validation study of the coding for bisphosphonate therapy in cancer patients (lung, prostate, breast, kidney, and multiple myeloma) in the DNPR.

Materials and methods

Through the DNPR, we identified cancer patients with a recorded treatment code for a bisphosphonate at Aalborg Hospital, Denmark, during 2005–2009. Aalborg Hospital is located in the northern part of Denmark and has a catchment area of approximately 640,000 inhabitants. Since 1977, the DNPR has recorded 99.5% of all nonpsychiatric discharges from Danish hospitals, including information on patient civil registration number, dates of admission and discharge, and up to 20 discharge diagnoses, coded according to the International Classification of diseases (ICD), 8th revision through 1993 and 10th revision thereafter. We restricted cancer patients to those with primary tumors of the lung (ICD-10 codes C33–C34), breast (C50), prostate (C61), kidney (C64–C65), and with multiple myeloma (C90). The treatment code used to identify bisphosphonate therapy was BWHB40. This treatment code represents bisphosphonate therapy independent of type of administration.

For each patient, the first author (MSN) reviewed all available medical records, from primary cancer date and onwards, to confirm or rule out bisphosphonate therapy and to determine the route of administration. We estimated the positive predictive value (PPV) as the proportion of patients registered with a code for bisphosphonate treatment in the DNPR whose treatment was confirmed by medical record review. The estimates are presented with the 95% CI, calculated using Jeffrey's method.[11]

Results

During the study period, there were 828 patients with the cancers included in this study, of whom 60 patients also had a bisphosphonate treatment code. We were able to locate all 60 (100%) relevant medical records. For the 60 patients, median age at cancer diagnosis was 67 (range 58–74) years and 50% of the patients were female. The most frequent cancer diagnosis was multiple myeloma followed by breast cancer, prostate cancer, and a small number of patients had lung cancer and kidney cancer (Table 1). All of the patients with cancers other than multiple myeloma had been diagnosed with bone metastases, and 37 patients had been diagnosed with skeletal-related events.

Review of medical charts revealed that intravenous pamidronate was used for all patients with multiple myeloma, whereas intravenous zoledronic acid was used for the remaining cancer sites except for one patient. Hence, 59 of the 60 patients with a treatment code of bisphosphonates in the DNPR had received intravenous therapy corresponding to a PPV of the treatment code for intravenous administration of 98.3% (95% CI 92.5–99.8). One remaining patient had prostate cancer with bone metastases and had received oral alendronate at the osteoporosis dose. We were unable to determine whether or not the therapy was initiated because of bone loss related to androgen deprivation therapy. When including this patient among the confirmed bisphosphonate

Table 1 Characteristics of the 60 cancer patients registered with bisphosphonate treatment in the Danish National Patient Registry, Aalborg Hospital, 2005–2009

Characteristics	
Age (years)	66.8
Sex n (%)	
Male	30 (50.0)
Female	30 (50.0)
Type of cancer n (%)[a]	
Multiple myeloma	23 (38.3)
Breast	19 (31.7)
Prostate	15 (25.0)
Lung	2 (3.3)
Kidney	2 (3.3)
Bisphosphonate n (%)	
Intravenous	59 (98.3)
Oral	1 (1.7)

Notes: [a]One patient was diagnosed with both cancer of the prostate and multiple myeloma. Hence, the total number of cancer patients adds up to 60 and not 61.

treatments, the PPV for any bisphosphonate treatment was 100% (95% CI 95.9–100.0).

Discussion

The validity of bisphosphonate treatment coding in the DNPR was high, as measured by a PPV of 98.3% (95% CI 91.1–100.0) for intravenous use and 100% (95% CI 94.0–100.9) for overall use, indicating that a registry-based in-hospital bisphosphonate administration record corresponds in the vast majority of cases to intravenous bisphosphonate treatment among cancer patients.

To our knowledge, our study is the first validation study of bisphosphonate coding in a large nationwide population-based hospital registry. The finding of an overall high PPV for the coding of bisphosphonate treatment is on a par with or better than validity reported for other procedures and for diagnostic coding. For example, a validation study of the data in the DNPR reported PPVs of 75%–90% for registered primary diagnoses classified according to clinical specialties.[7,12] In addition, a study investigating the quality of coding of acute total colectomy in patients with inflammatory bowel disease in the DNPR found a PPV of 97% (95% CI 93–99).[13] Furthermore, a large validation study of coding of the 19 conditions included in the Charlson Comorbidity Index found PPVs varying from the lowest of 82% for diabetes with complications to the highest of 100% for conditions such as chronic pulmonary disease and liver disease.[9] Nonetheless, for other conditions, such as venous thromboembolism, the PPV of coding in the DNPR has been shown to be as low as 30%,[10] indicating the importance of conducting validation studies.

We focused on validating the bisphosphonate hospital treatment code among cancer patients. The validity of bisphosphonate treatment among patients receiving bisphosphonates for other indications, such as osteoporosis, may be different from that reported here. We did not have a sample of independently ascertained true in-hospital bisphosphonate treatments and therefore could not estimate the sensitivity of hospital coding. Furthermore, completeness of DNRP with respect to bisphosphonate treatment could not be estimated because the true prevalence of such treatments in the population is unknown. It would be important to address completeness in the studies aiming to estimate true occurrence of bisphosphonate treatment in the population.

However, because data in the DNPR are registered for administrative purposes, the risk for most systematic errors (recall bias, nonresponse bias) is low.[15] Aalborg Hospital is a large hospital serving approximately 11% of the Danish population. Given the centralized, tax-supported universal medical coverage in Denmark, high generalizability to the entire Danish population is expected. Knowing the validity of hospital-administered drugs is of great value in future studies of cancer patients registered with a coding for bisphosphonate treatment, because of high certainty that the drug entered the patient's circulation. In conclusion, codes for in-hospital administration of bisphosphonates in the Danish National Registry of patients invariably corresponded to true treatment among cancer patients, and the route of administration was nearly always intravenous.

Disclosure

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