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Fall-related injuries in elderly cancer patients treated with neurotoxic chemotherapy: A retrospective cohort study

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ABSTRACT

Background: Fall-related injuries are a well-described cause of morbidity and mortality in the community-dwelling elderly population, but have not been well described in patients with cancer. Cancer treatment with chemotherapy can result in many unwanted side effects, including peripheral neuropathy if the drugs are potentially neurotoxic. Peripheral neuropathy and other side effects of chemotherapy may lead to an increased risk of fall-related injuries.

Methods: We conducted a retrospective cohort analysis using the records of 65,311 patients with breast, colon, lung, or prostate cancer treated with chemotherapy in the SEER-Medicare database from 1994 to 2007. The primary outcome was any fall-related injury defined as a traumatic fracture, dislocation, or head injury within 12 months of the first dose of chemotherapy. The sample population was divided into 3 cohorts based on whether they most frequently received a neurotoxic doublet, single agent, or a non-neurotoxic chemotherapy. Cox proportional-hazards analyses were adjusted for baseline characteristics to determine the risk of fall-related injuries among the 3 cohorts.

Results: The rate of fall-related injuries for patients receiving a doublet of neurotoxic chemotherapy (9.15 per 1000 person-months) was significantly higher than for those receiving a single neurotoxic agent (7.76 per 1000 person-months) or a non-neurotoxic agent (5.19 per 1000 person-months). Based on the Cox proportional-hazards model risk of fall-related injuries was highest for the cohort receiving a neurotoxic doublet after the model was adjusted for baseline characteristics.

Conclusions: Among elderly patients with cancer, use of neurotoxic chemotherapy is associated with an increased risk of fall-related injuries.

1. Introduction

The incidence of cancer in individuals aged 60 years and older is approaching 60% and is projected to increase.[1] Studies have shown that fit older patients with cancer may benefit from chemotherapy as much as younger patients.[2–4] As the age of patients with cancer treated with chemotherapy continues to rise, there is a growing need to recognize and try to prevent complications of treatment that are common in this population. Fall-related injuries (FRIs) are a frequent cause of morbidity and mortality in the elderly. In 2005, 1.8 million patients over the age of 65 years were treated in the emergency room for non-fatal fall injuries and 433,000 of these patients were hospitalized as a result of their injuries.[5] Every year, approximately one-third of community dwelling elderly people will experience a fall, and 5–10% of falls will result in a serious injury (major head trauma or fracture) related to the fall.[6] The rate of fall-related deaths has risen over the past decade,[7] highlighting the need for more efforts to prevent and lower the risk of falls in the elderly.

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Peripheral neuropathy can lead to and exacerbate balance and gait problems and is associated with a 2- to 3-fold increased risk of falling in community-dwelling elderly patients.[8,9] Some chemotherapeutic agents, such as platinum compounds, taxanes, and vinca alkaloids, may be neurotoxic and lead to peripheral neuropathy. Chemotherapy-induced peripheral neuropathy (CIPN) can occur in 10–40% of patients treated with neurotoxic chemotherapy and is often a dose-limiting side effect.[10] A retrospective study of the SEER-Medicare database showed that patients who received taxane-based chemotherapy are twice as likely to develop CIPN and patients treated with taxane–platinum chemotherapy combinations are 3 times as likely to develop CIPN compared to similar patients with cancer who did not receive chemotherapy.[11] Deficits caused by CIPN can include loss of sensation to touch, pinprick, and vibratory sensation and more commonly affect nerves in the lower extremities. This can lead to loss of proprioception, which can result in ataxia and significant functional impairment. In addition, CIPN can result in motor deficits, hyporeflexia, and loss of autonomic nervous function. These neurologic changes can manifest clinically as foot drop, dizziness, or orthostatic hypotension, which are syndromes that commonly contribute to falls in the elderly.[12]

Falls and FRIs are uncommonly measured outcomes and elderly patients are underrepresented in most oncology clinical trials.[13] A systematic review of the literature identified seven studies that reported an incidence of falls in patients with cancer (22–37% of patients reporting at least one fall in 12 months) that was similar to those in community-dwelling people 65 years of age or older. The authors of the review found several significant methodological problems with these studies, which limited the conclusions regarding risk factors for falls in patients with cancer.[14] A small, single institution study showed that among patients with lymphoma who are hospitalized for an autologous stem cell transplant, in-hospital falls were associated with lower overall survival and higher non-relapse mortality.[15] In another prospective longitudinal study, patients with a history of a fall in the 6 months prior to starting chemotherapy were more likely to experience grade 3–5 toxicities from chemotherapy.[16]

Falls and FRIs appear to play an important role in the treatment outcomes of elderly patients with chemotherapy, but there is little information in the literature about how often these events occur and which patients are at greatest risk. The primary aim of this retrospective cohort study was to describe the prevalence of fall-related injuries in a specific population of elderly patients with cancer. The secondary aim of the study was to explore the correlation between neurotoxic chemotherapy and fall-related injuries in the elderly cancer population. Based on the increased risk of falls in elderly individuals with peripheral neuropathy, we hypothesize that elderly patients treated with neurotoxic chemotherapy have a greater risk of FRIs.

2. Methods and Materials

2.1. Sample

We analyzed the SEER-Medicare database from 1994 to 2007. The SEER (Surveillance, Epidemiology, and End Results) program is a population-based cancer registry that encompasses about 14% of the US population. The registry includes information on cancer incidence, staging, initial therapy, and survival. It is linked to Medicare administrative claims data, which includes information on demographics, Medicare enrollment, and outpatient and inpatient claims. Approximately 97% of all adults in the US older than 65 years of age have Medicare as their primary insurance.[17]

We included patients who were diagnosed with breast, colon, lung, and prostate cancer between the years 1995 and 2007, who received their first dose of chemotherapy within 12 months of diagnosis. These four tumor types were chosen because of their high prevalence. Despite the differences between patients with these separate tumor types, we chose to include all of these patients in order to have a large enough sample size to detect differences in the rates of FRIs between the different chemotherapy groups. The observation period was defined as 12 months before the diagnosis of cancer (to account for baseline comorbidity) until 12 months after the first dose of chemotherapy. Patients were excluded for the reasons outlined in Fig. 1. For patients who had different cancers diagnosed more than 2 years apart, we only observed the period of time surrounding the first cancer diagnosis. We also excluded any patient who had a FRI at any time in the year prior to cancer diagnosis. We did this because a history of prior FRI is already known to be the strongest predictor of future FRIs and these patients were thought to be too frail to be included.

2.2. Design

The use of ICD-9 codes and J codes to identify the administration of chemotherapy has been previously well described.[18,19] The administration of chemotherapy was identified by the ICD-9 codes listed in Appendix A. The neurotoxic chemotherapy agents of interest were: cisplatin, carboplatin, vinorelbine, vincristine, vinblastine, oxaliplatin, paclitaxel, and docetaxel. Patients were divided into two cohorts depending on whether they most frequently received a neurotoxic doublet or a single neurotoxic agent within the 12-month period after the first chemotherapy administration. For example if a patient received 3 months of doublet neurotoxic chemotherapy and 1 month of single agent neurotoxic chemotherapy, they were placed in the doublet group. These cohorts were compared to a non-neurotoxic cohort composed of patients that received any other specific chemotherapeutic drug as listed in Appendix B. Patients were excluded from the analysis if there was a code for chemotherapy administration, but no specific chemotherapeutic agent could be identified by J code.

2.3. Definitions

The primary outcome was any FRI within one year of a patient being given their first dose of chemotherapy. A FRI was defined as a code for hip fracture (excluding codes for pathologic or spontaneous fractures), head injury, joint dislocation, or other traumatic fracture codes (ICD-9 codes: 800–839, 850–854). In order to limit type I error, a FRI was only counted when 2 codes were found in the outpatient files (because these codes can be abstracted from radiology orders and exams as “rule out” diagnoses) or one code was found in