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Unplanned hospitalizations in a racially and ethnically diverse population of women receiving chemotherapy for epithelial ovarian cancer

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HIGHLIGHTS

- Hospital readmission rates may be higher in diverse populations.
- Body mass index and hypertension are predictors for readmission.
- Readmission may be a predictor for overall survival and disease-free survival.

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ABSTRACT

Objectives. Unplanned hospital admission following chemotherapy is a measure of quality cancer care. Large retrospective datasets have shown admission rates of 10–35% for women with ovarian cancer receiving chemotherapy. We sought to evaluate the prevalence and associated risk factors for hospital admission following chemotherapy in our racially diverse urban population.

Methods. After IRB approval, clinicopathologic and treatment data were abstracted from all patients with newly diagnosed epithelial ovarian cancer who received chemotherapy at our institution from 2005 to 2016. Two-sided statistical analyses and Cox regression analysis were performed using Stata.

Results. Of 217 evaluable patients, 87 (40%) had unplanned admissions following chemotherapy: adjuvant 64 (74%) and neoadjuvant 23(26%). Thirty (14%) had more than one admission. In total, there were 1314 days of hospitalization. The median readmission duration was 3 days. Body mass index and hypertension were predictive of readmission ($p < 0.05$). When comparing those readmitted more than once to those admitted once, both race and aspirin use were predictive of readmission ($p < 0.05$). Of those admitted more than once the self-identified race and ethnicity was 12 (40%) Hispanic, 8 (27%) White, 8 (27%) Black and 2 (7%) other. There was a significant difference in disease free ($p = 0.01$) and overall survival ($p = 0.004$) for patients with unplanned admission after chemotherapy as compared to those without admission.

Conclusions. Readmission rates in our racially diverse patient population were higher than previously reported in the literature. Identifying patients at risk of readmission may play a role in chemotherapy decision-making, and resource allocation including patient care navigators.

1. Background

Chemotherapy has contributed to improved survival of ovarian cancer patients seen over the last several decades [1]. Following data supporting the benefit of platinum based chemotherapy agents in ovarian cancer, paclitaxel with cisplatin was adopted as the gold standard of chemotherapy treatment. Subsequently, it was found that carboplatin

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in combination with paclitaxel had decreased side effects compared to cisplatin and paclitaxel, and is non-inferior [8–10]. Paclitaxel and Carboplatin have become the standard of care for epithelial ovarian cancers [2–4]. Studies show that patients often do not receive the treatments that demonstrate the best efficacy as recommended by the National Cancer Care Network (NCCN) Guidelines [1]. A potential cause for this is that while treatments may be efficacious in highly selected clinical trial participants, these findings may not be generalizable and the toxicities may be greater in clinical practice [5,6].

With the advent of the Affordable Care Act, the accountable care organization (ACO) introduced the concept of rewards based on savings. The ACO developed the oncology care model, which creates a discrete instance of care associated with chemotherapy and the six-months that follow. Providers receive a combination of fee-for-service payments, monthly payments for additional care and performance-based payments [11,12]. Unplanned hospitalizations are a performance-based measure that is used as a metric of quality care by the Oncology Care Model.

While there are limited studies looking at unplanned hospitalization readmission rates in patients receiving chemotherapy, the literature suggests rates between 10 and 35% [12,13]. The purpose of our study was to describe toxicity of adjuvant chemotherapy for women with epithelial ovarian cancer as measured by unplanned hospital admission in an ethnically, racially and socioeconomically diverse urban population at our tertiary care medical center.

2. Methods

After institutional review board approval, all patients with newly diagnosed primary epithelial ovarian cancer from 2005 to 2016 who received at least one cycle of chemotherapy were identified from our tumor registry. The cohort included both patients who received neoadjuvant chemotherapy and those who received primary debulking surgery followed by adjuvant chemotherapy. Clinicopathologic and treatment data were recorded from the electronic medical record and included: age, race, parity, menopausal status, body mass index, diabetes, hypertension, hyperlipidemia, aspirin use, hormone replacement, tobacco use, histology, stage, grade, optimal debulking status, date of chemotherapy cycles, type and dosing of chemotherapy, and date of hospitalizations. The Charlson comorbidity index score was also calculated for each patient [19].

During the study time period, three chemotherapy regimens were used in either the adjuvant or neoadjuvant setting at our institution. The first was carboplatin area under the curve (AUC) of 6 and paclitaxel 175 mg/m^2 every 3 weeks. The second was dose dense chemotherapy consisting of carboplatin area under the curve (AUC) of 6 every 3 weeks and paclitaxel 80 mg/m^2 weekly. Lastly, intravenous and intraperitoneal chemotherapy was administered as intravenous paclitaxel 135 mg/m^2 on day 1, intravenous cisplatin 75–100 mg/m^2 on day 2 and intraperitoneal paclitaxel 60 mg/m^2 on day 8. At the time of chemotherapy, patients received palonosetron and dexamethasone for chemotherapy induced nausea and vomiting prophylaxis. Patients were prescribed prochlorperazine and ondansetron for at home management of nausea and vomiting.

The primary outcome of the analysis was hospitalization for the management of a chemotherapy associated complication. Hospitalization was defined as an unplanned admission to one of the three hospitals affiliated with our institution within thirty days of day one of a chemotherapy cycle. The chemotherapy regimens prescribed to our patients had 21-day cycles. Admissions were attributed to cycles that happened in the antecedent 30 days, provided the next cycle had not been given on day 21. Readmissions were not counted twice. In instances where additional doses of chemotherapy were administered after day one of the cycle, hospitalization was still defined as within thirty days after day one of the cycle.

The secondary outcome of the study included risk factors associated with unplanned hospitalizations and reasons for admission. Definitions for each category of reason for readmission were as follows: neutropenic fever defined as fever with absolute neutrophil count less than 1500 neutrophils per microliter of blood. Hematologic toxicity included anemia with a hemoglobin less than 12.3 g/dL and thrombocytopenia with platelets less than 150 k/uL. Gastrointestinal toxicity included nausea and vomiting, abdominal pain, constipation, diarrhea, small bowel obstruction, lower tract bleeding, colostomy malfunction, and bowel perforation. Venous thromboembolism encompassed both deep vein thromboses and pulmonary emboli. Neurologic toxicities were defined as syncope, numbness and tingling and mental status change not related to electrolyte disturbances or infection. Cardiovascular included chest pain and atrial fibrillation. Poor nutrition was encompassed electrolyte disturbances and malnutrition. The remaining categories were infection with a known source, pleural effusion and other.

Summary statistics were used to report the data. Two-sided statistical analyses were performed using Stata. A p value of <0.05 was considered statistically significant. Analyses were performed comparing cohorts of unplanned admission versus not admitted, as well as comparing patients who were not admitted, admitted one time, and admitted more than once during chemotherapy treatment. Univariable analyses were calculated with each clinical and pathologic factor. Multivariable logistic regression analysis was performed and included all variables with statistical significance ($p < 0.05$) on univariate analyses in addition to variables with clinical significance regardless of statistical significance. Kaplan Meier survival analysis was performed between cohorts of patients who were not admitted versus those who were admitted.

3. Results

A total of 217 evaluable patients were identified. The mean age for the entire cohort was fifty-nine years (Table 1). The self-described race and ethnicity of the cohort was White (34%), Black (29%), Hispanic non-white (18%), and other (19%). The cohort included 50 (23%) patients who received neoadjuvant chemotherapy and 167 (77%) patients who received primary surgical debulking followed by adjuvant chemotherapy. For the adjuvant chemotherapy group, the median days between surgery and initial chemotherapy cycle was thirty-five days. Of those treated with adjuvant chemotherapy, 110 (66%) received IV carboplatin and paclitaxel every 3 weeks, 52 (31%) received IV/IP cisplatin and paclitaxel every 3 weeks and 5 (3%) received IV carboplatin and weekly paclitaxel. Forty-seven (94%) patients treated with neoadjuvant chemotherapy were given IV carboplatin and paclitaxel every 3 weeks, 2 (4%) were treated with IV carboplatin and weekly paclitaxel and 1 (2%) was given IV carboplatin and paclitaxel every 3 weeks followed by IV/IP cisplatin and paclitaxel after secondary debulking surgery.

There was a total of 141 admissions in the entire cohort with a corresponding 1314 days of hospitalization. The median readmission duration was 3 days. Eighty-seven (40%) of the patients had an admission within thirty days of their chemotherapy dose: adjuvant 64 (74%) and neoadjuvant 23 (26%). Within the adjuvant group, 41 (34%) of the patients had an admission after adjuvant IV chemotherapy and 23 (46%) of the patients had an admission after adjuvant IV/IP chemotherapy. Cycle one of chemotherapy was the most common (41, 31%) cycle for hospitalizations. Cycle two through six of chemotherapy had roughly the same number of hospitalizations (range 16 to 22). The demographics for those hospitalized were: 27 White (31%), 28 Black (32%), 20 Hispanic non-white (23%) and 12 other (14%) (Table 1). When looking over multiple cycles of chemotherapy, 30 (14%) of the patients had an admission after more than one cycle. Of those admitted more than once, 12 (40%) were Hispanic, 8 (27%) were White, 8 (27%) were Black and 2 (7%) self-identified as other (Table 2).

The most common reasons for readmission were for gastrointestinal complaints (32%), neutropenia (18%) and hematologic disturbances not

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