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Chemotherapy is administered to a minority of hospitalized patients with diffuse large B-cell lymphoma and is associated with less likelihood of death during hospitalization

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ABSTRACT

Background: While treatment of DLBCL is largely outpatient, some patients require planned or unplanned admissions for chemotherapy, new diagnosis, relapse, or toxicity. We examined risk factors for receipt of inpatient chemotherapy and death during hospitalization.

Methods: We analyzed data from the 2012–2013 HCUP-NIS. We identified patient and hospital characteristics that were associated with chemotherapy administration and death.

Results: Chemotherapy was given in 3260/11,150 (29.2%) of hospitalizations. Younger age, urban teaching hospitals, fewer chronic conditions, male sex, non-Medicare insurance, and "less likelihood of dying" were associated with chemotherapy. Chemotherapy portended lower odds of death; older age and longer hospitalizations were associated with increased odds of death.

Conclusion: We identified socio-demographics and clinical characteristics associated with inpatient chemotherapy in DLBCL patients. Chemotherapy is associated with lower odds of death during hospitalization, suggesting that most chemotherapy is given appropriately to non-critically ill patients. Clinical acuity is a stronger predictor of death than socio-demographics.

1. Introduction

The integration of "CHOP" chemotherapy in the treatment of diffuse large B-cell lymphoma (DLBCL) has shifted treatment of newly diagnosed patients to the outpatient setting [1,2]. However, patients with DLBCL may still require inpatient admission for infusional chemotherapy or management of toxicity during diagnosis, active treatment, or relapse. Admissions may be planned (e.g., infusional regimens for high-risk disease, salvage chemotherapy for relapsed disease, hematopoietic cell transplant, HCT) [3,4] or unplanned (e.g., toxicity during treatment, new diagnosis, relapse). Unplanned admissions may result in urgent chemotherapy delivered during hospitalization, which has implications for inpatient resource utilization and cost of care. There are limited data about which patients are more likely to receive chemotherapy in the hospital, and which patients are more likely to suffer fatal complications during hospitalization. We examined patient and hospital characteristics associated with receiving inpatient chemotherapy and death during hospitalization for adults with DLBCL using a large US national database, the Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS).

2. Materials and methods

HCUP-NIS samples comprise 20% of discharges from non-rehabilitation hospitals in the US. The data describe patient demographics, hospital characteristics, calculated risk of mortality during hospitalization (a classification based on the All Patient Refined Diagnosis Related Groups system, which assigns patients a risk of mortality, based on severity of illness), and ICD-9-CM diagnosis and procedure codes for each discharge. HCUP-NIS provides weights to calculate nationally representative estimates. Combined, the 2012 and 2013 samples include data for 14,416,531 discharges. Weighted, this approximates 72,082,638 discharges across all diagnoses.

We identified hospitalizations for patients ≥18 years old with a diagnosis of DLBCL (ICD-9-CM 200.7) that were discharged from an inpatient setting between January 1, 2012 and December 31, 2013. We

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excluded patients with outlier insurance (self-pay, no-charge, other, invalid) and income (invalid) categories. Our primary outcomes were receipt of chemotherapy during hospitalization and death during hospitalization. We evaluated whether patient characteristics (age, sex, risk of mortality, chronic conditions, income), hospital characteristics (type, geographic region), insurance payor, charge per day (CPD), and length of stay (LOS) were associated with receiving chemotherapy (defined by codes ICD-9-M V58.11, 99.24). We included these variables, as well as chemotherapy administration to identify factors associated with death during hospitalization.

We collapsed the upper three income quartiles into high (top 75%) vs. low (0–25%) income, as modified from prior studies [5]. Black, Hispanic, Asian/Pacific Islander, Native American, and "Other" races were combined into one "non-white" race, and rural and urban non-teaching hospitals were collapsed into non-academic (versus urban teaching) hospitals. For chemotherapy administration, we performed univariate analysis using the chi-squared and Kruskal-Willis tests for categorical variables and the Wilcoxon rank-sum method for continuous variables. We performed logistic regression to identify factors associated with death during hospitalization. We included all variables for risk of death except "risk of mortality" due to collinearity. We applied the HCUP-NIS weights, strata, and clustering in all analyses. We computed standard errors following the methods recommended by HCUP [6]. All analyses were completed using the survey procedures in SAS EG 7.1.

3. Results

We included 11,150 weighted discharges associated with DLBCL in 2012–2013. We excluded 1,675 weighted (335 unweighted) discharges due to either missing data in our variables of interest (n = 1,165 weighted) or outlier insurance category (n = 610 weighted). Median age was 70 years (25–75 percentile, %: 59–78), and over half (54%) of hospitalizations occurred in males. The majority (63.8%) of patients carried Medicare insurance and was White (79.1%). Over half of admissions were in an academic urban hospital. Median number of chronic conditions was 5 (25–75% 2.8–7.1), and less than 10% of cases were categorized in HCUP-NIS as having an "extreme likelihood of dying". Median LOS was 4.1 days in the entire cohort (25–75% 2.3–7.5). Median CPD was $6217 (25–75% $3895–9716). (Table 1)

Chemotherapy was administered in 3260/11,150 (29.2%) of hospitalizations. Those who received chemotherapy in the hospital were younger (64 vs. 72 years, $p < 0.001$), more often in urban teaching hospitals ($p < 0.001$), had fewer chronic conditions (median 3.6 vs. 5.3, $p < 0.001$), were more often male (58% vs. 53%, $p = 0.01$), more frequently had private or Medicaid insurance (vs. Medicare, both $p < 0.001$), and were less likely to have an "extreme likelihood of dying" ($p < 0.001$) than those who did not receive chemotherapy. Hospitalizations associated with chemotherapy were more costly (median CPD $7682 vs. 5731, $p < 0.001$), but were not longer (median LOS 4.1 vs. 4.1 days, $p = 0.10$). Characteristics between chemotherapy vs. no chemotherapy cases are outlined in Table 1.

Death occurred in 585/11,150 (5.2%) admissions. Patients who died during hospitalization were older (median 74.9 vs. 69.3 years, $p < 0.001$), had an extreme likelihood of dying (66% vs. 6.5% $p < 0.001$), had more chronic conditions (5.9 vs. 4.7, $p < 0.001$), experienced longer LOS (7 vs. 4 days, $p < 0.001$) and had higher CPD ($8175 vs. $6127, $p = 0.004$) compared to those who did not die. Patients who did not receive chemotherapy during admission were more likely to die compared to those who received chemotherapy (6.5 vs. 2.3%, $p < 0.001$). There was no difference in hospital type (rural/urban-nonteaching, vs. urban teaching), sex, geographic region, race, and income. In multivariable regression, older age (OR = 1.38 for 10-year increase, $p = 0.01$) and longer LOS (OR = 1.05, $p < 0.001$ were associated with higher odds of dying during hospitalization), while receiving chemotherapy (OR = 0.38, $p = 0.002$) was associated with lower odds of dying (Table 2).

Table 1
Cohort characteristics.

Variable, % (SE)	All Admissions	No Chemotherapy	Chemotherapy	p-value
Sample Size, n	11,150	7,890	3,260	
Age in years, median (q1, q3)	69.6 (59.0, 77.8)	71.5 (61.4, 79.5)	64.1 (52.7, 73.4)	< .0001
Risk of mortality				< .0001
Minor to moderate likelihood of dying	90.4 (0.6)	69.3 (1.2)	30.7 (1.2)	
Extreme likelihood of dying	9.6 (0.6)	84.6 (2.4)	15.4 (2.4)	
Region				0.0564
Northeast	22.1 (1.3)	72.4 (2.7)	27.6 (2.7)	
Midwest	23.6 (1.0)	73.6 (2.1)	26.4 (2.1)	
South	36.8 (1.1)	71.0 (1.8)	29.0 (1.8)	
West	17.5 (0.7)	64.5 (2.5)	35.5 (2.5)	
Hospital Type				< .0001
Not academic (rural and urban nonteaching)	42.9 (1.1)	78.0 (1.3)	22.0 (1.3)	
Academic (urban teaching)	57.1 (1.1)	65.4 (1.6)	34.6 (1.6)	
Died During Hospitalization				< .0001
No	94.8 (0.5)	69.9 (1.2)	30.1 (1.2)	
Yes	5.2 (0.5)	87.2 (3.1)	12.8 (3.1)	
Sex				.0127
Male	54.5 (1.1)	68.6 (1.5)	31.4 (1.5)	
Female	45.5 (1.1)	73.3 (1.4)	26.7 (1.4)	
Number of Chronic Conditions				< .0001
≤3	27.4 (1.0)	55.6 (2.1)	44.4 (2.1)	
4–5	25 (0.9)	68.3 (2.3)	31.7 (2.3)	
6–7	21.5 (0.9)	78.3 (1.9)	21.7 (1.9)	
≥8	26.1 (0.9)	82.8 (1.6)	17.2 (1.6)	
Insurance				< .0001
Medicare	63.8 (1.1)	78.1 (1.2)	21.9 (1.2)	
Medicaid	7.8 (0.6)	57.2 (4.1)	42.8 (4.1)	
Private	28.5 (1.1)	58 (2.0)	42.0 (2.0)	
Race				.0653
White	79.1 (1.0)	71.7 (1.2)	28.3 (1.2)	
Not White	20.9 (1.0)	67.1 (2.3)	32.9 (2.3)	
Income				.6724
0-25th percentile	23.0 (1.0)	71.5 (2.2)	28.5 (2.2)	
26-100th percentile	77.0 (1.0)	70.5 (1.2)	29.5 (1.2)	
Chemotherapy Administration				
No	70.8 (1.1)			
Yes	29.2 (1.1)			
LOS, median (q1,q3)	4.1 (2.3, 7.5)	4.1 (2.6, 7.2)	4.1 (2.2, 7.5)	.1036
Charge Per Day, median (q1,q3)	6217.3 (3894.8, 9715.6)	7681.8 (5089.2, 11442)	5731.0 (3579.8, 8972.0)	< .0001

4. Discussion

We highlight three important findings about hospitalizations in patients with DLBCL in an analysis of a large inpatient population database. First, the demographics of DLBCL inpatients provide insight into patient care practices. Inpatient hospitalizations occurred relatively infrequently—11,150 over two years (2012–2013). In a disease with 27,650 projected new diagnoses in 2016 [7], only a small proportion required inpatient care. Of these inpatients, almost half were hospitalized in a non-urban academic center, reinforcing that DLBCL may be