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Brief Report

High-risk medication use for *Clostridium difficile* infection among hospitalized patients with cancer

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Patients with cancer are vulnerable to *Clostridium difficile* infection (CDI); hospitals with larger oncology populations may have worse CDI performance. Among 71 academic hospitals studied, there were significant differences in oncology patient-days per 1,000 admissions across CDI standardized infection ratio categories of better, no different, and worse; worse hospitals had the greatest number of patient-days. Oncology patients' most commonly used high-risk CDI medications were quinolones, third- and fourth-generation cephalosporins, and proton pump inhibitors.

Clostridium difficile infection (CDI) occurs in persons who have taken antibiotics, which disrupt the microbiome and lead to toxin-producing *C difficile* proliferation.[1] Another factor is gastric acid suppressant receipt. Modifying medications has served as an antimicrobial stewardship program strategy toward CDI reduction.[2]

Hospitals are assigned a standardized infection ratio (SIR), which relays the number of infections occurring to the predicted number. Hospitals are assigned a SIR category of better, no different, or worse, signifying that the number of infections was either less than, the same as, or greater than predicted given the national benchmark per the Centers for Disease Control and Prevention's National Healthcare Safety Network, respectively.[3] In previous work, we evaluated patient factors and medications and their association with the SIR category for health care facility–onset CDI. We identified that better hospitals used fewer antibiotics and proton pump inhibitors. However, while accounting for medications in multivariable analyses, only a proportion of patients >65 years and days of therapy (DOTs) per 1,000 patient-days (PDs) of cancer chemotherapeutic agents (control variable for immunosuppressed patients) were associated with a lower SIR category (no different vs better or worse vs no different). Thus, there are implications for hospitals with large oncology populations regarding their CDI performance. To identify possible target areas for antimicrobial stewardship programs in the modification of high-risk CDI medication use among oncology patients, the primary aim of this study was to describe use among inpatients with cancer and to ascertain if there were differences across SIRs.

METHODS

A hospital-level, cross-sectional analysis was conducted using data from 71 academic medical centers of Vizient, Inc (https://www.vizientinc.com/) that had antibiotic data available for oncology services. Data on adult inpatients ≥18 years of age from 2013 were obtained from the Clinical Resource Manager, which contains charge-based medication data.

Use was measured in DOTs per 1,000 PDs for antipseudomonal antibiotics (β-lactam/β-lactamase inhibitors [piperacillin/tazobactam]), third- and fourth-generation cephalosporins (cefepime, ceftazidime), quinolones (levofloxacin, ciprofloxacin), carbapenems (meropenem, imipenem, doripenem), and gastric acid suppressant agents (proton pump inhibitors, histamine receptor antagonists). We examined use among 6 oncology-related Vizient clinical service lines (CSLs): bone marrow transplant (BMT), gynecologic oncology, medical oncology/hematology (MEDHEM), medical oncology/radiation, medical oncology/solid tumor, and surgical oncology. Each hospital's

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Table 1
Mean (SD) number of oncology clinical service line PDs per 1,000 admissions and medication days of therapy per 1,000 PDs according to *Clostridium difficile* standardized infection ratio category

	Total (n = 71)	Better (n = 19)	No different (n = 32)	Worse (n = 20)	*P* value
Oncology clinical service line PDs per 1,000 admissions					
Total oncology	65.0 (34)	49.0 (32)	66.0 (27)	80.0 (39)	**.013**
Bone marrow transplant	14.0 (13)	7.6 (12)	14.0 (12)	19.5 (14)	**.022**
Gynecologic oncology	4.0 (2)	3.4 (2)	4.3 (2)	4.2 (4)	.316
Medical oncology/hematology	27.0 (15)	21.0 (14)	27.0 (12)	34.0 (19)	**.031**
Medical oncology/radiation	0.4 (3)	0.1 (0)	0.1 (0)	1.3 (5)	.254
Medical oncology/solid tumor	15.8 (5)	14.0 (4)	16.0 (6)	17.0 (4)	.085
Surgical oncology	4.3 (2)	3.7 (3)	4.0 (2)	5.4 (3)	**.044**
Medication days of therapy per 1,000 PDs					
Total antipseudomonal use	82.0 (38)	68.0 (34)	91.0 (44)	83.0 (24)	.104
β-Lactam/β-lactamase inhibitors	5.5 (4)	3.9 (3)	6.4 (4)	5.4 (5)	.117
Third- and fourth-generation cephalosporins	25.0 (14)	22.0 (14)	26.0 (15)	25.0 (13)	.629
Quinolones	38.0 (25)	31.0 (21)	43.0 (30)	35.0 (17)	.223
Carbapenems	15.0 (15)	11.0 (10)	16.0 (13)	17.0 (20)	.333
Proton pump inhibitors	270.0 (231)	199.0 (288)	215.0 (190)	283.0 (293)	.471
Histamine receptor antagonists	40.0 (23)	35.0 (23)	45.0 (27)	37.0 (18)	.254

NOTE. Data represent 11,340,272 total PDs and 771,144 oncology-related PDs. *P* values in bold indicate statistically significant differences.
PDs, patient-days.

2013 SIR category was obtained from the Hospital Compare Web site (https://www.medicare.gov/hospitalcompare/search.html?). One-way analysis of variance was used to assess whether statistically significant differences in oncology CSL PDs per 1,000 admissions and medications across SIRs existed; an alpha level of <0.05 was considered significant.

RESULTS

Overall, 27% of hospitals had a SIR of better, 45% were no different, and 28% were worse. Table 1 displays oncology CSL PDs per 1,000 admissions for total oncology and the 6 individual CSLs, as well as medications by class. Significant differences existed in total CSL PDs per 1,000 admissions. Worse and better hospitals, respectively, had the highest (80) and lowest (49) mean compared with no different (mean, 66). Of the 6 oncology CSLs, MEDHEM had the highest mean number of PDs per 1,000 admissions, and there were significant differences across categories. Worse hospitals had the highest PDs per 1,000 admissions (34) and better hospitals had the lowest (21) compared with hospitals that were no different (mean, 27). There were also significant differences for BMT and surgical oncology PDs per 1,000 admissions, with worse hospitals having the highest among the SIR categories.

Quinolones were most commonly used in terms of mean total oncology DOTs per 1,000 PDs (38), followed by cephalosporins (25) and carbapenems (15). Although use was generally lowest in the better category and highest in the no different category, no differences existed in antibiotic DOTs per 1,000 PDs across SIRs.

Figure 1 depicts the proportion of high-risk CDI medication use by class out of total oncology use (antibiotics and gastric acid suppressants) for the 3 highest CSLs in terms of PDs—BMT, MEDHEM, and medical oncology/solid tumor—and other CSLs grouped as other. The proportions ranged for the most commonly used medications, proton pump inhibitors, quinolones, and third- and fourth-generation cephalosporins from 0.67-0.88, 0.44-0.62, and 0.24-0.41, respectively, among the oncology CSLs. The proportion of use was highest in BMT for proton pump inhibitors, in medical oncology/solid tumor for quinolones, and in MEDHEM for third- and fourth-generation cephalosporins.

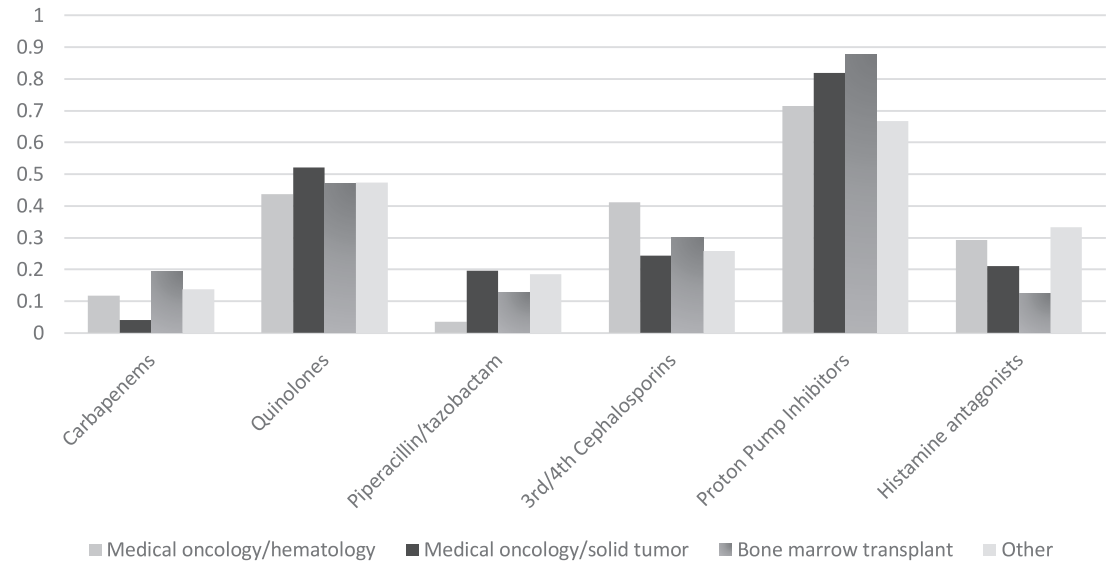

Fig 1. Proportion of medication use among individual oncology clinical service lines out of total antibiotic and gastric acid suppressant oncology clinical service line medication use. Gynecologic oncology, surgical oncology, medical oncology/radiation, and medical oncology/solid tumor were combined into the "other" category owing to lower medication use.

DISCUSSION

Results showed that hospitals with a SIR category of worse had more oncology PDs, suggesting that hospitals providing more care days for oncology patients may face challenges in obtaining better CDI performance. The most commonly used high-risk CDI medications were proton pump inhibitors, quinolones, and third- and fourth-generation cephalosporins, but there were no significant usage differences across SIRs. In assessing which individual oncology CSLs used greater proportions of high-risk medications, the proportion ranges were not very wide among the 3 most commonly used medications, indicating that there may not be a specific oncology CSL for targeting antimicrobial stewardship program interventions.

Few data are available that describe the epidemiology of CDI-specific risk factors among hospitalized oncology patients.[4,5] Patients with a cancer diagnosis are a population subgroup that is especially vulnerable to CDI development. In addition to frequent hospitalizations, antibiotic administration is common for infections that develop as a result of decreased immunity from the administration of chemotherapeutic regimens.[6] Prophylactic antibiotic regimens are also commonly administered to neutropenic patients, such as quinolones, which are high-risk agents.[7] Moreover, the administration of chemotherapeutic agents has been independently associated with CDI.[8] We did not evaluate chemotherapeutic medications, because they are often administered in outpatient settings, which serves as a study limitation. Another limitation is that the SIR represents hospital-wide rather than oncology-specific performance.

Although the number and types of oncology admissions are not modifiable, findings suggest that there may be potential target areas for medication modification to decrease CDI risk. Evaluation of proton pump inhibitor appropriateness could serve as a potential strategy. Previous studies recommended quinolones as a reasonable target, including strategies to limit their prophylaxis duration.[9,10] The need for antimicrobial coverage to treat and prevent infections for optimal outcomes needs to be weighed carefully with microbiome disruption and the risk of CDI. There is a definitive need for further research in this area to identify CDI-specific risk factors among patients with cancer, and how these various factors interplay to affect the risk level of CDI development and the impact of hospital oncology populations on CDI performance.

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