Effect of Postoperative Complications on Adjuvant Chemotherapy Use for Stage III Colon Cancer

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Objective: The National Quality Forum has endorsed a quality metric concerning the use of adjuvant chemotherapy administration in stage III colon cancer, yet a substantial treatment gap exists. Our objective was to evaluate the association of postoperative complications on the use of adjuvant therapy after colectomy for cancer.

Patients and Methods: Data from the American College of Surgeons National Surgical Quality Improvement Program and National Cancer Data Base were linked to augment cancer registry information with robust clinical data on comorbidities and postoperative complications (2006–2008). The association of complications on adjuvant chemotherapy use was assessed using hierarchical multivariable regression models.

Results: From 126 hospitals, 2368 patients underwent resection for stage III colon adenocarcinoma. Overall utilization of adjuvant chemotherapy was 63.2% (1497/2368). Of the 871 patients who did not receive chemotherapy, 652 met National Quality Forum exclusion criteria: death, severe comorbidity, refusal of care, advanced age ($\geq$80 years), or prior malignancy. Of the remaining 219 patients, 19.1% (42/219) had 1 or more serious postoperative complications (eg, pneumonia, pulmonary failure). After accounting for the aforementioned potential explanations, the utilization rate was 87.2% (1497/1716). The strongest predictors of adjuvant chemotherapy omission were prolonged postoperative ventilation, renal failure, reintubation, and pneumonia (all *P*s < 0.05). Superficial surgical site infection did not decrease adjuvant therapy receipt but delayed the time to its use by 3-fold. Serious complications increased time to chemotherapy by 65%. Abscess/anastomotic leak increased time to adjuvant chemotherapy by more than 5-fold.

Conclusions: Serious postoperative complications explained nearly 20% of the adjuvant chemotherapy treatment gap for patients with stage III colon cancer. The use of clinical data remains important when judging provider performance.

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In 2012, an estimated 103,170 new cases of colon cancer were be diagnosed in the United States, making it the fourth most common malignancy.[1] Although colon cancer incidence rates are declining, approximately 37% of patients will have regional disease at the time of diagnosis due, in part, to the continued low rate of screening.[1–3]

Nodal metastasis has long been recognized as having important implications both for prognosis and for decisions regarding systemic therapy for colon cancer.[4] Randomized trial data have demonstrated improvements in recurrence- and disease-free survival with the use of adjuvant 5-flourouracil–based chemotherapy regimens,[5,6] which became the standard of care after a National Institute of Health consensus statement in 1990.[7] Most recently, the American College of Surgeons (ACS) Commission on Cancer, American Society of Clinical Oncology, and the National Comprehensive Cancer Network established the use of adjuvant chemotherapy in stage III colon cancer as a quality metric.[8] This measure was subsequently endorsed by the National Quality Forum (NQF) in 2007[9] and will be implemented by the Centers for Medicare & Medicaid Services for public reporting and reimbursement purposes.[10]

Nevertheless, evidence suggests substantial treatment variation with respect to adjuvant chemotherapy utilization in the United States, and adherence to the adjuvant chemotherapy quality metric for stage III colon cancer remains an issue.[11,12] It is now well established that patient comorbidity profiles influence treatment patterns[13–15]; however, it is not well understood how postoperative complications influence adjuvant chemotherapy administration. Because colon surgery is associated with appreciable morbidity,[16] complications could substantially influence the use of guideline-recommended adjuvant therapy. The objective of this study was to evaluate the influence of postoperative complications on adjuvant chemotherapy treatment use and to determine the relative effect of complications on adjuvant chemotherapy delays after surgery for stage III colon cancer.

METHODS

Data Sources

To evaluate the association of postoperative complications and adjuvant chemotherapy use, we linked the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP), which contains patient demographic, comorbidity, and outcomes data, and the National Cancer Data Base (NCDB), which contains cancer-specific tumor and treatment information. Because a unique patient identifier common to each data set does not exist, patients from ACS NSQIP were linked to the NCDB on the basis of a probabilistic matching algorithm using the following variables: American Hospital Association number, patient age, sex, and date

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of operation. The final match rate was 83%, which is comparable with the linkage of NSQIP with other data sources and considered excellent without the use of direct patient identifiers.[17]

The ACS NSQIP is a surgical outcomes quality improvement program that originated in the Veterans Health Administration in 1994 and established in the private sector by the ACS beginning in 2001.[18,19] The ACS NSQIP case inclusion, exclusion, and sampling strategy has been previously described.[18,20] Using data definitions standardized across all hospitals, data are collected by trained surgical clinical reviewers and on-site audits are conducted to ensure data reliability.[21] The primary objective of the program is to report risk-adjusted 30-day outcomes information to participating hospitals for internal quality improvement purposes.

The NCDB is a joint program of the ACS Commission on Cancer and the American Cancer Society.[22] It is the largest cancer registry in the world, capturing more than 70% of all newly diagnosed malignancies in the United States from more than 1500 hospitals.[23] Data are abstracted by trained cancer registrars who are audited periodically to ensure data reliability.

Patient Selection

From the ACS NSQIP, patients undergoing colon resection for cancer from January 1, 2006, to December 31, 2008, were identified on the basis of *Current Procedure Terminology*[24] and *International Classification of Disease, Ninth Revision*,[25] codes. Patients from the NCDB were identified using *International Classification of Disease—Oncology, Third Revision*,[26] codes. Patients were included in this study if a colectomy was performed for pathologically determined stage III colon cancer on the basis of American Joint Committee on Cancer, Seventh Edition, pathological staging criteria.[27] Exclusion criteria were as follows: American Association of Anesthesiology (ASA) class V (ie, moribund at the time of surgery), use of preoperative chemo- or radiotherapy, and histological subtype other than adenocarcinoma.

Adjuvant Chemotherapy Use

The primary variable of interest was the use of adjuvant chemotherapy after surgical resection for stage III colon adenocarcinoma. We therefore assessed both its receipt (yes vs no) and, among patients who were treated, the number of days from surgery to chemotherapy initiation. The NCDB captures chemotherapy use if it was delivered as part of first-course therapy (ie, not for recurrent disease or the treatment of another cancer). Time to adjuvant therapy was measured in days from the date of surgery to chemotherapy initiation. Treatment delay was defined as 60 days or more, which was the approximate upper quartile number of days from surgery to chemotherapy initiation. This time interval is clinically appropriate and consistent with other studies.[28]

Outcomes

Thirteen 30-day outcomes were evaluated. First, a serious complication composite outcome was evaluated that included major surgical and medical adverse events. A serious complication was defined as the occurrence of at least 1 of the following: organ space surgical site infection (SSI), deep SSI, wound dehiscence, sepsis/shock, venous thromboembolism (VTE), pneumonia, prolonged ventilation, reintubation, return to the operating room, urinary tract infection, renal failure, myocardial infarction, or cardiac arrest. We also separately focused on the following individual complications: overall SSI, superficial SSI, organ space infection, wound dehiscence, prolonged ventilation, reintubation, pneumonia, VTE, renal failure, urinary tract infection, sepsis/septic shock, and return to the operating room. Patients were precluded from being categorized as having the following complications if the condition was documented preoperatively: wound infection, pneumonia, ventilator dependence/reintubation, or renal failure. Specific outcome definitions are described elsewhere.[18]

Statistical Analysis

Descriptive statistics were calculated using the χ^2 test for categorical variables and the Mann-Whitney *U* test to compare medians. We first assessed the proportion of adjuvant chemotherapy omission potentially explained by postoperative complications after applying the NQF measure exclusion criteria: age 80 years or older, prior neoplasm, severe patient comorbidities, chemotherapy offered but not administered (eg, patient refused), and death. Next, we evaluated the association between postoperative complications and adjuvant therapy use. Because many NQF exclusion criteria may actually reflect the direct effects of postoperative complications and we wanted to measure an unbiased association of complications with adjuvant treatment, the remainder of the analysis excluded patients who died before chemotherapy administration (n = 47). As a sensitivity analysis, we performed the analysis after the NQF exclusion criteria with

TABLE 1. Characteristics of Stage III Colon Cancer Patients (N = 2368) Who Underwent Surgical Resection (2006–2008)

Characteristic	n	%
Age, median (IQR), yr	68 (57–79)	
Sex (female)	1224	51.7
ASA class		
I/II	1151	48.6
III/IV	1217	51.4
Functional status		
Independent	2198	92.8
Dependent	170	7.2
Albumin <3.0 g/dL	187	7.9
BMI, kg/m^2		
Underweight	62	2.7
Normal	729	31.1
Overweight	818	34.9
Obese	428	18.3
Morbidly obese	307	13.1
Previous cardiac event	329	13.9
HTN	1312	55.4
PVD	37	1.6
Dyspnea	341	14.4
Diabetes	421	17.8
Income		
≥$60,000	436	24.8
$45,000–$59,000	482	27.4
$35,000–$44,000	446	25.3
<$35,000	397	22.5
Tumor grade		
Low	155	6.7
Intermediate	1454	62.9
High	701	30.4
Operative approach		
Open	1517	64.1
Laparoscopic	851	35.9
Surgical volume status* (cases/yr)		
<80	646	27.8
80–160	1158	49.7
≥160	524	22.5

Missing values: albumin, 705 (29.8%); BMI, 24 (1.0%); income, 607 (25.6%); grade, 58 (2.5%).

*Surgical volume status variable was calculated on the basis of the full NCDB data set.

BMI indicates body mass index; HTN, hypertension; PVD, peripheral vascular disease.

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similar results. Regression models were developed using generalized linear mixed models to evaluate the association of postoperative complications on (1) adjuvant therapy omission and (2) treatment delay (≥60 days from surgery to initiation of chemotherapy). These models accounted for the hierarchical nature of patients nested within hospitals by including the hospital as a random effect.[29] Variables were included in all models if they had a univariate association with the dependent variable at a $P < 0.2$ level or were considered clinically important. Final models included the following explanatory variables: age, sex, ASA class, functional status, preoperative dyspnea, previous neurological, cardiac, or vascular event, hypertension, body mass index, diabetes, preoperative albumin, tumor grade, income, and average annual colorectal surgical case volume, which was calculated from the full NCDB data set (<80, 80–160, ≥160 cases/yr). For both dependent variables assessed (ie, adjuvant therapy omission and treatment delay), postoperative complications were separately evaluated. The level of statistical significance was set at $P < 0.05$, and all analyses were performed using SAS 9.3 (SAS Institute, Cary, NC). The Northwestern University institutional review board approved this study as exempt.

RESULTS

From January 1, 2006, to December 31, 2008, a total of 2368 patients from 126 hospitals who underwent resection for stage III colon adenocarcinoma were evaluated. The median age at the time of surgery was 68 years (interquartile range, 57–79). Most patients were ASA class II (45.7%) or III (45.6%), with independent functional status (92.8%) and a normal serum albumin level (92.1%). Most patients underwent open resection (64.1%). Additional characteristics are detailed in Table 1.

Thirteen complications were evaluated, and event rates varied considerably. Eighty percent of patients did not experience any postoperative complication, whereas 15.8% of patients experienced at least 1 serious complication. The most common complications were overall SSI (10.9%), superficial SSI (7.7%), return to the operating room (5.0%), and sepsis/septic shock (5.0%). The least common complication was renal failure (1.0%).

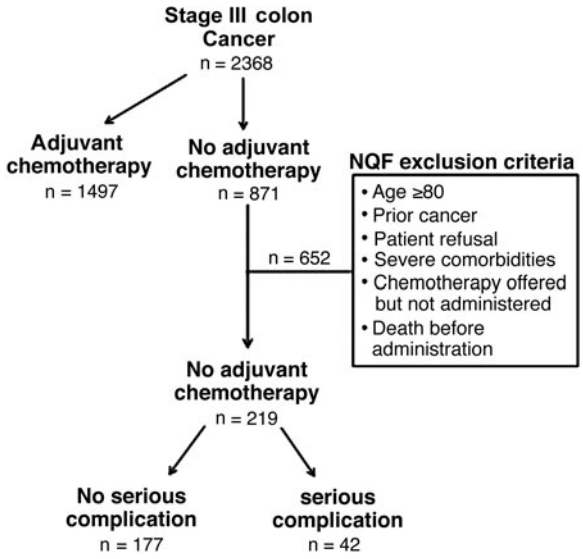


FIGURE 1. Adjuvant chemotherapy flow diagram incorporating NQF exclusion criteria in patients with stage III colon cancer (2006–2008). Serious complications include organ space SSI, deep SSI, wound dehiscence, sepsis/shock, VTE, pneumonia, prolonged ventilation, reintubation, return to operating room, urinary tract infection, renal failure, myocardial infarction/cardiac arrest.

Adjuvant Chemotherapy Utilization

The overall utilization of adjuvant chemotherapy was 63.2% (1497/2368). Among the 871 patients who did not receive adjuvant treatment, 77.5% (652/871) met NQF exclusion criteria: death, severe comorbidity, refusal of care, advanced age (≥80 years), and prior neoplasm (in situ or invasive). Thirty-day mortality was 1.7% (40/2368), and an additional 0.3% (7/2368) died before adjuvant chemotherapy initiation. Of the remaining 219 patients who did not have another

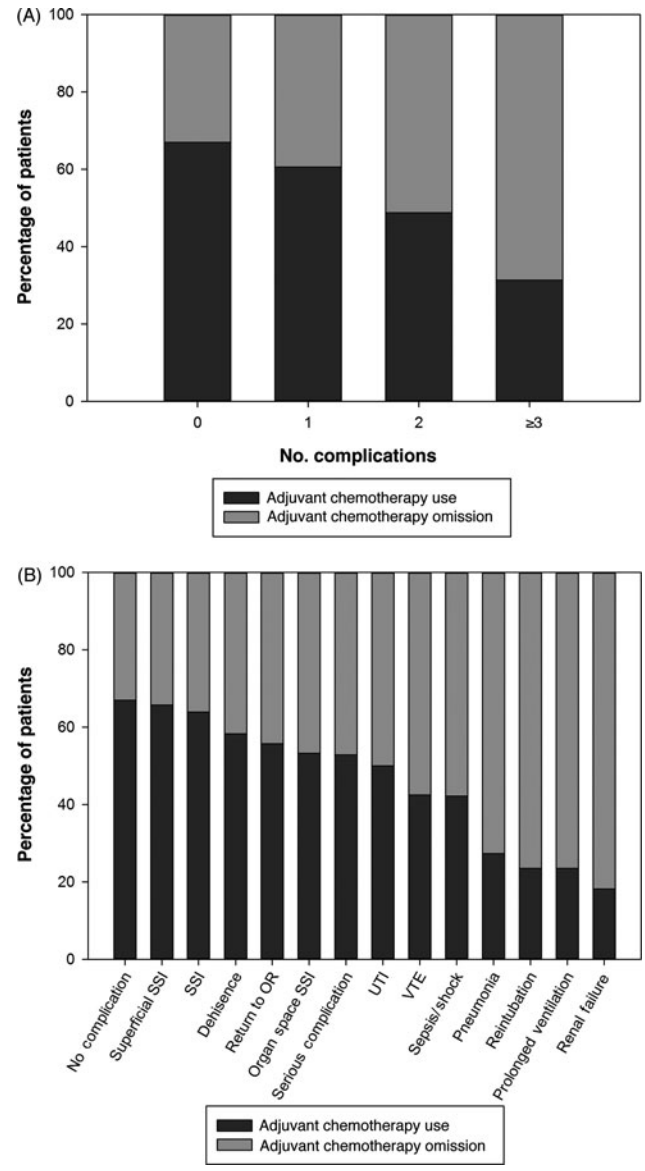


FIGURE 2. Adjuvant chemotherapy use by (A) complication number (0, 1, 2, ≥3) and (B) complication type after surgical resection among patients with stage III colon cancer. OR indicates operating room; UTI, urinary tract infection.

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reason precluding adjuvant chemotherapy receipt, 19.1% (42/219) experienced a serious postoperative complication. After accounting for these potential explanations for not receiving adjuvant chemotherapy, the overall utilization rate was 80.7% (1497/1855 patients) (Fig. 1).

After excluding deaths, we then assessed the influence of the number and type of postoperative complications on adjuvant therapy use. As the number of complications increased from 0 to 3 or more, the use of adjuvant chemotherapy decreased from 67.0% to 31.3% (Fig. 2A). Chemotherapy use also varied by specific complication type, from 65.7% for superficial SSI to 18.2% after renal failure (Fig. 2B).

Effect of Complications on Adjuvant Chemotherapy Omission

Table 2 provides details of the association of postoperative complications and adjuvant therapy receipt. After adjustment, the occurrence of any serious complication increased the likelihood of not receiving adjuvant chemotherapy by more than 50% [odds ratio (OR): 1.56; 95% confidence interval (CI), 1.20–2.04]. The strongest predictors of adjuvant chemotherapy omission were prolonged postoperative ventilation (OR: 7.36; 95% CI, 2.77–19.60), renal failure (OR: 6.69; 95% CI, 1.81–24.77), reintubation (OR: 5.28; 95% CI, 2.00–13.94), and pneumonia (OR: 3.80; 95% CI, 1.98–7.28). Other complications associated with chemotherapy omission were organ space SSI, VTE, sepsis/shock, and return to the operating room.

Effect of Complications on Adjuvant Chemotherapy Initiation

The overall time to adjuvant chemotherapy initiation after resection was a median of 45 days. Among patients without any complication, the median days from surgery to adjuvant therapy was 43, which increased substantially after most postoperative complications (any serious complication: 50 days; superficial SSI: 57 days; wound dehiscence: 60 days; organ space SSI: 73 days; sepsis/septic shock: 60 days; reintubation or prolonged ventilation: 77 days) (Fig. 3). After adjustment, the occurrence of a serious complication increased the likelihood of adjuvant chemotherapy treatment delay by 65% (OR: 1.65; 95% CI, 1.10–2.50). Other complications associated with treatment delay were overall SSI (OR: 3.35; 95% CI, 2.14–5.26), superficial SSI (OR: 2.80; 95% CI, 1.68–4.66), organ space SSI (OR: 5.74; 95% CI, 2.27–14.15), and sepsis/septic shock (OR: 3.65; 95% CI, 1.68–7.95) (Table 2).

Effect of Patient and Hospital Factors on Adjuvant Chemotherapy Utilization

The influence of patient-level factors on adjuvant chemotherapy omission and treatment delay was also assessed (Table 3). Age, ASA class, functional status, hypoalbuminemia, history of a cardiac event, and low-income level all increased the likelihood of chemotherapy omission. The strongest predictor of failure to receive adjuvant chemotherapy was age 75 years or older (vs <55 years) (OR: 5.48; 95% CI, 3.91–7.67). The only patient-level predictors of adjuvant chemotherapy treatment delay were history of a cardiac event and

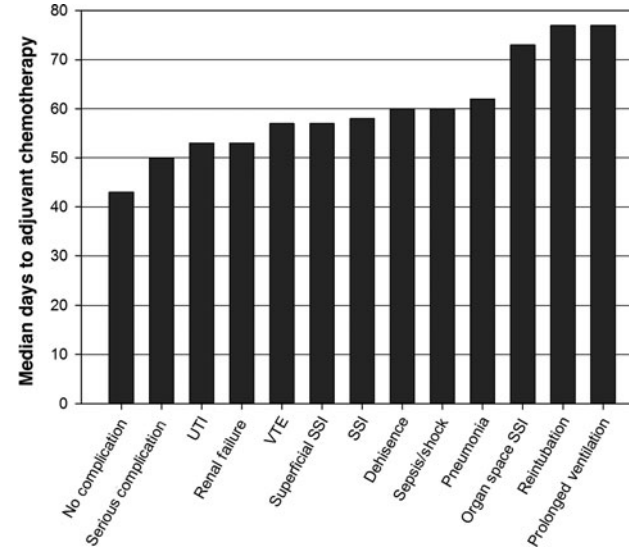


FIGURE 3. Median number of days from surgery to adjuvant chemotherapy initiation among patients with stage III colon cancer (2006–2008). UTI indicates urinary tract infection.

TABLE 2. Association Between Postoperative Complication and Omission or Delay of Adjuvant Chemotherapy* Administration Among Patients With Stage III Colon Cancer After Resection (2006–2008)

	Adjuvant Chemotherapy Omission*		Delay in Adjuvant Chemotherapy†	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Serious complication	1.78 (1.42–2.23)	1.56 (1.20–2.04)	1.60 (1.08–2.38)	1.65 (1.10–2.50)
SSI	1.03 (0.78–1.35)	1.19 (0.86–1.65)	3.25 (2.15–4.92)	3.35 (2.14–5.26)
Superficial SSI	0.94 (0.68–1.30)	1.04 (0.71–1.53)	2.68 (1.69–4.26)	2.80 (1.68–4.66)
Organ space SSI	1.62 (0.97–2.68)	1.92 (1.04–3.53)	6.10 (2.58–14.44)	5.74 (2.27–14.15)
Wound dehiscence	1.30 (0.57–2.94)	1.47 (0.55–3.90)	2.91 (0.72–11.74)	2.27 (0.39–13.17)
Prolonged ventilation	6.05 (2.73–13.43)	7.36 (2.77–19.60)	—	—
Reintubation	6.05 (2.73–13.43)	5.28 (2.00–13.94)	—	—
Pneumonia	5.07 (2.93–8.78)	3.80 (1.98–7.28)	2.81 (0.90–8.78)	2.22 (0.52–9.44)
VTE	2.49 (1.33–4.70)	2.43 (1.12–5.27)	1.11 (0.35–3.57)	1.16 (0.27–4.95)
Renal failure	8.30 (2.80–24.60)	6.69 (1.81–24.77)	—	—
UTI	1.86 (1.23–2.82)	1.33 (0.81–2.20)	2.18 (1.12–4.24)	2.14 (0.97–4.72)
Sepsis/shock	2.61 (1.79–3.81)	2.20 (1.39–3.48)	2.90 (1.51–5.56)	3.65 (1.68–7.95)
Return to operating room	1.47 (1.01–2.15)	1.66 (1.06–2.60)	0.92 (0.47–1.80)	0.87 (0.41–1.85)

*Calculations excluded patients who died before chemotherapy initiation.
†Delay to chemotherapy defined as 60 days or more after the index procedure.
UTI indicates urinary tract infection; —, model did not converge.

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TABLE 3. Association of Patient Characteristics and Omission of Adjuvant Chemotherapy, Accounting for Serious Postoperative Adverse Events, Among Patients With Stage III Colon Cancer (2006–2008)

	Adjuvant Chemotherapy Omission*		Delay in Adjuvant Chemotherapy†	
	Unadjusted OR (95% CI)	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**
Sex (female)	0.94 (0.79–1.12)	1.00 (0.81–1.22)	1.19 (0.91–1.56)	1.11 (0.82–1.52)
Age, yr				
<55	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
55–64	1.64 (1.19–2.27)	1.48 (1.04–2.10)	1.06 (0.72–1.56)	0.92 (0.60–1.41)
65–74	2.43 (1.79–3.30)	2.10 (1.49–2.95)	1.19 (0.81–1.74)	1.09 (0.70–1.69)
≥75	7.34 (5.54–9.73)	5.48 (3.91–7.67)	1.58 (1.08–2.31)	1.44 (0.90–2.31)
ASA class				
I/II	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
III/IV	2.62 (2.19–3.12)	1.53 (1.21–1.93)	1.62 (1.23–2.12)	1.27 (0.90–1.79)
Functional status				
Independent	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Dependent	5.34 (3.73–7.65)	3.07 (2.00–4.71)	0.84 (0.36–1.98)	0.73 (0.27–2.03)
Albumin <3.0 g/dL	2.57 (1.85–3.56)	1.60 (1.08–2.38)	0.70 (0.35–1.39)	0.63 (0.29–1.36)
BMI, kg/m^2				
Underweight	1.19 (0.69–2.03)	0.90 (0.49–1.67)	1.30 (0.55–3.10)	1.37 (0.53–3.52)
Normal	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Overweight	0.68 (0.55–0.84)	0.74 (0.58–0.95)	1.12 (0.79–1.59)	1.13 (0.76–1.67)
Obese	0.67 (0.52–0.86)	0.71 (0.53–0.96)	1.41 (0.95–2.09)	1.31 (0.84–2.06)
Morbidly obese	0.50 (0.37–0.67)	0.57 (0.40–0.82)	1.03 (0.66–1.61)	0.85 (0.50–1.44)
Previous cardiac event	2.31 (1.82–2.94)	1.40 (1.03–1.90)	2.11 (1.40–3.18)	1.75 (1.05–2.93)
HTN	1.71 (1.44–2.04)	0.94 (0.75–1.19)	1.45 (1.11–1.90)	1.15 (0.81–1.63)
PVD	2.70 (1.40–5.24)	1.54 (0.68–3.48)	0.93 (0.25–3.44)	0.40 (0.08–2.08)
Dyspnea	1.48 (1.17–1.87)	1.01 (0.76–1.35)	1.17 (0.80–1.72)	1.03 (0.65–1.63)
Diabetes	1.37 (1.10–1.70)	1.13 (0.86–1.48)	1.38 (0.97–1.96)	1.10 (0.72–1.69)
Income				
≥$60,000	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
$45,000–$59,000	1.02 (0.78–1.35)	0.98 (0.69–1.39)	1.05 (0.65–1.69)	1.91 (1.12–3.23)
$35,000–$44,000	1.03 (0.78–1.37)	1.15 (0.82–1.61)	1.88 (1.19–2.99)	1.12 (0.66–1.89)
<$35,000	1.47 (1.11–1.96)	1.50 (1.04–2.14)	2.06 (1.26–3.36)	1.98 (1.13–3.47)
Tumor grade				
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Intermediate	0.81 (0.57–1.15)	1.00 (0.66–1.52)	1.19 (0.66–2.14)	1.18 (0.62–2.25)
High	0.97 (0.67–1.39)	0.96 (0.62–1.49)	1.02 (0.55–1.89)	1.09 (0.55–2.17)
Serious complication	1.78 (1.42–2.23)	1.57 (1.20–2.05)	1.60 (1.08–2.38)	1.65 (1.09–2.49)
Surgical volume status‡ (cases/yr)				
<80	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
80–160	1.0 (0.81–1.22)	1.01 (0.40–2.53)	0.91 (0.69–1.21)	1.65 (0.05–59.51)
≥160	0.92 (0.72–1.17)	1.06 (0.45–2.50)	0.78 (0.55–1.12)	1.17 (0.04–33.67)

*Calculations excluded patients who died before chemotherapy initiation.
†Defined as 60 days or more from surgery to adjuvant therapy.
‡Surgical volume status variable was calculated on the basis of the full NCDB data set.
BMI indicates body mass index; HTN, hypertension; PVD, peripheral vascular disease.

low-income level. Average annual surgical case volume was not associated with adjuvant therapy omission or treatment delay.

DISCUSSION

Hospital performance with respect to cancer care will soon be measured, in part, on established quality-of-care metrics such as adjuvant chemotherapy utilization in stage III colon cancer. Previous work has focused on the association of patient factors (eg, comorbidity, demographics) on adjuvant treatment patterns[11,13–15]; however, postoperative complications directly influence chemotherapy receipt.[28] At present, the NQF colon cancer adjuvant chemotherapy quality measure does not consider clinical information such as the occurrence of postoperative complications, and it is unknown how these events could influence utilization patterns. In the present study using national clinical and cancer registry data, we found that serious postoperative complications such as major cardiac, pulmonary, wound occurrence, and infectious events were associated with substantial reductions in adjuvant chemotherapy utilization and treatment delays.

In a previous study, Kahn and colleagues[30] demonstrated that chemotherapy use varied from 92% among patients aged 18 to 54 years to 50% in those 75 years or older. In a separate report using SEER-Medicare data, overall adjuvant chemotherapy use was 66%, which decreased to 54% among patients who experienced at least 1 complication according to administrative data.[28] However, administrative data can underreport postoperative complications by nearly 20%, as claims-based complication information is not reliably or consistently captured.[31,32] Using linked clinical and cancer registry data, we found that among 2368 patients, only 63.2% received guideline-recommended care. After applying all NQF exclusion criteria (death, severe comorbidity, refusal of care, age ≥80 years, history of neoplasm), a serious complication accounted

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for almost 1 in 5 of the remaining patients. As a result, using current NQF exclusion criteria as a baseline, if certain serious postoperative complications were additionally considered as valid reasons for not receiving chemotherapy, the proportion of patients not receiving guideline-recommended care would be reduced by nearly 20%. Thus, clinical data on postoperative complications can impact provider profiling for quality-of-cancer-care metrics.

We next assessed the risk-adjusted association of individual complications on adjuvant therapy omission. In a recent study based on administrative data, Hendren and colleagues[28] found that complications were significantly associated with adjuvant chemotherapy omission (OR: 1.76; 95% CI, 1.59–1.95). However, this work did not focus on individual complications and identified adverse events on the basis of *International Classification of Disease, Ninth Revision*, billing codes. In the present study, we used clinically collected data and also found that serious complications increased the likelihood of adjuvant chemotherapy omission (OR: 1.56; 95% CI, 1.20–2.04). We additionally evaluated specific postoperative adverse events and found pulmonary (prolonged ventilation, reintubation, pneumonia), organ space SSI, renal failure, VTE, and septic complications were significantly associated with adjuvant chemotherapy omission.

The Institute of Medicine has identified the timeliness of care as 1 of the 6 domains of quality health care.[33] Time lines of cancer care may not only reflect intrinsic factors such as hospital efficiency and resource utilization but may also be influenced by clinical events such as postoperative complications. A recent meta-analysis of adjuvant therapy treatment times in colorectal cancer revealed that a 4-week treatment delay was associated with reductions in both overall survival and disease-free survival.[34] However, no previous study has detailed the contribution of specific complications to treatment delay in colon cancer. Hendren and colleagues[28] evaluated the association of complications on treatment delays and found that the occurrence of any complication increased adjuvant therapy treatment delay (defined $\geq$60 days from surgery) by 21%. In the present study, we found that the occurrence of at least 1 serious postoperative complication increased the likelihood of treatment delay by 65%. Moreover, specific complications were especially associated with treatment delay, namely, overall SSI, superficial SSI, organ space SSI, and postoperative sepsis. Notably, superficial SSIs, which are common and generally considered minor postoperative events, were not associated with adjuvant therapy omission; however, they increased the likelihood of treatment delay by nearly 3-fold.

These findings broaden our understanding of adherence with the use of adjuvant chemotherapy for colon cancer. Although most studies have focused on comorbidity burden, this work demonstrates that even after controlling for these predictors, postoperative complications have a dramatic effect on chemotherapy omissions and treatment delays. Although patients who are older and possess greater comorbidity burden may be at an increased risk, many post–colectomy complications also occur in younger, healthier populations.

Extensive work has detailed the influence of patient comorbidity and demographics on guideline adherence in colon cancer.[12,14,30] In a recent observational study by Chagpar and colleagues[14] using cancer registry data, patient age 75 years or older was the strongest predictor of nonadherence to guideline treatment in stage III colon cancer. However, limited comorbidity information is available in cancer registries, raising concerns regarding residual confounding. Nevertheless, our results also demonstrate the influence of age after controlling for detailed patient comorbidities and postoperative complications using high-quality clinical data. Specifically, age increased the likelihood of adjuvant therapy omission by more than 5-fold. These data suggest that underuse of chemotherapy in the older population is not merely a reflection of comorbidity burden, but it may reflect other issues such as referral patterns, patient preferences, and provider biases. Although older patients are excluded from the NQF measure, evidence indicates that these patients benefit from adjuvant therapy and perhaps should not necessary be removed from the measure denominator.[12] With respect to hospital characteristics, similar to other studies, surgical case volume status did not influence adjuvant treatment utilization.[13]

Limitations

This work has several limitations that should be considered. First, we were only able to evaluate hospitals in both the ACS NSQIP and the NCDB and therefore these findings may not be generalized to other hospitals. Nevertheless, this study included data from 126 hospitals and is the only national data set that includes clinical demographic, comorbidity, and short-term outcomes data and detailed tumor, staging, and cancer-specific treatment information. Second, these results are from an observational study that included more than 2000 patients with stage III colon cancer and could therefore only determine associations, not causal relationships, between complications and detailed adjuvant therapy utilization patterns. Although comorbidities certainly explain part of the association between complications and adjuvant treatment, this is not the only possibility and it remains feasible that there is a direct link. For example, young and healthy patients without comorbidities were also less likely treated with adjuvant therapy after a postoperative complication. Finally, this study was limited to the variables and outcomes included in the ACS NSQIP and NCDB data sets. However, the merged data set contains more than 300 patient demographic, comorbidity, outcomes, cancer staging, and treatment variables that capture most relevant information.

Conclusions

Serious postoperative complications explained nearly 20% of the adjuvant chemotherapy treatment gap among patients with stage III colon cancer. Adjuvant chemotherapy omission and treatment delays were influenced by postoperative 30-day complications even after controlling for comorbidity and demographic factors. Consideration of complications using clinical data is clearly important in quality measure development and ultimately to adequately assess provider performance.

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