Adjuvant Chemotherapy Use and Adverse Events Among Older Patients With Stage III Colon Cancer

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Context Randomized trials suggest adjuvant chemotherapy is effective for older patients with stage III colon cancer. However, older patients are less likely to receive this therapy than younger patients, perhaps because of concern about adverse effects.

Objective To evaluate adjuvant chemotherapy use and outcomes for older patients with stage III colon cancer from well-defined population-based settings and health care systems.

Design Observational study of adjuvant chemotherapy use and outcomes by age using Poisson regression to estimate the number of adverse events adjusted for demographic and clinical factors, including comorbid illness and specific elements of chemotherapy regimens documented with clinically detailed medical record reviews and patient and surrogate surveys.

Setting Five geographically defined regions (Alabama, Iowa, Los Angeles County, northern California, and North Carolina), 5 integrated health care delivery systems, and 15 Veterans Affairs hospitals.

Patients Six hundred seventy-five patients diagnosed with stage III colon cancer from 2003 through 2005 who underwent surgical resection and were followed up for as long as 15 months postdiagnosis.

Main Outcome Measures Chemotherapy regimen, dose, duration, and annualized mean number of adverse events stratified by age.

Results Of 202 patients aged 75 years and older, 101 (50%) received adjuvant chemotherapy compared with 87% of 473 younger patients (difference, 37%; 95% confidence interval [CI], 30%-45%). Among patients who received adjuvant chemotherapy, 14 patients (14%) aged 75 years and older and 178 younger patients (44%) received a regimen containing oxaliplatin (difference, 30%; 95% CI, 21%-38%). Older patients were less likely to continue treatment, such that by 150 days, 99 patients (40%) aged 65 years and older and 68 younger patients (25%) had discontinued chemotherapy (difference, 15%; 95% CI, 7%-23%). Overall, 162 patients (24%) had at least 1 adverse clinical event, with more events among patients treated with vs without adjuvant chemotherapy (mean, 0.39 vs 0.16; difference, 0.23; 95% CI, 0.11-0.36; P < .001). Among patients receiving adjuvant chemotherapy, adjusted rates of late clinical adverse events were lower for patients 75 years and older (mean, 0.28) vs for younger patients (0.35 for ages 18-54 years, 0.52 for ages 55-64 years, and 0.45 for ages 65-74 years; P = .008 for any age effect).

Conclusion Among patients with stage III colon cancer who underwent surgical resection and received adjuvant chemotherapy, older patients in the community received less-toxic and shorter chemotherapy regimens, and those treated had fewer adverse means of adverse events than younger patients.

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Of randomized controlled trials evaluating the effectiveness of adjuvant chemotherapy for patients older than 80 years as well as comorbid conditions and drug toxicities as the most common reasons for not treating older patients with adjuvant chemotherapy. Patients in clinical trials are systematically different from those in the community, where most decisions about chemotherapy are made. Compared with patients diagnosed nationally with stage III colon cancer, trial patients are younger, more likely to be white, and less likely to have comorbidities or functional impairment than community-dwelling adults.

Therefore, we analyzed the use of adjuvant chemotherapy and clinical adverse events by age in a large multiregional cohort of patients with stage III colon cancer.

METHODS
Study Design and Sample
The Cancer Care Outcomes Research and Surveillance (CanCORS) study examined care delivered to population-health system–based cohorts of patients, including 4713 patients newly diagnosed with colorectal cancer between 2003 and 2005 and followed up for as long as 15 months. Patients were living in northern California, Los Angeles County, North Carolina, or Alabama (Iowa research included only patients with lung cancer and thus was not included in this analysis) or received care in 1 of 5 large health maintenance organizations or 15 Veterans Affairs hospitals. Human subjects committees at all participating institutions approved the study. All interviewed participants provided verbal consent based on interviewer scripts approved by relevant institutional review boards, and all living patients provided written consent for medical record review.

This analysis included 675 patients with stage III colon cancer who underwent surgical resection and had survey and medical record data (Figure 1). We used data from a baseline patient survey approximately 4 months after diagnosis and from the review of medical records from multiple providers from 3 months before to 15 months after diagnosis. Surveys were conducted in English, Spanish, and Chinese and included 4 options: a 45-minute full survey (71%); a 20-minute brief survey for patients too sick to complete the full one (13%); and 2 surrogate surveys, one for patients alive but too sick to participate (9%) and one for patients deceased at the time of the baseline survey (7%). Self-reported patient demographics, including age, sex, race/ethnicity, income, and marital status, were included to control for sociodemographic factors related to access and use. We used data from medical records to assign American Joint Committee on Cancer collaborative stage to 76% of study patients; where complete stage data were not available from medical records, we obtained collaborative stage data from participating cancer registries.

We assessed comorbidity from 3 months before diagnosis to the time of initial treatment from the medical record using the Adult Comorbidity Evaluation 27 instrument. Patients’ recalled health status during the 4 weeks prior to diagnosis was obtained from the baseline survey. Other measures of patient-level burden of illness included a history of prior cancer and assignment of a do-not-resuscitate (DNR) order prior to the first hospitalization with an admission date more than 30 days after surgical resection.

Adverse Events
We defined adverse clinical events as the first occurrence of each of a subset of 39 clinical diagnoses that could reliably be abstracted from the medical record and that were important enough to adversely affect the patient’s process of care, quality of life, and survival. Events were included regardless of whether the events could be directly attributed to treatment.

Using the same list of clinical diagnoses, we defined early and late adverse events. Those that occurred before or at 30 days after surgical resection were considered early and were used as predictor variables. Events that occurred between 31 days after surgical resection and 15 months after diagnosis were used as a surrogate for events attributable to chemotherapy and considered late. (See eTable 1, available at http://www.jama.com, for complete listing of late adverse events.) We defined outcomes as annualized late adverse event rates, calculated by dividing the sum of each patient’s unique clinical events by the total number of days alive subsequent to 30 days after resection.
Adjuvant Chemotherapy Use
Chemotherapy was defined as adjuvant if the first dose was administered within 6 months after surgical resection and prior to any cancer recurrence. We classified initial chemotherapy regimens into oxaliplatin-containing, non–oxaliplatin-containing, and unknown. Chemotherapy initiation was categorized as days from surgical resection to first chemotherapy. Patients were considered to have received reduced-dose chemotherapy if their initial regimen included at least 1 dose of fluorouracil bolus less than 350 mg/m², fluorouracil continuous less than 600 mg/m², capecitabine less than 850 mg/m², or oxaliplatin less than 75 mg/m². Duration of treatment was categorized by specifying the proportion of patients discontinuing chemotherapy by a specified date (eg, before 6 months) and also as a continuous variable counting the number of days from first to last chemotherapy dose.

We validated the accuracy of medical record abstraction by comparing 146 medical record abstractions with gold-standard records specified by the research team. The mean (SD) agreement score was 0.83 (0.22).

Statistical Analyses
We used univariate analyses to describe study patients, chemotherapy initiation, initial regimen, dose, duration, and adverse event rates using CanCORS core and medical record abstraction data sets. All significance tests were 2-sided at the .05 level. Analyses used SAS version 9.1.3 (SAS Institute, Cary, North Carolina) and Stata version 9.2 (StataCorp, College Station, Texas).

We used a Poisson model to describe the count of unique patient-level adverse events with exposure defined as their total number of days alive subsequent to 30 days postresection.23 We also used recycled predictions, a method that produces adjustments in the event rate scale,24 to estimate the yearly late rate scale,24 to estimate the yearly late

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adverse event rates of patients with vs without chemotherapy stratified by age.

Independent variables included age, sex, race/ethnicity, income, marital status, burden of illness (survey type, prediagnosis health status, comorbidity, early adverse events, prior cancer, and early DNR order), initial adjuvant chemotherapy regimen (with or without oxaliplatin, missing regimen, or none), chemotherapy initiation date, reduced-dose chemotherapy, chemotherapy duration less than 6 months, and number of days from first to last chemotherapy. We treated sites as fixed rather than random effects because we studied a limited number of sites that were purposively selected rather than sampled from a larger number of sites. The model also adjusted for calendar time trends and days from diagnosis to survey.

We compared patients aged 75 years and older with patients in younger age categories and tested for interactions between age and survey type, prediagnosis health status, comorbidity, and postoperative adverse events; between age and chemotherapy type (oxaliplatin vs not); and between comorbidity and chemotherapy (oxaliplatin vs not). Two statistically significant interactions were included in the model: youngest age category × no adjuvant chemotherapy and surrogate survey × nonoxaliplatin chemotherapy use.

We assessed whether results were sensitive to the model chosen by fitting an alternative model using inverse probability of treatment weights based on propensity score for receiving any chemotherapy and separately for receiving individual chemotherapy regimens.25,26 Alternative models were compared on coefficient values and statistical significance.

## Table 2. Burden of Illness Characteristics for Adjuvant Chemotherapy Users and Nonusers Overall and by Age Categories (Unadjusted)\(^b\)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients</th>
<th>Aged 18-54 y</th>
<th>Aged 55-64 y</th>
<th>Aged 65-74 y</th>
<th>Aged 75 y</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health status, mean (95% CI)</td>
<td>43 (41-45)</td>
<td>45 (44-46)</td>
<td>.08</td>
<td>45 (37-53)</td>
<td>44 (41-46)</td>
</tr>
<tr>
<td>Comorbidity, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>26 (16)</td>
<td>150 (29)</td>
<td>&lt;.001</td>
<td>4 (36)</td>
<td>58 (44)</td>
</tr>
<tr>
<td>Mild</td>
<td>68 (41)</td>
<td>219 (43)</td>
<td>.08</td>
<td>4 (36)</td>
<td>51 (39)</td>
</tr>
<tr>
<td>Moderate</td>
<td>36 (22)</td>
<td>87 (17)</td>
<td>.047</td>
<td>1 (9)</td>
<td>16 (12)</td>
</tr>
<tr>
<td>Severe</td>
<td>34 (21)</td>
<td>57 (11)</td>
<td>.001</td>
<td>2 (18)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Survey, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full</td>
<td>86 (63)</td>
<td>387 (75)</td>
<td>&lt;.001</td>
<td>9 (62)</td>
<td>116 (89)</td>
</tr>
<tr>
<td>Brief</td>
<td>17 (13)</td>
<td>71 (14)</td>
<td>.16</td>
<td>1 (9)</td>
<td>12 (9)</td>
</tr>
<tr>
<td>Surrogate survey, alive or deceased</td>
<td>59 (38)</td>
<td>55 (11)</td>
<td>.01</td>
<td>1 (9)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Early clinical adverse events score, mean (95% CI)</td>
<td>0.59 (0.42-0.77)</td>
<td>0.35 (0.26-0.41)</td>
<td>&lt;.001</td>
<td>0.27 (0.14-0.40)</td>
<td>0.35 (0.23-0.47)</td>
</tr>
<tr>
<td>Prior cancer, No. (%)</td>
<td>41 (25)</td>
<td>54 (11)</td>
<td>&lt;.001</td>
<td>2 (18)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Early DNR order, No. (%)</td>
<td>4 (2.47)</td>
<td>1 (0.19)</td>
<td>.01</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: chemo, chemotherapy; DNR, do not resuscitate; IQR, interquartile range.

\(^b\)Burden of illness is the phrase used to describe prediagnosis health status, comorbidity, type of survey, early clinical outcomes, prior cancer, and DNR order prior to first hospitalization following resection surgery.

\(^c\)P-values are generated as follows for comparisons of variables by age: Fisher exact tests for dichotomous variables and categorical variables; Poisson tests for count variables, and F tests from analysis of variance for continuous variables.

\(^d\)Surveys were conducted to optimize patient participation, including the 45-minute full survey (71%), the 20-minute brief survey for patients too sick to complete the full (13%), and a surrogate survey for patients alive but too sick (9%) and for patients deceased at the time of the baseline survey (7%).
Adjuvant Chemotherapy

Overall, patients receiving adjuvant chemotherapy were significantly less burdened with comorbid illness. Among adjuvant chemotherapy users, 150 (29%) had no comorbidity compared with 26 (16%) among patients not receiving chemotherapy (difference, 13%; 95% CI, 6%-20%) (Table 2).

Overall, 513 of 675 patients with stage III colon cancer (75%) received any adjuvant chemotherapy. Of the 202 patients 75 years and older, 101 (50%) received adjuvant chemotherapy compared with 87% of 473 younger patients (difference, 37%; 95% CI, 30%-45%; P < .001). Among adjuvant chemotherapy users, 14 (14%) of patients 75 years and older and 178 (44%) of younger patients used an oxaliplatin-containing regimen (difference, 30%; 95% CI, 21%-38%).

Patients initiated adjuvant therapy a median of 47.3 days from surgery (51 days for patients aged ≥75 years and 46 days for those aged <75 years). Overall, 18% of patients had at least 1 drug in their initial regimen delivered at a reduced dose and this did not vary according to age. Although the recommended duration of stage III adjuvant chemotherapy regimens is at least 24 weeks, 27-29 by 21 weeks (150 days) from adjuvant chemotherapy initiation, more than one-quarter of patients had discontinued treatments.

Patients aged 65 years and older were more likely than younger patients to discontinue chemotherapy at all follow-up times, a finding that was statistically significant within 30, 120, and 150 days after initiating chemotherapy (Figure 2). For example, by 150 days, 99 patients at least 65 years old (40%) and 68 younger patients (25%) had discontinued chemotherapy (difference, 15%; 95% CI, 7%-23%).

Rate of Late Clinical Adverse Events

The frequency of adverse events according to treatment is shown in eTable 2 and Table 3. Overall, 162 patients (24%) had at least 1 late adverse event. Late events occurred in more than twice as many patients receiving vs not receiving adjuvant chemotherapy (142 [28%] vs 21 [13%]; difference, 15%; 95% CI, 8%-21%) (Table 3). The mean number of unique adverse events was also higher for adjuvant chemotherapy users vs nonusers (0.39 vs 0.16; difference, 0.23; 95% CI, 0.11-0.36).

Late adverse events were associated with adjuvant chemotherapy (both oxaliplatin and nonoxaliplatin regimens) (P = .02) as well as surrogate survey type (P < .001), early DNR order (P < .001), and male sex (P = .05) after adjustment for other variables in the model (eTable 3). Among adjuvant chemotherapy users (Figure 3), adjusted rates of late clinical adverse events showed a reverse U distribution across increasing age categories with the oldest patients having a lower adverse event rate than patients in the other age categories (0.35 for ages 18-54 years, 0.52 for ages 55-64 years, 0.45 for ages 65-74 years, and 0.28 for ages ≥75 years; P = .008 for any age effect and P = .01 for analysis of the effect of age categories beyond that explained by the youngest age category × no chemotherapy interaction). Regardless of whether the model included adjuvant chemotherapy as a single indicator variable or as oxaliplatin vs nonoxaliplatin regimens, adjuvant chemotherapy was significantly associated with late adverse events (0.37 with adjuvant vs 0.20 without adjuvant chemotherapy; difference, 0.17; 95% CI, 0.07-0.27). Across all tested regimens, the inverted U pattern of late adverse effects was preserved.

Late adverse event rates were higher with oxaliplatin vs nonoxaliplatin regimens (0.58 vs 0.40; difference, 0.18; 95% CI, 0.07-0.28) (Figure 3). The higher rates of late adverse events with oxaliplatin were accounted for by the higher rates of neuropathy among oxaliplatin users.

In sensitivity analyses, no statistically significant differences between results of the primary and alternate model were observed. Results were also similar when we constrained the close of the observation window for adverse outcomes to 6 months after surgical resection and again separately by the date of the last documented medical record visit. Results were similar when we omitted DNR order from the model and when we omitted deceased patients (7%) whose baseline survey was completed by a surrogate.

COMMENT

We analyzed adverse events in patients with stage III colon cancer in relation to adjuvant chemotherapy treatment and age. Patients in our study were enrolled from defined populations and health care systems throughout the United States. Therefore, these results describe care across diverse settings and patients in academic centers and community practices, complementing descriptions of adverse events in randomized controlled trials in which patients are highly selected.
We found that use of adjuvant chemotherapy differed substantially from evidence-based recommendations, especially for older patients. Despite evidence from selected patients accrued to clinical trials showing improved outcomes for patients receiving adjuvant chemotherapy regardless of age, only 50% of patients aged 75 years and older initiated this treatment. Starting doses were lower than in the standard regimens tested in trials for 18% of patients, but such dose attenuation did not vary by age. Older patients were less likely to receive oxaliplatin-containing regimens, which have been shown in clinical trials of patients younger than 75 years to be more effective, but also more toxic, than standard regimens. In contrast to trial-based recommendations for a 6-month course of adjuvant chemotherapy, only two-thirds of patients were still receiving chemotherapy at 6 months, with higher discontinuation rates with increasing age. Among patients receiving adjuvant chemotherapy, older patients did not experience more adverse events than younger patients in either unadjusted analysis or after controlling for comorbidity and treatment characteristics.

Older patients receiving adjuvant chemotherapy in our study had lower burden of illness than age-matched patients not receiving chemotherapy. Selection of less vulnerable patients might be one reason that older patients tolerated adjuvant chemotherapy better than younger patients. Adjustment for 6 dimensions of illness beyond measures of demographics and chemotherapy initiation, regimen type, and duration did not alter the finding that older patients were no more likely to have late adverse events than younger patients. These results were confirmed with propensity score methods as a means to reduce selection bias by equating treated and untreated patients based on observable characteristics. Nevertheless, residual confounding remains possible and some of our results may reflect selection of healthier older patients for chemotherapy use. Our population-based findings are consistent with those of published clinical trials and observational studies demonstrating that older patients with stage III colon cancer receiving chemotherapy do not experience more adverse events than younger patients.

Table 3. Late Clinical Adverse Events for Patients With Stage III Colon Cancer By Adjuvant Chemotherapy Status and Age (Unadjusted) rollout

<table>
<thead>
<tr>
<th>Late Adverse Events</th>
<th>Patients Without Chemotherapy by Age, y (n = 162)</th>
<th>Patients With Chemotherapy by Age, y (n = 513)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Late adverse event count, mean (95% CI)^d</td>
<td>P Value</td>
</tr>
<tr>
<td></td>
<td>18-54 (n = 11)</td>
<td>55-64 (n = 23)</td>
</tr>
<tr>
<td>Late adverse event count, mean (95% CI)^d</td>
<td>0.27 (0.00-0.59)</td>
<td>0.04 (0.00-0.13)</td>
</tr>
<tr>
<td>Yearly late adverse event rate (95% CI)^f</td>
<td>0.27 (0.00-0.59)</td>
<td>0.04 (0.00-0.13)</td>
</tr>
<tr>
<td>Any late adverse clinical outcome, No. (%)^d</td>
<td>3 (27) (1 4)</td>
<td>4 (15)</td>
</tr>
<tr>
<td>Infection^d</td>
<td>0 0 2 (7)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Sepsis^e</td>
<td>0 0 2 (2)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Surgical outcome^d</td>
<td>2 (18)</td>
<td>0 2 (2)</td>
</tr>
<tr>
<td>Bowel obstruction^e</td>
<td>2 (18)</td>
<td>0 2 (2)</td>
</tr>
<tr>
<td>Cardiac arrest^d</td>
<td>1 (9)</td>
<td>0 2 (7)</td>
</tr>
<tr>
<td>Cardiac arrest^e</td>
<td>1 (9)</td>
<td>0 2 (7)</td>
</tr>
<tr>
<td>Thromboembolic^d</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Deep venous thrombosis^e</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Indwelling venous catheter clott^e</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Gastrointestinal^d</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Lower gastrointestinal tract bleeding^e</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Pulmonary^d</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Respiratory failure requiring intubation^e</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Neurological^d</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Neurosurgery^e</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Other^d</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Acute renal failure^e</td>
<td>0 0 2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Any new hospitalization &gt;30 d after resection^d</td>
<td>1 (9)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

aLate clinical adverse events were defined as the first occurrence for each patient of any of 39 adverse events measured occurring from day 31 after surgical resection through 15 months after diagnosis (listed in eTable 1; available at http://www.jama.com). Only individual adverse events with significant differences by chemotherapy or age are displayed here.

bCalculated as the mean number of unique, individual adverse events sustained by each patient. For this count, each first episode of the event was counted for the patient. For example, 3 events were assigned to a patient’s count if the patient sustained each of fever with neutropenia, pneumonia, and sepsis.

cDefined as the sum of adverse events divided by the sum of alive exposure time from 30 days after resection through 15 months after diagnosis.

dMultiple individual clinical events were sustained. For example, a patient who sustained a fever with neutropenia, pneumonia, and sepsis is represented as 1 patient sustaining infection even though each 1 patient sustained 3 different individual types of infections. P values were generated using y^2 test.

ePatients sustained at least 1 episode of individual adverse events (eg, sepsis). P values were generated with Fisher exact tests to account for the observed small counts noted within cells.

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Adjuvant chemotherapy is generally intended to prevent disease recurrence and prolong survival for patients expected to live at least 5 years; it is not usually indicated for patients with more limited life expectancy, regardless of age. Women and men who reach age 70 years have an additional median life expectancy of 16.2 and 13.7 years, respectively, and those who survive to age 80 years have an additional life expectancy of 9.8 and 8.2 years, respectively, suggesting that adjuvant chemotherapy should be considered for many older patients. However, clinical trial data for older patients are lacking.

Older patients who received chemotherapy, including 41 patients at least 80 years old, did not experience higher rates of adverse events than younger patients, but the duration of follow-up of this cohort is not sufficient to know whether survival benefits expected from adjuvant chemotherapy were preserved for older patients using lower doses and shorter durations of treatment. We plan to follow up this cohort for measures of clinical benefit to learn whether the lower doses and shorter courses of treatment represent a clinical advance for older patients or whether these modified regimens affect cancer recurrence and disease-free survival.

Our findings underscore that practical clinical trials of adjuvant chemotherapy for older patients with stage III colon cancer are needed, including patients with comorbidities and functional impairment. Such trials should include patients across diverse community practice settings regardless of whether they have comorbidity. Our study documents the use of adjuvant chemotherapy for older patients across diverse community settings, while also noting only half of older patients receive adjuvant chemotherapy and those who do receive shorter than recommended duration. Strategies to help clinicians uncertain about the safety of adjuvant chemotherapy for older patients with comorbidity could increase the likelihood that evidence-based chemotherapy benefits are realized in population-based settings. Using decision support tools built on published trials and population-based analyses such as these can help clinicians predict effectiveness of chemotherapy, even for patients with comorbid conditions and advanced age. Systematic monitoring of symptoms and signs among chemotherapy users, combined with interventions to evaluate and treat these clues, could help clinicians support patients in meeting evidence-based treatment dosage and duration goals. Clinicians who identify symptoms and signs early and take steps to avoid serious adverse outcomes may enable their patients to complete recommended treatment courses while also improving quality of life.

Our study has several strengths. Patients were identified in representative populations or health systems with relatively few exclusion criteria and so are likely to broadly represent care in the community. The sample size was large enough to yield relatively stable

Figure 3. Adjusted Yearly Late Adverse Event Rates by Chemotherapy Use

Poisson models were adjusted for sex (reference, female); married or living together; race/ethnicity (Hispanic, black, Asian, reference, white); survey type (brief, surrogate; reference, full); age (<55 years, 55-64 years, 65-74 years; reference, ≥75 years); income ($20 000 and $20 000-$40 000; reference, >$40 000); prediagnosis health status; comorbidity (none, mild, moderate; reference, severe); early (from 30 days before diagnosis to ≤30 days after surgical resection); history of prior cancer; early do-not-resuscitate order; study sites, calendar date for colon cancer diagnosis; adjuvant chemotherapy (vs none); number of days from diagnosis to chemotherapy initiation; reduced-dose adjuvant chemotherapy; chemotherapy duration ≥6 months; and number of days from first to last chemotherapy dose. Adjuvant chemotherapy significantly predicted late adverse events. Among nonchemotherapy users, rates were highest among youngest patients (P=.01). Rates were significantly higher for patients using oxaliplatin compared with patients using nonoxaliplatin regimens across all 4 age categories (P<.001). Rates differed significantly among oxaliplatin users (P=.02) according to whether neuropathy was included or excluded in the definition of the adverse events. Rates for oxaliplatin users vs nonusers were higher when neuropathy was included in the model. Once neuropathy was excluded from the list of late adverse events, there was no difference between oxaliplatin and nonoxaliplatin users.
estimates of rates in subgroups defined by treatment and age (including 109 patients at least 80 years old), and to support modeling for other covariates. We included numerous adverse events that are likely to affect a patient’s quality and quantity of life and that occurred during the time window that corresponds with adjuvant chemotherapy use. Adverse events were identified from the various physicians caring for these patients using inpatient and ambulatory records from oncologists, surgeons, other specialists, and primary care physicians.

Our study also has limitations. Follow-up is not yet complete for analyses of recurrence rates and longer-term survival. Although we adjusted for numerous covariates using rigorous statistical methods, patients might have been selected for treatment according to unmeasured characteristics, which might have also been related to adverse events. We collected clinically important adverse events rather than use the Common Toxicity Criteria (CTC) grading scheme developed for clinical trials. Of note, CTC were designed to be collected prospectively by trial staff so that its classification scheme is not well suited for abstraction from medical records alone. Nevertheless, our abstracted rate of neuropathy (11%) among patients younger than 75 years is consistent with the prevalence of grade III neuropathy noted in the MOSAIC trial. The use of different measures and data sources means we cannot directly compare the event rates we observed with clinical trials involving the same agents. However, because we focused on events that were documented by clinicians rather than transient symptoms or isolated abnormal laboratory values, our data may be even more appropriate for informing clinical decision making with future patients.

Among older patients selected by clinicians for adjuvant chemotherapy (usually the less-toxic non–oxaliplatin-based regimens), this analysis shows older patients tolerate adjuvant chemotherapy, although more often with earlier discontinuation of treatment. However, this empirical analysis cannot answer the question of whether other older patients who were untreated might also tolerate and benefit from the use of adjuvant chemotherapy.

In conclusion, in this multisite community sample of patients with stage III colon cancer who underwent surgical therapy, approximately 50% of older patients received adjuvant chemotherapy, and doses and durations were lower than recommended based on clinical trial data. Further research is needed to determine the effects of this treatment on survival and recurrence rates.

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