The incidence of colorectal cancer (CRC) increases considerably with age. Each year in the United States, nearly 150,000 patients are diagnosed with CRC and 50,000 die from the disease (1).

Older individuals often present with chronic conditions that complicate the diagnostic and clinical management of cancer (2,3). Population-based studies of outcomes in cancer patients using the linked Surveillance, Epidemiology, and End Results (SEER)–Medicare files have relied on comorbidity scores derived from diagnosis codes documented in claims records (4,5). However, because of the absence of more detailed data on the patients’ clinical presentation in these files, it has not been possible to incorporate relevant additional measures to study cancer-related outcomes at the population level. In particular, functional limitations (FL) and geriatric syndromes (GS), both of which are components of the Comprehensive Geriatric Assessment (CGA) (6–10), have not been accounted for in these studies.

The importance of these factors in disease management and prognostication should not be underestimated because their presence reflects reduced functional and physiological reserves. The resulting increased state of vulnerability, which may be associated with poor survival, may also dictate treatment-related decisions, with physicians likely to favor less aggressive treatment when FL or GS are present (10). There have been only a few studies on cancer-related outcomes incorporating these clinical factors. However, these studies are small and based on primary clinical data (11,12). Larger-scale and population-based studies are absent, given that such data are not available in the SEER–Medicare files, as noted above.

To address these gaps in knowledge, we resort to the home health care (HHC) Outcome and Assessment Information Set (OASIS), which includes detailed clinical data for HHC patients. Counts of COM, FL, and GS at baseline were retrieved from the OASIS. Multivariable logistic and survival models were developed to examine the association between clinical attributes and outcomes, adjusting for demographic covariates and cancer stage.

Purpose. To examine patterns of colorectal cancer (CRC) treatment and survival in relation to comorbidities (COM), functional limitations (FL), and geriatric syndromes (GS).

Methods. Our study population consisted of Ohio elders diagnosed with incident invasive CRC in the period August 1999 to November 2001 and admitted to home health care (HHC) in the 30 days before or after cancer diagnosis \((n = 1009)\). We used data from the Ohio Cancer Incidence Surveillance System, vital records, and Medicare administrative data, including the HHC Outcome and Assessment Information Set (OASIS), which includes detailed clinical data for HHC patients. Counts of COM, FL, and GS at baseline were retrieved from the OASIS. Multivariable logistic and survival models were developed to examine the association between clinical attributes and outcomes, adjusting for demographic covariates and cancer stage.

Results. Comorbidities were associated with increased likelihood of surgery-only, but not with surgery + chemotherapy. Both FL and GS were associated with lower likelihood to undergo surgery-only or surgery + chemotherapy. Two or more GS was associated with disease-specific mortality \((\text{adjusted hazard ratio [AHR]}: 2.71; 95\% \text{ confidence interval [CI]}: 1.80–4.07)\) and overall mortality \((\text{AHR}: 2.34; 95\% \text{ CI}: 1.74–3.15)\). Two or more FL was associated with overall mortality \((\text{AHR}: 1.33; 95\% \text{ CI}: 1.10–1.62)\), but not with disease-specific mortality. COM was not associated with overall mortality, but was negatively associated with disease-specific mortality at borderline level of significance \((\text{AHR}: 0.78; 95\% \text{ CI}: 0.61–1.00)\).

Conclusion. Our findings demonstrate the importance of accounting for FL and GS, in addition to COM, when studying cancer-related outcomes in elders.

Key Words: Comorbidities—Functional limitations—Geriatric syndromes—Colorectal cancer.
but more than .7 for most items (17,18). Based on these findings, the reliability of these items in the OASIS has been deemed “sufficient for use in research” (17). To be reimbursed by Medicare, home health agencies must submit the OASIS forms to CMS. This requirement ensures that patient assessment is available for all Medicare beneficiaries receiving HHC.

In addition to patient identifiers, the OASIS includes detailed clinical assessment data, including diagnosis codes in International Coding of Disease Clinical Modification, Ninth Edition (ICD9-CM) and variables evaluating activities of daily living (ADLs) and cognitive status. These data served as the basis in this study to describe patients’ clinical presentation by the presence or absence of COM, FL, and GS. To characterize clinical presentation at baseline, we used variables referring to the patient’s condition within 14 days prior to the date of assessment. The date of cancer diagnosis from the OCISS was compared against the date of OASIS assessment in order to select patients admitted to HHC in the 30 days before or after cancer diagnosis.

The Ohio death certificate files include a record for each decedent who was resident of the State. In addition to identifiers, the death certificate record carries the date and cause of death in ICD-CM 10th Edition.

**Study Population**

The study population included all Ohio residents 65 years of age or older, diagnosed with invasive CRC in the period August 1, 1999, through November 30, 2001, and admitted to HHC in the 30 days before or after the date of initial cancer diagnosis ($n = 1,233$). Because of incomplete claims history, we excluded Medicaid-only patients ($n = 4$) and those enrolled in managed care in the year following cancer diagnosis ($n = 220$). Our final study population included 1,009 patients.

**Variables of Interest**

**Outcome variables.—**a) Treatment variables: Treatment was categorized as follows:

- Surgery + chemotherapy, including patients who underwent colorectal resection as well as chemotherapy
- Surgery-only, for those who underwent colorectal resection but no chemotherapy
- Palliative care, including the following two groups of patients: (a) those who underwent palliative surgery, including excision and bypass and (b) those who received chemotherapy only, but no surgical intervention of any sort.

Colorectal resection was identified using ICD9-CM and Common Procedural Terminology, Fourth Edition (CPT-4) procedure codes 45.71-45.76, 45.79, 45.8, 48.41, 48.49, 48.5, 48.61-48.69, 44140-44160, 45110-45121 in the 30- to 180-day-window relative to cancer diagnosis.
Receipt of chemotherapy was identified in the presence of ICD9-CM procedure code 99.25; ICD9-CM diagnosis code V58.1, V66.2, and V67.2; CPT-4 codes 96400-96549; and HealthCare Common Procedural Coding System (HCPCS) codes J9000, J9001, J9010, J9070, J9080, J9090-J9097, J9190, J9250, J9260, J9999, Q0083-Q0085 in the 30- to 180-day-window relative to cancer diagnosis.

b) Survival:

Defined as the time elapsed from the date of cancer diagnosis to death or the end of the follow-up period (December 31, 2005). Death was categorized as disease specific if the cause of death ICD10-CM was any of the following: C18, C19, C20.

Independent variables.—Demographic variables included patient age, race, and sex. Age at diagnosis was grouped in 5-year increments (65–69, 70–74, 75–79, 80–84, and ≥85 years). Because of the very small representation of other minorities in the State of Ohio, race was categorized as African American and All others.

Tumor stage, according to the SEER summary stage, included local, regional, distant, and unstaged.

Clinical presentation was characterized through the presence or absence of COM, FL, and GS. Consistent with our previous study (14), we relied on ICD9-CM codes documented in the OASIS to identify the presence of any of the codes of the National Cancer Institute/National Institute on Aging (NCI-NIA) list of comorbidities (COM) (2). These conditions were recorded in the OASIS only if they were symptomatic and required medical management (14). The presence of FL was based on limitations in any of the ADLs. GS indicated the presence of any of the following conditions: dementia, delirium, depression, incontinence, fall, osteoporosis, and malnutrition.

To examine the association between COM, FL, GS, and cancer treatment and outcomes in a more nuanced fashion, we created variables reflecting the count of each of COM, FL, and GS as 0, 1, and 2 or more (2+).

Analysis

We examined treatment and survival patterns by each of the independent variables. Descriptive analyses were conducted and bivariable comparisons were made using chi-square statistics.

We developed multivariable logistic regression models to assess the association between the treatment modalities, as defined above, and each of COM, FS, and GS, after adjusting for patient demographics and cancer stage. In addition to age, race, sex, and cancer stage, the multivariable models included the variables COM, FL, and GS simultaneously, thus adjusting for each other. We also tested models in which we included comorbidities only, FL only, or GS only, along with patient demographics and cancer stage. We reported findings from the latter models only when notable changes occurred in any of the regression coefficients. In all our models, the group of patients receiving palliative care served as the reference category.

Except in descriptive analyses, in an effort to create parsimonious multivariable models, we modeled age as a continuous variable and stage as a binary variable (local–regional vs distant–unknown). This strategy also helped us to improve statistical power in our analyses by having fewer parameters to estimate.

We also developed multivariable Cox regression models to analyze patient survival in relation to COM, FL, and GS, after adjusting for patient demographics, cancer stage, and cancer treatment. We developed overall survival models and disease-specific survival models. Similar to the logistic regression models described earlier, the survival models account simultaneously for the effects of COM, FL, and GS, thus adjusting for each other. We also tested alternative models in which we accounted for the presence of comorbidities only, FL only, or GS only, along with patient demographics, cancer stage, and cancer treatment. To correct for violations of the assumption of proportional hazard, we included time-varying covariates when the situation presented.

SAS 9.1 (Cary, NC) was used in all the analyses.

Results

The descriptive statistics are shown in Table 1. The proportions of patients in the three treatment categories of surgery + chemotherapy, surgery-only, and palliative care–no surgery were respectively 31.4%, 53.2%, and 15.4%. Whereas 51.3% of patients in the 65–69 years age group underwent surgery and received chemotherapy, only 8.7% of patients in the oldest age group did so. Conversely, the proportion of patients undergoing surgery-only was 30.3% in the youngest age group and 73.8% in the oldest.

Significant variations in treatment modalities were also observed by race, cancer stage at diagnosis, and clinical presentation. The proportion of patients undergoing surgery and receiving chemotherapy was lower in African Americans than in all others (24.4% vs 32.0%) and in patients diagnosed in earlier than in later stages of cancer (29.5% vs 37.0%). Additionally, we consistently observed a gradual decrease in the proportion of patients in the surgery + chemotherapy group across the categories of 0, 1, and 2+ counts of comorbidities, FL, and GS (respectively, 36.9%, 35.4%, and 10.4% for comorbidities; 36.7%, 28.4%, and 18.4% for FL; and 37.2%, 29.5%, and 16.8% for GS).

Results from the multivariable logistic regression analysis (Table 2) indicated that, adjusting for patient demographics and cancer stage, and compared with palliative care, comorbidities were associated with a greater likelihood to undergo surgery-only (adjusted odds ratio [AOR]: 1.82, 95% confidence interval [CI]: 1.09–3.04, for one COM, and AOR: 1.56, 95% CI: 0.99–2.46, for 2+ COM). However, comorbidities
were not associated with receipt of surgery + chemotherapy. Conversely, the presence of FL and GS was associated with a decreased likelihood to undergo surgery and to receive chemotherapy, but only in the presence of two or more such conditions. Patients were equally likely to be in this treatment category whether their count of FL and GS was 0 or 1.

The association between the count of FL and GS with surgery-only was less consistent than what was observed with the surgery + chemotherapy category. Relative to palliative care, we report a decreased likelihood to undergo surgery-only among patients with limitations in one ADL compared with those with no FL, but at borderline significance, and among patients with 2 or more GS compared with their counterparts with no GS (respectively, AOR: 0.58, 95% CI: 0.34–1.00; and AOR: 0.55, 95% CI: 0.33–0.91).

We tested our models by adjusting for comorbidities only, FL only, or GS only (i.e., without simultaneously adjusting for COM, FL, and GS), and the only notable change was in the association of two or more limitations in ADLs and surgery-only, which became significant at $p = .04$ (AOR: 0.62, 95% CI: 0.40–0.97).

Results from the survival analysis (Figure 1A and B and Table 3) indicated that the presence of two or more FL and two or more GS was associated with significantly greater mortality in the overall survival models over 6 years (respectively, adjusted hazard ratio [AHR]: 1.33, 95% CI: 1.10–1.62, and AHR: 2.34, 95% CI: 1.74–3.15). For the CRC-specific survival model, we observed increased likelihood of death associated with the presence of two or more GS (AHR: 2.81, 95% CI: 1.80–4.07) and borderline significant decreased likelihood associated with two or more COM (AHR: 0.78; 95% CI: 0.61, 1.0) over 6 years. The presence of FL was not associated with CRC-specific survival. The hazard ratios for both overall and disease-specific mortality decreased with time when patients with two or more GS were compared with those without GS.

The alternative models including comorbidities only, FL only, or GS only yielded the following notable change: The
presence of two or more comorbidities was no longer associated with disease-specific survival (AHR: 0.82, 95% CI: 0.64–1.04).

**DISCUSSION**

Our findings indicate that in a population-based cohort, FL and GS are associated with mortality in CRC patients, whereas comorbidities are not. This finding has important clinical and methodological implications. From a clinical perspective, it implies that comorbidities are unlikely to be associated with mortality, so long as the functional reserve is not compromised and the patient is not frail, and that CGA-driven interventions may improve overall and disease-specific mortality. From a methodological standpoint, especially when using administrative population-based data, it is important to employ caution when interpreting association between comorbidities and survival outcomes when FL and GS are not incorporated in the analyses.

The absence of a consistent dose–response relationship between COM, FL, GS, and the outcomes of interest deserves some discussion. We note that the approach adopted in this study to group patients by the number of COM, FL, and GS (0, 1, and 2+) is a simplistic one that likely masks important nuances in clinical presentation. Given the relatively small sample size, we were unable to account for patients with combinations of COM, FL, and GS, when we have shown that the majority of patients do in fact have such complex clinical presentation (14). Also, we did not account for individual clinical conditions contributing to the comorbidities or GS, their severity, or for individual ADLs in which the patients present impairment and the extent to which there is such impairment. Future studies in larger cohorts and incorporating these nuances in the analyses would elucidate the association between individual conditions and outcomes and, further, between more complex clinical presentations and outcomes.

The finding that patients with comorbidities are more likely than their counterparts with no comorbidities to undergo surgery-only versus palliative care is of interest, although, as noted below, this finding was sensitive to how we defined comorbidities in this study. Although the relationship between comorbidities and utilization of cancer-related services has yet to be fully understood, we note that previous studies have in fact reported favorable outcomes in the presence of comorbid conditions, including greater use of cancer screening services (19) and lower use of emergency CRC resection (20). Like others (19), we speculate that more frequent contact with the health care system by patients with comorbidities may explain this finding, at least to some extent. In an observational cohort study by Min and colleagues (21), multimorbidity was associated with greater overall health care quality scores, even after controlling for the number of office visits. These results are in contrast to that presented by Wolff and colleagues (22), showing an increased likelihood among patients with higher number of comorbidities to be hospitalized for ambulatory care sensitive conditions (ACSCs), an indicator of adequacy of primary care (22). Min and colleagues provide several explanations for their favorable findings, including greater perceived need to provide better care in patients with multimorbidity (21), or with any comorbid condition, as it is the case in our study. The debate to this effect continues, and all explanations to date remain speculative. The negative association between FL and receipt of chemotherapy is consistent with other studies of cancer-related outcomes, indicating a lower likelihood of patients with FL to receive certain screening services (23,24) or to undergo axillary lymph node dissection after breast-conserving surgery (25). Future studies involving larger patient cohorts should investigate the independent and interactive effects of deficiency in individual ADLs and each of the GS relative to the outcomes of interest. As well, the association of cancer outcomes with other patient covariates should be explored. One such covariate is Medicaid status, the association of which with disparate outcomes has been well documented (15,26,27,28).

The use of multiple sources of data to study cancer-related outcomes in association with FL and GS, in addition to comorbidities, constitutes a major strength of this study. On the other hand, because we resorted to the OASIS to draw the relevant clinical factors, we had to limit our study population to those admitted to HHC. Because of our selection criteria restricting our study population only to those admitted to
HHC for the first time in the 30 days before or after being diagnosed with cancer, we believe that the study subjects are likely comparable in functional status to those in the community and not receiving HHC. Patients represented in this study may have been referred to HHC following changing complexity of care needs resulting from cancer-directed treatment.

Although the generalizability of our findings may be limited, we also point out to similarities in treatment rates between this study population and rates derived from nationally representative samples. The proportion of patients in this study undergoing resection (84%) or any kind of colorectal surgery (98%) is somewhat comparable to a proportion of 92% derived from a study using SEER data for the period 1991–2002 (29). However, the latter proportion is representative of the entire population, including those younger than 65 years. Also, in our study, the proportion of patients receiving chemotherapy was 13.0%, 41.3%, 54.3%, and 35.5%, respectively, in those diagnosed with SEER summary stage local, regional, distant, and unknown. These proportions compare with 27% in elders 65–75 years of age and diagnosed with American Joint Committee on Cancer Staging (AJCC) stage II cancer and receiving adjuvant chemotherapy within 3 months of surgery (30) and 55% among elders 65 years of age or older and diagnosed with AJCC stage III cancer (31).

Finally, given the small size of our study population, we note our inability to account for individual comorbid conditions, GS, or impairment in a particular ADL, or the combination thereof. The analysis of data obtained from larger cohorts would be most helpful in this regard, especially to evaluate whether the findings reported herein hold true across various study populations. Also of note is that the NCI/NIA-defined comorbid conditions in this study were identified from a single clinical HHC assessment, in contrast to other studies that rely on Charlson–Deyo-based conditions (32) identified from claims history for services received in the entire year preceding cancer diagnosis. In testing our

Figure 1. A. Overall survival by comorbidities functional limitations, and geriatric syndromes. B. Disease-specific survival by comorbidities functional limitations, and geriatric syndromes.
models with the use of Charlson and Deyo claims–based history to identify comorbidities, we observed two notable changes: (a) The AOR of one comorbid condition in relation to surgery-only changed from AOR: 1.82, 95% CI: 1.09–3.04 to AOR: 1.50, 95% CI: 0.92–2.44, p > .05 and (b) In the disease-specific model, the AHR associated with two or more comorbid conditions became statistically significant at p = .02 (AHR: 0.67, 95% CI: 0.48–0.95). Future studies should further explore potential differences associated with the two methodological approaches.

In closing, we reiterate the importance of accounting for FL and GS, in addition to comorbidities, when studying cancer-related outcomes in elders. Outcomes studies incorporating comorbidities alone may be confounded by FL and GS.

FUNDING
Career Development Grant from the National Cancer Institute (K07 CA096705 to S.M.K.) and a National Institutes of Health Cancer-Aging Research Development Grant (P20 CA103736).

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Acknowledgments
The authors thank Ms Georgette Haydu of the Ohio Department of Health for her review of an earlier version of this manuscript. Cancer incidence data were obtained from the Ohio Cancer Incidence Surveillance System (OCISS), Ohio Department of Health. Use of these data does not imply that the Ohio Department of Health either agrees or disagrees with any presentation, analyses, interpretations, or conclusions. Information about the OCISS may be obtained at ohs.state.oh.us/ODH-Programs/CL_SURV/ci_surv1.htm. A version of this study was presented at the “Geriatric Oncology and Primary Care: Promoting Partnerships in Practice and Research Conference,” April 3–4, 2008, Case Comprehensive Cancer Center of Case Western Reserve University, Cleveland, Ohio. A related manuscript titled Assessment and Interpretation of Comorbidity Burden in Elders with Cancer presenting a summary of the results from this study presented at the above-referenced conference is currently in press in the Journal of the American Geriatrics Society.

References

Table 3. Multivariable Survival Analysis

<table>
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<th>Variable of Interest</th>
<th>Overall Survival</th>
<th>Disease-Specific survival</th>
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<tbody>
<tr>
<td></td>
<td>AHR (95% CI)</td>
<td>AHR (95% CI)</td>
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<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Age (continuous)</td>
<td>1.02 (1.00–1.03)*</td>
<td>1.00 (0.98–1.02)</td>
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<tr>
<td>Race</td>
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<tr>
<td>African American</td>
<td>0.94 (0.71–1.25)</td>
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<td>All others</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Men</td>
<td>1.10 (0.94–1.29)</td>
<td>1.01 (0.82–1.24)</td>
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<td>Women</td>
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<td>Distant/unknown</td>
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<td>6.49 (4.64–9.08)†</td>
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<td>Stage × Time</td>
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<td>0.98 (0.97–1.00)†</td>
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<td>0.56 (0.42–0.75)†</td>
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<td><strong>Clinical presentation</strong></td>
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<td>0.78 (0.61–1.00)*</td>
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<td>2+</td>
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<td>2.71 (1.80–4.07)†</td>
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<tr>
<td>Geriatric 2+ × Time</td>
<td>0.98 (0.97–1.00)*</td>
<td>0.96 (0.94–0.98)†</td>
</tr>
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</table>

Note: *p ≤ .01; †p < .001; ‡p < .001; †p ≤ .05 ≤ p < .01; all other statistics not significant at p < .05. AHR = adjusted hazard ratio; CI = confidence interval.

Received October 30, 2008
Accepted October 27, 2009
Decision Editor: Luigi Ferrucci, MD, PhD