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Survival after recurrence of stage I–III breast, colorectal, or lung cancer

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ABSTRACT

Background: The experiences of patients with recurrent cancer are assumed to reflect those of patients with *de novo* stage IV disease; yet, little is truly known because most registries lack recurrence status. Using two databases with excellent recurrence and death information, we examined determinants of survival duration after recurrence of breast (BC), colorectal (CRC), and lung cancers (LC).
Methods: Recurrence status was abstracted from the medical records of patients who participated in the Cancer Care Outcomes Research and Surveillance study and who received care at two Cancer Research Network sites—the Colorado and Northwest regions of Kaiser Permanente. The analysis included 1653 patients who developed recurrence after completing definitive therapy for stages I–III cancer. Multivariable modeling identified independent determinants of survival duration after recurrence, controlling for other factors.
Results: Through 60 months' average follow-up, survival after recurrence for BC, CRC, and LC were 28.4, 23.1 and 16.1 months, respectively. Several factors were independently associated with shorter survival for all three cancers, including higher initial stage (III vs. I: BC −9.9 months; CRC −6.9 months; LC −7.4 months; $P \leq 0.01$). Factors associated with shorter survival for selected cancers included: distant/regional recurrence for BC and CRC; current/former smoker for LC; high grade for CRC; and <4-year time-to-recurrence for BC.
Conclusions: Initial stage predicts survival duration after recurrence, whereas time-to-recurrence usually does not. The impact of biologic characteristics (e.g., grade, hormone-receptor status) on survival duration after recurrence needs further study. Predictors of survival duration after recurrence may help facilitate patient decision-making.

1. Introduction

Nearly all cancer deaths occur as a result of metastatic disease. In some patients, metastatic disease is present when cancer is first diagnosed, but in many patients metastatic disease represents recurrence that develops among patients previously treated for earlier stage cancer. Most large data sets, including tumor registries, electronic medical records, and health insurance claims, do not capture recurrence status. Consequently, much of what we believe about metastatic cancer comes from patients with *de novo* stage IV disease. We face a dearth of population-based research on the patterns-of-care provided to and outcomes experienced by patients with recurrent cancer.

Among patients with newly diagnosed non-metastatic cancer, the factors that predict survival duration have been well described. Nevertheless, these same factors may not predict survival duration from the point of recurrence for the subset of patients whose cancers recur. While one may assume the experiences of patients with recurrent cancer mimic those of patients with *de novo* stage IV cancer, these experiences may differ for a number of reasons. Patients with recurrence may have more aggressive disease, considering that their cancer recurred despite prior therapy. Because of cumulative toxicity or dose limits, previously administered treatments may not be an option at the time of recurrence. And the treatment preferences of patients with recurrence could diverge from those with *de novo* stage IV disease.

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Few reliable determinants of survival duration for recurrent or *de novo* metastatic cancer have been identified. Studies of locally recurrent breast cancer among patients initially treated on National Surgical Adjuvant Breast and Bowel Project (NSABP) clinical trials suggest that initial stage and time-to-recurrence influence outcomes [1,2]. However, these studies did not include patients with distant recurrence, and little is known about outcomes after recurrence of other cancers. Investigators have looked at how treatments and surveillance practices impact development of recurrence and/or survival from the initial cancer diagnosis, but these studies usually did not focus on the events that followed recurrence [3–8]. Several National Comprehensive Cancer Network studies and many clinical trials have examined the association between patient features, tumor characteristics, and/or treatment factors, on survival among patients with metastatic cancer. These analyses, however, usually grouped patients with recurrent and stage IV disease together [9,10], and the treatments provided to and outcomes experienced by patients treated in these research settings may not reflect those of patients treated in community settings.

Our goals were to use a unique pair of datasets that offered high-quality information on cancer incidence, recurrence, and health services utilization to identify factors associated with survival duration following recurrence of breast, colorectal, and lung cancers. We also described patterns-of-care among patients with recurrent cancer treated in community settings.

2. Materials and methods

2.1. Data sources

The databases used in this analysis came from the Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium, and the Cancer Research Network (CRN). CanCORS was a large, prospective, population and health-system based study of lung and colorectal cancer patients diagnosed in 2003–2005 [11,12]. Data collected through CanCORS were derived from multiple data sources through extensive medical records reviews and patient surveys. The CRN (http://crn.cancer.gov/) is a consortium of large health care systems affiliated with the Health Care Systems Research Network (HCSRN) and the National Cancer Institute. Two CRN sites, whose certified tumor registrars collect high quality recurrence data, contributed to this analysis: Kaiser Permanente Colorado, Denver, CO, and Kaiser Permanente Northwest, Portland, OR. The CRN maintains a Virtual Data Warehouse (VDW) [13] that links tumor registry data, diagnosis and procedure codes documented in an EPIC®-based EHR, claims for services delivered by external contract providers, health plan eligibility, and member demographic data.

Institutional Review Boards from the Dana-Farber/Harvard Cancer Center and the participating CRN sites approved and provided oversight for the project.

2.2. Study cohorts and recurrence status

All patients 1) were diagnosed with invasive, non-metastatic breast (BC), colorectal (CRC), or lung (LC) cancer when ≥21 years old; 2) completed definitive local-regional therapy for their initial cancer; 3) survived and were followed for at least 30 days after definitive therapy; and, 4) subsequently experienced recurrence. Definitive local-regional therapy was defined as organ-directed surgery appropriate for the specific cancer (i.e., mastectomy for BC, colectomy for CRC, lobectomy for LC), with or without radiation therapy. For patients with stage IIIa lung cancer, receiving both chemotherapy and radiation therapy was also considered definitive local-regional therapy. Patients with stage IV BC and CRC, and stages IIIb-IV LC were excluded, as were those who developed recurrence or died before definitive therapy or had another cancer diagnosis (Fig. 1).

Presence of recurrence and date of recurrence were derived from the abstracted medical record and/or tumor registry [13,14]. Recurrent events were classified as “local only” or “regional/distant”. Unless explicity stated, ‘recurrence’ herein refers to both types of events (i.e., local and regional/distant). Vital status was ascertained from health plan records or state and national death records. CanCORS patients were followed until death or study end date (12/31/11). CRN patients were followed through death, health plan disenrollment, or study end date (12/31/12).

Patient and disease characteristics were derived from survey and/or medical record abstraction for CanCORS and from tumor

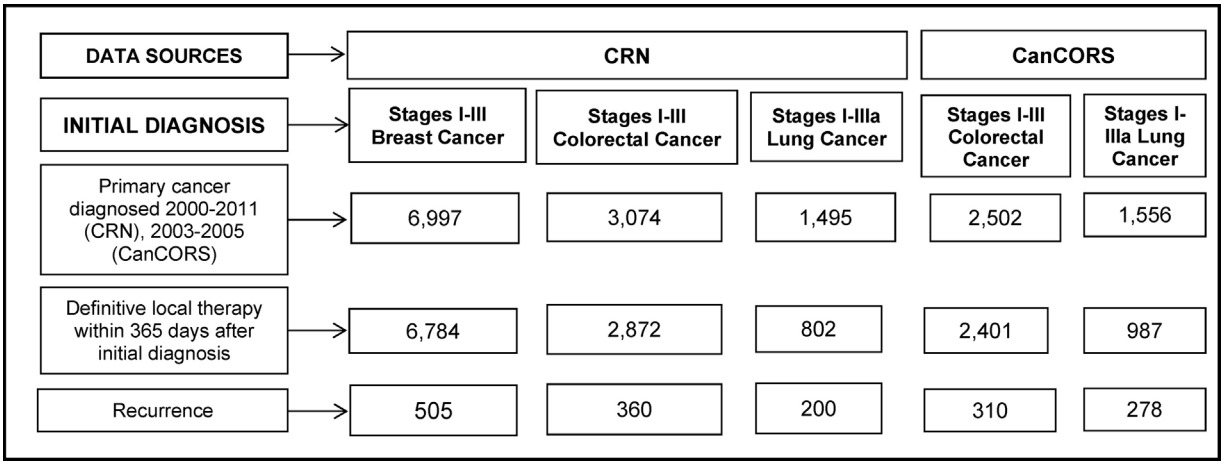

Fig. 1. Flow diagram of breast, colorectal and lung cancer patients from the CRN and CanCORS who were included in this analysis. For the Cancer Research Network (CRN) cohort, inclusion criteria included: first cancer diagnosis only (i.e., no previous cancer diagnosis), enrolled in one of two participating CRN institutions at diagnosis, and at least age 21 at diagnosis. For the Cancer Care Outcomes Research and Surveillance Consortium (CanCORS) cohort, inclusion criteria included: CanCORS participant, first cancer diagnosis only (i.e., no previous cancer diagnosis), at least age 21 at diagnosis, and both baseline interview and medical record abstraction data were available. CanCORS only enrolled colorectal and lung cancer patients so did not contribute breast cancer patients to this analysis. Patients from Kaiser Permanente Northwest who enrolled in CanCORS were excluded from the CanCORS cohort, because they were part of the CRN cohort. All patients must have had stage I–III cancer (excluding stage IIIb lung cancer) treated with