Are Deaths Within 1 Month of Cancer-Directed Surgery Attributed to Cancer?

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Background: **Cancer mortality should include not only deaths from cancer but also deaths from cancer treatment. By convention, deaths within 30 days of a surgical procedure are considered treatment-related deaths in the calculation of operative mortality—that is, the chance of dying from surgery. How cause of death is attributed in patients who die within 1 month of cancer-directed surgery is unknown.** ***Methods:*** **The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program data from 1994 through 1998 were used to examine the cause of death in patients diagnosed with one of 19 common solid tumors who had died within 1 month of diagnosis and had also received cancer-directed surgery. We determined the proportion of deaths not attributed to the cancer and the magnitude of the undercount in cancer-specific mortality.** ***Results:*** **Among 4135 patients with only one cancer who died within 1 month of diagnosis and cancer-directed surgery, the proportion of deaths not attributed to the coded cancer was 41% (1714/4135), ranging from 13% (1/8) for cervical cancer to 81% (13/16) for laryngeal cancer. Selected intermediate values include 25% (14/56) for esophageal cancer, 34% (177/525) for lung cancer, 42% (719/1695) for colorectal cancer, 59% (110/186) for breast cancer, and 75% (80/106) for prostate cancer. Restricting the analysis to deaths following specific major procedures (e.g., esophagectomy, pneumonectomy, colectomy) had little effect on the findings. If all deaths within 1 month of cancer-directed surgery were attributed to cancer, cancer mortality would rise about 1%.** ***Conclusion:*** **Some deaths that are conventionally attributed to surgery are not being attributed to the cancer for which the surgery was performed. Although the estimated effect of this misclassification on overall cancer mortality is modest, it may be indicative of more widespread confusion about how to code treatment-related deaths of patients with cancer. [J Natl Cancer Inst 2002;94: 1066–70]**

Cancer mortality is the single best measure of progress against cancer *(1).* This measure depends on the accurate determination of the underlying cause of death, defined by the World Health Organization as "the disease or injury which initiated the train of morbid events leading directly to death" *(2).* To both satisfy this definition and to ensure that observed progress is not illusory, cancer mortality should include not only deaths from cancer but also deaths from cancer treatment.

There is some evidence that treatment-related deaths are not being attributed to cancer. Brown et al. *(3)* found that noncancer mortality was considerably higher in cancer patients than in the general population. The excess mortality was most evident in the year immediately following a cancer diagnosis, suggesting that much of it could be attributable to treatment. The investigators were quick to acknowledge, however, the challenges involved in accurately determining the cause of death.

Attribution of the underlying cause of death depends not only on data from the physician completing the death certificate but also on subjective judgments about the likely causal pathway of death (both by the physician and the coder in the state health department). In surgery, researchers and quality managers typically bypass this complexity by using a simple rule: Deaths within 30 days of a surgical procedure are considered treatment-related in the calculation of operative mortality *(4–6).* To determine if this rule is being applied to patients with cancer, we examined the coded cause of death in patients who died within 1 month of cancer-directed surgery.

Methods

Data and Sample Frame

We analyzed the most recent 5 years of available data (1994–1998) from the 9 Registries Public Use file maintained by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER)[1] program. SEER data relevant to this analysis include information on the cancer site, number of primary cancers, initial surgical therapy, and survival time. In addition, SEER includes data on cause of death as reported on the state death certificate.

Because of our interest in selecting patients likely to have received surgery, we focused on patients with solid tumors. The sample frame included patients diagnosed with one of the 19 solid tumors regularly reported in SEER's summary table of changes in incidence, mortality, and 5-year survival *(7).* The sample frame was further restricted to patients who had received an operation for cancer, such as a lobectomy for lung cancer. These patients were identified in the database as having one of the surgical procedures categorized by SEER as "cancer-directed" *(8).* (Note: biopsy procedures are not considered cancer-directed surgical procedures.)

Death Within 1 Month of Surgery

Because of the limited data available, we were unable to precisely measure 30-day mortality following surgery. SEER codes the dates of diagnosis and death by simply using month and year; there is no date coded for cancer-directed surgery. Given SEER coding rules, however, the date of diagnosis must

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precede any cancer-directed therapy. We considered patients who died in the same month as diagnosis or in the subsequent month to have died within 1 month of surgery.

There is obviously some error associated with this approach. An extreme case would be a patient who was diagnosed, underwent surgery on July 1, and then died on August 31—61 days later. On the other hand, a typical patient would be expected to have been diagnosed somewhere toward the middle of the month and to have experienced some delay before having had surgery. Given this reality, we chose to include both deaths within the month of diagnosis and those within the subsequent month for estimating 30-day mortality.

Analysis

For simplicity, we first focused on patients with only one cancer. We determined what proportion of deaths within 1 month of diagnosis and cancer-directed surgery were *not* attributed to that same cancer. To see whether attribution was affected by the extent of the surgery, we then repeated the analysis on a subset of patients who received more extensive surgeries (i.e., those with higher operative mortality).

Next, we attempted to estimate the magnitude of the undercount in cancer-specific mortality, with the assumption that all deaths within 1 month of diagnosis and cancer-directed surgery should have cancer as the underlying cause. For each cancer, we estimated the death rate based on all the deaths that occurred within 1 month of diagnosis and cancer-directed surgery; we refer to this as the 1-month perioperative death rate (annual rate per 100 000 age-adjusted to the 1970 U.S. population). We multiplied this rate by the proportion of deaths *not* attributed to the diagnosed cancer. We considered the resulting number to be the rate of undercount, which has the same dimensions as cancer-specific mortality collected by the National Center for Heath Statistics and reported in SEER publications (annual rate per 100 000 age-adjusted to the 1970 U.S. population) *(7)*. Thus, we were able to calculate the potential undercount as a percentage of reported cancer-specific mortality.

Finally, we examined how the death rate and pattern of attribution change with time elapsed from diagnosis and surgery. Here, we considered as a group all patients receiving surgery for any one of the 19 solid tumors, and we included those patients with multiple cancers. Our hypothesis regarding the death rate was that it would be highest in the months immediately following surgery and would then fall with time. Our hypothesis for the pattern of attribution was that the proportion of deaths *not* attributed to any cancer would rise as more time elapsed from surgery (i.e., as the risk of operative mortality fell). In a final step, using the same approach outlined above, we estimated the potential undercount as a percentage of total cancer mortality for all 19 tumors (132.6 per 100 000 population) as a function of the number of months elapsed from the time of diagnosis. Analyses were performed using SEER*Stat 4.0 (National Cancer Institute, Bethesda, MD) and Excel 98 (Microsoft, Redmond, WA).

Results

Among patients with only one cancer, there were 4135 deaths within 1 month of diagnosis and cancer-directed surgery for the 19 solid tumors. Of these deaths, 1707 (41%) were attributed to something other than the coded cancer. There was considerable variation in the pattern of attribution among the 19 tumors (Table 1). The proportion *not* attributed to the coded cancer ranged from 13% for cervical cancer to 81% for laryngeal cancer. Selected intermediate values include 25% for esophageal cancer, 34% for lung cancer, 42% for colorectal cancer, 59% for breast cancer, and 75% for prostate cancer. Restricting the analysis to major procedures with higher mortality risks (e.g., esophagectomy, pneumonectomy, colectomy) had little effect on the proportion *not* attributed to the coded cancer (44% overall). This restriction was as likely to result in a higher proportion of deaths

Table 1. Proportion of deaths within 1 month of cancer diagnosis and cancer-directed surgery *not* attributed to cancer in the SEER data 1994–1998*

	Any cancer-directed surgery		Major surgical procedures†		
Type of cancer	No. of deaths	Percentage not attributed to coded cancer	Procedure	No. of deaths	Percentage not attributed to coded cancer
Oral cavity	44	64	Radical excision and/or radical neck dissection	24	58
Esophageal	56	25	Esophagectomy‡	38	32
Stomach	236	39	Gastrectomy	203	33
Colorectal	1695	42	Colectomy or rectosigmoidectomy	1583	46
Liver	65	51	Lobectomy or hepatectomy‡	32	56
Pancreatic	135	27	Complete/partial pancreatectomy	85	27
Laryngeal	16	81	Partial/total laryngectomy	7	100
Lung	525	34	Lobectomy or pneumonectomy	277	40
Melanoma	61	57	Radical excision or amputation	4	25
Breast	186	59	Mastectomy	68	66
Cervical	8	13	Hysterectomy	2	0
Uterine	88	48	Hysterectomy	74	47
Ovarian	242	24	Oopherectomy with hysterectomy	92	30
Prostate	106	75	Radical prostatectomy	18	56
Testicular	8	25	Orchiectomy	6	0
Bladder	256	54	Cystectomy	12	25
Kidney	129	45	Nephrectomy	107	43
Brain	257	26	Partial/radical resection	39	41
Thyroid	22	41	Lobectomy or thyroidectomy	18	50

*Restricted to patients with only one cancer; SEER = Surveillance, Epidemiology, and End Results.

†More radical forms of the procedure listed are also included (e.g., hysterectomy includes pelvic exoneration).

‡Before 1998, cancer-directed surgery was not specified for this cancer. For the years 1994–1997, we instead relied on the following generic codes for these sites: "partial/simple removal" and "radical surgery" (codes 40, 50, and 60).

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Table 2. Estimate of the magnitude of undercount in cancer-specific mortality due to misattribution of deaths within 1 month of surgery*

Type of cancer	1-month perioperative death rate (SEER)†‡ (a)	Percentage misattributed (Table 1) (b)	Perioperative mortality not included in cancer-specific mortality (c = a × b)	Cancer-specific mortality rate (U.S.)‡ (d)	Undercount as a % of cancer-specific mortality (e = c/d)
Bladder	0.152	54	0.082	3.2	2.57
Colorectal	1.032	42	0.433	16.9	2.56
Thyroid	0.014	41	0.006	0.3	1.91
Uterine	0.061	48	0.029	1.9	1.54
Stomach	0.151	39	0.059	4	1.47
Testicular	0.005	25	0.001	0.1	1.25
Brain	0.188	26	0.049	4.1	1.19
Kidney	0.088	45	0.040	3.5	1.13
Melanoma	0.04	57	0.023	2.2	1.04
Ovarian	0.159	24	0.038	4.2	0.91
Oral cavity	0.031	64	0.020	2.6	0.76
Laryngeal	0.012	81	0.010	1.3	0.75
Liver	0.047	51	0.024	3.6	0.67
Prostate	0.063	75	0.047	9.2	0.51
Breast	0.116	59	0.068	13.5	0.51
Pancreatic	0.096	27	0.026	8.3	0.31
Esophageal	0.041	25	0.010	3.6	0.28
Lung	0.385	34	0.131	48.7	0.27
Cervical	0.006	13	0.001	1.4	0.05

*Restricted to patients with only one cancer.
†SEER = Surveillance, Epidemiology, and End Results.
‡Rate per 100 000 population.

being attributed to some other cause as it was to result in a lower proportion.

Our estimate of the magnitude of the undercount in cancer-specific mortality is shown in Table 2. The calculations for the undercount are based on the assumption that all deaths within 1 month of diagnosis and cancer-directed surgery should be attributed to cancer. The magnitude of the undercount is primarily a function of the ratio of column a to column d—in other words, how large the 1-month perioperative death rate is relative to cancer-specific mortality (Table 2). Thus, although bladder and colorectal cancer have an intermediate proportion of deaths misattributed (54% and 42%, respectively) because of their relatively high 1-month perioperative death rates, they have the most substantial undercount problem (roughly 2.5% of reported mortality).

The death rate changed with the time elapsed from diagnosis and surgery (Fig. 1). The data provide support for our hypothesis that death rates would be highest in the months immediately following surgery and would then fall with time—in other words, that many of these deaths are a consequence of cancer-directed surgery. The data in Table 3, however, do not provide support for our hypothesis about the relationship between attribution and elapsed time. In fact, the proportion of deaths *not* attributed to cancer was highest during the period immediately following surgery (i.e., precisely the time when treatment-related death would be most likely).

Finally, changing the duration of follow-up for defining perioperative deaths affected the undercount in cancer mortality (Table 3). If only deaths within 1 month of diagnosis and surgery were considered attributable to cancer, then the undercount would be 0.9% of reported cancer mortality. If, however, the duration were increased to 4 months (a time during which the death rates are still elevated and, for some patients with lengthy diagnostic evaluations, may still be within 1 month of surgery), then the undercount increased to 2%. If all deaths in the year following cancer-directed surgery were attributed to cancer, then the reported cancer mortality would increase from 2% to 4%.

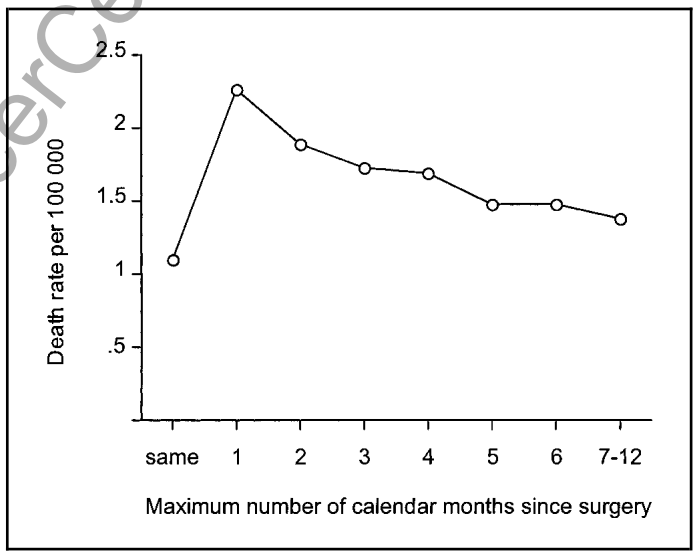

Fig. 1. Perioperative death rate—rate of death following surgery—as a function of the time elapsed from cancer-directed surgery. Analysis is based on all individuals (including those with multiple cancers) receiving cancer-directed surgery for one of 19 solid tumors reported to Surveillance, Epidemiology, and End Results (SEER), 1994–1998. The ***x*-axis** shows the maximum number of calendar months since surgery. The ***y*-axis** shows the death rate per 100 000 population.

Discussion

Our findings suggest that some deaths that are conventionally attributed to surgery are not regularly coded to the cancer for which the surgery was performed. Consequently, cancer mortality may be underestimated by about 1%–2%. For perspective,

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Table 3. Potential undercount in reported cancer mortality as a function of time elapsed from cancer-directed surgery*

Maximum No. of calendar months since surgery	Perioperative death rate† (a)	Percentage of deaths not attributed to any cancer (b)	Perioperative mortality not included in cancer-specific mortality (c = a × b)	Percentage of reported cancer mortality (d = c/132.6)	Cumulative undercount, % (e = ∑ d)
Same	1.093	37	0.402	0.3	0.3
1	2.256	35	0.778	0.6	0.9
2	1.877	30	0.569	0.4	1.3
3	1.721	28	0.489	0.4	1.7
4	1.676	26	0.436	0.3	2.0
5	1.475	24	0.357	0.3	2.3
6	1.464	24	0.351	0.3	2.6
7–12	1.374§	24	1.979‖	1.4	4.0

*Analysis based on all individuals (including those with multiple cancers) receiving cancer-directed surgery for one of 19 solid tumors reported to Surveillance, Epidemiology, and End Results (SEER), 1994–1998.

†Deaths per 100 000 population for the calendar month noted.

‡For all the 19 cancers considered here, annual mortality is 132.6 per 100 000 population.

§Average rate for months 7–12.

‖Total rate for the 6-month period.

from 1973 through 1998, the reported overall cancer mortality decreased 0.3% (from 162.0 to 161.5 per 100 000 population) and, if lung cancer deaths are excluded, decreased 10.7% (from 127.3 to 113.6 per 100 000 population) *(7).* Thus, a modest proportion of the reported decrease in non-lung-cancer mortality could be a result of the misclassification of deaths from cancer-directed surgery. Equally important, this misclassification may be indicative of more widespread confusion about how to code treatment-related deaths in patients with cancer.

Admittedly, reasonable concerns could be raised about our inability to precisely measure the time interval between surgery and death. Because SEER codes dates of diagnosis and death using only the month and year, we probably included some deaths that occurred almost 2 months after surgery when we estimated the percentage of deaths within 1 month of surgery that were attributed to other causes. However, when we restricted the analysis to deaths that occurred within the same month as diagnosis and surgery (for the typical patient probably within a week of surgery, given a mid-month diagnosis and some delay to surgery), we found an almost identical percentage of deaths attributed to other causes. In fact, for 12 of 19 cancers, the proportion of deaths not attributed to cancer nominally increased with the restricted time period. This finding reinforces our hypothesis that some treatment-related deaths are not being properly attributed to cancer.

Determination of Underlying Cause

In fairness, we should note that clear guidelines for classifying treatment-related deaths in cancer do not exist. Determination of the underlying cause of death is a complex process. It begins when the pronouncing physician—who may or may not be familiar with the patient's history—completes the death certificate. The physician makes a decision about which diagnoses to include and which one to label the "underlying cause." Coders in the state health department may change the underlying cause, but in most cases, they rely entirely on the information provided on the death certificate.

Although detailed instructions exist for coding underlying cause of death *(9),* these are quite abstract and require considerable subjective medical judgment about the causal pathway. For example, the so-called general rule reads, "Select the condition entered alone on the lowest used line of Part I unless it is highly improbable that this condition could have given rise to all the conditions entered above it." There are 12 subsequent rules. Rule 3, for example, reads "If the condition selected by the General rule, Rule 1, or Rule 2 can be considered a direct sequel of another reported condition, whether in Part I or Part II, select this primary condition."

Each rule is followed by a series of cases that provide some insight into how the authors intended that the rules be applied and, at the same time, highlight the contradictory messages about treatment-related deaths. Rule 3, for example, is illustrated by a death certificate that contains mesenteric thrombosis as an underlying cause of death and mentions colectomy for cancer of the sigmoid under "other significant conditions." Coders are supposed to recognize mesenteric thrombosis as a postoperative complication and to code the underlying cause to cancer of the sigmoid. In contrast, Rule 12 makes it clear that medical misadventures should be coded to errors and accidents and not to the disease for which therapy was initiated. In the two examples, peritonitis resulting from a perforated bowel (from a barium enema in the first example and a laparotomy in the second) is to have "accident" coded as the underlying cause (despite the death certificate listing of colon cancer on the first and carcinoma of the small bowel on the second). Similarly, a patient with malignant lymphoma who dies of acute renal failure secondary to gentamycin toxicity is to be coded an accidental death, not a cancer death (even if the patient was septic following immunosuppression from chemotherapy).

Policy Implications

The more we look for cancer and the more we treat people with the diagnosis, the more important it will be to properly assign diagnostic and treatment-related deaths. Otherwise, observed mortality trends may make harmful interventions appear beneficial.

There are a number of reasons why an enhanced ability to find cancer early may magnify the undercount in cancer-specific mortality described here. First, because a higher proportion of new cancer cases are likely to be resectable, surgery will become more common for some cancers—particularly those of the lung and brain. Second, because both serendipitously and screen-detected cancers tend to be very small, treatment-related deaths will appear to have nothing to do with the cancer and will likely

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be classified as caused by something else. Comparing the data reported here with what was observed in SEER 20 years ago (1974–1978) (data not shown), there is a trend toward increasing misclassification among those cancers in which early detection has increased substantially. Among patients who died within 1 month of diagnosis and cancer-directed surgery, the proportion *not* attributed to the coded cancer has increased from 49% to 59% for breast cancer, from 68% to 75% for prostate cancer, from 35% to 57% for melanoma, from 36% to 45% for renal cell carcinoma, and from 19% to 26% for brain cancer. Finally, an enhanced ability to find cancer will also detect an increasing number of abnormalities that look like but are not histologically confirmed to be cancer (either because they are not cancer or because no definitive tissue samples are available). Deaths from the invasive evaluation of these abnormalities will not be attributed to the suspected cancer because no such guidelines exist, even within randomized clinical trials of cancer screening. These misclassification problems related to cancer screening may explain why several randomized clinical screening trials have shown reductions in disease-specific mortality but not in all-cause mortality *(10)*.

Furthermore, there are reasons to believe that treatment-related deaths may occur well after a 1-month period. A person who has a lobectomy for an early lung cancer may be "cured" of cancer but die of pneumonia 6 months later. Although the surgery increased the likelihood of getting pneumonia, under current guidelines it would not be coded as a lung cancer death. Similarly, a person who has a colectomy may also be "cured" of cancer but die of an intestinal obstruction 6 months after the surgery. Although the surgery increased the likelihood of the obstruction, under current guidelines it would not be coded as a colon cancer death. Other treatments for cancer may also increase the long-term chance of death [e.g., radiation and vascular disease *(11)*, chemotherapy/radiation, and second cancers *(12)*] and theoretically should be included in cancer mortality.

A number of steps ought to be taken to ensure that cancer mortality remains a valid indicator of progress against cancer. The first is to be clear about what we want measured. The National Center for Health Statistics should clearly articulate the basic construct to both clinicians and coders: all treatment-related deaths should be attributed to cancer (regardless of whether the death was the result of a complication or an accident). Second, more effort should be made to identify specific long-term complications for particular therapies. For each cancer, this might involve a panel comprised of clinicians most familiar with specific treatment-related morbidities and possibly some complication-specific rules (e.g., for colon cancer patients with just one abdominal surgery, code all deaths that result from mechanical bowel obstruction to colon cancer). Finally, serious consideration should be given to developing some simple rules, such as a rule under which all deaths within 1 month of surgery, radiation therapy, or chemotherapy are to be attributed to the cancer for which the treatments were initiated. Although this will cause some deaths to be attributed to cancers that arguably should not be (e.g., a newly diagnosed cancer patient who is killed in a car accident), it will also miss some deaths that arguably should be. The virtue of simplicity is that at least it would provide comparability from cancer to cancer and across time.

Of course, how deaths should be classified depends on the purpose of classification. If the purpose is to determine how various exposures relate to the development of lethal cancers, then a narrow definition of deaths due to cancer is appropriate. However, if the purpose is to make judgments about progress against cancer, then we need to also count deaths from cancer treatment and diagnosis. In addition, we should try to distinguish treatment deaths from the deaths that are due to the disease, recognizing that this distinction is secondary and may not always be reliable. This strategy would allow us to more accurately track our progress against cancer overall while still providing some indication of the side effects of diagnosing and treating the disease.

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Notes

[1]*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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