Causes of Death of Patients With Lung Cancer

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• Context.—The causes of death for patients with lung cancer are inadequately described.

Objective.—To categorize the immediate and contributing causes of death for patients with lung cancer.

Design.—The autopsies from 100 patients who died of lung cancer between 1990 and February 2011 were analyzed.

Results.—Tumor burden was judged the immediate cause of death in 30 cases, including 26 cases of extensive metastases and 4 cases with wholly or primarily lung tumor burden (causing respiratory failure). Infection was the immediate cause of death for 20 patients, including 8 with sepsis and 12 with pneumonia. Complications of metastatic disease were the immediate causes of death in 18 cases, including 6 cases of hemopericardium from pericardial metastases, 3 from myocardial metastases, 3 from liver metastases, and 3 from brain metastases. Other immediate causes of death were pulmonary hemorrhage (12 cases), pulmonary embolism (10 cases, 2 tumor emboli), and pulmonary diffuse alveolar damage (7 cases). From a functional (pathophysiologic) perspective, respiratory failure could be regarded as the immediate cause of death (or mechanism of death) in 38 cases, usually because of a combination of lung conditions, including emphysema, airway obstruction, pneumonia, hemorrhage, embolism, resection, and lung injury in addition to the tumor. For 94 of the 100 patients, there were contributing causes of death, with an average of 2.5 contributing causes and up to 6 contributing causes of death.

Conclusions.—The numerous and complex ways lung cancer kills patients pose a challenge for efforts to extend and improve their lives.


Lung cancer kills in many ways. Bronchial obstruction from lung cancer can cause pneumonia, making pneumonia the immediate cause of death.1 Lung cancer burden can invade and disrupt blood vessels with resulting fatal hemorrhage.2,3 The hypercoagulable state of malignancy from lung cancer can cause fatal pulmonary thromboembolism.4 The burden of tumor in the lungs or the liver can cause these organs to fail, resulting in a patient’s demise.5 The tumor burden of extensive widespread metastases can essentially starve to death a patient with lung cancer.6 These are only some of the mechanisms of death from lung cancer. Although lung cancer is the leading cause of cancer death worldwide, including more than 150,000 deaths/y in the United States, little is published identifying or quantifying the causes of death for patients with lung cancer. Knowledge of the immediate and contributing causes of death could potentially guide interventions to extend the lives of these patients.7 For instance, if pulmonary thromboembolism is identified as a common, immediate cause of death, vena cava filters or anticoagulation could forestall these fatal complications. Of course, if hemorrhage is a common immediate cause of death as well, that would favor placing vena cava filters over anticoagulation as a measure to extend the lives of patients with lung cancer. If the immediate causes of death are untreatable, providing patients and health care proxies with the understanding of the prognosis and clinical course may relieve the patients’ suffering from aggressive care near the end of life.8 Autopsies are determinations of the cause of death and can provide the best possible data about the immediate, underlying, and contributing causes of death. Hence, we used data from the autopsies of patients with lung cancer to shed light on the mechanisms of death for these patients. We also used those data to characterize the extent and types of comorbidities contributing to their deaths.

MATERIALS AND METHODS

The electronic medical records of autopsies at the University of Pittsburgh Medical Center (Pittsburgh, Pennsylvania) were searched to identify 100 cases of autopsies on patients with lung cancer as the underlying cause of death. A data spreadsheet was created with demographic information (age, sex, race), smoking history, histologic type of lung cancer, sites of metastases, and the immediate, underlying, and contributing causes of death. The immediate cause is the final disease or condition resulting in death. The underlying cause is the disease that initiated the events leading to death. Contributing causes are comorbidities or conditions that significantly contributed to the death. Tumor burden was counted as the immediate cause of death when (1) extensive, widespread metastases were associated with malfunction of the organs involved, commonly with cachexia as well, and there were no other specific, pathophysiologic mechanisms of death; (2) when knowledge of extensive, widespread metastases...
led to a comfort measures–only treatment regimen; and (3) when
the amount of tumor in the lungs was the most important factor
in causing fatal respiratory failure. The search for cases
encompassed the years 1990 through January 2011. Selected
statistical differences were analyzed for significance by compar-
ing the proportions of groups with $\chi^2$ testing. This study was
approved by the University of Pittsburgh Medical Center
Committee for Oversight of Research Involving the Dead.

RESULTS

The average age of the patients who died of lung
cancer was 66 years (range, 33 to 88 years). Sixty-three
were men, and 37 were women; 82 were white, 17 were
black, and 1 was East Asian; and 82 patients had a
definite history of smoking, 3 patients had a definite
history of not smoking, and the smoking history of the
other 15 patients was not recorded in the medical record.
As shown in Figure 1, the lung cancer of 44 of the
patients was adenocarcinoma, 24 had squamous cell
carcinoma, 19 had small cell carcinoma, and 7 had large
cell undifferentiated carcinoma. Four cases had to be left
classified as non–small cell carcinoma because the slides
were not available for review. One case was a mucoeipi-
dermoid carcinoma, and one was an adenosquamous
carcinoma. All 3 of the patients who were definite
nonsmokers had adenocarcinoma. As shown in Table 1,
of the 100 patients, 91 had metastases at the time of
death, in lymph nodes ($n = 73; 80\%$), lung ($n = 43; 47\%$),
liver ($n = 37; 41\%$), adrenal glands ($n = 30; 33\%$), brain
($n = 25; 27\%$), and various other sites.

The most common immediate cause of death was tumor
burden, which was the immediate cause of death of 30% of
the patients, as shown in Figure 2. The second most-
common cause was infection, which was the immediate
cause of death of 20% of the patients. This was followed by
various complications of metastases, the immediate cause
of death for 18% of the patients; pulmonary hemorrhage,
the cause in 12% of cases; pulmonary thromboembolism in
10% of cases; pulmonary diffuse alveolar damage for
7% of patients; and miscellaneous causes in 3%. The 3
miscellaneous causes of death included one case of
intestinal hemorrhage, one case of tumor invasion, and
one case of thrombotic disease.

The 30% of the cases with tumor burden as the
immediate cause of death included 26 cases of extensive
widespread metastases and 4 cases with wholly or
primarily lung tumor burden as the immediate cause of
death. The type of lung cancer in these cases was
adenocarcinoma in 16 cases, small cell carcinoma in 8

Figure 1. Types of lung cancer. Other: non–small cell lung cancer, $n = 4$; mucoid, $n = 1$; and adenosquamous, $n = 1$.

Figure 2. Lung cancer: immediate causes of death.

Figure 3. Cardiac metastasis.

Figure 4. Pulmonary embolism.
cases, squamous cell carcinoma in 4 cases, and undifferentiated large cell carcinoma in 2 cases.

Infection was the immediate cause of death in 20% of the cases. This included 8 cases with sepsis and 12 cases with pneumonia without sepsis as the immediate cause of death. The cases of sepsis included 5 directly caused by pneumonia. Of the 17 cases with pneumonia (5 with sepsis from it and 12 without sepsis), the pneumonia was presumptively caused by therapy for the lung cancer in 9 of the cases, including 4 postoperative pneumonias following lobectomy, 3 following chemotherapy, 1 following radiation, and 1 following chemotherapy plus radiation. Four (24%) of the pneumonias were presumptively caused by altered mental status, induced in 2 cases by pain control for bone metastases, in 1 case by brain metastases, and in 1 case by paraneoplastic encephalitis.

Three (18%) of the pneumonias were caused by bronchial obstruction, and 1 case (6%) of pneumonia was caused by a bacteria-seeding, necrotic tumor. The type of lung cancer leading to fatal infection (n = 20 cases) was squamous cell carcinoma in 9 cases, adenocarcinoma in 5 cases, small cell carcinoma in 4 cases, undifferentiated large cell carcinoma in 1 case, and non–small cell carcinoma in 1 case.

The next-largest category of immediate causes of death was complications of metastatic disease (18% of cases). This included 6 cases of pericardial metastases leading to hemorrhage and fatal hemopericardium; cofactors for those fatal hemorrhages included anticoagulation in 3 cases and antiplatelet therapy plus mild coagulopathy in 1 case. The category of complications of metastatic disease included 3 presumptive cardiac arrhythmias, all caused by myocardial metastases. In one case, as shown in Figure 3, there was a 7-cm metastasis in the right atrial wall, extending into the right ventricle and through the interatrial septum. The category of complications of metastatic disease also includes 3 cases of liver failure because of metastases (involving approximately 90% of the liver in 2 cases and approximately 80% in 1 case). Two patients in this category died of cerebral infarctions and one cerebral hemorrhage. There was one case of cerebral tonsillar herniation caused by cerebral edema because of meningeal carcinomatosis. This category also includes one case of bowel metastasis, which led to obstruction, perforation, and fatal peritonitis. There was also one case of Lambert-Eaton syndrome. The type of lung cancer in the patients who died of complications from metastases was adenocarcinoma in 10 cases, small cell carcinoma in 5 cases, squamous cell carcinoma in 2 cases, and non–small cell carcinoma in 1 case.

Pulmonary hemorrhage was the immediate cause of death in 12 of the cases. Seven of these were due to vascular invasion by tumor. One was due to a cavitated tumor, which became infected, causing an abscess, which then eroded an artery. One was due to tumor invasion and necrosis, which ruptured an emphysematous bleb. One was due to a wedge resection of the primary tumor. One was attributable to a bleeding diathesis from disseminated intravascular coagulation. One was due to anticoagulation for pulmonary thromboembolism from a right heart mural thrombus, which developed after a pneumonectomy caused right heart failure. The type of lung cancer leading to fatal hemorrhage into the lungs was squamous cell carcinoma in 6 cases, adenocarcinoma in 3 cases, mucoepidermoid carcinoma in 1 case, undifferentiated large cell carcinoma in 1 case, and non–small cell carcinoma in 1 case. Of these 12 patients, 6 (50%) had squamous cell carcinoma, whereas only 18 of the other 88 patients in the study (20%) had squamous cell carcinoma (P = .02).

Pulmonary embolism was the immediate cause of death in 10 of the cases. This included 8 cases of thromboembolism, 1 case of tumor emboli, and 1 case with bilateral macroscopic thromboemboli and microscopic tumor emboli. Seven of these cases were attributable to a presumptively deep vein thrombosis caused by the hypercoagulable state of malignancy. One fatal embolism was attributable to a presumptively postoperative deep vein thrombosis, after having a right pneumonectomy. One embolism (Figure 4) was caused by manipulation of the leg during orthopedic surgery for a pathologic fracture caused by a bone metastasis. In the tumor emboli case, the patient had platypnea-orthodeoxia syndrome with a patent foramen ovale, where the increased venous blood return from reclining apparently allowed enough additional blood to go through the largely obstructed pulmonary vasculature to decrease the patient’s hypoxemia in the terminal phase of his illness. The type of lung cancer in these cases was adenocarcinoma in 7 cases, squamous cell carcinoma in 1 case, undifferentiated large cell carcinoma in 1 case, and adenosquamous carcinoma in 1 case. Of the 10 patients who died, 70% of pulmonary embolism had adenocarcinoma, whereas only 37 of the other 90 patients (41%) had adenocarcinoma (P = .08).

Diffuse alveolar damage (acute lung injury) was the immediate cause of death in 7 of the cases. This included 3 cases of radiation-induced diffuse alveolar damage and 4 cases of infection-induced diffuse alveolar damage, 2 from pneumonia and 2 from sepsis. One of the 2 cases from pneumonia was postoperative after a double lobectomy, and 1 was attributable to chemoradiation. In the 2 cases of fatal acute lung injury from sepsis, the sepsis was due to pneumonia from bronchial obstruction in 1 case and neutropenia from chemotherapy in the other case. The type of lung cancer in these cases was adenocarcinoma in 3 cases, small cell carcinoma in 2 cases, squamous cell carcinoma in 1 case, and undifferentiated large cell carcinoma in 1 case.

### Table 1. Sites of Metastases

<table>
<thead>
<tr>
<th>Site of Metastasis</th>
<th>Cases, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes</td>
<td>73</td>
</tr>
<tr>
<td>Lung</td>
<td>43</td>
</tr>
<tr>
<td>Liver</td>
<td>37</td>
</tr>
<tr>
<td>Adrenal</td>
<td>30</td>
</tr>
<tr>
<td>Brain</td>
<td>25</td>
</tr>
<tr>
<td>Pleura</td>
<td>19</td>
</tr>
<tr>
<td>Bone</td>
<td>18</td>
</tr>
<tr>
<td>Kidney</td>
<td>17</td>
</tr>
<tr>
<td>Pericardium</td>
<td>16</td>
</tr>
<tr>
<td>Pancreas</td>
<td>10</td>
</tr>
<tr>
<td>Heart, bone marrow</td>
<td>9 each</td>
</tr>
<tr>
<td>Esophagus, diaphragm</td>
<td>7 each</td>
</tr>
<tr>
<td>Small intestine</td>
<td>6</td>
</tr>
<tr>
<td>Thyroid, chest wall</td>
<td>5 each</td>
</tr>
<tr>
<td>Colon, stomach</td>
<td>4 each</td>
</tr>
<tr>
<td>Mediastinum, retroperitoneum, major vessels, prostate</td>
<td>3 each</td>
</tr>
<tr>
<td>Omentum, skin, and subcutaneous fat</td>
<td>3</td>
</tr>
<tr>
<td>Ovaries, breast</td>
<td>2 each</td>
</tr>
<tr>
<td>Paranasal sinuses, pituitary, gallbladder, mesentery, skeletal muscle</td>
<td>1 each</td>
</tr>
</tbody>
</table>

a Bilateral, n = 17; right, n = 7; left, n = 6.

b Bilateral, n = 10; right, n = 4; left, n = 3.

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carcinoma in 1 case, and undifferentiated large cell carcinoma in 1 case.

Of the 3 patients with miscellaneous immediate causes of death, 1 patient (with squamous cell carcinoma) died of an intestinal hemorrhage because of anticoagulation for a deep vein thrombosis because of the hypercoagulable state of malignancy. The other 2 patients died of primary tumor invasion. One patient (with undifferentiated large cell carcinoma) died of a presumptive cardiac arrhythmia because the primary tumor extended into the left ventricle, and one patient (with non–small cell carcinoma) died from thrombosis of the pulmonary artery and the superior vena cava after both were stented to keep them open because the primary tumor had invaded them.

Of the 100 patients, 94 had contributing causes of death, with up to 6 contributing causes and an average of 2.5 contributing causes of death. As shown in Table 2, the contributing causes of death were emphysema in 30 cases, infection in 24 cases, organ failure in 23 cases, pneumonectomy or lobectomy in 16 cases, pulmonary edema in 15 cases, pulmonary thromboembolism in 12 cases, and various other conditions. Many of the patients in this study had multiple lung diseases. Most commonly, they had both lung cancer and chronic obstructive pulmonary disease related to smoking, but others had lung cancer and pulmonary edema or other lung diseases not directly related to smoking. In many cases, the combination of these multiple lung diseases led to respiratory failure. From a functional (pathophysiologic) perspective, respiratory failure could be regarded the immediate cause of death (or mechanism of death) in 38 cases.

**COMMENT**

Our finding that tumor burden was the most common immediate cause of death fits with the importance of stage (the anatomic extent of tumor) in the prognosis of patients with lung cancer. It also fits well with the results of a study showing that gross tumor volume determined by manual contouring on computed tomography images as part of a 3-dimensional, conformal, radiation treatment plan predicts survival. The prognostic importance of tumor burden is also evidenced by a study showing that metabolic tumor burden determined by 18F-fluoro-2-deoxy-D-glucose positron emission tomography is a significant predictor of progression to death after controlling for stage, treatment intent (definitive versus palliative), age, Karnofsky performance status, and weight. This is because the study results from the positron emission tomography scan suggest that the burden of tumor robbing the patient of metabolic resources leads to the patient’s death somewhat like a nonsymbiotic parasite leaving too little nutrition for a host to survive. Another way of looking at this tumor-burden effect is to assess the nutritional status of the patient. One of the most common, albeit imperfect, ways to assess the effect of tumor burden on a patient’s nutritional status is serum albumin. In a meta-analysis of 10 studies of pretreatment serum albumin as a predictor of survival for patients with lung cancer, all but 1 found lower serum albumin levels to be associated with shortened survival. Part of the reason that malignant tumors so avidly take up nutrition is the Warburg effect, the characteristic inefficient aerobic glycolytic metabolism of tumor cells, which generates 2 molecules of adenosine triphosphate per molecule of glucose compared with more than 20 molecules of adenosine triphosphate per molecule of glucose from mitochondrial oxidative phosphorylation. In addition to depriving the patient of nutrition, malignant tumors create a catabolic bodily response mediated by tumor necrosis factor and other cytokines, which combine with the simple stealing of nutrients to cause the fatal effect of tumor burden.

Our conclusion that respiratory failure was, by far, the most frequent immediate cause of death from a functional (pathophysiologic) analysis fits with the conclusion of other studies. In one study of 313 patients who died of lung cancer in Japan, the immediate cause of death was classified as respiratory failure in 109 (34.8%), pneumonia in 59 (19%), cachexia in 38 (12%), brain metastasis in 26 (8.3%) and digestive organ disease in 7 (2% patients, including hepatic insufficiency in 10 and gastrointestinal bleeding in 8 cases). The 34.8% of deaths attributed to respiratory failure in these Japanese patients is very close to the 38% attributed to respiratory failure in our study of American patients. In addition, in a study of the immediate causes of death of thyroid cancer patients in Japan, the immediate cause of death was attributed to respiratory failure in 43%, also very close to the 38% in the patients with lung cancer in our study. In a study of causes of death of the patients in a tertiary care oncology center in India, the most common cause of death of the 22 patients with lung cancer was judged to be progressive disease, which accounted for 12 (55%) of the deaths. This most likely corresponds to tumor burden from an anatomic perspective or respiratory failure from a functional point of view.

### Table 2. Contributing Causes of Death

<table>
<thead>
<tr>
<th>Contributing Causes of Death</th>
<th>Cases, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emphysema</td>
<td>30</td>
</tr>
<tr>
<td>Infection</td>
<td>24</td>
</tr>
<tr>
<td>Organ failure</td>
<td>23</td>
</tr>
<tr>
<td>Pneumonectomy or lobectomy</td>
<td>16</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>15</td>
</tr>
<tr>
<td>Pulmonary thromboembolism</td>
<td>12</td>
</tr>
<tr>
<td>Pulmonary fibrosis, tumor burden</td>
<td>10 each</td>
</tr>
<tr>
<td>Radiation</td>
<td>9</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>8</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>7</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>6</td>
</tr>
<tr>
<td>Diffuse alveolar damage</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary hemorrhage, marantic endocarditis</td>
<td>4 each</td>
</tr>
<tr>
<td>Hemorrhage, hypercoagulable state of malignancy, coagulopathy, anticoagulation, cardiopulmonary arrest</td>
<td>3 each</td>
</tr>
<tr>
<td>Anoxic encephalopathy, cerebral infarcts, second lung cancer, anemia, diverticulitis, pneumothoraces</td>
<td>2 each</td>
</tr>
<tr>
<td>Pleural effusions, hemorhohces, hepatic cirrhosis, brain metastasis, intestinal perforation, colonic dilatation, patent foramen ovale, intracardiac right-to-left shunt, Alzheimer disease, heavy narcotic use, extracorporeal membrane oxygenation, atrial fibrillation, left vocal cord paralysis, surgical manipulation of a leg, chronic steroid therapy, chest tube, hemiparesis, hyperkalemia, lumbar spinal cord compression, morbid obesity and diabetes mellitus</td>
<td>1 each</td>
</tr>
</tbody>
</table>

*Drs. A. and B. were the authors of the paper that was published in the journal. The paper was later found to have errors in the data analysis, and the conclusions of the paper were retracted. The authors have issued a public apology for the errors.*

Arch Pathol Lab Med—Vol 136, December 2012

_Causes of Death for Patients With Lung Cancer—Nichols et al_ 1555
Respiratory failure was the most common immediate cause of death (mechanism of death) for the patients with lung cancer in this study, probably because most of them had lung disease besides cancer, so that the impairment of lung function caused by the lung cancer was additive with the impairment caused by the other lung disease. If the lung cancer was the most important lung disease leading to the respiratory failure, the lung cancer was the underlying cause of death, and the other lung disease was a contributing cause of death, following the logic of the death certificate format. Lung cancer can cause respiratory failure in many ways. It obliterates alveoli and the gas exchange that they would have performed. It obstructs bronchi, removing large numbers of alveoli from the pulmonary workforce. Lymphatic tumors (lymphangitic carcinomatosis) impair lung expansion and contraction, adding a component of restrictive lung disease to the lung impairment. Surgical removal of lung cancer inevitably removes some functional lung tissue along with the tumor, especially during the removal of an entire lung (pneumonectomy), making the therapy an intermediate cause of death in that case. Radiation therapy damages the lung parenchyma, particularly the blood vessels, so that is another way that lung cancer leads to respiratory failure with therapy as an intermediate cause. Chemotherapy damages any dividing cell population, and that can also be an intermediate cause of respiratory failure caused by lung cancer.

The frequency and contribution of other simultaneous lung disease is evident in the surgical outcomes and survival of patients with lung cancer. In a study of 237 patients who underwent surgical removal of lung cancer, 43.4% also had emphysema, and their survival was 40.6 months compared with 51.2 months for those without emphysema. In another study of 1143 patients with lung cancer, 404 (35.3%) also had emphysema, 101 (8.9%) had both emphysema and fibrosis, and 15 (1.3%) had fibrosis without emphysema, so that 45% of the patients had at least one additional lung disease. The median survival of patients with all 3 lungs diseases (10.8 months) was significantly less than that of patients with only emphysema and lung cancer (21.9 months) and far less than that of patients with only lung cancer (53 months). A fourth lung disease, acute lung injury, occurred in 20 (19.8%) of the patients with emphysema, fibrosis, and lung cancer. A few of the less-common, immediate causes of death in our study deserve specific discussion. The heart is an uncommon site of metastases from lung cancer, occurring in only 9 of the 100 patients in our study, but myocardial metastases can cause arrhythmias and sudden death. In one reported case, the first and only cardiac manifestation of cardiac metastasis of lung cancer was irreversible, sustained, ventricular arrhythmia leading to death. Three patients in our study similarly died of presumptive cardiac arrhythmias from myocardial metastases. One unique patient in our study presented with platypnea (dyspnea on standing) and orthodeoxia (hypoxemia on standing) because of pulmonary hypertension from tumor emboli in combination with a patent foramen ovale that created a right-to-left intracardiac shunt and the reduced venous return to the heart on standing left an insufficient amount of unshunted blood to keep him from deoxygenation.

Two of the specific immediate causes of death in our study were more common with specific histologic types of lung cancer. Pulmonary thromboembolism was more common in patients with adenocarcinoma, although the correlation failed to reach statistical significance. That greater frequency is most likely because of the thrombogenicity of the mucus produced by those tumors. Pulmonary hemorrhage was correlated with squamous cell carcinoma, and that correlation was statistically significant. Squamous cell carcinoma of the lung is the histologic type most likely to cavitate, and one might wonder if that is because the squamous type is more likely to invade blood vessels, cut off blood supply, and cause ischemic necrosis. Alternatively, hemorrhage from blood vessel invasion by squamous cell carcinoma may be more likely fatal because it is more likely to involve a larger blood vessel because squamous cell carcinomas are usually centrally located in the lung, in contrast to adenocarcinomas, which are more likely to be peripherally located. Squamous cell–type lung cancer has become a contraindication for therapy with bevacizumab, which inhibits vascular endothelial growth factor, because of the frequency of pulmonary hemorrhage caused by this inhibition, so one might speculate that the repair response to vascular invasion is more important in squamous cell carcinomas because blood vessel invasion is more common with this histologic type of lung cancer.

Determination of the cause of death by autopsy enhances the accuracy of the determination in all patients and specifically in patients with cancer. In a study of 86 patients with cancer who died in an oncologic intensive care unit, 22 (26%) had major, missed diagnoses, including 17 opportunistic infections, such as vancomycin-resistant enterococcal pneumonia, Legionella pneumonia, pneumocystis, aspergillosis, Candida empyema, herpes encephalitis, and disseminated toxoplasmosis. Our use of autopsy reports, rather than medical record audits, to determine the causes of death is a strength of this study.

Contributing causes of death, which are additional to the immediate, intermediate, and underlying causes, are nearly universal in adults, especially for those who die of cancer. In the study of the immediate causes of death for patients of thyroid cancer, the physician investigators seem to have sidestepped an assessment of the role of contributing causes of death by analyzing only the 106 of 171 cases (66%) in which they felt they could determine a single, specific, immediate cause of death and leaving the other 55 patients (34%) out of their analysis. Including a full assessment of the contributing causes of death yields a more complete appreciation of the challenge in extending the lives of patients with lung cancer. If our patients are representative of patients with lung cancer in general, knowing that 94% of them have contributing causes of death, an average of 2.5 contributing causes, suggests the unfortunate possibility that saving a patient with lung cancer from one cause may only allow another disease process to become the immediate cause of death.

Respiratory failure from pulmonary emphysema and/or cancer in the lungs despite therapy is not a reversible condition. Aggressive ventilatory support with high inspired oxygen, high airway pressures, nitric oxide, prolonged mechanical ventilation, tracheostomy, and other measures for patients with irreversible respiratory failure is most likely to extend life without quality and with the suffering of being unable to speak or perform any activities of daily living. Knowing the likelihood of this clinical course would steer many patients or their health...
care proxies away from aggressive ventilatory support and toward comfort measures, decreasing the patients' suffering. Evidence that this sort of knowledge can have this effect comes from a study\textsuperscript{26} of patients with advanced dementia. Patients whose proxies had an understanding of the poor prognosis and clinical complications expected in advanced dementia were much less likely to have burdensome interventions in the last 3 months of life than were those whose proxies did not have that understanding (odds ratio, 0.12). Pretreatment assessment of the global quality of life and physical function for patients with lung cancer can enable a prediction of their survival posttreatment.\textsuperscript{27} Such knowledge can help patients with lung cancer make more informed therapy choices aimed at maximizing the quality of the limited life most of them have left, while they are still in a position to make the choices, before it is their health care proxies who have to make the choices. The numerous and complex ways lung cancer kills patients pose a challenge for efforts to extend and improve the lives of these patients, but knowing the mechanisms of death is important for these efforts.

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References