

# Causes and Outcomes of Spontaneous Pneumothoraces in Solid Tumor Cancer Patients: An Update for the Medical Oncologist

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**Purpose:** Defined as lung collapse in the absence of a recent invasive thoracic procedure, a spontaneous pneumothorax can be a catastrophic event, leading to abrupt shortness of breath, chest pain, hypotension, and occasionally death. A dearth of present day information on this entity in solid tumor cancer patients prompted this single-institution retrospective study on current causes and outcomes.

**Methods:** All patients with diagnoses of “spontaneous pneumothorax” and “cancer” between 1990 and 2004 had their records retrieved and reviewed. Among 546 patients with a diagnosis of spontaneous pneumothorax, only 25 (5%) met predefined inclusion criteria that included an antecedent diagnosis of an invasive solid tumor malignancy. Lung ( $n = 5$ ) and bladder cancer ( $n = 4$ ) were the most common malignancies; eight patients had received radiation and one had received carmustine. Of note, 78% were smokers, 13 had chronic obstructive pulmonary disease, and 12 had no known active cancer at the time of the pneumothorax.

**Results:** Pneumothorax management was associated with great morbidity, including hospitalization in 24 patients and chest tube placement and/or surgery in most patients. Median survival for the group as a whole was 31 months, but patients with known active cancer tended to do poorly, with only a 3-month median survival.

**Conclusion:** A spontaneous pneumothorax is rare, and patients with known active cancer tend to do poorly. However, even patients with no known active cancer are at risk, perhaps in part from smoking. The fact that patients with no known active cancer can live for years after this event suggests that the pneumothorax should not be assumed to be related to cancer recurrence, that cancer restaging is not always mandatory, and that there is justification for managing the pneumothorax in this subgroup aggressively.

**Key Words:** Spontaneous pneumothorax, Lung cancer, Bladder cancer, Survival.

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A spontaneous pneumothorax can be a catastrophic event. Defined as lung collapse in the absence of a recent invasive thoracic procedure, a spontaneous pneumothorax can lead to abrupt shortness of breath, chest pain, hypotension, and occasionally death. Although it can resolve with conservative management, patients typically undergo hospitalization and often require chest tube placement. Previous studies suggest that fewer than 1% of cancer patients suffer from a spontaneous pneumothorax, but when it does occur, it can bring with it tremendous morbidity.<sup>1,2</sup>

How does a spontaneous pneumothorax occur in cancer patients? The medical literature provides three plausible explanations<sup>3</sup>: (1) a bronchopleural fistula develops within necrotic tumor, establishes a communication between the bronchus and pleura, and thereby results in a spontaneous pneumothorax; (2) a tumor-induced rupture of a subpleural bleb leads to an imbalance of intrathoracic pressures and results in a spontaneous pneumothorax; and (3) direct pleural invasion by the tumor again causes an imbalance of intrathoracic pressures and once again results in a spontaneous pneumothorax.

Such putative mechanisms add to our understanding of this entity but do not address the clinical circumstances and implications underlying a diagnosis of a spontaneous pneumothorax. Multiple case reports and small case series are invaluable in this regard. Such reports tell us that spontaneous pneumothoraces are more commonly observed in patients with lung cancer and sarcoma but can also occur in patients with gynecologic malignancies, rectal cancer, renal cell carcinoma, testicular cancer, and lymphoma.<sup>1,2–7</sup> A spontaneous pneumothorax often suggests cancer recurrence or progression and heralds demise within only a few months.<sup>1,4</sup> Prior treatment, such as radiation or carmustine-based chemotherapy, is often associated with its development.<sup>8–12</sup>

However, the need to revisit this entity is evident: most recent reports and case series on this topic are now over two decades old. Are the typical cancer patients (those with lung cancer, sarcoma, carmustine exposure, and radiation exposure) still heavily represented, or should oncologists remain vigilant for this rare entity in other settings as well? Do cancer patients who develop a spontaneous pneumothorax still commonly have metastatic cancer as the cause? Do cancer patients who develop a spontaneous pneumothorax still carry a poor prognosis of only a few months, even with modern improvements in cancer care? These unanswered

questions invite a modern day reexamination of the causes and outcomes of spontaneous pneumothoraces in solid tumor cancer patients.

## PATIENTS AND METHODS

### Identification of Patients

The study was approved by the Mayo Clinic Institutional Review Board. Thereafter, the Mayo Clinic Patient Registry in Rochester, Minnesota, identified all patients with diagnoses of “spontaneous pneumothorax” and “cancer” between 1990 and 2004. Patients were not required to have an active cancer to be included in this study; only a prior or concurrent solid tumor cancer diagnosis was necessary. Patients with leukemia or hematologic malignancies were excluded, except for lymphoma patients. Patients with squamous cell or basal cell carcinoma of the skin or with a noninvasive malignancy were also excluded, given the low likelihood of metastasis.

### Review of Medical Records

One investigator (S.N.C.) reviewed all the medical records, and select information was re-reviewed and confirmed by another investigator (A.J.). Spontaneous pneumothorax is not well defined in the literature.<sup>13</sup> Thus, for purposes of this study, a spontaneous pneumothorax was defined as a pneumothorax that was diagnosed in the absence of an invasive procedure in the preceding 7 days. This 7-day interval seemed conservatively appropriate, was derived from the clinical experience of the investigative team, and was thought unlikely to result in a traumatic pneumothorax as being misconstrued as a spontaneous one. Patients who did not meet this definition were not included.

The following information was retrieved and recorded for each patient: (1) age at the time of the pneumothorax; (2) cancer type; (3) cancer status (known active cancer or not); (4) prior cancer therapy; (5) smoking history; (6) prior diagnosis of nonmalignant lung disease, such as chronic obstructive pulmonary disease; (7) recent radiographic testing with results (recent chest radiographs were assumed to have been completed); (8) method of management of the pneumothorax; (9) number of days in the hospital; and (10) date of death or last day of follow-up. Types of prior cancer therapy were described by treatment modality and not further classified on the basis of whether they targeted the thorax. This approach was used because cancer treatments can have unforeseen effects on the chest; for example, even abdominal surgery might entail manipulation of the diaphragm and possibly pneumothorax at a later date.<sup>14</sup>

In reviewing the medical record, only information that was clearly documented was recorded on the data sheets. For this reason, speculation as to whether the spontaneous pneumothorax was primary or secondary or specifically caused by the cancer is not included.

### Statistical Analyses

Patient demographics are presented descriptively. Survival was defined as the interval from the date of diagnosis of the spontaneous pneumothorax until the date of death. If the

latter was unknown, data were censored from the date of last follow-up. Time intervals were rounded up to the nearest month. JMP, Version 5.1 (SAS Institute, Inc., Cary, NC), was used for statistical graphics. If a patient had had more than one spontaneous pneumothorax, the date of diagnosis of the first pneumothorax was used in summarizing the data. Kaplan-Meier curves were constructed for all patients, with a separate curve for patients with known active cancer at the time of the spontaneous pneumothorax.

## RESULTS

### Overview

A total of 546 patients were identified with the assistance of the Mayo Clinic Tumor Registry with a diagnosis of spontaneous pneumothorax between 1990 and 2004. Excluding all noncancer patients, those without an antecedent, concurrent, or almost concurrent cancer diagnosis, and those who did not meet the other criteria described earlier, yielded a remaining 25 solid tumor cancer patients, approximately 5% of the original group. This report focuses on these 25 patients.

### Patient Demographics

The average age of the group at the time of development of a spontaneous pneumothorax was 65 years (Table 1). Twenty were men. Prior cancer therapy included radiation ( $n = 8$ ), chemotherapy ( $n = 5$ ), surgery ( $n = 19$ ), and other ( $n = 2$ ), such as hormonal therapy, with many patients having received multiple treatment modalities for their cancer. Chemotherapy consisted of paclitaxel, carboplatin, 5-fluorouracil, cisplatin, etoposide, cyclophosphamide, procarbazine, and carmustine. To our knowledge, only one patient had received carmustine.

A variety of cancer types were represented, although lung cancer and bladder cancer were the most common (Table 2). Two patients, one with non-small cell lung cancer and another with renal cell cancer, presented with a pneumothorax within a few days of their cancer diagnoses. Thirteen patients had known evidence of active cancer at the time of

**TABLE 1.** Baseline Characteristics\*

Age, mean (SD)	65 (18)
Gender	205
Male	
Female	
Prior cancer therapy	
Radiation	8
Chemotherapy	5
Surgery	19
Other	2
Smoker†	18
Nonmalignant lung disease	
Chronic obstructive pulmonary disease	13
Hamartoma, resected	1
Tuberculosis	1
Lymphangiomyomatosis	1
Sleep apnea	1
Sarcoidosis	1

\*Denotes numbers of patients unless otherwise specified. †Defined as having smoked at least 1 year.

**TABLE 2.** Cancer Types

Cancer Type	No. of Patients (n = 25)*
Non-small cell lung	4
Bladder	4
Gynecologic	3
Prostate	3
Colorectal	2
Head and neck	2
Brain tumor	2
Renal cell	1
Sarcoma	1
Carcinoid	1
Melanoma	1
Esophageal	1
Breast	1
Hodgkin's	1
Small cell lung	1
Hurthle cell	1
Unknown primary	1

\*Does not add up to 25 because five patients had more than one cancer.

diagnosis of the spontaneous pneumothorax. Of the 12 patients who did not have known active cancer, eight had been diagnosed with cancer in the preceding 5 years.

Notably, the majority of patients within the group as a whole were smokers, defined as the use of inhaled tobacco products over the course of 1 year. As many as 18 patients, or 72% of the group, were deemed smokers. Thus, not surprisingly, a sizable number of patients carried a history of chronic obstructive pulmonary disease ( $n = 13$ ) and other non-cancer-related lung disease (Table 1).

## Management

Interestingly, a total of eight patients suffered more than one episode of spontaneous pneumothorax. One patient had as many as four successive episodes over a span of roughly 8 years, and another patient had as many as three over a span of roughly 5 months. Five of these patients had underlying, noncancerous lung disease that appeared to be responsible for these multiple events.

Management of this entity entailed notable morbidity. Within the entire group, 22 events required a chest tube. Within the entire group, 14 events required surgery that entailed either a pleurodesis or a wedge resection of diseased lung. A video-assisted thorascopic procedure accounted for seven of these surgical procedures. A surgical approach or pleurodesis occurred more often in patients with known active cancer, with eight of 13 such patients requiring it. Also, within the entire group, only two events required no invasive procedure.

Similarly, the average number of days ( $\pm$ SD) in the hospital for each event that required hospitalization was  $10 \pm 7$ . One patient was not hospitalized and therefore not included in the calculation of average hospital stay. Only eight patients underwent cancer restaging with a computed tomographic scan of the chest within 7 days before or after the spontaneous

pneumothorax, although we cannot rule out the possibility that patients might have had recent scans completed at an outside facility.

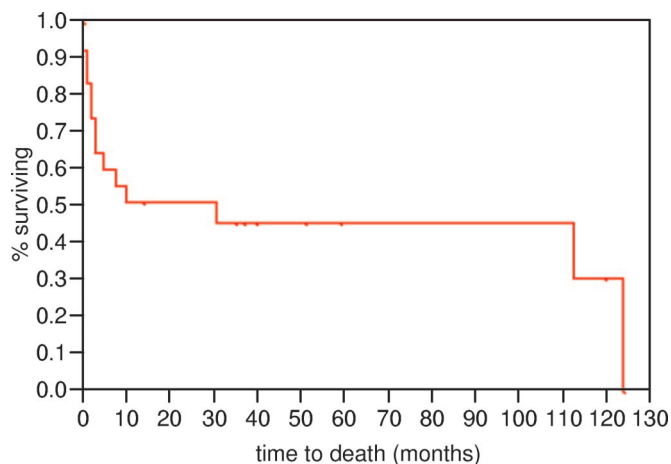
## Survival

The median survival for the group as a whole after a first-time diagnosis of spontaneous pneumothorax was 31 months (Figure 1). Within the group with known active cancer, the median survival was only 3 months, although patients with more indolent tumors lived longer (Figure 2). The median survival of the 12 patients with no active cancer was 113 months. One patient died in the hospital while being managed for a spontaneous pneumothorax.

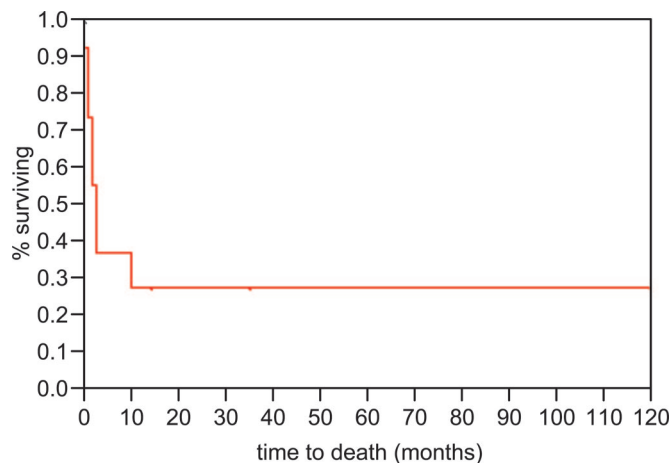
## DISCUSSION

The purpose of this study was to update our current understanding of the causes and outcomes of spontaneous pneumothoraces in solid tumor cancer patients. This entity remains rare, accounting for less than 5% of all spontaneous pneumothoraces. Lung cancer patients (20%) continue to be overrepresented. Moreover, this study provides confirmatory evidence that a spontaneous pneumothorax—specifically, in patients with known active cancer—continues to be a serious event associated with morbidity and a median survival of only 3 months.

Updated observations are discussed below. First, 48% of cancer patients in this study developed a spontaneous pneumothorax in the absence of known active cancer. Many were smokers and may well have had more than one reason to explain their pneumothorax. Thus, continued vigilance for this rare entity, particularly among smokers, who can suffer great morbidity and mortality from this event as a result of chronic obstructive pulmonary disease,<sup>15</sup> should continue even in patients who are thought to be cancer free. Second, in patients without known active cancer, it is reasonable to treat these patients aggressively. We define “aggressively” as using a multidisciplinary approach to determine the best, possibly invasive, approach for a given patient. It is true that only a small fraction of patients in this study were restaged for



**FIGURE 1.** Median survival from the time of pneumothorax was 31 months for the group as a whole.



**FIGURE 2.** When survival was examined only in patients with active cancer, median survival was 3 months.

their cancer at the time of pneumothorax diagnosis. However, the fact that many of these patients went on to live for many months—even years—suggests that this entity should not be assumed to be indicative of cancer recurrence, that cancer restaging is not absolutely mandatory, and that there is clear justification for treating this subgroup of patients aggressively when this catastrophic event occurs.

Third, although the earlier literature points to specific cancers (e.g., lung cancer and sarcoma) as predisposing patients to the development of a spontaneous pneumothorax and although it points to certain therapy (e.g., carmustine and radiation) as putting patients at higher risk, the present series shows that patients with a variety of malignancies under a variety of clinical circumstances can develop this complication. In fact, only eight patients in this group had received radiation, only five had lung cancer, only one had sarcoma, and only one had received carmustine. Thus, the vigilance suggested above should occur regardless of type of cancer or type of prior therapy with perhaps a higher degree of watchfulness reserved for those patients with a smoking history.

It is important to point out that this study carries the same limitations inherent in any retrospective study. Bias in identifying cases can be exacerbated by inaccuracies of the medical record diagnoses, by an overrepresentation of patients with certain cancers based on unique expertise within a specific cancer center, and by referral patterns that often funnel more complicated patients to tertiary care medical

centers. Moreover, gaps in information are inevitable. Despite such limitations, a relatively rare entity, such as spontaneous pneumothorax in solid tumor cancer patients, must rely on a retrospective approach, and this approach remains the only way to permit timely study completion.

## CONCLUSIONS

This study provides updated information on the demographics and management of solid tumor cancer patients who develop a spontaneous pneumothorax in an effort to allow medi. As more contemporary studies begin to refocus on this entity, the optimal method for counseling and managing patients will be defined with greater clarity.

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