

“The Air Got to It:” Exploring a Belief About Surgery for Lung Cancer

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Background: The belief that exposure of lung cancer to air during surgery causes tumor spread is prevalent but poorly understood.

Purpose: The purpose of the study was to summarize the published literature on the potential historical origins of this belief, study the recurrence rates of surgically treated stage I non-small cell lung cancer, research the mechanisms by which surgery might promote tumor growth and metastasis, and examine the social and cultural implications of this belief.

Data Sources: Various databases, reference lists, and expert contacts were the sources of data.

Findings: Although the origin of this belief is obscure, its emergence may have been due to early debates within the medical community about the risks of lung biopsies, the significant surgical morbidity initially associated with thoracic surgery, and the difficulty early on of staging lung cancer patients before surgery. Approximately one-third of patients undergoing curative surgery for stage I lung cancer experience a recurrence of the tumor. Most recurrences are detected in the first 24 months after resection and likely reflect the presence of undetected, occult metastases at the time of surgery. Mechanisms by which surgery could promote tumor growth and worsen prognosis include direct seeding of tumor at local sites, tumor manipulation, stimulation of subclinical tumor by postsurgical inflammation, and accelerated metastatic tumor growth due to loss of inhibitory factors derived from the primary tumor. These beliefs are more likely to be prevalent, and resistant to change, in minority and disadvantaged groups.

Conclusions: These findings provide the basis for an approach to patients who fear the spread of their cancer by surgery.

Keywords: lung ■ cancer ■ surgery ■ cultural competence ■ health disparities ■ folk beliefs

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INTRODUCTION

Mr Thomas, a 65-year-old African American retired bus driver, was referred for evaluation of an asymptomatic lung nodule. He smoked 1 pack of cigarettes daily for 50 years but had quit 1 year ago. A computed tomography (CT)-guided needle biopsy established the diagnosis of non-small cell lung cancer. Radiographic studies disclosed no evidence of metastases, consistent with stage I lung cancer. Surgical resection was recommended to the patient and his wife, but both were very hesitant about proceeding with the surgery. They indicated that several family members had told them that lung cancer spreads when exposed to air during surgery, and a close friend had died less than 6 months after undergoing lung cancer surgery.

The belief that exposure of lung cancer to air during surgery causes tumor spread, and thus leads to a poor outcome, is not uncommon. In a study of more than 600 patients in pulmonary and thoracic surgery clinics, 40% believed that exposure to air promotes lung cancer metastasis.¹ Further, 10% said they would refuse surgery for lung cancer on these grounds, with 9% indicating their physicians could not convince them otherwise.¹ Consistent with this report was the finding of an American Cancer Society telephone survey of the general public, which found that 41% endorsed the belief that surgery spreads cancer.² This belief that surgery spreads lung cancer has the potential to lead to refusal of life-saving surgery. It may be more prevalent in minority and economically disadvantaged communities,¹ and thus has been suggested as a cause of disparities in lung cancer outcomes in these groups.

In order to more effectively engage patients who fear that surgery will cause the spread of their lung cancer, the literature relevant to this belief was reviewed to better understand the historical, medical, and cultural aspects of this belief. The literature reviewed was obtained through searches of online databases (Medline; PubMed; and the

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History of Science, Medicine, and Technology database), printed databases (Index Medicus and the Index-Catalog of the Surgeon General of the United States), reference lists, bibliographies, and citations in articles and books and by expert contacts. This paper will therefore review possible historical origins of this belief, tumor recurrences after surgery for stage I lung cancer, potential mechanisms by which surgery might lead to tumor dissemination, and the social and cultural implications of this belief. These findings will then provide the basis for a suggested approach for engaging patients who express concerns about spread of the cancer by surgery.

HISTORICAL PERSPECTIVES ON SURGERY FOR LUNG CANCER

The notion that exposure of lung cancer to air during surgery spreads the tumor probably began at the time of the first lung resections in the opening decades of the 20th century. Although the origin of this belief is obscure, at least 3 historical factors may have contributed to its emergence and then establishment in the collective psyche of the public: early debates within the medical community about the risks of performing lung biopsies, the significant surgical morbidity initially associated with thoracic surgery, and the difficulty in those early years of staging patients before the operation.

Debates About the Risks of Tumor Biopsies

In the first decades of the 20th century, there was a vigorous debate within the medical community about the risk of cutting into a tumor to obtain a biopsy and then returning later to remove it. When the New York Department of Health's started a tumor diagnosis service in 1917, Thomas L. Stedman, the editor of the *Medical Record*, argued that biopsy would cause metastasis and therefore was tantamount to homicide.³ For physicians, subsequent studies in mice demonstrating that biopsies could be performed without spread of the tumor helped to settle this issue.⁴⁻⁶ However, during this time, some of the medical debate about the safety of biopsies may have caught the attention of the general public and led to an initial sense in the minds of many lay people

that manipulation of lung cancers (or maybe any tumor) might be hazardous.

Surgical Morbidity Initially Associated With Thoracic Surgery

The development of artificial means of ventilatory support, first in the form of negative pressure surgical chambers and then by endotracheal intubation with positive-pressure ventilation, ushered in the modern era of thoracic surgery in the 1930s.⁷⁻¹⁰ Prior attempts to perform surgery within the chest in the late 19th century had proved unsuccessful because of death due to respiratory failure, either during or shortly after the procedure.¹¹ By 1933 successful pneumonectomies had been performed by surgeons in Europe, Canada, and the United States.¹²⁻¹⁹ Although these reports established the surgical feasibility of the procedure, intraoperative hemorrhage and respiratory failure remained the principal dangers during surgery, while pneumonia, empyema, and sepsis emerged as major causes of early postoperative death. As a result, the mortality rates of pneumonectomies in the 1930s were high, ranging from 45% to 90%.²⁰ In light of this significant mortality, it would not have been unexpected that surgery involving the lung could have come to be viewed as risky. It was not until the 1950s, with improvements in surgical techniques and the use of blood transfusions and antibiotics, that the surgical mortality associated with lung resections fell to less than 10%.²¹

Initial Limitations of Preoperative Lung Cancer Staging

During the 1930s, the ability to stage patients with lung cancer prior to surgery was limited since conventional x-rays and the physical examination were the only means available for noninvasively evaluating patients. Therefore, exploration of the chest at the time of the thoracotomy became the standard approach in many patients for evaluating the extent of disease within the thorax.^{22,23} As asserted by Alton Ochsner and Michael DeBaakey, leading surgeons of the time,

Table. Resection Rates in Early Thoracotomy Series

Source	Years	Total Lung Cases in the Series	Number Taken to Thoracotomy	No. (%) of Thoracotomy Patients Whose Cancers Could Not Be Resected
Reinhoff ²⁴	1933-1944	Not noted	181	110 (61%)
Adams ²⁵	1931-1946	157	94	45 (47.8%)
Jones ²⁶	1943-1947	197	66	27 (41%)
Churchill ²⁷	1937-1944	996	152	77 (50.7%)
Ochsner, DeBaakey, Dixon ²⁸	1931-1947	2034	594	272 (45.8%)
Bernatz and Clagett ²⁹	1947-1951	Not noted	203	60 (29.6%)
Reinhoff, King, Dana ³⁰	1933-1956	Not noted	699	450 (64.4%)
Boyd et al ³¹	1933-1959	628	340	145 (42.7%)

*It is our firm conviction that borderline cases should always be given the benefit of exploration even at the risk of closing up a relatively large number without removing the tumor; because it is the only means by which operability can be absolutely determined in these instances.*²⁰

As a result, surgical series published through the 1940s (Table) reported that up to 65% of lung cancer patients who went to thoracotomy were deemed inoperable at the time of surgery.²⁴⁻³¹ With so many patients undergoing “open and close” procedures because the tumor had spread further than originally thought, it would not be difficult for a folk belief to emerge in which the opening of the chest (and its subsequent exposure to air) came to be seen as the reason why the tumor could not be removed, or the cause of a worse outcome. Beginning in the 1950s, however, the ability to stage lung cancer patients steadily improved with the introduction of mediastinoscopy and the use of surgical exploration of the abdomen for metastases in the late 1950s and early 1960s,^{32,33} followed by the emergence in the 1970s of noninvasive imaging technologies such as radionuclide bone scans and computer-assisted tomography.^{34,35} As a result, by 1980 patients whose cancers were deemed unresectable at thoracotomy had fallen to less than 10%,³⁶ but probably not before the belief in the dangers of exposing a cancer to air had gained a foothold within segments of the lay community.

RECURRENCE OF STAGE 1 NON-SMALL CELL LUNG CANCER AFTER SURGERY

The recurrence rate after surgery for pathologic stage I non-small cell lung cancer has been well studied. In 2001 Jones and Detterbeck published a comprehensive review of existing data on more than 11 000 patients, summarizing 19 studies published from 1980-2000 involving at least 250 patients each.³⁷ The overall 5-year survival for surgically treated stage I tumors was 65% (71% for stage IA cases and 55% for stage IB); about 33% of patients suffered a recurrence. A recently published study reported only slightly better 5-year survival: 77% for stage IA and 61% for stage IB.³⁸

Further analysis by Jones and Detterbeck of 7 large series disclosed that, on average, 57% of the deaths were related to recurrent lung cancer, 11% to new primary lung cancers, and 33% to nonpulmonary cancers and nonneoplastic conditions.³⁷ Thus, about 17% of patients undergoing surgery for stage I non-small cell lung cancer died of recurrent disease within 5 years of the operation. Risk factors for recurrence include tumors staged as T2 disease based on the tumor, node, and metastases (TNM) staging system, adenocarcinoma, visceral pleural invasion, vascular invasion, symptoms at the time of presentation, and an elevated carcinoembryonic antigen level. Finally, these authors detailed the nature of lung

cancer recurrence in 11 large studies: 32% were local or regional recurrences, while 68% were distant or both local-regional and distant. Most recurrences (60%) were detected within the first 24 months after resection, but the exact time to recurrence was variable and not explicitly stated. In 1 series the recurrence rate was 15 cases per 100 patient-years of observation in the first postoperative year;³⁹ in another the median time to recurrence was 13 months (range, 2-58 months).⁴⁰ The most common distant sites of recurrence were brain, bone, and liver. The likelihood of recurrence decreases after 24 months but is still 7% to 9% in patients who are clinically disease free after 5 years.

One factor that likely contributes to what is termed *lung cancer recurrence* is the presence of occult metastases at the time of resection that were undetected by preoperative scans, leading to the erroneous classification of a patient who actually harbors advanced disease as resectable. This is not so much a recurrence as the failure to accurately stage the patient at the time of surgery followed by the delayed clinical presentation of previously unrecognized metastatic disease. In a 1973 study 28.5% of 140 patients considered to have had a curative surgical resection and then subsequently autopsied within 30 days of surgery showed evidence of residual, local, or metastatic disease.⁴¹ As preoperative scanning becomes more sophisticated, this should be less of a problem, but recent data indicate that clinical understaging remains a significant issue. For example, a study from the Mayo Clinic in 2004 reported that 16% of 32 patients who had undergone autopsy within 30 days of “curative” surgery for non-small cell lung cancer were found to harbor metastatic disease, despite the use of CT in preoperative staging.⁴² More recently, Ost et al, reporting on Surveillance, Epidemiology, and End Results (SEER) registry data from 1988-2000, described a worse prognosis for stage I adenocarcinomas (particularly those with initial size >3 cm), likely due to late recurrences and deaths which seemed to emerge from micrometastases after 2 years.³⁸ These data are consistent with studies employing sensitive immunochemical techniques that have detected circulating tumor cells or micrometastases in bone marrow and/or regional lymph nodes in 18-60% of patients with operable lung cancer.^{43,44} Whether still more sophisticated scanning techniques, such as PET and PET-CT, would impact these findings and reduce the number of unnecessary thoracotomies is unknown.^{45,46} Genetic changes, such as methylation of key promoter genes, may prove helpful in detecting micrometastases in histologically normal nodes, as these types of alterations have been associated with a 25-fold increased risk of recurrence after resection of stage I lung cancer.⁴⁷ On an individual level recurrences due to understaging are the kinds of experiences that might help to reinforce beliefs about the hazards of exposing a tumor to air.

MECHANISMS BY WHICH SURGERY MIGHT PROMOTE TUMOR GROWTH AND DISSEMINATION AFTER SURGERY

Although there is no scientific basis for the notion that the actual exposure of tumors to air negatively affects outcome, there are at least 4 possible mechanisms by which surgery could promote tumor growth and worsen the patient's prognosis: direct seeding of tumor at local sites, tumor manipulation, stimulation of subclinical tumor foci by postsurgical inflammation, and accelerated metastatic tumor growth due to loss of inhibitory factors derived from the primary tumor.

Direct Local Seeding

The intraoperative spillage of tumor cells at local sites and in the surgical wound has long been recognized as a complication of cancer surgery.^{48,49} Video-assisted thoracoscopic resections of lung malignancies, though less invasive, have also been associated with local seeding, albeit rarely.⁵⁰⁻⁵² Reported sites of tumor implantation following these procedures have included port sites, pleura, resection margins, and other lung parenchymal sites. It is also important to note that tumor implantation may occur along the tract of previous diagnostic needle biopsy that could manifest as a recurrent tumor in the chest wall or pleura after the presumably curative surgery.^{53,54}

Tumor Manipulation

Beyond local seeding that might occur with perturbing and removing the tumor, there is evidence that manipulation of the tumor may result in hematogenous dissemination of the malignancy. This includes animal data demonstrating that surgical manipulation of tumors may enhance the formation of metastases,^{55,56} and studies of patients undergoing cancer surgery in which tumor manipulation increased the seeding of malignant cells into the circulation.^{57,58}

Postsurgery Inflammation

The host response to infection or injury involves the elaboration of inflammatory mediators that enhance the adhesiveness of circulating leukocytes to the endothelium and thus promotes leukocyte recruitment.⁵⁹ It is now well established that recruited leukocytes, particularly infiltrating macrophages, may promote tumorigenesis.⁶⁰ Consequently, the postsurgical inflammatory state could lead to increased trafficking of leukocytes out of the circulation and their accumulation in microdeposits of tumor with the potential for stimulating the growth of subclinical tumor foci. Further, the molecules on activated endothelium that mediate adhesiveness to leukocytes also promote tumor-endothelial cell adhesion *in vitro*⁶¹ and have been implicated in the development of tumor metastases *in vivo*.^{62,63} Moreover, these data are consistent with the finding of animal studies demonstrating that the postsurgical inflammatory state facili-

tates the establishment of metastatic deposits.⁶⁴ Thus the trauma of thoracic surgery with the resulting inflammation has the potential of promoting the endothelial attachment of circulating tumor cells and the establishment of new metastatic deposits.

Loss of Inhibitory Factors Derived From the Primary Tumor

Lastly, a number of elegant studies have established that a large primary tumor may suppress the growth of small and dormant metastatic deposits of the tumor.⁶⁵ The explanation of these data involves a model in which the primary tumor induces the expression of not only tumor-promoting proangiogenic mediators but also tumor-inhibiting antiangiogenic factors, with the inhibitors having a significantly longer circulating half-life than that of the stimulators. It is proposed that the size of the primary tumor is such that local/tissue concentrations of proangiogenic factors are sufficiently high to counter the suppressive effects of the inhibitors. However, the long half-life of the antiangiogenic factors permits them to reach the metastatic tumor deposits in amounts where they are able to exert suppressive effects due to the small sizes of the metastatic foci and their relatively low output of pro-angiogenic factors. Therefore it would be predicted that removal of the primary tumor and the resulting loss of factors suppressing metastatic foci could lead to accelerated growth of clinically unrecognized tumor deposits.⁶⁵

SOCIAL AND CULTURAL IMPLICATIONS

Improvements in diagnosis, surgery, and chemotherapy in the past century have made lung cancer a survivable cancer for those with early-stage disease. Unfortunately, the overall 5-year survival for all patients with lung cancer is still only 15.2% based on the most recent SEER data, weighted heavily by the fact that the majority of patients have metastatic disease at the time of diagnosis.⁶⁶ Lung cancer disproportionately affects the poor and members of racial minorities, who also have shorter survival times on average.⁶⁷⁻⁶⁹ Some of these disparities may be due to a later stage at diagnosis and/or poor access to health care.^{70,71} Because surgery represents the greatest chance for cure, numerous studies have tried to understand disparities in the use of surgery for early-stage lung cancer, attempting to separate medical comorbidities, health care access, physician advice, and the world view and preferences of the patient.⁷²⁻⁷⁷

What has been presented above provides some understanding of the possible origins of the belief that exposure to air causes the spread of a tumor. Many physicians, however, will still find it baffling that such notions continue to persist in the era of modern medicine, particularly in minority and disadvantaged communities, despite scientific evidence to the contrary. As Roger Bacon noted centuries ago,⁷⁸ personal experience forms

the basis for many beliefs, even in the face of overwhelming scientific fact. That is, evaluations by patients of the likely outcome of cancer are based not only on what they learn from their physicians (“science”), but also their personal experiences and the experiences of their friends and family members. Since disparities in lung cancer outcomes make it less likely that people from poor socioeconomic backgrounds and members of racial minorities will have positive outcomes,⁶⁷⁻⁷¹ the collective experiences of these groups would lead to the understanding that lung cancer is likely to be fatal. These experiences are consistent with and help to reinforce more general notions about the risks of cancer spread during surgery. Further specific social or cultural experiences may lead to an overall group distrust of physicians and their scientific claims. This has certainly been the case for some African American communities, where specific histories of discrimination in medical settings, particularly when viewed in the context of the notorious Tuskegee Syphilis study, have contributed to distrust of the medical community.⁷⁹⁻⁸²

The writings of Charles Sanders Peirce,⁸³ a 19th-century philosopher whose theories of belief remain influential,⁸⁴ provide further insights into the development of belief. He described 4 processes, or “methods,” that drive and sustain belief. In addition to the method of science, which he preferred, and the a priori method—that is, common sense reasoning arising from experience—he recognized 2 other possible bases of belief: the methods of authority and tenacity. Authority argues that communities preserve belief through group consensus, coercion, and sometimes force. In impoverished communities and among many racial minorities, community leaders and tradition represent authority. Relevant to beliefs about the dangers of lung cancer surgery, leadership and cultural traditions within segments of these groups have long fostered suspicions of medical authority. Tenacity represents an individual’s personal commitment to his or her beliefs. Once a community has accepted a belief, tenacity causes individuals within the group to maintain that belief and is often at work when respondents indicate that nothing could change their minds.

The significance of all this is that regardless of the origins of beliefs about the hazards of lung cancer surgery, these beliefs are more likely to be prevalent in minority and disadvantaged groups, often as an attempt to explain poor outcomes in their communities. They are also more resistant to change, due to certain shared experiences, community leadership, and traditions that are distrustful of medical authority, and the inertia associated with changing established patterns of belief.

RESPONDING TO PATIENTS WHO EXPRESS THIS BELIEF

It is easy to dismiss beliefs about the hazards of exposing lung cancers to air as mere superstition. We

believe, however, that a more effective response is to carefully listen to the patients’ concerns and then respectfully engage them in a discussion about their beliefs. The physician certainly has the obligation to ensure that the patient is making an informed decision and to advocate for the treatment that is felt to be in the best interest of the patient. A dismissive approach is much more likely to distance the physician from the patient and to make the patient less willing to accept the physician’s recommendations.

In developing a response, several things should be kept in mind. First, belief in the hazards of exposing tumors to air may have been reinforced by the personal experiences of the patient. Such experiences need to be identified and “unpacked.” Second, while exposure of a cancer to air might not stimulate its growth, there are plausible scientific mechanisms by which factors associated with lung cancer surgery could promote the development of subclinical metastatic tumor foci. It is important to acknowledge this while affirming the benefits of surgery. Last, expression of this belief may actually reflect other unspoken concerns, such as a more general fear of surgery or distrust of the physician, which may also need to be explored. Suggested questions and/or responses to the patient could include:

- You are not alone in having this belief, as many lung cancer patients who are deciding whether or not to have lung cancer surgery have the same concern. Has something like this happened to someone close to you?
- In many ways what you are asking is, “Will the surgery itself make the cancer worse?” Although we are not entirely sure, in a small number of instances it is possible that surgery for lung cancer may stimulate the spread of the tumor. However, the good news is that research has told us that even with this possibility, you are much more likely to be alive with surgery than without it.
- What fears do you have about the surgery itself?
- Do you have any concerns about how you have been or will be treated?

As noted above, these beliefs can be quite strong and the patient may still be reluctant to consider surgery, even after a respectful and careful conversation with the physician. In these situations it is appropriate to schedule a follow-up visit for further discussion and to encourage the patient to use the intervening time to reflect on the conversation with the physician.

In the end, the decision to accept or reject surgery rests with the patient. Although the physician advocates for what is potentially lifesaving therapy, the physician’s ultimate responsibility is to ensure that the patient has made an informed decision. Understanding that beliefs about the dangers of lung cancer surgery are not crude

manifestations of superstition or ignorance will enable the physician to do this with patience, humility, and sensitivity.

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