Pulmonary Resection for Non–Small Cell Lung Cancer in Patients With Prior Spinal Cord Injury

Louis S. Brunworth, MD^{1,2}; Dharson Dharmaasena, MBBS^{2,3}; Katherine S. Virgo, PhD^{1,2}; Frank E. Johnson, MD^{1,2}

¹Department of Surgery, Saint Louis University Health Sciences Center, St. Louis, Missouri; ²Surgical Service, Department of Veterans Affairs Medical Center, St. Louis, Missouri; ³Guy's, King's and St. Thomas' College, London, United Kingdom

Received May 18, 2005; accepted January 8, 2006

Abstract

Background/Objective: We sought to determine the clinical course of patients with spinal cord injury (SCI) who subsequently developed bronchogenic carcinoma and underwent pulmonary resection.

Methods: A nationwide retrospective study was conducted of all veterans at Department of Veterans Affairs Medical Centers for fiscal years 1993–2002 who were diagnosed with SCI, subsequently developed non–small cell lung cancer, and were surgically treated with curative intent. Inclusion criteria included American Spinal Injury Association type A injury (complete loss of neural function distal to the injury site) and traumatic etiology. Data were compiled from national Department of Veterans Affairs data sets and supplemented by operative reports, pathology reports, progress notes, and discharge summaries.

Results: Seven patients met the inclusion/exclusion criteria and were considered evaluable. Five (71%) had one or more comorbid conditions in addition to their SCIs. All 7 underwent pulmonary lobectomy. Postoperative complications occurred in 4 patients (57%). Two patients died postoperatively on days 29 and 499, yielding a 30-day mortality rate of 14% and an in-hospital mortality rate of 29%.

Conclusions: This seems to be the only case study in the English language literature on this topic. Patients with SCI who had resectable lung cancer had a high incidence of comorbid conditions. Those who underwent curative-intent surgery had high morbidity and mortality rates. Available evidence suggests that SCI should be considered a risk factor for adverse outcomes in major surgery of all types, including operations for primary lung cancer.

J Spinal Cord Med. 2006;29:133–137

Key Words: Spinal cord injuries; Veterans Administration database; Lung cancer, non–small cell; Smoking; Pulmonary resection; Lobectomy; Surgical risk; Morbidity; Mortality; Outcomes

INTRODUCTION

In the United States, lung cancer is the leading cause of cancer-related deaths in both men and women. This highly prevalent disease is largely attributable to tobacco smoking. The diagnosis is usually made at advanced clinical stages when treatment is typically noncurative and the overall survival rate is approximately 15% at 5 years. The prognosis is highly dependent on the pathological stage of the initial lung cancer. No screening test to date has led to a reduction in lung cancer-specific mortality (1–5). In the United States, the prevalence of

spinal cord injury (SCI) is approximately 183,000 to 230,000 persons, with approximately 11,000 new cases each year (annual incidence). Currently, veterans comprise approximately 22% of the SCI population in the United States (6). The prevalence of smoking is higher among veterans than nonveterans and higher among veterans seeking care within the Department of Veteran Affairs (DVA) system than in veterans seeking care elsewhere (7). Patients with SCI have a significantly higher prevalence of smoking (41% are current smokers) than the general population (26% are current smokers) and are thus a group at particularly high risk of developing lung cancer (8,9), but clinical details about surgery for lung cancer in patients with SCI have not been reported to our knowledge.

We hypothesized that patients with SCI would be at higher risk for adverse outcomes of pulmonary resection

Please address correspondence to Frank E. Johnson, MD, Department of Surgery, Saint Louis University Health Sciences Center, 3635 Vista Avenue at Grand Boulevard, St. Louis, MO 63110; phone: 314.577.8316; fax: 314.771.1945 (e-mail: frank.johnson@med.va.gov).

than neurally intact patients. SCI has been reported to affect the clinical presentation and/or outcomes of operative management of many disorders such as appendicitis (10), gallbladder disease (11), bladder cancer (12), colorectal cancer (13), severe pressure ulcer (14), renal cell carcinoma (15), and abdominal aortic aneurysm (16). Because many patients with SCI within the VA medical care system smoke, this is an ideal population for the study of outcomes of surgery for lung cancer in these patients. Table 1 provides rates of common complications from lung resection for primary lung cancer in the general population from several recent reports (17–22). The morbidity rates in a recent report from the DVA National Surgical Quality Improvement Program (NSQIP) were 24% for lobectomy and 26% for pneumonectomy (17). The 30-day mortality rates from the same study were 4% for lobectomy and 12% for pneumonectomy.

We compared rates from the NSQIP to those of the DVA patients with SCI who developed lung cancer and had potentially curative resection. Patients with SCI, particularly those with high spinal lesions, have decreased pulmonary function and decreased ability to maintain a clear airway because of an ineffective cough. They often suffer from other comorbid conditions related to their SCI such as pressure ulcers, contractures, and side effects of the injury that caused the spinal cord transection. We hypothesized that they would be at higher risk than neurally intact patients of developing complications after potentially curative lung cancer surgery.

METHODS

Records of DVA Medical Centers from fiscal years 1993–2002 were reviewed for this study. Informed consent was

Table 1. Reported Rates of Adverse Outcomes After Pulmonary Resection for Primary Carcinoma of the Lung in the General Population

	Percentage
30-day mortality	2.9–7.5
Overall morbidity	8.8–25.7
Arrhythmia	11.5–26
Atelectasis	1.3–15.0
Pneumonia	8–19.0
Prolonged mechanical ventilation	2.0–6.6
Bronchopleural fistula	1.8–5.4
Empyema	2.8–5.0
Wound infection	1.2–7.9
Postoperative bleeding	2.9–3.2
Deep venous thrombosis	1.7–1.9
Myocardial ischemia	0.8–2.0

Data from Harpole et al (1999), Handy et al (2002), Sabiston et al (1995), Canver et al (1998), Myrdal et al (2001), and Ploeg et al (2003) (17–22).

not required. Institutional Review Board approval was obtained. The DVA Data Processing Center in Austin, TX, maintains the administrative databases for all DVA facilities. Its main components are an IBM mainframe computer linked with several direct-access IBM-emulating EMC storage computers. This computer complex has 265 terabytes of storage capacity and the ability to respond to more than 1.4 billion instructions per second. This is the largest data center in the DVA and one of the largest in the world.

The DVA Patient Treatment File (PTF) was used to identify patients with a diagnosis of SCI. This was identified by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 344.0–344.99, which included complete and incomplete SCI. We included these identifiers to be as certain as possible that all suitable patients would be found in our computer search. Next, the PTF was used to identify patients with a diagnosis of bronchogenic carcinoma who had undergone potentially curative wedge resection, lobectomy, or pneumonectomy (ICD-9-CM codes 32.3–32.59). The 2 data sets were matched to identify patients who were coded for SCI, had a subsequent code for bronchogenic carcinoma, and received their resections in the DVA system. Clinical presentation, tumor stage, and histologic type are not available in these data sets and must be obtained through chart review.

Operative notes, progress notes, radiology reports, and pathology reports were requested from the DVA Medical Center where the treatment had been given. Categorical and count data from computer resources and chart review were entered into an SPSS database and analyzed. Only patients with American Spinal Injury Association type A (23) injuries (resulting in complete loss of motor and sensory perception distal to the injury site) were included. Patients with American Spinal Injury Association type B–E injuries (Brown-Sequard syndrome, central cord syndrome, etc) were excluded. To further ensure homogeneity, only patients with traumatic causes of injury were included. Patients with SCI caused by metastatic cancer, multiple sclerosis, cervical degenerative disease, and the like were excluded, as were those in whom the cause of injury was not specified. Only patients treated with curative intent for primary non-small cell lung cancer were included. Thus, patients with lung metastases and small cell lung cancer were excluded. Patients were also excluded if records were judged to be too incomplete for evaluation or improperly coded.

RESULTS

During fiscal years 1993–2002, 12,634 patients had codes for surgical treatment for lung cancer at DVA Medical Centers nationwide, of which 55 also had ICD-9-CM codes for previous SCI. Of these 55 subjects, 48 were excluded for the following reasons: we did not receive information from the facility at which the care was provided (4), the information provided was insufficient

(14), the patient did not have SCI (4), the patient's injury was of nontraumatic origin (4), the SCI was incomplete (10), the patient's neurologic deficit was from multiple sclerosis (4), vascular accident (3), or degenerative joint disease of the spine (3), or the lung mass was not a primary non-small cell lung cancer (2). The remaining 7 patients met the inclusion and exclusion criteria and were considered evaluable.

Table 2 shows the clinical status of the patients in the study. All were men, with a mean age of 64 ± 12 (SD) years. Five (71%) were white, and 2 (29%) were African American. Five were paraplegic, and 2 were tetraplegic.

Six of the 7 patients had sufficient clinical data to permit assessment of clinical presentation. All 6 were smokers (mean, 60 pack-years; range, 10–100 pack-years). Two of the 6 had typical signs and symptoms (cough, hemoptysis, chest pain, dyspnea, wheezing, weight loss, or hoarseness); 4 had an asymptomatic mass found on chest radiograph or computed tomography. Four patients had enough information to evaluate the time elapsed from their SCI to the subsequent development of a lung neoplasm (mean, 33 years; range, 7–48 years). Any patient with a recorded preoperative diagnosis of any comorbid condition was considered to have that condition. If no mention was made of a historical finding or abnormality on physical examination, it was assumed to be absent. Recorded comorbid conditions were diabetes mellitus, hypertension, chronic heart disease, peripheral vascular disease, cerebrovascular accident, chronic obstructive pulmonary disease, emphysema, chronic sepsis, urinary tract infection, and other malignancy. The total length of stay in DVA inpatient facilities ranged from 5 to 499 days. With one extreme outlier removed and the data set winsorized at the 99th percentile, time spent in DVA facilities ranged from 5 to 175 days, with a mean length of stay of 74 days. The extreme outlier resulted from the DVA practice of including the time spent in a DVA nursing home within the inpatient admission length of stay in an acute care facility.

All 7 patients underwent a curative-intent resection; all had a lobectomy. None suffered intraoperative mortality. Postoperative complications occurred in 4 patients (57%; Table 2). Two patients died postoperatively on days 29 and 499, resulting in a 30-day mortality rate of 14% and an in-hospital mortality rate of 29%. Because of the small final sample size, no statistical comparisons were possible. Thus, for example, the impact of level of injury on outcomes could not be assessed.

DISCUSSION

Injury to the spine has undoubtedly occurred for as long as humans have existed (24). There is paleopathological evidence documenting spinal injury in prehistoric man. Its catastrophic consequences are prominently mentioned in the Edwin Smith Papyrus (25), the earliest

Table 2. Clinical Features of 7 Patients With SCI Presenting With Non-Small Cell Lung Cancer and Subsequently Undergoing Lobectomy

Variable	No. of patients (n)	Percentage
Comorbid conditions*	5/7	71
1	2/7	29
>1	3/7	43
Tumor stage†	6/7	86
IA or IB	4/6	67
IIA or IIB	0/6	0
IIIA or IIIB	2/6	33
Level of SCI	7/7	100
C3–C5	2/7	29
C6–S2	5/7	71
Postoperative complications‡	4/7	57
Nosocomial pneumonia	3/7	43
Ventilation difficulties	2/7	29
Retroperitoneal bleed	1/7	14
Arrhythmia	1/7	14
Skin infection	1/7	14
Prolonged air leak	1/7	14
Altered mental status	1/7	14
30-day mortality	1/7	14
In-hospital mortality	2/7	29

*Any patient with a preoperative diagnosis of a comorbid condition was considered to have that condition. These included diabetes mellitus, hypertension, chronic heart disease, peripheral vascular disease, cerebrovascular accident, chronic obstructive pulmonary disease, emphysema, chronic sepsis, urinary tract infection, and other malignancy.

†Tumor stage based on American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 6th edition. Complete staging data were available for only 6 of the 7 patients.

‡Complications are defined as any morbid states that occurred within 30 days postoperatively. If a complication was not mentioned in the medical record material available to us, it was considered to be absent. Some patients had more than one complication.

||In-hospital mortality is defined as a death that occurred during the initial admission for curative-intent lung cancer surgery.

known document clearly describing human illness and treatment. It dates from 2500–3000 BC, the time of the Pharaoh Zoser in ancient Egypt, and describes several patients with spinal injury. Imhotep, the presumed physician-author, comments on case 31 as follows:

“If thou examinest a man having a dislocation in a vertebra of his neck, shouldst thou find him unconscious of his two arms and his two legs on account of it, while his phallus is erected on account of it; his flesh has received wind; his two eyes are blood-shot; it is

a dislocation of a vertebra of his neck extending to his backbone which causes him to be unconscious of his two arms and his two legs. Thou shouldst say concerning him:...an ailment not to be treated."

In modern times, the life expectancy of those who sustained this injury has lengthened greatly. In the United States, a 20-year-old person without SCI can expect to live another 57 years; a 20-year-old with SCI resulting in paraplegia who survives the first 24 hours after injury currently can expect to live another 45 years (26).

This retrospective study presents detailed clinical information about patients with SCI who subsequently undergo lung resection for lung cancer. We believe it is the only series on this topic reported to date. To accomplish this, we used large national DVA computer data sets to identify patients of interest. There are approximately 25 million veterans eligible for care at more than 150 DVA medical centers (27). Approximately 5 million obtain care in DVA facilities each year. This is the largest medical system in the United States, treating 52,856 SCI patients during the 10-year period of this study. This represents approximately 20% of the total national pool. The identification of 55 candidates for study from a sample of more than 11 million DVA patients is testimony to the power of computers and cooperation of the DVA to facilitate clinical research. All 7 evaluable patients had a complete SCI of traumatic etiology, all had non-small cell lung cancer, and all had curative-intent surgical resection. All were middle-aged or elderly male smokers, thus constituting a relatively homogenous population. This limits the generalizability of the data to other populations of patients with SCI with bronchogenic carcinoma who may be candidates for surgery. However, our report should enable clinicians to anticipate the clinical course of patients with SCI with lung cancer who are eligible to receive potentially curative surgery, counsel them about operative risks, and perhaps take steps to avoid predictable complications.

Patients with SCI constitute a high-risk category. Some patients are nutritionally depleted, but obesity is also common. They typically have at least one chronic illness (diabetes mellitus, bronchitis, hypertension, peripheral vascular disease, etc). This places them at high risk of postoperative complications. In our study, 71% of patients had more than one comorbid condition (Table 2). These patients also have high rates of pressure ulcers, spasticity, contractures, stomas, and areas of ectopic ossification, which may make the technical conduct of surgery more difficult. Some may have residual spinal fixation devices in place that can degrade computed tomography images, make magnetic resonance imaging unfeasible, and make surgery more difficult. Patients with SCI in general have a diminished pulmonary reserve as a result of respiratory muscle weakness (28,29). Not surprisingly, smokers with SCI have worse function than nonsmokers with SCI (30). Treatment of lung disorders

can be effective (29); a summary of evidence has been published by the US Agency for Healthcare Research and Quality (31).

SCI can alter the presentation and surgical outcome of many disease processes. This case study suggests, but does not definitively prove, that the rate of adverse outcomes of surgery for lung cancer may be related to preexisting SCI. The postoperative mortality rate after pulmonary lobectomy in recent articles ranged from 2.9% to 7.5% (Table 1). In the prospectively collected data from NSQIP, it was 4% (17). In our series, all received a lobectomy, and 2 of 7 (29%) died without leaving the hospital. Data concerning SCI as a possible risk factor for adverse outcomes have recently led NSQIP to add SCI to its registry of putative risk factors.

The study has several limitations. Our main limitations were the retrospective design, lack of reliable pulmonary function test data, and small study population. Because of the small final sample size, no statistical comparisons were possible. Nonetheless, this is the only series on this topic available. Another limitation was the absence of female patients with SCI. Our screening computer search yielded 55 patients, but only 7 met our inclusion criteria for evaluation. We were unable to obtain detailed medical records on all suitable patients who had SCI followed by lung resection for lung cancer within the VA system.

Current treatment protocols and improvements in our understanding of SCI have enabled this group of patients to have much prolonged life expectancy and quality of life. Until the 20th century, the major cause of death after SCI was sepsis secondary to urinary tract infection. Currently, patients with SCI are living longer, and their comorbid conditions reflect those of the general age-adjusted population. However, patients with SCI often have several serious comorbid conditions and seem to experience complications of surgery frequently. Comorbid conditions constitute a major independent risk factor affecting prognosis in cancer patients (32), and the mortality and morbidity rates we observed were quite high. Data from this report and previous articles (dealing with other types of surgery in patients with SCI) have generally indicated that patients with SCI have worse outcomes after surgery than the neurally intact population. We believe that the SCI itself is largely responsible for this. We hope this report stimulates others with access to suitable patient populations to study the topic of lung cancer surgery in patients with SCI to increase the generalizability and credibility of our conclusions.

CONCLUSION

Pulmonary resection in patients with SCI who develop lung cancer is feasible. Comorbid conditions are common, however, and individuals who undergo resection have high morbidity and mortality rates. The available evidence suggests that SCI should be considered a risk

factor for poor outcomes in patients undergoing major pulmonary surgery.

REFERENCES

- Fontana RS, Sanderson DR, Woolner LB, Taylor WF, Miller WE, Muhm JR. Lung cancer screening: the Mayo program. *J Occup Med.* 1986;28:746–750.
- Tockman MS. Survival and mortality from lung cancer in a screened population: the Johns Hopkins study. *Chest.* 1986;89(suppl 4):324S–326S.
- Melamed MR, Flehinger BJ, Zaman MB. Impact of early detection on the clinical course of lung cancer. *Surg Clin North Am.* 1987;67:909–924.
- Kubik A, Parkin DM, Khat M, Erban J, Polak J, Adamec M. Lack of benefit from semi-annual screening for cancer of the lung: follow-up report of a randomized controlled trial on a population of high-risk males in Czechoslovakia. *Int J Cancer.* 1990;45:26–33.
- Fontana RS, Sanderson DR, Woolner LB, et al. Screening for lung cancer: a critique of the Mayo Lung Project. *Cancer.* 1991;67(suppl 4):1155–1164.
- Lasfargues JE, Custis D, Morrone F, Carswell J, Nguyen T. A model for estimating spinal cord injury prevalence in the United States. *Paraplegia.* 1995;33:62–68.
- McKinney WP, McIntire DD, Carmody TJ, Joseph A. Comparing the smoking behavior of veterans and non-veterans. *Public Health Rep.* 1997;112:212–218.
- Spungen AM, Lesser M, Almenoff PL, Bauman WA. Prevalence of cigarette smoking in a group of male veterans with chronic spinal cord injury. *Mil Med.* 1995;160:308–311.
- Centers for Disease Control. Cigarette smoking among adults—United States, 1990. *MMWR.* 1992;41:354–355,361–362.
- Strauther GR, Longo WE, Virgo KS, Johnson FE. Appendicitis in patients with previous spinal cord injury. *Am J Surg.* 1999;178:403–405.
- Ahmed HU, Smith JB, Rudderow DJ, Longo WE, Virgo KS, Johnson FE. Cholecystectomy in patients with previous spinal cord injury. *Am J Surg.* 2002;184:452–459.
- West DA, Cummings JM, Longo WE, Virgo KS, Johnson FE, Parra RO. Role of chronic catheterization in the development of bladder cancer in patients with spinal cord injury. *Urology.* 1999;53:292–297.
- Stratton MD, McKirgan LW, Wade TP, et al. Colorectal cancer in patients with previous spinal cord injury. *Dis Colon Rectum.* 1996;39:965–968.
- Chan JWH, Virgo KS, Johnson FE. Hemipelvectomy for severe decubitus ulcers in patients with previous spinal cord injury. *Am J Surg.* 2003;185:69–73.
- Brandes SB, Smith JB, Longo WE, Virgo KS, Johnson FE. Renal cell carcinoma in patients with prior spinal cord injury. *J Spinal Cord Med.* 2001;24:251–256.
- Jacobs DL, Longo WE, Peterson GJ, McKirgan LW, Virgo KS, Johnson FE. Outcome of abdominal aortic aneurysm repair in patients with previous spinal cord injury in the Department of Veterans' Affairs hospitals. *Cardiovasc Surg.* 1997;5:286–290.
- Harpole DH, DeCamp MM, Daley J, et al. Prognostic models of thirty-day mortality and morbidity after major pulmonary resection. *J Thorac Cardiovasc Surg.* 1999;117:969–979.
- Handy JR, Asaph JW, Skokan L, et al. What happens to patients undergoing lung cancer surgery? *Chest.* 2002;122:21–30.
- Sabiston DC, Spencer FC. *Surgery of the Chest.* Philadelphia, PA: WB Saunders; 1995.
- Canver CC, Cooler SD, Nichols RD. The influence of cardiopulmonary function on outcome of veterans undergoing resectional therapy for lung cancer. *J Cardiovasc Surg.* 1998;39:497–501.
- Myrdal G, Gustafsson G, Lambe M, Horte LG, Stahle E. Outcome after lung cancer surgery. Factors predicting early mortality and major morbidity. *Eur J Cardiothorac Surg.* 2001;20:694–699.
- Ploeg AJ, Kappetein AP, van Tongeren RB, Pahlplatz PV, Kastelein GW, Breslau PJ. Factors associated with perioperative complications and long-term results after pulmonary resection for primary carcinoma of the lung. *Eur J Cardiothorac Surg.* 2003;23:26–29.
- American Spinal Injury Association. *International Standard For Neurologic Classification of Spinal Cord Injury, Revised 2000.* Chicago, IL: American Spinal Injury Association; 2000.
- Bedbrook GM, Sedgley GI. The management of spinal injuries—past and present. *Int Rehabil Med.* 1980;2:45–61.
- Breasted JH. *The Edwin Smith Surgical Papyrus. Vol. 1. Hieroglyphic Transliteration, Translation, and Commentary.* Chicago, IL: University of Chicago Press; 1930.
- Spinal cord injury: facts and figures at a glance. *J Spinal Cord Med.* 2000;23:51–53.
- Principi AJ. Department of Veterans Affairs strategic plan for employees 2003–2008. US Government Printing Office; 2003.
- Baydur A, Adkins RH, Milic-Emili J. Lung mechanics in individuals with spinal cord injury: effects of injury level and posture. *J Appl Physiol.* 2001;90:405–411.
- Sassoon CSH, Baydur A. Respiratory dysfunction in spinal cord disorders. In: Lin VW, ed. *Spinal Cord Medicine.* New York, NY: Demos Medical Publishing; 2003:155–168.
- Linn WS, Spungen AM, Gong H, Bauman WA, Adkins RH, Waters RL. Smoking and obstructive lung dysfunction in persons with chronic spinal cord injury. *J Spinal Cord Med.* 2003;26:28–35.
- Agency for Healthcare Research and Quality Evidence Report/Technology Assessment Number 27. *Treatment of Pulmonary Disease Following Cervical Spinal Cord Injury.* Available at: <http://www.ahrq.gov/clinic/epcsums/spinalsum.htm>. Accessed January 26, 2006.
- Piccirillo JG, Tierney RM, Costas I, Grove L, Spitznagel EL. Prognostic importance of comorbidity in a hospital-based cancer registry. *JAMA.* 2004;291:2441–2447.