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Management of pleural space infections: A population-based analysis

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Supplemental material is available online.

Objective: Management options for pleural space infections have changed over the last 2 decades. This study evaluated trends over time in the incidence of disease and use of different management strategies and their associated outcomes.

Methods: A retrospective study was performed by using a statewide administrative database of all hospitalizations for pleural space infections between 1987 and 2004.

Results: Four thousand four hundred twenty-four patients (age, 57.1 ± 18.6 years; 67% male; comorbidity index, 1.1 ± 1.9) were hospitalized with pleural space infections. The incidence rate increased 2.8% per year (95% confidence interval, 2.2%-3.4%; $P < .001$). Overall, 51.6% of patients underwent an operation, and the proportion increased from 42.4% in 1987 to 58.4% in 2004 ($P < .001$). The risk of death within 30 days was less for patients undergoing operations compared with that for patients not undergoing operations (5.4% vs 16.6%, $P < .001$); however, patients undergoing operations were younger (52.9 ± 17.6 years vs 61.5 ± 18.6 years, $P < .001$) and had a lower comorbidity index (0.8 ± 1.6 vs 1.4 ± 2.1, $P < .001$). After adjusting for age, sex, comorbidity index, and insurance status, patients undergoing operative therapy had a 58% lower risk of death (odds ratio, 0.42; 95% confidence interval, 0.32-0.56; $P < .001$) than those undergoing nonoperative management.

Conclusions: The incidence of pleural space infections and the proportion of patients undergoing operative management have increased over time. Patients undergoing operations were younger and had less comorbid illness than those not undergoing operations but had a much lower risk of early death, even after adjusting for these factors.

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Read at the Thirty-second Annual Meeting of the Western Thoracic Surgical Association, Sun Valley, Idaho, June 21-24, 2006.

Received for publication June 16, 2006; revisions received Aug 28, 2006; accepted for publication Sept 29, 2006.

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J Thorac Cardiovasc Surg 2007;133:346-51

0022-5223/$32.00

doi:10.1016/j.jtcvs.2006.09.038

Pleural space infections are associated with considerable morbidity, mortality, and health care resource use.[1-4] Although drainage of the pleural space is a key component of care, the extent of drainage and debridement has long been debated.[5] Options include nonoperative (thoracentesis and tube thoracostomy) and operative (thoracotomy with decortication) intervention. Recent additions to these 2 management approaches include image-guided catheters and operations performed by using video-assisted thoracoscopic surgery (VATS), respectively.

A meta-analysis of largely retrospective cohort studies and historically controlled case series revealed lower early mortality (2%-5% vs 9%-10%) and reintervention (0%-11% vs 40%-46%) rates for primary operative versus nonoperative drainage.[1] However, different patient characteristics among the different treatment groups might have influenced these outcomes. Only one randomized trial addressed this issue, comparing operative (primary VATS) with nonoperative (primary tube thoracostomy and fibrinolytic therapy) therapy, with the findings that patients undergoing VATS experienced significantly fewer treatment failures and hospital and chest tube days.[6] Unfortunately, an insufficient number of patients (n = 20) was

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Abbreviations and Acronyms

CI = confidence interval
ICD-9 = *International Classification of Diseases, Ninth Revision*
ICF = institutional care facility
VATS = video-assisted thoracoscopic surgery

enrolled to meaningfully evaluate whether early VATS actually decreased the risk of death. Because of these limitations, the approach to pleural space infection varies between physicians. Practice patterns are likely influenced by specialization, access to thoracic surgeons, and conventional wisdom and training.

It is unclear how the growing availability of new management options for pleural drainage has affected clinical practice in the community at large. The management of pleural space infections has never been described at the population level. We examined trends in the incidence of disease and operative management over an 18-year period in the state of Washington, and evaluated differences in baseline characteristics and outcomes between patients undergoing operations and those not undergoing operations.

Materials and Methods

Study Design

A retrospective cohort study was performed by using a statewide hospital discharge database. This study was exempted from human subject review by agreement of the University of Washington Subject Review Committee and the Washington State Department of Health. The data set contains no direct identifiers and is considered within the public domain.

Setting and Data Source

The Washington State Comprehensive Hospital Abstract Reporting System database contains records of all hospitalizations occurring between 1987 and 2004, except those at Veterans Affairs and US military hospitals. This data set includes demographic information (age and sex); *International Classification of Diseases*, *Ninth Revision* (ICD-9) diagnostic and procedure codes; administrative details of hospitalization (insurance status, length of stay, charges, and disposition); and coded hospital identifiers. Thirty-day mortality was determined by means of linkage of the Comprehensive Hospital Abstract Reporting System to the Washington State Department of Health vital records database. Estimates of the statewide population were derived from the US Census Bureau.

Patients and Definitions

Cases were defined as all patients hospitalized between 1987 and 2004 with a pleural space infection (ICD-9 diagnostic codes for either empyema with or without fistula [510.0, 510.9] or infected pleural effusion [511.1]) whose hospitalization also included a pleural drainage procedure (ICD-9 procedure codes for operative drainage of the pleural space [34.0, 34.01, 34.02, 34.09, 34.21], decortication [34.51, 34.59], closure of a bronchopleural fistula [33.42, 34.73], thoracentesis [34.91], or tube thoracostomy [34.04]). Patients less than 18 years of age were excluded. ICD-9 diagnostic codes for the cause or chronicity of infection do not exist, and thus categorization by cause, chronicity, or both was not possible. Categorization by the presence or absence of a fistula was not attempted because ICD-9 diagnostic codes are unlikely to reliably identify that level of clinical detail. Patients with procedure codes (see Appendix E1) for thoracic operations performed for conditions other than pleural space infection were also excluded. The latter were believed to more likely represent patients who had pleural space infection as a complication of their thoracic operations. Operative therapy was defined by procedure codes for operative drainage of the pleural space, decortication, or closure of a bronchopleural fistula. Nonoperative therapy was defined by procedure codes for thoracentesis or tube thoracostomy. Because ICD-9 procedure codes do not capture the timing or number of interventions and because the reliability of these codes for procedures that occur at the bedside, as opposed to the operating room, is unknown, we did not analyze subcategories of operative and nonoperative therapy.

Outcomes

Outcomes of interest included 30-day mortality, readmission within 30 days of discharge for a diagnosis of pleural space infection, discharge to an institutional care facility (ICF), length of stay, and costs. Discharge to an ICF was a dichotomized variable indicating whether a patient went to another facility, such as a skilled nursing, intermediate-care, or rehabilitation facility, versus home. Calculation of the proportion discharged to an ICF excluded patients who died in the hospital. Costs were calculated from hospital charges using the Medicare charge-to-cost ratio for Washington State[7] and adjusted for inflation by using the Consumer Price Index for Medical Care.[8]

Covariates

The Deyo modification of the Charlson comorbidity index (0-3) was calculated by using ICD-9 diagnostic codes from index admissions.[9] A value of zero indicates no comorbid conditions, whereas an index of 3 or greater indicates the greatest extent of comorbidity. Insurance status was considered a marker for economic status and was a dichotomized variable indicating whether the primary payer was Medicaid or the case was considered "charity" versus all other types of payers, such as Medicare, a health maintenance organization, Blue Cross/Blue Shield, or commercial insurance.

Analysis

Poisson regression was used to test for a change in the incidence of pleural space infection over the time of the study by using age- and sex-standardized data. Data were directly standardized for age and sex by using year 2000 population data as a reference. Trends in patient characteristics, management, and outcomes were reported across three 6-year time categories. Tests for trends over time were based on linear (for continuous variables) and logistic regression (for categoric variables) analyses by using yearly time categories as the independent variable.

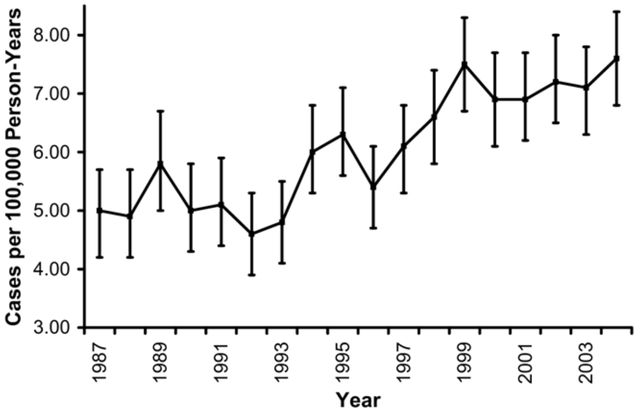

Figure 1. Age- and sex-adjusted incidence of pleural space infection in Washington State from 1987 through 2004.

For comparisons of outcomes between patients treated operatively and nonoperatively, χ^2 tests were used for categoric variables, and the unpaired *t* test was used for continuous variables. Logistic regression was used to examine the association between receipt of operative therapy and death within 30 days of discharge, readmission, and discharge to an ICF. The cumulative patient fatality rate was estimated for the entire cohort and operative and nonoperative groups by using the Kaplan–Meier method. A log-rank test was used to test for an unadjusted difference in patient fatality rate between the 2 groups. Cox regression was used to provide adjusted estimates of the instantaneous hazard of death. Regression models were built to first include unadjusted variables and then added patient age, sex, comorbidity index, and insurance status as confounding variables. Adjustments for clustering at the hospital level were performed to account for similarities among patients treated in the same hospital. Statistical analyses were performed by using STATA version 9 (STATA Corp, College Station, Tex).

Results

Four thousand four hundred twenty-four patients (mean ± standard deviation age, 57.1 ± 18.6 years; 66.8% men) were hospitalized with pleural space infection and underwent some form of drainage procedure in Washington State between 1987 and 2004. A large percentage of patients (16.7%) was considered to have low socioeconomic status based on the payer source described as either Medicaid or charity care. The age- and sex-adjusted incidence of pleural space infection increased 2.8% per year (95% confidence interval [CI], 2.2%-3.4%; $P < .001$), with a peak of 7.6 cases per 100,000 state residents in 2004 (Figure 1).

Table 1 demonstrates differences in patient characteristics, operative management, and outcomes averaged across 6-year time periods. Mean age and sex distribution did not change over the study period ($P = .64$ and $P = .54$, respectively), although the mean comorbidity index and proportion of patients with Medicaid/charity care increased ($P < .01$ and $P < .01$, respectively). Overall, 51.6% of patients underwent an operation, and the proportion increased from 42.4% in 1987 to 58.4% in 2004 ($P < .001$). The proportion of patients discharged to an ICF increased from 23.1% in 1987 to 30.6% in 2004 ($P < .001$). Length of stay decreased from 16.9 days in 1987 to 13.9 days in 2004 ($P = .001$), but adjusted costs increased from $23,240 in 1987 to $38,659 in 2004 ($P < .001$). The 30-day mortality rate was 12.1% in 1987 and 9.4% in 2004, although the test of trend revealed no statistically significant differences over time ($P = .24$).

Patients undergoing operations were younger, had fewer comorbid conditions, were more commonly men, and were more often Medicaid/charity care beneficiaries compared with patients not undergoing operations (Table 2). Patients undergoing operative therapy had better outcomes, with lower 30-day mortality (5.4% vs 16.6%, $P < .001$), read-

TABLE 1. Temporal trends in patient characteristics, management, and outcomes

	All (n = 4424)	1987-1992 (n = 1053)	1993-1998 (n = 1407)	1999-2004 (n = 1964)
Characteristics				
Age (y, mean ± SD)	57.1 ± 18.6	57.5 ± 19.2	56.2 ± 18.5	57.5 ± 18.3
Male sex (%)	66.8	67.0	68.1	65.7
Comorbidity index (mean ± SD)	1.1 ± 1.9	0.9 ± 1.8	1.1 ± 1.9	1.1 ± 1.9
Medicaid/charity (%)	16.7	15.1	15.4	18.5
Management				
Operative (%)	51.6	44.4	51.6	55.4
Outcomes				
30-d Mortality (%)	10.8	10.9	11.4	10.3
Readmission (%)	4.4	4.7	4.1	4.6
Discharge to ICF (%)	26.0	19.5	24.8	30.3
LOS (d, mean ± SD)	14.1 ± 11.8	15.9 ± 14.1	13.3 ± 10.1	13.7 ± 11.6
Costs ($, mean ± SD)	27,368 ± 34,578	21,723 ± 27,729	23,949 ± 27,779	32,843 ± 40,910

SD, Standard deviation; *ICF*, institutional care facility; *LOS*, length of stay.

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TABLE 2. Patient characteristics and outcomes by management

	Operative (n = 2281)	Nonoperative (n = 2143)	*P* value
Characteristics			
Age (y, mean ± SD)	52.9 ± 17.6	61.5 ± 18.6	<.001
Male sex (%)	70.1	62.7	<.001
Comorbidity index (mean ± SD)	0.8 ± 1.6	1.4 ± 2.1	<.001
Medicaid/charity (%)	19.4	13.8	<.001
Outcomes			
30-d Mortality (%)	5.4	16.6	<.001
Readmission (%)	3.0	5.9	<.001
Discharge to ICF (%)	21.8	30.1	<.001
LOS (d, mean ± SD)	15.5 ± 12.5	12.6 ± 10.9	<.001
Costs ($, mean ± SD)	32,112 ± 36,060	22,318 ± 32,174	<.001

SD, Standard deviation; *ICF*, institutional care facility; *LOS*, length of stay.

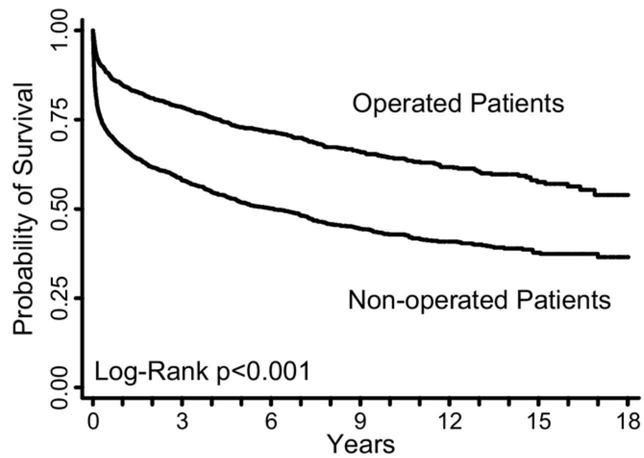

Figure 2. Kaplan–Meier plots of cumulative case fatality rates by management.

mission (3.0% vs 5.9%, $P < .001$), and discharge to an ICF (21.8% vs 30.1%, $P < .001$) rates compared with those of patients undergoing nonoperative therapy. Interestingly, patients undergoing operations had longer hospitalizations and greater hospital costs, but we could not assess the relative contribution of preintervention hospitalization time and costs.

After adjusting for age, sex, comorbidity index, and insurance status, patients who had an operation were 58% less likely to die within 30 days (odds ratio, 0.42; 95% CI, 0.32-0.56), 58% less likely to be readmitted (odds ratio, 0.42; 95% CI, 0.31-0.57), and 17% less likely to be discharged to an ICF (odds ratio, 0.83; 95% CI, 0.71-0.98). Patients undergoing operations had a 29% reduction in the adjusted risk of death over time (hazard ratio, 0.71; 95% CI, 0.63-0.80). The greatest effect of an operation on survival appeared within the first year of follow-up, with an apparently similar risk of death beyond 1 year (Figure 2). Overall, 39.6% of patients died (median survival, 13.2 years) within the follow-up period.

Discussion

This study aimed to describe changes in the incidence of pleural space infections and the proportion of patients undergoing operative therapy over time and to compare differences in patient characteristics and outcomes between operative and nonoperative groups. We found an increasing incidence of pleural space infections and an increase in the use of operative interventions. This study also found that patients undergoing operations had more favorable outcomes, even after adjusting for differential characteristics that might influence outcome, such as age, sex, burden of comorbid conditions, and insurance status.

It is unclear why the incidence of pleural space infections is increasing. Although older patients might be more likely to have pleural space infections, the aging US population alone might not account for this observation. For example, we found that the mean age of patients with pleural space infection did not change significantly during the study period. Alternatively, the growing number of patients living with chronic illness might explain this increase. Potential risk factors for pleural space infections include cardiac disease,[2] chronic lung disease,[2] diabetes,[2,10,11] obesity, and tobacco and alcohol use.[2,12] An increasing comorbidity index over time confirms that patients with pleural space infections bear an increasing burden of comorbid conditions. Finally, it is possible that the observed increase in incidence could be an artifact of increased clinical awareness, identification, and coding of this disease.

We found that the proportion of patients undergoing an operation increased over time. One explanation for this growth is an increase in access to and use of better imaging technology. Ultrasonography and computed tomography are well suited to detect loculations and pleural and extrapleural fat enhancement,[13] findings that might influence a surgeon's decision to operate. A second possibility is an increase in access to well-trained thoracic surgeons and their influence in the community to consider earlier and more aggressive surgical intervention. The introduction of VATS in the 1990s as a less-invasive and apparently effective approach for many thoracic operations might also have contributed to the increasing proportion of operations being performed. In 2 different studies of patients with pleural space infections,[14,15] those undergoing VATS had a shorter duration of preoperative symptoms than those undergoing thoracotomy. This observation is consistent with the hypothesis that the availability of VATS has lowered the threshold to operate, possibly because of greater patient and physician acceptance of this less-invasive option.

Compared with patients who did not undergo an operation, patients who did undergo operative management had markedly different baseline characteristics and outcomes. The observation that patients undergoing operations were younger and apparently healthier (although also more likely male and economically disadvantaged) supports the hypothesis that patient characteristics influence treatment selection. It seems likely that physicians managing patients who were older and with higher comorbidity were more hesitant to refer for operative intervention, that thoracic surgeons were less likely to advise surgical intervention, or both. After adjustment, patients undergoing operations still had a lower risk of early mortality, readmission, and discharge to an ICF. This finding is consistent with the hypothesis that operative drainage of the pleural space is more efficacious than nonoperative drainage, but this study could not completely distinguish the effect of other important but unmeasured patient characteristics on these outcomes.

We found a higher risk of death for both patients undergoing operations (5.4%) and patients not undergoing operations (16.6%) than previous estimates derived from aggregate published data (1.9%-4.8% and 4.3%-10.3%, respectively).[1] Publication and selection bias might account for lower published risks of death for the 2 management strategies. Another possible explanation is that care in the community at large, especially nonoperative management, is less effective compared with care in institutions that publish research on pleural space infections.

Our investigation has several limitations. Administrative data sets do not contain sufficient clinical information to adequately adjust for potential confounding based on the severity of infection or underlying comorbidity. Additionally, administrative data do not contain information on the timing of procedures, and therefore a distinction between primary and secondary procedures was not possible. ICD-9 procedure codes do not exist for therapeutic VATS drainage/decortication or image-directed catheters, and thus direct evaluation of the effect of new technology was not possible. We aimed to minimize misclassification of patients included in our cohort by requiring all patients to have an associated ICD-9 procedure code, given that some form of drainage of pleural space infection is the standard of care. Although diagnostic codes are susceptible to miscoding or undercoding, procedure codes have a higher yield because procedures are discrete billing events. This approach, however, might have excluded patients who truly had pleural space infections that were never drained. This bias would likely underestimate the true incidence of pleural space infection. We also excluded patients who had ICD-9 procedure codes for thoracic operations used to treat conditions other than pleural space infection. We believe these patients likely represent a group that had pleural space infection as a consequence of a thoracic operation and accordingly have a different risk profile for adverse outcomes compared with the population that typically acquires pleural space infection as a result of pneumonia. Concerned that attempts to conservatively define our cohort might have significantly altered the results, we performed several post-hoc analyses of temporal trends and comparisons across treatment groups, varying the definition of pleural space infection to include patients we had originally excluded. Although absolute estimates were slightly different, neither trends nor tests of significance were different than those reported.

In summary, the incidence of pleural space infection and the proportion of patients undergoing operative management are increasing. Patients who undergo operative therapy have a lower risk of death, readmission, and being discharged to an ICF, although these patients are also typically younger and with less comorbid illness. Thoracic surgeons can use these findings to (1) better inform their patients that an 18-year statewide experience confirms that operative management is a relatively safe and effective procedure for selected patients with pleural space infections and (2) better educate their medical colleagues about the importance of early referral for thoracic surgical consultation. Future investigations should aim to describe the proportion of patients undergoing primary operative therapy, better identify potential confounders, measure quality of life and functional status, and evaluate the cost-effectiveness of competing therapies.

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Appendix E1

Lung resection (32.0, 32.09, 32.1, 32.21, 32.22, 32.29, 32.3, 32.4, 32.5, 32.6, 32.9, 33.0, 33.1, 33.25, 33.26, 33.28), destruction of phrenic nerve (33.31), artificial pneumothorax for collapse of lung (33.32, 33.39), thoracoplasty (33.34), suture of laceration of the bronchus (33.41), closure of laceration of lung (33.43), other repair and plastic operation on bronchus (33.48), lung transplantation (33.50, 33.51, 33.52, 33.6), other repair and plastic operation on lung (33.49), ligation of bronchus (33.92), puncture of lung (33.93), other operation of lung or bronchus (33.98, 33.99), incision of mediastinum (34.1), pleural biopsy (34.24), open biopsy of mediastinum (34.26), biopsy of diaphragm (34.27), pleurodesis (34.6, 34.92), other repair of chest wall (34.79), excision of lesion or tissue of diaphragm (34.81), suture of laceration of diaphragm (34.82), closure of fistula of diaphragm (34.83), other repair of diaphragm (34.84), implantation of diaphragmatic pacemaker (34.85), other operations on diaphragm (34.89), repair of pleura (34.93), other operations on thorax (34.99), closed heart valvotomy (35.00-35.04), open heart valvuloplasty without replacement (35.10-35.14), replacement of heart valve (35.20-35.28), operations on structures adjacent to heart valves (35.31-35.35, 35.39), creation of septal defect in heart (35.42), repair of atrial and ventricular septa with prosthesis (35.50, 35.51, 35.54), repair of atrial and ventricular septa with tissue graft (35.60-35.63), other and unspecified repair of atrial and ventricular septa (35.70-35.73), total repair of certain congenital cardiac anomalies (35.80-35.84), other operations on valves and septa of heart (35.90-35.95, 35.98, 35.99), operations on vessels of heart (36.03), bypass anastomosis for heart revascularization (36.10-17, 36.19), heart revascularization by arterial implant (36.20), other heart revascularization (36.31, 36.32, 36.39), other operations on vessels of heart (36.91, 36.99), cardiotomy and pericardiotomy (37.10-37.12), biopsy of pericardium or heart (37.24, 37.25), pericardiectomy and excision of lesion of heart (37.31-37.35), repair of heart and pericardium (37.41, 37.49), heart replacement procedures (37.51-37.54), implantation of heart and circulatory assist system (37.62-37.68), insertion of left atrial appendage device (37.90), incision of esophageal web (42.01), other incision of esophagus (42.09), esophagostomy not otherwise specified (42.1), exteriorization of esophageal pouch (42.12), other external fistulization of esophagus (42.19), operative esophagoscopy by incision (42.21), open biopsy of esophagus (42.25), local excision of esophageal diverticulum (42.31), local excision of other lesion or tissue of esophagus (42.32), other destruction of lesion or tissue of esophagus (43.39), esophagectomy (42.40-42.42), intrathoracic anastomosis of esophagus (42.50-42.56, 42.58, 42.59), antesternal anastomosis of esophagus (42.60-42.66, 42.68, 42.69), esophagomyotomy (42.7), insertion of permanent tube into esophagus (42.81), other repair of esophagus (42.82-42.87, 42.89), and ligation of esophageal varices (42.91).