Treating Malignant Pleural Effusions Cost Consciously*

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Malignant pleural effusions are associated with significant morbidity. Prompt clinical evaluation followed by aggressive treatment often results in successful palliation. This report summarizes the traditional and experimental approaches used in the management of malignant pleural effusion and provides an attempt at analysis of cost comparison and resource utilization associated with the use of various sclerosing agents. The standard sclerotherapy for malignant pleural effusions has routinely been performed as an inpatient procedure using a large-bore chest tube for drainage and instillation of a sclerosing agent. Use of a small-bore catheter for drainage and pleurodesis is associated with reduced patient discomfort and appears to be feasible and equally efficacious in the ambulatory setting. Results with the ambulatory procedure are preliminary but promising. Future comparisons with the traditional approach will allow therapy to be based not only on efficacy, but also on the use and expense of related resources. (CHEST 1998; 113:78S-85S)

Pleural effusions in patients with malignancy are usually due to the underlying neoplastic process and often signify advanced disease, but they can occur as the initial manifestation of malignancy or as a first sign of its recurrence. Malignancies of the breast, lung, and ovary, together with lymphomas, account for almost 75% of all malignant effusions. The remaining cases are associated with malignancies of the GI tract, genitourinary tract, unknown primary site malignancies, and a variety of other solid tumors. Most patients with pleural effusions have symptoms, presenting with severe dyspnea, cough, and chest discomfort that have diminished overall quality of life and reduced the patient's ability to perform routine daily activities. The average survival time for patients with advanced refractory malignancy who present with malignant pleural effusion is 4 to 6 months. Goal of management is thus prompt clinical evaluation followed by aggressive treatment using cost-effective strategies to achieve successful palliation. This report summarizes the various standard and experimental approaches to managing malignant pleural effusion and their efficacy and outlines related expenses to the patient and the healthcare system.

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Diagnosis
A systematic approach to the diagnosis of malignant pleural effusion begins with a patient history and thorough physical examination. The severity of symptoms often depends on the rate of fluid accumulation rather than on the total quantity of fluid. In addition to the symptoms of dyspnea, cough, and chest pain, systemic complaints due to underlying malignancy include weight loss, anorexia, malaise, and fatigue. Physical findings include decreased vocal fremitus, dullness to percussion, and decreased breath sounds over the areas of effusion. Massive pleural effusions are identified via bulging of the intercostal spaces, contralateral tracheal deviation, and reduced diaphragmatic excursion.

The chest radiograph is a low-cost and sensitive way of confirming the presence and size of pleural effusion. As little as 175 mL of fluid can be detected on an upright view of the chest, with blunting of the costophrenic angle. Decubitus views can detect as little as 100 mL of fluid in the pleural space. CT can detect even smaller quantities of fluid, but it is not performed routinely for diagnosis.

The diagnosis of malignant pleural effusion is usually relatively straightforward, with thoracentesis yielding an exudative effusion containing malignant cells. Removing large fluid volumes rapidly may result in reexpansion pulmonary edema. Approximately 50% of all malignant pleural effusions are diagnosed based on first cytologic study and the yield increases by 10% with the second cytologic study. Used alone, pleural biopsy is less sensitive in making a definitive diagnosis—probably owing to the focal nature of the disease process and the blind sampling procedure—and thus it is not recommended routinely. Pleural effusions associated with lymphomas and mesothelioma have a low diagnostic yield on cytologic examination and usually require a large tissue sample obtained at thoracoscopy or open biopsy to confirm the diagnosis. Immunocytochemical techniques using monoclonal antibodies and polyclonal antiserum to epithelial membrane antigen and rare pleural fluid studies like chromosomal analysis or measurement of creatine kinase BB are less sensitive and usually not helpful in the day-to-day diagnosis of malignant pleural effusion. Despite all the above tests, 25% of pleural effusions remain undiagnosed and require either thoracoscopy or limited thoracotomy for definitive diagnosis. The diagnostic yield of thoracoscopy is as high as 96%, and the procedure is increasingly replacing thoracotomy, which is associated with significant patient discomfort, lengthier hospitalization, increased morbidity, and greater expense.

Management
The management of malignant pleural effusions depends on the treatment potential of the primary malignancy. Systemic treatment may control primary malignancies like lymphoma, small cell lung cancer, or germ cell cancer, although therapeutic thoracentesis may still be required to improve symptoms. If effective systemic treatment is not available for the underlying disorder, the goal of treatment is successful palliation of symptoms with local therapy. The choice of locoregional therapy should aim at
avoiding unnecessary hospitalization, minimizing expenses, and ensuring fewer treatment-related complications. The various local management techniques currently include thoracentesis, tube thoracostomy and drainage, tube thoracostomy with instillation of a sclerosing agent, talc poudrage, pleuroperitoneal shunt, and pleurectomy (Table 1).

Thoracentesis

Thoracentesis plays an important therapeutic role in patients with symptomatic effusions, but the effect is short lived and symptoms recur in almost all patients.29 Repeated thoracenteses should be avoided because of the risk of adhesions and loculations, making future management more difficult.

Tube Thoracostomy and Drainage

Tube thoracostomy and drainage are effective in only a small number of patients.22 It is not recommended routinely to treat patients with malignant pleural effusions.

Tube Thoracostomy and Drainage With Instillation of a Sclerosing Agent

This is the treatment most often used for malignant pleural effusion. The chest tube is placed by an experienced physician or surgeon through the sixth or seventh interspace in the midaxillary line into the pleural cavity and connected to the water-seal drainage system, and negative wall suction (15 to 20 cm H2O) is applied. Drainage is usually continued until it decreases to ≤100 ml in a 24-h period, with lung reexpansion and apposition of the visceral and parietal pleura. Patients usually require some analgesia before the sclerosing agent is instilled. The agent is instilled through the drainage tube, after which the tube is clamped. The patient is asked to change positions every 15 min for 2 h to ensure uniform distribution of the sclerosing agent throughout the pleural space. The tube is then unclamped and opened to drain for an additional 24 h before removal. The success of sclerotherapy is ascertained by assessing changes in signs and symptoms and by monthly chest radiographs to rule out recurrence.

Choice of Sclerosing Agent

A number of sclerosing agents have been used to treat malignant pleural effusion, but many have proved less than optimal because of poor efficacy, a high incidence of adverse effects, difficulty in administration, or expense. The optimal sclerosing agent has high molecular weight, high chemical polarity, low regional clearance, high systemic clearance, and a steep dose-response curve, and it must be tolerated well by local tissue. The efficacy of currently available sclerosing agents is outlined in Table 2.

Talc: A mechanical sclerosing agent, talc is one of the oldest treatments for malignant pleural effusion and is still used extensively. Its overall utility in this setting, however, has become controversial. Talc is administered intrapleurally following thoracentesis, either injected into the chest tube as a slurry (in 0.9% NaCl) or insufflated during thoracotomy or a thoroscopic procedure. The insufflation procedures are conducted in the operating room by appropriately trained personnel, with the patient under general anesthesia. Talc pleurodesis is highly effective, with a 72 to 100% response rate after a single administration22 (Table 2). It is not always regarded favorably, however, owing to the severe pain and the variety of complications associated with the procedure such as fever, dyspnea, pneumothorax, acute pneumonitis, granulomatous pneumonitis, and ARDS.23-28 Because general anesthesia adds to the risk of morbidity and mortality, video-assisted thoracoscopy is being used increasingly in place of thoracotomy to assure uniform distribution of talc.27,28

The dose of talc for pleurodesis has ranged from 2 to 10.5 g (recommended dose, 5 g). The talc itself is relatively inexpensive at $0.15 to $0.50 for a 2.5- to 10-g dose, unsterilized.29 However, when procedural costs for thoracoscopy, operating room and surgical staff time, anesthesia and postanesthesia monitoring, and adverse effect management are taken into account, the total cost of talc pleurodesis has been determined to be $20,996 (1992 US dollars).30 In a recently published analysis that considered this high initial cost, the low recurrence rate of 3 to 8%, and the single-administration effectiveness of 98% (Table 2), we determined that talc pleurodesis results in a 6-month cost of $149 per symptom-free day,30 which is higher than other treatments30 (Table 3). Despite its well-documented efficiency, the role of talc as a sclerosing agent continues to be controversial because of its unattractive side effect profile and associated difficulties with sterilization and administration.

Bleomycin and Other Chemotherapeutic Agents: Inves-

| Table 2—Efficacy of Currently Available Sclerosing Agents |
|---------------------------|--------------------|---------------|
| Agent                  | Mean % Response | Range     |
| Talc                    | 98                | 72-100      |
| Quinacrine              | 86                | 64-100      |
| Bleomycin               | 64                | 31-85       |
| Tetracycline            | 72                | 25-100      |
| Doxycycline*            | 73                | 67-88       |
| Doxorubicin             | 70                | 70          |
| Nitrogen mustard        | 44                | 27-95       |

*Multiple instillations of drug were made in some studies.
tigators have evaluated a wide range of antineoplastic drugs as sclerosing agents to treat malignant pleural effusion, including doxorubicin,31 etoposide,32 combination cisplatin/cytarabine,33,34 fluorouracil,35 and bleomycin.36-42 Except for bleomycin, these agents, with their low response rates and serious side effects, have shown little potential in this setting.29 Intrapleurally administered bleomycin, however, has produced response rates of 31 to 85%36-42 (Table 2). Comparative trials have shown bleomycin also is associated with a lower recurrence rate than tetracycline (36 to 54% vs 58 to 67% after 30 days, and 30% vs 53% after 90 days). Adding to the attractiveness of bleomycin is the typically low intensity of side effects associated with its use. Adverse effects include mild fever, localized pain, and GI complaints.29,30,42 The recommended dose is 60 U in 50 mL normal saline solution. As bleomycin usually does not cause myelosuppression, it can be administered safely to patients with compromised immune function, including those who are receiving other chemotherapeutic agents.

The cost per dose of bleomycin was reported as $1,104 (average US wholesale price, 1993 to 1994).29 Yet, the total cost of treatment (1992 US dollars) was relatively low, $8,657, owing to the high efficacy achieved with a single administration of this drug and its moderate adverse effect profile. The 6-month cost per symptom-free day was the lowest in our analysis,30 ie, $132 (Table 3).

**Tetracycline:** While no longer in use as a sclerosing agent, tetracycline is still often used as a standard in the comparison of new agents. Tetracycline had been the most commonly used agent for pleurodesis in the United States. The average response rate in patients with malignant pleural effusion was 75%.42-43 (Table 2). Tetracycline treatment was inexpensive, and its associated side effects, including localized pain and fever,41-44 were minimal. It had the additional advantage of producing local antibacterial activity, which helped reduce the risk of infection common with thoracentesis procedures.44 In 1991, however, production of injectable tetracycline in the United States was discontinued by its sole manufacturer.45

The cost of tetracycline ranged from $19.77 per 500-mg dose to $39.54 per 1,000-mg dose.29 Single-agent treat-
ment was effective and had few side effects, but 30-day recurrence rates were high, ranging from 54 to 67%.42,43 These factors resulted in a total treatment cost of $8,066 and a 6-month cost per symptom-free day of $159 (Table 3). As tetracycline is no longer available in the United States, bleomycin has been suggested as a suitable alternative.

**Doxycycline:** Because of its pharmacologic similarities to tetracycline, doxycycline has been investigated for use in the treatment of malignant pleural effusion. Three small, uncontrolled clinical trials have reported response rates of 67 to 88%,46-48 with response durations ranging from 2 to 10 months. Side effects are minimal and similar to those seen with tetracycline. The problem with doxycycline treatment is the need for repeated instillations on a biweekly basis. In the reported studies, only 15% of patients responded to a single treatment, and 9% required four or more treatments.48 Overall, the average was three treatments before adequate response to fluid reaccumulation was obtained. Additional procedures require that the chest tube either remain in place for several days or be removed and reinserted repeatedly, greatly increasing patient discomfort and the possibility of infection and pneumothorax.

The cost per 500-mg dose of doxycycline was reported as $86, with patients typically requiring three doses at a cost of $258.29 The total cost of treatment, which was most affected by the need for repeated administration and consequent hospitalization, was determined to be $8,061 with a cost per symptom-free day of $218, the highest in our analysis30 (Table 3).

**Interferons:** Not the agents of choice for pleurodesis, interferons have been used intrapleurally to obtain local immune modulation, including stimulation of natural killer cells.49-51 Response rates, however, have not been impressive. Side effects with interferon-β (IFN-β) are minimal and include local pain and fever.49-51 Use of high-dose recombinant interferon-α2b, however, has been associated with a flu-like syndrome and severe hematologic toxic reactions.49 Interferons were not included in our meta-analysis, but the costs per dose were calculated from the pharmaceutical average wholesale price. The cost

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Agent Cost</th>
<th>Total Cost of Treatment</th>
<th>Cost per Symptom-Free Day</th>
<th>Cost Drivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talc</td>
<td>$0.15-0.50 (2.5-10 g)</td>
<td>$20,996</td>
<td>$149</td>
<td>OR facilities, thoracic surgeon, complications</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>$1,104.00 (60 U)</td>
<td>$8,657</td>
<td>$132</td>
<td>High agent cost, toxicity potential with chemotherapy</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>$19.77 (500 mg)</td>
<td>$9,066</td>
<td>$159</td>
<td>NA for use</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>$255.00 (3 × 500 mg)</td>
<td>$8,061</td>
<td>$218</td>
<td>Repeated instillations required</td>
</tr>
<tr>
<td>IFN-β</td>
<td>$45.00-$134.00 (5-35 × 10^6 units)</td>
<td>NA</td>
<td>NA</td>
<td>Low response rate, high recurrence rate</td>
</tr>
<tr>
<td>IFN-α2b</td>
<td>$66.00 (1 million units)</td>
<td>NA</td>
<td>NA</td>
<td>High recurrence rate, limited data</td>
</tr>
<tr>
<td>rIL-2</td>
<td>$4.20-$8.00 (14,000-30,000 U)</td>
<td>NA</td>
<td>NA</td>
<td>Repeated instillations required, limited data</td>
</tr>
</tbody>
</table>

*OR=operating room; IFN-β=interferon; NA=not available.

1Average wholesale price in 1993-1994 US dollars.
21992 US dollars.
3Average wholesale price in 1995 US dollars.
per treatment for IFN-β ranged from $45 to $134 for one to seven doses, and the cost for interferon-α2b (Roferon) was $66 for the 1-million unit dose.

Interleukins: Recombinant interleukin-2 (rIL-2) was evaluated in patients with malignant pleural effusion in a small clinical trial by Suzuki et al. Patients received daily instillations of rIL-2 through a thoracostomy tube for an average of 24 days. Complete or partial response was seen in 100% of patients with no recurrence of symptoms (average survival period, 15.9 months). Side effects included fever and a transient increase in effusion lasting 3 to 10 days. Occasional conversion to normal results of cytologic examination has been reported with rIL-2, in addition to its relief of the symptoms of malignant effusion. Cost evaluation of interleukin-2 (Proleukin) was also not included in our meta-analysis, but the cost per treatment was calculated from the pharmaceutical average wholesale price as $4.20 to $9.00 a day for a 14- to 30-day supply of 1,000-U daily doses. Further investigations are needed to determine the intrapleural dose schedule and appropriate vehicle (eg, ethiodized oil emulsion, liposomes) to obtain an optimal biological effect.

Radioactive Isotopes

Radioactive gold (198Au) and Cr32PO4 have been the two radioisotopes most frequently used in sclerotherapy for malignant pleural effusions. Response rates range from 55 to 63%, with nausea being the most common side effect. The availability of the radioisotopes is limited not only because of their short half-lives but also because health-care personnel require protection to prevent exposure. They are rarely used clinically.

Pleuroperitoneal Shunts

Pleuroperitoneal shunts are occasionally beneficial in patients with intractable effusions and trapped lungs. They are, however, expensive and have limited efficacy. The shunt consists of a subcutaneous pumping chamber, one end of which is inserted into the chest cavity and the other into the abdomen. This permits the fluid in the pleural space to be diverted into the abdomen. The need to actively pump the shunt a minimum of 400 times daily limits its usefulness in patients with excellent performance status. In addition, the shunt may malfunction over time, further limiting its usefulness. Thus, it is one of the last alternatives for patients with refractory effusions that are not amenable to traditional thoracostomy and pleurodesis.

Pleurectomy

Pleurectomy and decortication have been attempted in patients with intractable malignant pleural effusions that have not responded to tube thoracostomy with sclerotherapy and talc insufflation. The procedure, however, is associated with prohibitive morbidity and mortality and requires general anesthesia. The use of safer, minimally invasive video-assisted thoracoscopic techniques may minimize these risks, but the associated costs probably outweigh the benefit in most patients.

Ambulatory Sclerotherapy

Traditionally, tube thoracostomy and pleurodesis are performed as inpatient procedures using a large-bore chest tube. New technology allows small-bore catheters to be used to drain malignant pleural effusions with a similar degree of efficacy. To avoid hospitalization and minimize discomfort, we have devised an ambulatory sclerotherapy procedure that uses radiologically placed small-bore catheters connected to a plastic bag with a one-way valve system for gravity drainage. Sclerotherapy was performed by instilling bleomycin, 60 U, in 50 mL normal saline solution when daily drainage decreased to <100 mL. Sixteen of 28 patients (57%) responded to this ambulatory procedure. Significant complications have included occasional pain, fever, infection, tube occlusion, and tube dislodgment. Overall, the ambulatory procedure is feasible and offers comparable palliation to traditional in-hospital procedures with greater patient comfort, reduced hospitalization, and lower health-care costs. The data are preliminary, and a larger randomized study is needed to compare the ambulatory procedure with the traditional tube thoracostomy with sclerotherapy. This study should include analyses of quality of life and resource utilization.

Cost Drivers: Sclerosing Agents

Studies have reported cost comparisons for many of the chemical sclerosing agents described. These reports compare total agent charges based on the US average wholesale price for 1993 to 1994 (Table 3). This information, however, is misleading when total treatment costs, which involve a number of additional factors that vary widely among the agents described, are considered. These factors include the number of instillations required for a complete response, route of administration, recurrence rate, anesthesia use, number of required personnel, hospitalization time, and adverse effects management. To derive a complete cost-effectiveness analysis, each of these factors must be considered in addition to the agent's cost.

Number of Required Instillations

The necessity for repeated dosing of an agent contributes significantly to the overall cost of therapy and duration of patient discomfort. Additional hospital stays, personnel time, diagnostic procedures, and pharmaceutical costs to manage pain all incur extra costs. Repeated dosing also enhances the risk of complications. Thus, whereas single administration of tetracycline or bleomycin provides a complete clinical response in >70% of cases, doxycycline requires an average of three biweekly administrations, and IFN-β requires one to seven biweekly administrations, and rIL-2 requires daily doses for 10 to 29 days.

The procedure required to administer a particular agent also affects the total cost of treatment. Typically, sclerosing agents are instilled via chest tube following optimal drainage. Pain is ameliorated by introducing a 1% lidocaine solution into the pleural space 10 to 15 min before the sclerosing agent. Talc pleurodesis is significantly more
intensive and costly than the other agents. Talc is usually insufflated either following thoracotomy or using a thoracosopic technique. Both procedures require operating room facilities and a specially trained thoracic surgeon. Additionally, the high degree of pain associated with this procedure requires general anesthesia.

Recurrence Rates

How often malignant pleural effusions recur with each method of pleurodesis is an important consideration in measuring cost-effectiveness. Typically, a particular agent is used only once after the effusion recurs. Following a second recurrence, talc pleurodesis is usually advised. Patients with effusions that are refractory to talc pleurodesis require pleurectomy or pleuropertitoneal shunting, provided their performance status is excellent. Each successive treatment required adds to the costs of therapy by necessitating additional hospital stays, personnel costs for repeated procedures, laboratory and radiology costs for diagnosis, and pharmacy costs for pain management and by increasing the risk of adverse effects. Talc is associated with the lowest recurrence rates, 3 to 8% after 30 days,20 followed by doxycycline with 30-day recurrence rates of 17 to 27%.4 The rate associated with bleomycin was highly variable, ranging from 36 to 83.9%,20,44 whereas rates with the remaining agents were relatively high (54 to 67% for tetracycline, 67 to 74% for interferons).21-25

Adverse Effects Management

Managing adverse effects can add a significant amount to the total costs of treating malignant pleural effusions. All agents administered following thoracentesis, especially those like doxycycline and the biological response modifiers that require repeated instillations, increase the risks of infection, empyema, pneumothorax, and acute heart failure. These risks stem not only from placing the chest tube but also from the drainage procedure itself. Bleomycin has been reported to cause nausea. Talc pleurodesis is associated with the most adverse effects, and published reports have documented pneumothorax, acute pneumonitis, granulomatous pneumonitis, and ARDS.23,28 General anesthesia is also associated with increased risks. More recent studies of talc, however, have reported a decreased incidence of serious side effects, probably due to procedural improvements in thoracoscopy.27,28

Cost Issues: Present and Future

To date and to our knowledge, our study is the most comprehensive analysis comparing the cost-effectiveness of the available treatments for malignant pleural effusions.20 We used the methods of meta-analysis to evaluate multi drug and placebo-controlled studies published between 1965 and 1992 (determined by a computer search of Medline and Cancerlit). The agents included in this analysis were tetracycline, bleomycin, doxycycline, and talc. The cost-effectiveness of each agent was compared as the cost per symptom-free day during a 6-month period. Total costs, reported in 1992 US dollars, included the costs of drugs, procedures, laboratory tests, and managing adverse effects. The cost analysis calculated the total cost of each possible outcome as a result of the probability matrix percentage and cost outcome total of each branch. The results of this study, outlined in Table 3, demonstrate that bleomycin is currently the most cost-effective agent available to treat malignant pleural effusion.

Although this study provided valuable information, it was limited in several respects, particularly in its inability to control for differences in patient characteristics, observation durations, and outcome measurements. These limitations are best overcome by analyses based on large-scale, randomized, controlled clinical trials. Such a trial is currently being conducted through the intergroup mechanism with participation by the Cancer and Leukemia Group B, the Eastern Cooperative Oncology Group, the Southwest Oncology Group, the Radiation Therapy Oncology Group, and the North Central Cancer Treatment Group. It is a randomized study comparing talc slurry vs talc instillation by thoracoscopy: the utility of these treatments will be evaluated based on the proportion of patients with successful pleurodesis at 30 days posttreatment as well as the cost and cost-effectiveness of the procedures. A minimum sample size was calculated, using the literature-reported response rates for each procedure, to detect a significant difference with 90% power at the 0.10 level of significance. Allowing for two interim analyses and assuming that 10% of the patients would not live the 30-day period, the investigators determined the minimum sample size for accrual to be 400. The economic end point will be calculated as a cost minimization study, based on the assumption that the two procedures provide equal benefits. A comparison of costs between the two groups will also be made using multiple regression to adjust for any clinical prognostic factors identified as having a significant impact on costs. However, if the more expensive procedure provides superior control, then a cost-effectiveness ratio will also be calculated, based on the comparison of the marginal cost of the more expensive procedure to the marginal benefit measured in probability of effusions controlled at 30 days.

The treatment plan will involve randomizing patients to either talc slurry or talc instillation, followed by a baseline radiograph and monitoring. Procedure performance will be determined by monthly chest radiographs for a total of 6 months. Pain will be assessed at baseline and for the 2 days the chest tube is in place, using a visual analog scale. Quality of life will also be assessed before and 30 days after treatment by standard quality of life instruments such as the Quality of Life Questionnaire-C30, a scale developed specifically for lung cancer and its treatment by the Lung Cancer Cooperative Group of the European Organization for Research and Treatment of Cancer.65 Samples of chest radiographs will be reviewed centrally to ensure consistent interpretation of radiographs.

The cost analysis will compare differences in the resources used and the associated costs for the two treatment arms. It will focus on collection of resource utilization data to generalize results to all clinical centers. Resource and cost data will be collected from the first day of protocol treatment until hospital discharge and will include number of hospital days following chest tube
placement, number and type of operating room procedures, operating room time, and number and type of chest radiographs, chest tubes, and procedure trays. These data will be collected at three sites: Fox Chase Cancer Center, Philadelphia; Brigham and Women’s Hospital, Boston; and SUNY Health Science Center, New York. The data will be used to calculate an estimate of the mean charge for each resource unit consumed by patients in each treatment arm. Costs will be estimated from these charges using a hospital-specific departmental ratio of costs to charges. The accuracy of these cost estimates will be assessed by comparing them with estimates derived from the application of the chart-based formula for calculating imputed charges developed by Kukall et al.67 The effects of all varying clinical and cost estimates will be examined using sensitivity analysis.

CONCLUSION

The results of these studies demonstrate that a number of factors contribute to the costs and cost-effectiveness of agents used to treat malignant pleural effusion. The largest proportion of the cost of pleurodesis appears to be attributable to the performance of the sclerosing agent, including complete response rate, number of administrations necessary to achieve complete response, and the relapse rate. These factors affect the length of hospital stay, personnel costs, diagnostic costs, and the risk of adverse effects. These properties make doxycycline and the interferon costly choices for treatment, despite high initial response rates and low frequencies of adverse effects. The second major contributor to cost-effectiveness appears to be procedural costs. The highly sophisticated procedures required to administer talc make it one of the more costly treatments, despite its low cost and strong efficacy. Efficacy and adverse effect profiles have to be considered when cost-effectiveness issues are analyzed. The flow diagram shown in Figure 1 can help physicians make decisions regarding the optimal treatment of patients with malignant pleural effusions. Future comparisons of the ambulatory approach with the traditional approach, requiring hospitalization to drain malignant pleural effusions followed by sclerosis, will allow therapy to be defined based not only on efficacy, but also on the use—and expense—of related resources.

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