June 2006

When to Begin, When to Withhold Therapy: An Update on Current Medical Practice With Implications for Both Patient Comfort and Health-care Utilization.

Madalina Minciu Macrea

Follow this and additional works at: https://opencommons.uconn.edu/uchcgs_masters

Recommended Citation
When to Begin, When to Withhold Therapy:
An Update on Current Medical Practice with Implications for both Patient Comfort and
Health-Care Utilization

Madalina Minciu Macrea

M.D., “Carol Davila” School of Medicine, 1997

A Thesis
Submitted in Partial Fulfillment of the
Requirements for the Degree of
Master of Public Health
at the
University of Connecticut
2006
Master of Public Health Thesis

When to Begin, When to Withhold Therapy:
An Update on Current Medical Practice with Implications for both Patient Comfort and Health-Care Utilization

Presented by
Madalina Minciu Macrea, MD

Major Advisor
David Gregorio, PhD

Associate Advisor
Joan Segal, MS

Associate Advisor
Roger Thrall, PhD

University of Connecticut
2006
ACKNOWLEDGEMENTS

I would like to acknowledge and extend my deepest appreciation to many individuals who have assisted and guided me throughout my MPH Program.

First and foremost, I would like to express my sincere appreciation to my major advisor, Dr. David Gregorio. Apart from supervising this project, he has believed in my capabilities as a graduate student during the past 2 years. His insightful suggestions and thought-provoking discussions related to this topic will always be remembered and used in future projects. I would also like to thank Dr. Segal and Dr. Thrall for their endless patience and graceful guidance over many years.

And once again, I would like to express my deepest appreciation to Dr. Lahiri for believing in me and forever enriching me as a physician and, most importantly as a person.
# Table of Content

Abstract .................................................................................................................. v

1. Introduction ........................................................................................................... 1

2. Background ......................................................................................................... 2

3. Methods ............................................................................................................... 7

4. Results ............................................................................................................... 9

5. Discussion ......................................................................................................... 16

6. Conclusions ...................................................................................................... 18

Bibliography ........................................................................................................... 20
Abstract

Objectives: To assess the outcome of patients who develop a parapneumonic effusion in the hospital while receiving appropriate antibiotic treatment. In the ever-changing field of medicine, it is important and necessary to have up-to-date information about new practice methods. Treatments often carry risks, and physicians need to weigh the balance between the potential for doing good and the potential for harm. Community-acquired pneumonia (CAP) is the leading cause of death from infectious diseases and the sixth-ranked cause of death overall in the United States. Diagnostic and therapeutic approach to patients with CAP may be now regarded of public health-importance knowing that 4 to 5 million cases of CAP occur annually, accounting for approximately 10 million physician visits, 500,000 hospitalizations, 45,000 deaths, and an annual cost of $23 billion dollars.

Design, setting and patients: Patients admitted to University of Connecticut Health Center between January 1st 1999 and December 31st 2001 with a diagnosis of community-acquired pneumonia was retrospectively identified from a medical record search. Computer-based radiology reports were studied and patients with minimal or no effusion on admission who subsequently developed a pleural effusion were included.

Measurements: One thousand twenty eight patients were admitted with the diagnosis of community-acquired pneumonia. One hundred ninety one patients had minimal or no effusion on the admission chest radiograph and subsequently developed a pleural effusion based on the computer-based radiology reports. After reviewing all 191
chest radiographs, 12 were excluded as the chest radiograph was lost; another 151 were excluded, as the chest radiograph did not definitively show an effusion, therefore leaving 28 patients to be included in the study. The parapneumonic effusion was detected at a mean of 3 days after admission. Seventy-one percent of parapneumonic the effusions were small (under the 1/3rd of the hemithorax) and 29 % were moderate (under the 2/3rd of the hemithorax. Twenty-two patients (79%) were alive at discharge and 6 (21%) died during the hospital stay. Twenty four patients (86%) had improvement in their symptoms related to the initial pneumonia episode. A total of 21 patients (75%) had radiographic improvement of the pleural effusion while receiving antibiotic therapy; of whom 12 (43%) had complete resolution of the pleural effusion and 8 (29%) had a decrease in the size of the pleural effusion at the follow-up CXR exam. The size of the effusion increased during antibiotic therapy in 3 patients (11%); 2 of these 3 patients had a complete resolution of their effusion at the follow-up and one patient was lost. The PPE remained unchanged in 2 (7%) of the patients and both of them had a complete resolution of their effusion at the follow-up. Only one patient out of the 5 patients whose PPE increased or remained unchanged during antibiotic therapy had a history of CHF. No association was found (p>0.05) between the size of the effusion developed under antibiotic therapy and the outcome of the PPE at follow up (PPE improved or resolved vs. unchanged or increased).

**Results:** Only 28 out of 1028 patients developed a parapneumonic effusion during antibiotic therapy. The majority of patients had clinical (90%) or radiographic (75%) improvement while receiving antibiotic only. None of the 20 patients followed after discharge required aggressive therapeutic approach.
**Conclusion:** Patients who are admitted to the hospital with a diagnosis of pneumonia and develop a PPE under appropriate antibiotic therapy may not require diagnostic or therapeutic thoracentesis for their PPE. We believe that the present study, by demonstrating that thoracentesis becomes an unnecessary medical procedure in a certain group of patients who develop PPE, may have further impact on both patient comfort and health-care utilization related to the very common diagnosis of CAP.
1. Introduction

In the ever-changing field of medicine, it is important and necessary to have up-to-date information about new practice methods. Treatments often carry risks, and physicians need to weigh the balance between the potential for doing good and the potential for harm. New guidelines are published quite frequently for conditions considered to be of public health importance; most of the time these guidelines appropriately call for an escalated rather than a de-escalated treatment. For example, the initial medical approach for patients with acute myocardial infarction became steadily more aggressive over years, once the medical literature showed that such aggressive intervention would improve the morbidity and mortality of these patients\(^1\). Occasionally the capacity of medicine to treat illness has prompted reconsiderations of basic concepts of biomedical ethics, regarding when to begin, withhold, or stop the therapy\(^2\).

We have the ability to treat conditions that if left alone tend to do little damage to the person. The majority of elderly men, for example, are found to have elevated blood levels of prostate-specific antigen (PSA). In such cases it would have been inappropriate during their lifetime to operate and remove the gland because the procedure carries risks\(^3\), would be costly and has a lengthy recovery phase\(^4\). In that instance an operation may be considered unnecessary over-treatment. The challenge for physicians is to spot those people for whom an operation to remove the prostate would be beneficial and to provide alternative therapy to others. Similarly, a decision regarding artificial hip replacement in a young person with bone disease is complicated. Most artificial hip joints last only ten years, so if the person is young he or she may need repeated operations. However, at the moment, the techniques used actually damage the bone, so
that it is unlikely a surgeon would be able to perform the procedure more than twice. Delaying treatment for as long as possible may benefit the patient. Therefore, knowing when not to intervene in order to "protect" patients from unnecessary and excessive risk is as important, if not more important, than knowing when to start an appropriate treatment.

In this article we will attempt to identify the possible clinical (i.e. the presence or absence of fever, chills, cough, purulent sputum and chest pain) and imaging data (i.e. the size of pleural effusion) that may help health care providers in identifying and perhaps deferring a medical procedure (i.e. diagnostic thoracentesis) that later would prove to be medically unnecessary for patients with pneumonia who develop pleural effusions.

2. Background

Despite recent advances in diagnosis and treatment, community-acquired pneumonia (CAP) is still a common and potentially lethal infectious disease. CAP is the leading cause of death from infectious diseases and the sixth-ranked cause of death overall in the United States. The age adjusted death rates for the 15 leading causes of death in the United States as per latest CDC National Vital Statistics Reports is described in Figure 1.
It is estimated that 4 to 5 million cases of CAP occur annually, accounting for approximately 10 million physician visits, 500,000 hospitalizations, 45,000 deaths, and an annual cost of $23 billion. The overall CAP-related mortality rate has ranged from 2% to 30% among hospitalized patients, whereas the mortality rate is less than 1% for patients who are not hospitalized. There are 1 million hospitalizations annually owing to
CAP in the United States, with a cost of approximately $9 billion dollars per year\(^\text{10}\). Cost-of-illness studies are necessary to provide a comprehensive estimate of a disease’s impact on the health-care system\(^\text{11}\). Although such studies do not directly assess alternative treatment strategies, cost of illness data can be used to evaluate whether current treatment (cost) patterns are consistent with clinical expectations of the patient outcomes with high-quality care. However, the economic issues surrounding the costs of treating pneumonia are critically important to the national health-care system.

The exact costs related to the inpatient and office visits related to the CAP are described in the Tables 1 and 2.

**Table 1**

<table>
<thead>
<tr>
<th>Age Group (y)</th>
<th>Physicians’ Offices</th>
<th>Emergency Departments</th>
<th>Outpatient Departments</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥65</td>
<td>0.589</td>
<td>0.458</td>
<td>0.048</td>
<td>1.095</td>
</tr>
<tr>
<td>≤64</td>
<td>2.438</td>
<td>0.798</td>
<td>0.156</td>
<td>3.392</td>
</tr>
<tr>
<td>All ages</td>
<td>3.027</td>
<td>1.256</td>
<td>0.204</td>
<td>4.487</td>
</tr>
</tbody>
</table>

Data from Medicare Standard Analytical File Part B, National Ambulatory Medical Care Survey\(^\text{12}\) and National Hospital Ambulatory Medical Care Survey\(^\text{13}\)

**Table 2**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of Discharges</th>
<th>Average Length of Stay</th>
<th>Average Cost of Stay</th>
<th>Total Cost of Stay (in billions)</th>
<th>MD Costs (in billions)</th>
<th>Total Cost of Stay + MD (in billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥65</td>
<td>615,780</td>
<td>7.8</td>
<td>$7166</td>
<td>$4.412</td>
<td>$0.305</td>
<td>$4.717</td>
</tr>
<tr>
<td>≤64</td>
<td>519,573</td>
<td>5.8</td>
<td>$6042</td>
<td>$3.139</td>
<td>$0.192</td>
<td>$3.331</td>
</tr>
<tr>
<td>All ages</td>
<td>1,135,353</td>
<td>6.9</td>
<td>$6652</td>
<td>$7.552</td>
<td>$0.497</td>
<td>$8.049</td>
</tr>
</tbody>
</table>

CAP is the forth most frequent discharge diagnosis for patients less than age of 65 and second most frequent discharge diagnosis for patients over age of 65\textsuperscript{12}. The CAP-related medical costs are tremendous and every effort should be made to appropriately and timely diagnose and treat these patients for the best outcome.

**Figure 2.**

![Graph showing hospital discharges for various diagnoses categorized by age group](image)

Disputes over diagnostic evaluations and therapeutic decisions exist for patients with CAP and appropriate therapeutic interventions will undoubtedly reduce the significant costs related to the treatment of CAP. One of the most debated subjects is that related to the appropriate therapeutic approach to pleural effusions that develop during antibiotic therapy in patients who develop CAP. Parapneumonic effusions (PPE) develop in up to 44% of patients with bacterial pneumonia who require admission to hospital\textsuperscript{13}.
While many PPE will resolve without specific treatment therapy other than antibiotic therapy of the underlying pneumonia, other PPE require an aggressive therapeutic approach, to prevent or ameliorate empyema or complicated pleural effusion. This aggressive therapeutic approach is called “thoracentesis” and represents the procedure by which some of the pleural fluid is removed by inserting a needle in the pleural cavity. Thoracentesis is associated with a certain risk of complications, out of which pneumothorax (i.e. collection of air or gas in the pleural space of the lung, causing the lung to collapse) is the most common. This complication is associated with increased morbidity and hospital stay, as well as patient discomfort. It is established, that the incidence of thoracentesis-related pneumothorax varies between 3% and 19%, with additional treatment (i.e. chest tubes) needed in 3.6% of all thoracenteses representing almost half of all patients (48%) in whom pneumothorax occurred. Therefore, thoracentesis is not a procedure devoid of medical complications and appropriate exclusion of patients that not need it is essential, both for the patient comfort and healthcare utilization.

The recent American College of Chest Physician (ACCP) consensus conference on the medical and surgical management of PPE stratifies the therapeutic intervention based on the risk for a poor outcome. Based on the ACCP consensus conference, any patient with a small to moderate free-flowing pleural effusion should have a diagnostic thoracentesis performed.

Some patients with pneumonia who do not have a PPE at the time of presentation to the hospital may develop one during the hospital stay. One expert has suggested an aggressive approach to these patients, while another has suggested that
patients who develop a PPE while on therapy do not need a thoracentesis. In both cases, the recommendations were made based on expert opinion. The appropriate therapeutic approach of such effusions is yet to be decided as the current medical literature provides only limited and controversial data. Therefore, our paper will review retrospectively the outcome of patients who develop pneumonia and pleural effusions while admitted to the hospital and receiving antibiotic therapy. It is not counterintuitive to speculate though that patients who are admitted to the hospital with a diagnosis of pneumonia and develop a pleural effusion under appropriate antibiotic therapy may not require further aggressive diagnostic approach, proven they improve clinically throughout their hospital stay.

3. Methods

Patient Selection and Definitions

All patients admitted to the University of Connecticut Health Center between January 1st 1999 and December 31st 2001 with a discharge diagnosis of pneumonia were retrospectively identified from a medical record search based on ICD coding for pneumonia (ICD 486) and bacterial pneumonia (ICD 482.0 to 482.9). Computer-based radiology reports for these patients were reviewed and patients with minimal (defined as a pleural effusion that blunted the costo-phrenic angle only) or no effusion on the admission chest radiograph (CXR) who subsequently developed a pleural effusion during their hospital stay were selected for further study. For many individuals, especially those with only a portable AP view, the findings were not reported as definitive. Nonetheless, these patients were considered for further review to maximize sensitivity. Chest radiographs of the selected patients were then examined by 2 pulmonary physicians jointly. Only those unequivocally confirmed as having developed a parapneumonic
effusion (defined as a pleural effusion with an ipsilateral infiltrate) were considered for inclusion in study. The last step of the screening process required confirmation of the clinical diagnosis of pneumonia, for which we required the radiographic finding of a new infiltrate and at least two of the following: fever or diaphoresis, cough, purulent sputum, dyspnea, hypoxemia or pleuritic chest pain.

Clinical improvement was defined as improvement or resolution of the signs or symptoms that the patient had on the admission to the hospital. The size of the effusion was defined as small if it occupied less than one third of the hemithorax, moderate if it occupied less than two-thirds and large if it occupied more than two-thirds of the hemithorax. The effusion was considered improved when it either decreased in size or resolved, as documented by subsequent CXR films.

Data collection

The following data were collected from the medical records: (1) Admission data: age, gender, comorbidities, symptoms on admission, antibiotics received prior to admission (if any); (2) In-hospital data: size of the effusion, antibiotics received during the hospital stay, time when the antibiotics were started, thoracentesis or other drainage procedure results (if any), number of days in the hospital; and (3) Post-discharge data: CXR findings, requirement for further therapy of pleural disease, disposition (home vs. facility), outcome (alive vs. deceased), follow up visit interval, cause of death (unrelated or related to the parapneumonic effusion).

Statistical analysis
Descriptive data for continuous variables are presented as means ± SD or medians with range, when appropriate. Statistical comparisons of nominal variables were made using Fisher's exact test. Statistical significance was defined as a two-tailed value of p<0.05.

Analyses were done with software from the Statistical Package for the Social Sciences (version 12; SPSS, Chicago, IL).

4. Results

Patient population

Based on the computer-based radiology reports of the 1,028 patients admitted consecutively to the University of Connecticut Health Center with the diagnosis of pneumonia, 191 individuals had minimal or no effusion seen at the time of admission CXR but subsequently developed a pleural effusion. Of these, 12 were excluded as the films could not be located; the two pulmonary physicians who reviewed all the films in the study excluded another 151 CXR that did not unequivocally show an effusion, leaving 28 patients included in the study (2.7%). The clinical characteristics of the patients who developed a PPE under the antibiotic therapy are described in Table 3. The mean patient age was 76±15 years (range 36-94) and 57% were female. Ninety-six percent of the patients had at least one comorbid condition. Underlying pulmonary disease was present in 8 patients (29%), congestive heart failure (CHF) in 6 patients (21%), neoplastic disease in 7 patients (25%) and HIV-infection in 2 patients (7%). Within 2 months prior to admission the CD4 counts of one of the HIV infected patients was 134 cells/mm³ and the viral load of the other HIV infected patient was 67500
copies/ml. The presenting symptoms included fever in 18 patients (64%), productive cough in 18 (64%), dyspnea in 14 (50%) and pleuritic chest pain in 1 patients (4%); 5 patients (18%) were hypoxic. Twenty six patients (93%) received antibiotics within 24 hours of admission to the hospital. Six patients (21%) had received antibiotics prior to admission, and 4 patients (14%) continued the same class of antibiotic during the hospital stay.

An etiologic diagnosis was assigned for 8 patients (29%) as follows: 2 *Streptococcus pneumoniae*, 3 *Staphylococcus aureus*, 1 *Pseudomonas aeruginosa*, 1 *Haemophilus influenzae* and 1 Influenza A. The diagnosis was based on blood culture in 2 patients (7%), on sputum culture in 5 patients (18%) and on both blood and sputum culture in 1 patient (4%).
Table 3.
Clinical Characteristics of the Patients who developed a Parapneumonic Effusion under the Antibiotic Therapy

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr (range)</td>
<td>36-94</td>
</tr>
<tr>
<td>Female (%)</td>
<td>16 (57%)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>8 (29%)</td>
</tr>
<tr>
<td>Coronary disease</td>
<td>6 (21%)</td>
</tr>
<tr>
<td>HTN</td>
<td>4 (14%)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>6 (21%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>HIV positive</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>CVA and/or dementia</td>
<td>4 (14%)</td>
</tr>
<tr>
<td>Reasons for hospital admission (any two of the following):</td>
<td></td>
</tr>
<tr>
<td>Fever and/or chills</td>
<td>18 (64%)</td>
</tr>
<tr>
<td>Productive cough</td>
<td>18 (64%)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>14 (50%)</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>5 (18%)</td>
</tr>
<tr>
<td>Pleuritic chest pain</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Antibiotic use</td>
<td></td>
</tr>
<tr>
<td>Hospital day number when the antibiotic was started (% patients)</td>
<td>1 (93%)</td>
</tr>
<tr>
<td>Time of development of the parapneumonic effusion</td>
<td></td>
</tr>
<tr>
<td>Hospital day number (mean and range)</td>
<td>3 (1-10)</td>
</tr>
<tr>
<td>Size of the parapneumonic effusion</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>20 (71%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>8 (29%)</td>
</tr>
<tr>
<td>Type of pneumonia</td>
<td></td>
</tr>
<tr>
<td>Unilobar</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>Multilobar</td>
<td>17 (61%)</td>
</tr>
</tbody>
</table>
Chest radiograph and PPE findings

The parapneumonic effusion was detected at median of 3 hospital days after the hospital admission. A small effusion was detected in 20 patients (71%) and moderate in 8 patients (29%). A diagnostic thoracentesis was attempted in 5 (18%) cases and was successful in 4 (14%).

The reasons for thoracentesis were as follows: Persistent fever in the presence of a small pleural effusion (1 patient) and worsening dyspnea in the presence of an increasing pleural effusion (4 patients). According to Light’s criteria\textsuperscript{18}, 2 patients (50%) had an exudative effusion and one patient (25%) had a transudative effusion; in one patient the culture and gram stain of the pleural effusion were negative with the rest of the data missing. According to the 2000 ACCP Guidelines\textsuperscript{2}, the 2 exudative PPE were considered to be associated with a moderate risk of poor outcome based on the pH value or pleural space anatomy. The pleural fluid characteristics for the 2 patients with exudative effusions were as follows: pH level of 7.0, white blood count (WBC) with 67% monocytes and negative pleural fluid culture (one patient); and LDH of 1307 U/L and glucose level of 127 mg/dl (the other patient). All 4 patients who successfully underwent thoracentesis had negative gram stains and cultures of the fluid. The amount of fluid removed at thoracentesis was 35cc for the exudative effusion and 400 cc for the transudative effusion. The patient whose pleural fluid chemistry was missing had 150 cc fluid removed. The amount of the fluid removed was not explicitly mentioned in the patient whose pleural fluid results were mentioned above (pH 7.0 and WBC of 345 cells/ul).
**Patient outcomes**

Twenty-two patients (79%) were alive at discharge and 6 (21%) died during the hospital stay. Twenty-four patients (86%) had improvement in their symptoms related to the initial pneumonic episode. A total of 21 patients (75%) had radiographic improvement of the pleural effusion while receiving antibiotic therapy; of whom 12 (43%) had complete resolution of the pleural effusion and 8 (29%) had a decrease in the size of the pleural effusion at the follow-up CXR exam. The size of the effusion increased during antibiotic therapy in 3 patients (11%); 2 of these 3 patients had a complete resolution of their effusion at the follow-up and one patient was lost. The PPE remained unchanged in 2 (7%) of the patients and both of them had a complete resolution of their effusion at the follow-up. Only one patient out of the 5 patients whose PPE increased or remained unchanged during antibiotic therapy had a history of CHF. No association was found (p>0.05) between the size of the effusion developed under antibiotic therapy and the outcome of the PPE at follow up (PPE improved or resolved vs. unchanged or increased).

None of the 28 patients who developed a PPE under antibiotic therapy required chest tube thoracostomy during the hospital stay or at the follow-up. Also, all but the 2 patients who were lost to follow had documented clinical improvement (follow-up range 13 days to more than a year). The 2 patients who did not receive antibiotics within 24 hours had complete resolution of their PPE at the follow up and clinically improved during their hospital stay. The median hospital stay for all 28 patients was 12 days and the median hospital stay for patients alive at discharge was 10 days.

Six patients (21%) died during the hospital stay; in 2 patients (7%) the pleural
effusion improved, in another 2 patients (7%) the pleural effusion remained stable and in the last 2 patients (7%) the effusion increased in size prior to the patients’ death. The causes of death for the 6 patients were as follows: gastro-intestinal hemorrhage (1 patient), chronic respiratory failure in a stable COPD patient who requested withdrawal of the mechanical ventilation (1 patient) and aspiration pneumonia with cardiopulmonary arrest (1 patient). The other 3 patients died unexpectedly. An improvement in their symptoms related to the initial pneumonic infection was documented in the medical records before they died. The major acute events before their death were listed in the electronic medical records as follows: gastro-intestinal hemorrhage (1 patient) and aspiration-related cardio-respiratory arrest in a patient who had tracheostomy-dependent chronic respiratory failure (1 patient) and fever with worsening congestive heart failure in a patient who had end-stage renal disease hemodialysis dependent (1 patient).

Of the 22 patients alive at discharge from the hospital, 2 (7%) were lost to follow up, therefore leaving 20 patients for follow up. One of these 2 patients underwent diagnostic thoracentesis and was discharged to a chronic rehabilitation facility. The first follow up visit after discharge occurred after 21 days for half of the patients. The follow-up intervals for the patients alive at discharge, as documented in the electronic medical records, are described in Table 4.
Table 4
The Clinical Outcome of Patients with a PPE and Alive at Discharge from the Hospital

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Size of the PPE developed during hospital stay</th>
<th>Distribution of the pneumonia associated with a PPE</th>
<th>Period of follow-up (post-discharged days)</th>
<th>Radiographic evolution of the PPE (during hospital stay or at follow up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Moderate</td>
<td>Multilobar</td>
<td>&gt; 1 year</td>
<td>Decreased in size</td>
</tr>
<tr>
<td>2</td>
<td>Small</td>
<td>Unilobar</td>
<td>19</td>
<td>Unchanged</td>
</tr>
<tr>
<td>3*</td>
<td>Small</td>
<td>Unilobar</td>
<td>&gt; 1 year</td>
<td>Resolved</td>
</tr>
<tr>
<td>4</td>
<td>Small</td>
<td>Unilobar</td>
<td>&gt; 1 year</td>
<td>Resolved</td>
</tr>
<tr>
<td>5</td>
<td>Small</td>
<td>Multilobar</td>
<td>17</td>
<td>Decreased in size</td>
</tr>
<tr>
<td>6</td>
<td>Moderate</td>
<td>Unilobar</td>
<td>&gt; 1 year</td>
<td>Resolved</td>
</tr>
<tr>
<td>7</td>
<td>Small</td>
<td>Unilobar</td>
<td>56</td>
<td>Decreased in size</td>
</tr>
<tr>
<td>8</td>
<td>Small</td>
<td>Multilobar</td>
<td>249</td>
<td>Increased in size</td>
</tr>
<tr>
<td>9</td>
<td>Small</td>
<td>Multilobar</td>
<td>&gt; 1 year</td>
<td>Resolved</td>
</tr>
<tr>
<td>10*</td>
<td>Small</td>
<td>Multilobar</td>
<td>&gt; 1 year</td>
<td>Decreased in size</td>
</tr>
<tr>
<td>11</td>
<td>Moderate</td>
<td>Unilobar</td>
<td>&gt; 1 year</td>
<td>Decreased in size</td>
</tr>
<tr>
<td>12</td>
<td>Small</td>
<td>Multilobar</td>
<td>25</td>
<td>Resolved</td>
</tr>
<tr>
<td>13</td>
<td>Moderate</td>
<td>Unilobar</td>
<td>&gt; 1 year</td>
<td>Resolved</td>
</tr>
<tr>
<td>14</td>
<td>Small</td>
<td>Multilobar</td>
<td>54</td>
<td>Resolved</td>
</tr>
<tr>
<td>15</td>
<td>Small</td>
<td>Multilobar</td>
<td>&gt; 1 year</td>
<td>Resolved</td>
</tr>
<tr>
<td>16</td>
<td>Moderate</td>
<td>Multilobar</td>
<td>78</td>
<td>Resolved</td>
</tr>
<tr>
<td>17</td>
<td>Small</td>
<td>Unilobar</td>
<td>13</td>
<td>Unchanged**</td>
</tr>
<tr>
<td>18</td>
<td>Small</td>
<td>Multilobar</td>
<td>33</td>
<td>Resolved</td>
</tr>
<tr>
<td>19*</td>
<td>Small</td>
<td>Unilobar</td>
<td>15</td>
<td>Increased in size</td>
</tr>
<tr>
<td>20</td>
<td>Small</td>
<td>Unilobar</td>
<td>&gt; 1 year</td>
<td>Resolved</td>
</tr>
<tr>
<td>21*</td>
<td>Moderate</td>
<td>Multilobar</td>
<td>Lost</td>
<td>Decreased in size</td>
</tr>
<tr>
<td>22</td>
<td>Small</td>
<td>Multilobar</td>
<td>Lost</td>
<td>Increased in size</td>
</tr>
</tbody>
</table>

* Denotes patients who underwent diagnostic thoracentesis.

** Denotes CXR findings during the hospital stay as the patient did not have a follow-up CXR.

None of the 20 patients followed after discharge required further diagnostic or therapeutic interventions for the PPE that developed while receiving antibiotic therapy.
5. Discussion

Currently, there are no recommendations as to what is the best therapeutic approach of a PPE that develops during antibiotic therapy. The absence of such recommendations impacts both patient comfort and health-care utilization. All previous studies agree on the importance of appropriate antibiotic coverage. While some experts believe that the development of pneumococcal empyema after initiation of proper therapy is unusual (and therefore diagnostic thoracentesis in patients who develop a PPE under antibiotic therapy may be unnecessary), others strongly recommend both diagnostic and therapeutic thoracentesis at the earliest sign of development of pleural fluid.

None of the 20 patients followed after hospital discharge developed empyema, requiring further aggressive diagnostic or therapeutic approach. We lost a total of 2 patients at follow up; one developed a small PPE and the other developed a moderate PPE considered of moderate risk of poor outcome based on the diagnostic thoracentesis. We cannot unequivocally affirm that none of them developed an empyema; however we consider this possibility very unlikely, as both of them clinically improved during their hospital stay and they were continued to be followed after the hospital discharge at a chronic rehabilitation facility. Six patients died during their hospital stay. All of them clinically improved during their hospital stay and after in-depth search of the electronic medical records their death was considered not to be related to the presence of the PPE. One of the patients that died had ESRD, CAD and valvular insufficiency and developed fever 24 hours before his death; we believe that his death was also unlikely to be the result of an empyema, as the size of the PPE was small and the rest of his symptoms (i.e.
cough and dyspnea) that prompted the hospital admission resolved during the hospital
stay.

The CXR often worsens initially after the antibiotic therapy is started, with the
development of a pleural effusion. In our study, in a majority of patients (71%) the size
of the PPE decreased or resolved during the antibiotic therapy. The PPE in the rest of the
patients remained unchanged or increased during the in-hospital antibiotic therapy, only
to improve after the hospital discharge. These findings are in agreement with the 2001
ATS Guidelines for the Management of Adults with Community-acquired pneumonia\textsuperscript{21}
that if the patient is showing an otherwise good clinical response, the CXR progression
may have no significance. In our study, none of the patients developed large PPE. One
potential explanation may be that large PPE are less likely to develop under appropriate
antibiotic therapy.

In summary, the most important findings of this study are that none of the 20
patients that developed a PPE while receiving antibiotic therapy and were followed after
hospital discharge developed empyema; therefore thoracentesis may not be required in
patients who develop a PPE under appropriate antibiotic therapy. In such circumstances,
close clinical follow up may benefit the patient more than an early aggressive therapy
that is associated with certain procedure-related risks.

Overall in our study, only 28 out of 1028 patients (2.7%) developed a PPE
while receiving antibiotic therapy. This low incidence of the PPE is most likely related to
the fact that we only selected patients who unequivocally developed a PPE during the
antibiotic therapy. This method of patient selection may slightly underestimate the
incidence of the PPE developed during the antibiotic therapy, but it also eliminates the
chance of having patients with infiltrates only on the CXR that also improve with antibiotic therapy (i.e. false positives).

The major limitation of our study is its retrospective design. The answer to what is the best therapeutic approach to patients that developed a PPE during the antibiotic therapy is yet to be ideally decided in a prospective setting. However, we believe that prospective studies in patients who develop a PPE under antibiotic therapy are difficult to perform because of the researcher’s ethical imperative to intervene if less than optimal care is observed.

6. Conclusions

So far, from our study, it appears that patients who are admitted to the hospital with a diagnosis of pneumonia and develop a PPE under appropriate antibiotic therapy may not require diagnostic or therapeutic thoracentesis for their PPE. We do not disagree with an early aggressive therapeutic intervention if clinical presentation is suggestive of such approach; we just recommend that certain category of patients to be closely monitored rather than undergoing early thoracentesis, procedure not devoid of certain risks and patient discomfort. We believe that the present study, by demonstrating that thoracentesis becomes an unnecessary medical procedure in a certain group of patients who develop PPE, may have further impact on both patient comfort and health-care utilization related to the very common diagnosis of CAP. Our conclusion, despite committing to a new and less invasive diagnostic approach for patients with CAP who develop a PPE, is not in argument with the current medical practice; it rather complements it, as clinical judgment will remain the most precious step for medical
practice.
Bibliography


