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The Prognostic Value of Longitudinal C-Reactive Protein Trends in Complicated Parapneumonic Effusion and Empyema

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ABSTRACT

Background: Parapneumonic effusion and empyema are complications of pneumonia and are linked to significant morbidity and mortality. Yet, the early assessment of patients at risk of treatment failure has remained an area of difficulty. C-reactive protein (CRP) is a biomarker of inflammation that has widespread clinical utility. The utility of CRP trend analysis in patients suffering from pleural infections has remained unproven.

Objective: To determine the relationship between the trend of C-reactive protein levels in patients and clinical outcomes in the treatment of complicated parapneumonic effusion and empyema.

Methodology: One hundred and sixty adult patients suffering from complicated parapneumonic effusion and/or empyema were included in a prospective observational study. CRP values at admission and during treatment (on Day 3, Day 7, and discharge) were determined. Multivariate logistic regression analysis was used to differentiate independent predictors for treatment failure and mortality.

Results: A total of 95 (59.4%) patients showed a rapid decline in CRP, 50 (31.3%) showed a slow decline, while 15 (9.3%) showed persistent elevation. Multivariate analysis showed that the persistently elevated CRP levels as an independent predictor for treatment failure (OR = 6.8, 95% CI 2.4-19.2, $p < 0.001$) and mortality (OR = 9.1, 95% CI 2.1-39.5, $p = 0.003$).

Conclusion: Serum CRP dynamics within a series of patients is an independent predictor of clinical outcome for complicated parapneumonic effusion and empyema. The rapid decrease of CRP values predicts favorable outcome, while persistent elevation is a marker of patients who are at high risk for treatment failure, complications, or death.

Keywords: C-reactive Protein; Parapneumonic Effusion; Empyema; Pleural Infection; Inflammatory Markers

Introduction

Complicated parapneumonic effusion (CPE) and empyema are serious infectious complications of pneumonia. Parapneumonic effusions have been observed in up to 40% of cases of hospitalized patients with bacterial pneumonia, while around 5-10% of cases of parapneumonic effusions develop further into CPE or empyema, which would require invasive procedures like chest drainage, fibrinolysis in the pleural space, or surgical decortication. Even with the improvement in antimicrobial therapies and surgical care, the mortality rate in empyema has not decreased significantly and still ranges from 10% to 30%, especially in older patients and those with associated conditions like diabetes, COPD, or immunodeficiency.[1]

The pathophysiological mechanism of CPE and empyema is characterized by a complex interaction between bacterial infection, the immune reaction of the host, and the biochemical microenvironment of the pleural space. First of all, in the case of pneumonia, the exudative fluid appears as a sterile effusion because of infection. Later on, bacterial infection leads to pleural thickening. This completes the transition process from a complicated effusion to empyema. Here, monitoring the progression of the infection as well as the effectiveness of treatment is an important aspect in clinical management.[2]

C-reactive Protein (CRP) is an acute protein that is produced by hepatocytes due to the presence of certain pro-inflammatory cytokines, specifically Interleukin-6. It is a highly accurate biological marker for inflammation, infection, or other such conditions. CRP values tend to increase within 6-12 hrs after any inflammatory insult, reaching a peak at about 48 hrs, after which the values decrease rapidly with treatment, making it a useful marker for following the course of infection. CRP has been studied extensively for predicting the severity, outcome, or resolution of respiratory infections. Its elevation has been assimilated with extensive infection, bacteremia, and a poor outcome for patients suffering from Community-Acquired Pneumonia. Similarly, it has also helped in predicting infection resolution, antibiotic treatment, and complications.[3]

In the scenario related to complicated parapneumonic effusions and empyema, the trends related to CRP can provide important prognostic data. There are certain studies which have indicated that an elevated level of CRP, despite receiving proper antibiotic therapy or drainage procedures, can suggest infection, loculations, or source control failure.[4] On the contrary, a rapid decrease in the level of CRP can provide an indication of successful infection eradication and better patient outcome. But in spite of this, the use of CRP for monitoring in cases related to CPE and empyema has not yet been standardized, and very less data related to the use of this protein for the prediction of certain clinical end points, such as success rates, duration of patient stay in the hospital, need for surgery, and death rates, has been obtained. In spite of it, the measurement of this protein is very easily accessible in resource-limited countries because it is very cheap and can be readily repeated.

So, the present study was planned to determine the trends of the C-reactive protein in those receiving treatment related to complicated parapneumonic effusions and empyema in order to correlate it with certain clinical outcomes in relation to success rates, patient stay in the hospital, surgical needs, and mortality rates.

Objective

To determine the relationship between the trend of C-reactive protein levels in patients and clinical outcomes in the treatment of complicated parapneumonic effusion and empyema.

Methodology

This was a prospective observational study conducted at Department of Medicine, Ziauddin University Hospital, Karachi from January 2024 to March 2025. This study was approved by the Institutional Review Board Ziauddin University Hospital, Karachi. Written consent was signed from all the participants before the study. Patients ≥18 years admitted for complicated parapneumonic effusion (CPE) or empyema were considered for recruitment. The diagnosis included findings such as The presence of clinical manifestations of pneumonia with pleural effusion, Pleural fluid examination revealing an exudative effusion according to the criteria used (protein >30g/L, Lactate dehydrogenase (LDH) >500 IU/L, pH <7.2), and Confirmatory pleural fluid evidence of infection demonstrated by positive gram stain/culture, and Loculated pleural effusion demonstrated on imaging. The criteria for exclusion included Patients with secondary non-infectious pleural effusion due to other conditions like malignancy, heart disease, or Renal disease, Patients with chronic inflammatory disease not secondary to infections but due to immunosuppression, Patients with insufficient data, Pregnant women.

Data on Demographic & Clinical variables were gathered, for instance, age, gender, comorbid conditions (diabetes, COPD, cardiovascular disease), smoking status, & symptoms (fever, chest pain, shortness of breath, cough), while Radiological Assessment may include Chest X-ray and/or computed tomography scans are done on admission for the extent of pleural effusion, the extent of loculations, and the extent of the pulmonary parenchyma. They are also done as clinically indicated for the response to therapy. Pleural Fluid Analysis and C-Reactive Protein Measurement values are also collected.

The data was entered and analyzed through SPSS. Continuous variables are presented as the mean and

standard deviation (SD), or median and interquartile range (IQR), according to the nature of the data. Categorical variables are presented in frequency and percentages. Comparison of groups (e.g., fast versus slow decline in CRP, survivors versus non-survivors) was done. The correlation of patterns in CRP decline and outcomes was evaluated using Pearson or Spearman correlation coefficient tests. Multivariate logistic regression analysis was performed to explore independent predictors of failure, prolonged hospital stays, and death. $p < 0.05$ was statistically significant.

Results

The study included a total of 160 patients diagnosed with complicated parapneumonic effusion or empyema. The mean age of the cohort was 52.6 ± 14.2 years, indicating a predominance of middle-aged and older adults. The majority of patients were male (102, 63.8%), while females accounted for 36.2% (58 patients), reflecting a slight male predominance in the study population. Several comorbid conditions were present, with diabetes mellitus observed in 48 patients (30%), hypertension in 52 patients (32.5%), and chronic obstructive pulmonary disease (COPD) in 35 patients (21.8%). Notably, 67 patients (41.9%) reported a history of smoking, which is a known risk factor for both respiratory infections and impaired pleural fluid clearance. Regarding clinical presentation, the majority of patients exhibited typical symptoms of pleural infection. Fever was the most commonly reported symptom, occurring in 148 patients (92.5%), followed by cough in 152 patients (95%), indicating that nearly all patients presented with significant respiratory involvement. Dyspnea was reported in 136 patients (85%), while chest pain was present in 112 patients (70%), often associated with pleuritic inflammation and pleural irritation.

Staphylococcus aureus was the most frequently isolated organism, identified in 50 patients (31.3%), followed by Streptococcus pneumoniae in 42 patients (26.3%). Gram-negative bacilli, including Escherichia coli and Klebsiella species, were isolated in 28 patients (17.5%), while mixed or less common organisms accounted for 20 patients (12.5%). Pleural fluid analysis demonstrated typical exudative characteristics associated with complicated infections. The mean pleural fluid protein level was 45.8 ± 12.5 g/L, indicating significant protein exudation due to increased vascular permeability. Lactate dehydrogenase (LDH) levels were markedly elevated, with a mean of 780 ± 215 IU/L, consistent with intense inflammatory and cellular turnover within the pleural space. The pleural fluid pH was low, averaging 7.12 ± 0.08, reflecting acidification secondary to bacterial metabolism and neutrophilic activity, which is characteristic of complicated effusions and empyema.

The majority of patients (95, 59.4%) demonstrated a rapid decline in CRP, defined as a ≥50% reduction by Day 7. In this group, the mean CRP on admission was 120 ± 35 mg/L, which decreased substantially to 65 ± 28 mg/L by Day 3 and 48 ± 20 mg/L by Day 7, ultimately reaching 15 ± 8 mg/L at discharge. Fifty patients (31.3%) exhibited a slow decline in CRP, with less than a 50% reduction by

Table 1. Patient Demographics and Clinical Characteristics

Variable	Total (n=160)	Percentage / Mean ± SD
Age (years)	160	52.6 ± 14.2
Gender		
Male Female	102 58	63.8% 36.2%
Comorbidities		
Diabetes Mellitus Hypertension COPD Smoking history	48 52 35 67	30% 32.5% 21.8% 41.9%
Presenting Symptoms		
Fever Dyspnea Chest pain Cough	148 136 112 152	92.5% 85% 70% 95%

Day 7. Their mean CRP values were slightly higher at baseline (125 ± 40 mg/L) and declined more gradually to 102 ± 35 mg/L on Day 3 and 85 ± 30 mg/L on Day 7, with a discharge value of 40 ± 18 mg/L. A smaller subset of patients (15, 9.3%) displayed persistent CRP elevation, with values remaining above 50 mg/L even at Day 7. Their mean CRP was 130 ± 30 mg/L on admission and declined minimally to 115 ± 25 mg/L by Day 3 and 110 ± 20 mg/L by Day 7, with a discharge value of 75 ± 12 mg/L..

The majority of patients, 100 (62.5%), were treated with chest tube drainage alone, which represents the standard initial intervention for uncomplicated drainage of infected pleural fluid. Thirty-five patients (21.9%) required chest tube drainage combined with intrapleural fibrinolytic therapy, typically administered in cases with loculated or complex effusions where simple drainage was insufficient. A smaller subset of patients, 25 (15.6%), underwent surgical intervention, either via video-assisted thoracoscopic surgery (VATS) or open decortication.

Among the 95 patients who exhibited a rapid CRP decline (≥50% by Day 7), treatment success was achieved in 90 patients (94.7%), indicating a favorable response to therapy. This group also had the shortest mean hospital stay of 8.2 ± 2.1 days, with only 5 patients (5.3%) requiring surgical intervention. Complications, including sepsis or recurrence of effusion, were infrequent, occurring in 8 patients (8.4%), and mortality was low at 2.1% (2 patients). In contrast, patients with a slow CRP decline (<50% by Day 7) had comparatively poorer outcomes. Treatment success was observed in 40 patients (80%), while the mean hospital stay was prolonged to 12.5 ± 3.6 days. Ten patients (20%) in this group required surgical intervention due to persistent or loculated effusions, and 12 patients (24%) experienced complications. Mortality was higher than the rapid-decline group, occurring in 3 patients (6%). The persistent CRP elevation group (>50 mg/L at Day 7), comprising 15 patients (9.3%), exhibited the worst clinical outcomes. Only 8 patients (53.3%) achieved treatment success, while the mean hospital stay was markedly prolonged at 18.3 ± 4.5 days. Two-thirds of these patients (10, 66.7%) required surgical intervention, and the same proportion experienced complications. Mortality in this group was substantially higher, affecting 4 patients (26.7%). Statistical analysis confirmed that differences across the three CRP trend groups were significant for all measured outcomes ($p<0.05$).

Table 2. Etiology and Pleural Fluid Findings

Variable	Total (n=160)	Percentage / Mean ± SD
Etiology (culture positive)		
Staphylococcus aureus	50	31.3%
Streptococcus pneumoniae	42	26.3%
Gram-negative bacilli	28	17.5%
Mixed / Others	20	12.5%
Pleural fluid analysis		
Exudative protein (g/L)	160	45.8 ± 12.5
LDH (IU/L)	160	780 ± 215
pH	160	7.12 ± 0.08

Patients exhibiting a rapid CRP decline (≥50% by Day 7) showed the most favorable outcomes, with treatment success achieved in 90 patients (94.7%). This group experienced the shortest mean hospital stay, averaging 8.2 ± 2.1 days, and had minimal need for surgical intervention, with only 5 patients (5.3%) requiring procedures such as VATS or decortication. Complications, including sepsis or recurrence of effusion, occurred in 8 patients (8.4%), and mortality was low at 2.1% (2 patients). In contrast, patients with a slow CRP decline (<50% by Day 7) had comparatively poorer outcomes. Treatment success was achieved in 40 patients (80%), while the mean hospital stay was prolonged to 12.5 ± 3.6 days. Surgical intervention was necessary in 10 patients (20%), and complications occurred in 12 patients (24%). Mortality in this group was 6% (3 patients). Multivariate analysis revealed that a slow CRP decline was associated with an increased risk of treatment failure (OR 3.2, 95% CI 1.1–9.4, $p=0.03$), although its association with mortality was not statistically significant (OR 2.9, 95% CI 0.6–14.1, $p=0.18$). Patients with persistent CRP elevation (>50 mg/L at Day 7) had the worst outcomes. Only 8 patients (53.3%) achieved treatment success, while the mean hospital stay was markedly longer at 18.3 ± 4.5 days. Two-thirds of these patients (10, 66.7%) required surgical intervention, and the same proportion experienced complications. Mortality in this group was significantly higher at 26.7% (4 patients). Multivariate logistic regression confirmed persistent CRP elevation as an

Table 3. CRP Trends During Treatment

CRP Trend	Number of Patients	Percentage	Mean CRP (mg/L) on Admission	Mean CRP (mg/L) Day 3	Mean CRP (mg/L) Day 7	Mean CRP (mg/L) at Discharge
Rapid decline (≥50% by Day 7)	95	59.4%	120 ± 35	65 ± 28	48 ± 20	15 ± 8
Slow decline (<50% by Day 7)	50	31.3%	125 ± 40	102 ± 35	85 ± 30	40 ± 18
Persistent elevation (>50 mg/L at Day 7)	15	9.3%	130 ± 30	115 ± 25	110 ± 20	75 ± 12

independent predictor of treatment failure (OR 6.8, 95% CI 2.4–19.2, p<0.001) and mortality (OR 9.1, 95% CI 2.1–39.5, p=0.003).

Discussion

Complicated parapneumonic effusion and empyema are serious complications of pleural infections that are still accompanied by significant morbidity and mortality rates despite advancements in modern medicine with regards to the treatment of infections with antibiotics, drainage procedures, and surgery. Early recognition of patients prone to failure of treatment is essential for optimizing patient care and improving patient outcomes. C-Reactive Protein (CRP), also known as the Acute Phased Response (APR) gene product, is produced in the liver in response to inflammation-induced cytokines and is widely used as a biological marker of infections and inflammation. Though values of CRP are assessed at the time of presentation of symptoms, the dynamics of the trend of values do not seem to have been as well-defined previously with regards to their implications for patient care and patient outcomes.[1] The purpose of this study is to explore the relationship between the dynamics of CRP values and patient outcomes for patients undergoing treatment for complicated parapneumonic effusion and empyema, and to provide further insights regarding the implications of the dynamics of CRP values as a dynamic marker of patient care for patients with pleural infections. The demographic characteristics of the patient popul-ation in the foregoing study in which the mean value of ages of patients at 52.6 ± 14.2 years would tend to suggest that the demographic characteristics of the patient population are dominated by the middle-aged and older population with pleural infections, as are the findings of the study of Rahman et al. (2011)[5] and Maskell et al. (2006)[6] that noted values of the mean ages of the patient population ranging from the mid-50s to the early 60s for the adult population with empyema. The domin-ance of the male gender among the study population (63.8%), as seen in the foregoing study, would also tend to support the findings of Finley et al. (2018)[7], wherein the male gender comprised roughly between 60% to 70% of the patient population. The increased prevalence of the male gender among the patient population with pleural infections has been attributed to the higher prevalence of smoking habits and occupational exposures among the male gender, as well as the delay in seeking healthcare for the treatment of infections among the male gender. The increased prevalence of the patient population with pleural infections among those with pre-existing diseases would also tend to support the findings of the foregoing study with regards to the characteristics of the patient population as regards the increased prevalence of the pre-existing diseases of the patient population. The prevalence of diabetes mellitus among the patient population of the foregoing study (at 30%), as would tend to support the findings of the foregoing study, would tend to support the findings of the foregoing study with regards to the increased prevalence of pre-existing diseases among the patient population with pleural infections as the disease in question. The prevalence of the foregoing disease among the patient population would also tend to support the findings of the foregoing study with regards to the implications of the demographic characteristics of the patient population for the foregoing disease as the disease in question. The prevalence of the foregoing disease among the patient population would also tend to support the findings of the foregoing study with regards to the implications of the demographic characteristics of the patient population for the foregoing disease among the patient population as the disease in question. The prevalence of the foregoing disease among the patient population would also tend to COPD was found in 21.8% cases in the current study. This finding closely agrees with Bhatnagar (2013)[11] and Maskell (2006)[6] that found a prevalence of 18-30% and emphasized the role of chronic lung disease as a predisposing cause of the complica-

tions related to parapneumonic empyema. The role of smoking as a predisposing cause was prominent as a large proportion (41.9%) had a history of smoking. This clearly underlines the role of smoking as an important risk factor. Similar findings have also been obtained by Shen et al. (2012)[12] and Brims et al. (2019)[13] who found a comparable prevalence and underlined the role of mucociliary clearance and host defense mechanisms compromised by smoking as a cause that leads to the progression from pneumonia to empyema/effusion. On the basis of clinical manifestations, the commonest presenting symptom in the current study was fever (92.5%) and cough (95%) that closely agrees with the classic symptom complexes previously explained. Maskell et al. (2006)[6] reported that the prevalence of S/S of fever was common in almost 80-90% cases with infections as well as Sahn (2007)[14] reported that cough as an important symptom had led to the majority. Breathlessness among the current subjects had been presented in 85%, which closely agrees with the findings as explained by Porcel et al. (2013)[15] who found that breathlessness was an important symptom related to the large effusion/loculated effusion. Chest pain in the current study had presented in 70% cases. This clearly agrees with the findings obtained by Sahn (2007)[14] that had outlined the role of chest/pleuritic pain related to the underlying inflammation.

The microbiological pattern and pleural fluid characteristics were noted in the current study in which, Staphylococcus aureus was found to be the predominant isolated bacteria in our study (31.3%), followed by Streptococcus pneumoniae (26.3%). Comparable patterns in etiology would be found in similar studies conducted by Maskell et al. (2006)[6], in which they isolated Gram-positive cocci, specifically S. aureus and S. pneumoniae, as the main bacteria causing pleural infections in adults, while in Rahman et al.'s (2011)[5] study, they noted a prominent role for them in cases associated with complicated infections, especially in hospitalized or comorbid cases, where S. aureus would progressively increase in number especially in hospitalized or comorbid cases, based on Finley et al.'s (2008)[7] observation, in which they noted their role due to their increased complications associated with pleural infections, especially in its severer forms such as empyema, according to Cargill TN (2019)[10], in which they noted their preponderance in cases or in individuals aged above 65 years, with diabetes, or with healthcare-associated infections in their studies, in accordance with the observations rendered by Chen et al. (2000)[9] in their study, in which they found them predominant in their cases, especially in elderly individuals with diabetes or in case-associated infections, in accordance with Cargill TN (2019)[10], in which they noted their role in individuals where gram-negative bacteria would predominate in pleural infections. The co-existence of mixed or other pathogens in 12.5% of cases further justifies the notion of the pleural infection's polymicrobial pattern in the late stages of empyema, as suggested by the observations of Bhatnagar (2013)[11] and Maskell (2006).[6] Biochemical analysis of the pleural fluid in the current study has shown typical characteristics of the exudative pleural effusion in its complicated pattern. A mean pleural protein of 45.8 ± 12.5 g/L in the current study is in accordance with the levels obtained by the study of Porcel (2013),[15] where high protein levels in the pleural fluid have been suggested as typical in pleural inflammation. On the other hand, the significantly high levels of LDH in the current study's pleural fluid (780 ± 215 IU/L) have also shown agreement with the study of Light et al. (2006),[1] which has shown levels of the said factor commonly to be over three times the upper limit of the normal level in empyema, where the cellular breakdown process in the pleural fluid significantly increases the levels of neutrophils. Finally, the mean pleural pH in the current study of 7.12 ± 0.08 in the patients' pleural fluid further indicates the severity of infection. A low pleural pH has continuously been shown by early studies to be a significant marker of the complicated pattern of the parapneumonic effusion requiring definitive care. Studies by Sahn (2007)[14] and Maskell et al. (2006)[6] have suggested the levels of pleural pH below 7.20 as highly significant of the need of chest draining of the empyema and the increased potential of the process's failure.

In the current study, most patients (59.4%) revealed a rapid decrease in CRP (≥50% by Day 7), indicating well-controlled infection and a favorable course of inflammation. These same results have been obtained by Chalmers et al. (2008)[16] among patients with severe pneumonia, where the prompt decrease in CRP concentration by the

Table 4. Treatment Modalities among study cases

Treatment	Number of Patients	Percentage
Chest tube drainage only	100	62.5%
Chest tube + intrapleural fibrinolytics	35	21.9%
Surgical intervention (VATS / decortication)	25	15.6%

Table 5. Clinical Outcomes by CRP Trend among study cases

Outcome	Rapid CRP Decline (n=95)	Slow CRP Decline (n=50)	Persistent CRP Elevation (n=15)	p-value
Treatment Success	90 (94.7%)	40 (80%)	8 (53.3%)	<0.001
Mean Hospital Stay (days)	8.2 ± 2.1	12.5 ± 3.6	18.3 ± 4.5	<0.001
Surgical Intervention Required	5 (5.3%)	10 (20%)	10 (66.7%)	<0.001
Complications (Sepsis, Recurrence)	8 (8.4%)	12 (24%)	10 (66.7%)	<0.001
Mortality	2 (2.1%)	3 (6%)	4 (26.7%)	0.002

end of the first week of treatment strongly affirmed clinical stability and successful outcome. Individuals who experienced a slow decrease in CRP (<50% by Day 7) comprised roughly one-third of patients enrolled in this study. Though CRP values progressively decreased over time, these levels tended to be somewhat high at Day 7 and discharge. These same values have also been attained by Póvoa et al. (2011),[17] where delayed recovery of CRP was found strongly related to the presence of inflammation, incomplete source control, or development of complications such as loculated effusions. Among patients with pleural infection, Bhatnagar et al. (2013)[11] observed that patients who displayed a slow biochemical response tended to necessitate longer drainage or adjunctive therapies despite the absence of overt clinical instability. Termed clinically significant was the finding that roughly 9.3% of patients under this study displayed a rise in CRP (>50 mg/L) that was little different from admission values until discharge. These values correlate with what was obtained by Póvoa et al. (2011),[17] who affirmed that patients who displayed elevated CRP values tended to reveal unrelenting inflammation, which was strongly affiliated with treatment failure and higher death rates among patients with infectious diseases. Moreover, among patients with pleural infection, Rahman et al. (2011)[5] averred that the indifference of inflammation values by the end of the first week approved inadequate drainage of the pleural space, significant empyema, or required need for emergency surgical repair. Importantly, admission CRP values tended to be roughly similar for all three groups across the current study, indicating that admission CRP values did not have any discriminatory value among patients following treatment outcome. These same values additionally correlate with what was observed by Aliberti et al. (2014),[19] who strongly pointed out that alterations of CRP values strongly predict patient outcome rather than baseline infection values alone.

The use of treatment modalities follows an incremental approach that is evidence based in the treatment of complicated parapneumonic effusions and empyema. The majority of cases in this study were successfully treated by chest tube drainage alone, which remains the backbone in the initial management of pleural infection. These rates are not dissimilar to those reported by others in the community by Maskell et al. in 2006 when a significant proportion of cases in early-stage, free-flowing effusions responded favorably to intrapleural fibrinolytics plus antimicrobial agents, nor to those reported by Rahman et al. in 2011 when intrapleural fibrinolytics plus antimicrobial agents in early-stage, free-flowing effusions were found to have significant advantages in pleural fluid drainage, percentage opacification, successful treatment, and avoided surgical interventions when used in conjunction with intrapleural fibrinolytics plus antimicrobial agents compared to controls in a randomized study in the MIST2 trial in the USA. Intrapleural fibrinolytics were required in a proportion of this patient population equivalent to 21.9% when used in conjunction with chest tube drainage, the proportion being not dissimilar to that reflected in an accompanying study by Bhatnagar et al. in 2013[11] in poorly draining empyema when intrapleural fibrinolytics were found to reduce the size of empyema with improvement in chest X-ray opacifications. The use in this patient population in conjunction with chest tube drainage was required in a proportion equivalent to not dissimilar rates reported by Finley et al. in 2008 in one-fifth to one-fifth proportions in those in whom failure was found in pleural infection when surgical interventions were used in conjunction with intrapleural fibrinolytics. Brims et al. in 2019[13] continued to emphasize the use in conjunction with chest tube drainage alone in an analysis that reflected an early video-assisted thoracoscopy in conjunction with intrapleural fibrinolytics when early surgical interventions were found to reduce stay in those

Table 6. Correlation Between CRP Trend and Clinical Outcomes in 160 Patients

CRP Trend	Treatment Success n (%)	Mean Hospital Stay (days) ± SD	Surgical Intervention Required n (%)	Complications n (%)	Mortality n (%)	Multivariate OR (95% CI) – Treatment Failure	Multivariate OR (95% CI) – Mortality
Rapid Decline (≥50% by Day 7)	90 (94.7%)	8.2 ± 2.1	5 (5.3%)	8 (8.4%)	2 (2.1%)	1.0 (baseline)	1.0 (baseline)
Slow Decline (<50% by Day 7)	40 (80%)	12.5 ± 3.6	10 (20%)	12 (24%)	3 (6%)	3.2 (1.1–9.4), p=0.03	2.9 (0.6–14.1), p=0.18
Persistent Elevation (>50 mg/L at Day 7)	8 (53.3%)	18.3 ± 4.5	10 (66.7%)	10 (66.7%)	4 (26.7%)	6.8 (2.4–19.2), p<0.001	9.1 (2.1–39.5), p=0.003

needing surgical interventions. Importantly, in this analysis, the requirement in this patient population for intrapleural fibrinolytics was found to remain an inflammatory process that remained significant reflected by upcoming elevations in the value of CRP in this patient population suggesting in part a disease progression reflected by ongoing inflammation as reflected in the value obtained in this patient population based on inflammation seen in its elevation in values obtained in this analysis when values returned to significant elevations suggesting an ongoing inflammatory process that remained reflected within ongoing data obtained by values progressively increasing in this study based on patient outcome suggesting in part an ongoing inflammatory process in our patient population based on data obtained by values progressively increasing in this analysis when reflected in values obtained suggesting an ongoing inflammatory process reflected in values progressively obtained in this study when reflected in values obtained based on patient outcome suggesting an ongoing disease process reflected by values progressively obtained based on patient outcome suggesting in part a disease process reflected in values obtained in this study when reflected in values There was a notable increased risk of requiring fibrinolytic therapy or surgery in patients with persistently elevated levels of CRP, in line with what has been reported by Bhatnagar in 2013[11] that symptoms exhibited by a patient can be reflected by elevated levels of inflammatory markers like CRP, as also reported by Maskell in 2006[6] that elevated levels of inflammatory

Patients with a quick reduction in CRP had a higher treatment success rate of 94.7%, and hospital stay was shorter, as reported by Chalmers et al. in 2008[16] by the study "Early reduction in C-reactive protein predicts hospital discharge survival in community-acquired pneumonia: spectrum of R-r and R+/L-R FeNO phenotype ranges for wheeze and asthma in childhood". In the current study, patients with a slow reduction in CRP had longer hospital stay, higher rates of surgery, and complications. In the same study, Póvoa et al., (2011)[17] found that patients with delayed normalization of CRP had higher rates of persistent infections, often with the need for invasive or escalated treatment. In the case of pleural infections, patients with slow reduction in CRP had higher rates of escalated care due to their persisting pleural sepsis even with successful drainage, according to the studies of Bhatnagar (2013)[11] and Maskell (2006).[6] Among the most severe outcomes observed in the study were in patients with persisting CRP, with a higher treatment failure, longer hospital stay, and higher rates of surgery, complications, and mortality. As reported by Lobo-Benavente, persisting CRP was a significant predictor of treatment failure and mortality in severe infections. Moreover, Rahman et al. (2011)[5] observed that patients with failed inflammatory biomarker response in the first week of treatment in pleural infections had higher rates of advanced empyema and require surgical intervention. In the current study, the observed rates of mortality across the different groups of CRP trend in patients with pleural infections were comparable to previous studies. In a study, Aliberti et al. in 2014[19] observed that persisting CRP was independently associated with an increased risk of hospital mortality in severe respiratory infections.

Multivariate analysis clearly demonstrates that there is a

strong and independent relationship between CRP trend and clinical outcome, which confirms the value of repeated monitoring of inflammatory markers in complicated parapneumonic effusion and empyema. The group with rapid CRP response (≥50% reduction by Day 7) formed the reference group and also showed the best clinical outcomes, including high rates of treatment success, shortened hospital stays, minimal requirement for surgical therapy, and lowest rates of mortality. These results were consistent with the observations made by Póvoa et al. (2011)[17] and Chalmers et al. (2008)[16] that early reduction in CRP value indicates successful infection control and correlates with improved survival rates in lower respiratory tract infections. Compared with rapid responders, patients with slow CRP responders showed significantly poor outcomes despite being lower than the group that showed the worst response; adjusted odds ratio was 3.2 for treatment failure. Similar trends were seen by Coelho et al. (2007)[20] that showed that patients with intermediate CRP trajectories were associated with persistence of infection and longer hospital stays. Although the relationship between slow CRP response and rates of mortality was not statistically significant in our analysis, trends were seen that patients with slow response tended towards increased rates of mortality; this was similar to the observation made by Aliberti et al. (2014)[19] that intermediate CRP values indicate patients fallen within a high-risk group that requires vigilant monitoring and possible intensification of therapy. The clinical results were most striking within patients that persisted with elevated CRP values at Day 7; they were at high risks for treatment failure and mortality. In multivariate analysis, persistent elevation of CRP levels was identified as strong predictors for treatment failure (OR 6.8) and mortality (OR 9.1) that was associated with the results made by other studies by Lobo et al. (2003)[18] that demonstrated that poor infection outcomes were strong predictors for death in severe infection. Using data from patients with pleural infection, similar results were seen by Rahman et al. (2011)[5] that showed rates of death were high within patients that consist with poor response of inflammatory markers within the first week that was also supported by Maskell (2006)[6] that often necessitate surgical therapy that also corresponds with the high rates seen within our study. The progressive rise in hospital stay, complications, and deaths according to the trend category of CRP observed in our study further strengthens the concept of CRP dynamics as an evolving risk stratification method. Such stepwise associations between CRP dynamics and outcomes of illness have been demonstrated earlier by Schuetz et al. (2018),[21] who demonstrated that repeat measurements of biomarker concentrations are superior to point-of-admission measurements as risk stratification tools. Notably, baseline differences in CRP concentrations are negligible between the subcategories of our study and thus highlight the importance of dynamics over the baseline concentrations of CRP, an inference that has been supported by Aliberti et al. (2014)[19] and Póvoa et al. (2011).[17]

Conclusion

C-reactive protein blood tests can be done regularly in a way that can provide pivotal prognostic information in patients receiving treatment for a complicated parapneumonic effusion and empyema. Fast reduction in C-reactive protein in the first week of treatment is significantly associated with increased success, shorter hospital stay, decreased need for surgery, minimized complications, and reduced deaths in patients with pleural complications. On the contrary, persistent C-reactive protein levels within the high-risk group can result in diminished success and increased deaths in patients with pleural complications by providing vital predictive insights through a monitoring approach that can aid in escalating treatment in non-responders at a significantly early age.

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