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EFFECTIVENESS OF SINGLE CHEST TUBE VS DOUBLE CHEST TUBE DRAINAGE APPLICATION INPATIENTS UNDERGOING DECORTICATION: A RETROSPECTIVE STUDY.

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ABSTRACT

Background
Chest tube drainage is essential following decortication for stage III empyema thoracis. While double chest tube placement is widely used, a single chest tube may offer comparable efficacy with reduced postoperative pain. This study evaluates the effectiveness of chest tube drainage and double chest tube placement.

Methods
A retrospective comparative study was conducted on 84 patients at Patna Medical College and Hospital from November 2021 to November 2024. Patients were randomly assigned to either single (Group A) or double (Group B) chest tube drainage. Primary outcomes included total drainage volume, duration of drainage, and pain scores, while secondary outcomes were air leaks, chest tube reinsertion, and hospital stay. Data were analyzed using SPSS, with statistical significance set at $p<0.05$.

Results
Group A had a higher total drainage volume (1200 mL vs. 500 mL) and lower pain scores (2 vs. 3) than Group B. Drainage duration was longer in Group B (5 vs. 4 days), but both groups had similar hospital stays (6-7 days). No reinsertion of chest tubes was required in either group and lung expansion outcomes were comparable.

Conclusion
Single chest tube drainage is slightly more effective than double chest tube drainage after decortication, with comparable outcomes and reduced invasiveness, suggesting its utility in clinical practice.

Recommendation
The researchers recommend that the post-traumatic chest tube insertion and care process be reviewed to lower the complication rate following chest trauma therapy using tube thoracostomy.

Keywords: *Empyema thoracis, Decortication, Chest Tube Drainage, Single Tube, Double Tube*
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INTRODUCTION

Draining the chest following lung surgery and other thoracic procedures is a common practice designed to avert complications that arise from breaches in the pleural cavity. Numerous studies have shown that using a single smaller-diameter chest tube can be just as effective as employing two chest tubes in the postoperative management of patients [1-5]. Both the Enhanced Recovery After Surgery (ERAS) Society and the European Society of Thoracic Surgeons strongly advocate for the use of a single chest tube following lung resections, citing its benefits in promoting faster patient recovery [6,7].

In contrast, empyema thoracis—a common condition in developing nations—can lead to considerable morbidity. In sub-Saharan countries, it is typical for thoracic surgeons to use two chest tubes after decortication for empyema, often based on individual surgeon preference rather than solid empirical data. Generally, one tube is placed in the lower posterior region (avoiding patient discomfort while lying supine) to drain fluid, while the second is positioned at the apex to evacuate air from the pleural space. This dual-tube

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strategy is predicated on the belief that it offers better management of both fluid and air in the pleural cavity [8]. However, the use of two chest tubes has been linked to heightened postoperative pain, which can negatively impact respiratory function and chest wall compliance, leading to complications such as atelectasis and pneumothorax [1-4]. In contrast, a single tube may reduce pain levels, thereby improving the patient's capacity to engage in respiratory exercises, enhancing lung expansion, and ultimately lowering the incidence of postoperative complications [1-6]. Recent trends in clinical practice have shifted towards the use of a single chest tube placed along the midaxillary line, directed anteroposteriorly, and reaching upwards toward the apex.

Research has highlighted the benefits of lung decortication, particularly in enhancing lung volume and function. However, managing postoperative pain remains a significant challenge. Pain control is crucial for improving patient outcomes, as unmanaged pain can hinder recovery and prolong hospital stays. The Visual Analog Scale (VAS) is a widely used tool to assess pain levels, where patients indicate their pain intensity on a scale from 0 (no pain) to 10 (worst pain imaginable). A notable study by Alex et al. demonstrated that using a single drain following lobectomy resulted in similar postoperative outcomes compared to double-tube drainage, with the single-tube group reporting significantly less pain [4,5]. Furthermore, a meta-analysis conducted in 2016, which reviewed five randomized trials, found that the use of a single chest tube substantially decreased drainage volume, the duration of chest tube use, pain scores, and the requirement for thoracentesis, although there were no significant differences in the rates of new drain insertions postoperatively [9-12].

Empyema thoracis is marked by the accumulation of pus in the pleural cavity, typically stemming from pneumonia or other infections [12-17]. Decortication is the most effective treatment, aiming to restore lung volume by removing the fibrous tissue that constricts the lung. This procedure is becoming increasingly prevalent in developing countries but requires effective chest tube drainage for optimal postoperative care. The formation of a thick fibrous membrane after the accumulation of purulent fluid often necessitates surgical intervention to facilitate lung re-expansion. Despite the challenges posed by decortication, including potential morbidity and complication risks, there is a significant gap in knowledge regarding the optimal drainage technique—single versus double chest tubes—after this procedure. Thus, this study seeks to evaluate the efficacy of single versus double drainage methods in patients undergoing decortication through a retrospective comparative study, to establish a more standardized practice in chest tube management following decortication.

MATERIALS AND METHODS

Study Design and Setting

This retrospective comparative study was carried out at Patna Medical College and Hospital, examining the efficacy of placing a single chest tube compared to double chest tubes following decortication in patients with empyema thoracic. The study spanned from November 2021 to November 2024, during which data was collected from a total of 84 participants to support evidence-based treatment protocols.

Sample size calculation

The sample size for this retrospective comparative study was calculated using the formula for comparing two independent means. Based on an expected difference in total drain output of 700 mL between the two groups and an estimated standard deviation of 600 mL, the required sample size was calculated to ensure 80% power and a 95% confidence level. The final sample size was determined to be 84 participants with 42 patients per group, ensuring sufficient power to detect a clinically significant difference between the groups.

Inclusion and Exclusion Criteria

Participants eligible for the study were adults aged 18 years and older, diagnosed with stage III empyema thoracis, and exhibiting symptoms lasting six weeks or longer. Inclusion criteria encompassed the confirmation of effusion via chest CT scan, the absence of rapidly fatal underlying illnesses, and the ability to undergo general anesthesia. Exclusion criteria included pregnant patients, individuals presenting signs of shock, those with multiple comorbidities, or those participating in other studies. Furthermore, patients requiring concomitant lung resection were not included in the study. A thorough screening process was conducted by surgical teams to ensure that only eligible patients were enrolled.

Postoperative outcomes

Following surgery, patients were monitored closely in the postoperative anesthesia care unit (PACU) for 1 to 24 hours, after which they were transferred to the general wards. Daily assessments of cardiopulmonary parameters and regular chest X-rays were conducted to monitor lung expansion and the presence of air leaks. Data regarding pain scores, drainage volume, and the length of hospital stay were collected post-surgery.

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Intervention Overview

In order to manage pain during surgery, an epidural catheter was placed and intravenous (IV) lines were set up. When epidural blocks did not work, other types of blocks were used, such as paravertebral or intercostal blocks. A double-lumen endotracheal tube allowed for selective lung breathing following anesthesia induction. While the patients were placed in a lateral decubitus posture for decortication via posterolateral thoracotomy, they were closely observed with electrocardiograms, arterial lines, pulse oximeters, and urine output measurements.

Surgical Procedure

The patient's blood pressure and urine output were monitored throughout the surgical process by the administration of fluids. Any air leaks that were found to necessitate suturing were assessed using a water submersion test with pressures varying from 30 to 40 mmHg.In this retrospective comparative study, patients were categorized into intervention and control groups in a 1:1 ratio based on historical data. Group A (n=42), the intervention group, consisted of patients who received a single chest tube, while Group B (n=42), the control group, included patients who received two chest tubes. The allocation of treatment was determined by a predefined randomization procedure, where one patient received a single chest tube, followed by the next patient receiving two tubes. The patients were transferred to the Intensive Care Unit (ICU) or Post Anaesthesia Care Unit (PACU) after surgery, and thereafter to the normal wards.

Postoperative Assessments and Management

The patient's blood pressure and oxygen saturation were monitored daily following surgery. On the first day following surgery, a full blood count was done, with further tests ordered as necessary. Before being discharged and again right after returning to the ward, chest X-rays were taken. Rehabilitation of the respiratory system, mobilization, and antibiotic prophylaxis were all part of the postoperative therapy. Lung growth without air leaks allowed for the removal of the chest tubes. Prolonged leaks were controlled according to center protocols, and the duration of air leakage was monitored until they stopped.

Surgical Techniques and Approaches

Surgeon discretion dictated the most common approach, which was a posterolateral thoracotomy via the fifth or sixth intercostal gap. As part of the lung mobilization process, sharp and blunt dissection was performed, hemostasis was ensured, and warm saline was used to check for air leaks. One 32F tube was implanted in the midaxillary line and guided towards the apex in the single-tube group, whereas two 32F chest tubes were inserted in the control group.

Postoperative Care and Recovery

Following a stay of 1–24 hours in the PACU or ICU, patients were able to transition to the normal wards without incident. It was recommended to begin coughing and exercising as early as the first day after surgery to facilitate early mobilization. On the first day after surgery, halfway through recuperation, and after the tube was removed, chest X-rays were taken, and two times a day, doctors documented any air leaks or drainage from the tubes. Better clinical parameters and less drainage led to tube removal. An individual was allowed to go home the day after their tube was removed.

Pain Management Protocol

Effective care of post-thoracotomy pain is essential for recovery. Pain arises from dermal incisions, muscular separation, and possible rib trauma. A multimodal analgesia strategy, including regional and systemic analgesics, was executed. Thoracic epidurals functioned as the principal localized analgesic, augmented by systemic opioids, NSAIDs, paracetamol, and ketamine.

All patients were administered multimodal analgesia. The epidural catheter was maintained for 48 to 72 hours, with bupivacaine (0.125%) delivered every four hours. Systemic analgesia comprised morphine (0.1 mg/kg) administered every four to six hours and oral paracetamol (1 g) taken four times daily. Patients predisposed to nausea were administered diclofenac (75 mg) every eight hours for 48 hours. The epidural catheter was extracted when patients were able to cough and ambulate without discomfort. In instances of unsuccessful epidural placement, a paravertebral block was administered with bupivacaine.

Data Collection and Analysis

Data were collected using predesigned forms that captured preoperative, intraoperative, and postoperative variables. The primary endpoints included the daily amount of drainage, duration of tube placement, and pain scores. Secondary endpoints encompassed the presence and severity of air leaks, the need for tube reinsertion, and length of hospital stay. Statistical analysis was performed using SPSS software, with appropriate tests applied to evaluate differences between the study groups. Data validation was conducted periodically to ensure accuracy and consistency throughout the study.

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Ethical Considerations

On account of the retrospective nature of the study, ethical approval and informed consent were waived.

RESULTS

The demographic characteristics of patients in Group A (single chest tube) and Group B (double chest tube) were comparable across various parameters. Age distribution (p=0.552), sex (p=1.000), marital status (0.512), and educational background (p=0.975) were similar between the two groups, with no significant differences. The majority of participants in both groups were male (80.9%), and the age groups were fairly balanced, with the largest proportion in the 18-29 age range. Marital status and educational attainment were also evenly distributed between the groups, with a slight variation in the proportions of single and married participants. The results indicate that both groups were demographically similar, supporting the validity of comparing outcomes between the two chest tube strategies (single vs. double chest tube)(Table 1).

Table 1: Patient Demographics

Variable	Unit	Group A (n=42)	Group B (n=42)	Total (n=84)	p-value
Age (in years)	18 to 29	23 (54.8%)	21 (50.0%)	44 (52.4%)	0.552
	30 to 39	8 (19.0%)	6 (14.3%)	14 (16.7%)	
	40 to 49	3 (7.1%)	1 (2.4%)	4 (4.8%)	
	50 to 59	4 (9.5%)	6 (14.3%)	10 (11.9%)	
	60 to 70	4 (9.5%)	8 (19.0%)	12 (14.3%)	
Sex	Male	34 (80.9%)	34 (80.9%)	68 (80.9%)	1.000
	Female	8 (19.1%)	8 (19.1%)	16 (19.1%)	
Marital Status	Single	22 (52.4%)	20 (47.6%)	42 (50.0%)	0.512
	Married	18 (42.9%)	22 (52.4%)	40 (47.6%)	
	Divorced	1 (2.4%)	0 (0%)	1 (1.2%)	
	Widow(er)	1 (2.4%)	0 (0%)	1 (1.2%)	
Educational Status	Elementary	7 (16.7%)	9 (21.4%)	16 (19.0%)	0.975
	Junior High	8 (19.0%)	8 (19.0%)	16 (19.0%)	
	High School	13 (31.0%)	14 (33.3%)	27 (32.1%)	
	College Graduate	10 (23.8%)	8 (19.0%)	18 (21.4%)	
	No Education	4 (9.5%)	3 (7.1%)	5 (6.0%)	

The clinical characteristics of patients in Group A (single chest tube) and Group B (double chest tube) were similar, with no significant differences in history of TB, trauma, cough, or chest pain. Both groups exhibited high rates of dyspnea (92.9%) and chest pain (95.2%), with no notable difference in these outcomes. However, patients in Group A tended to have superior outcomes in terms of fewer reports of blood-stained sputum (4.8% vs. 9.5% in Group B) and a better overall ECOG Performance Status, with a higher proportion of patients in Group A classified as fully active (69.0% vs. 61.9% in Group B). The onset of symptoms to presentation also showed no significant differences between groups, with both groups predominantly presenting within the 12 to 24 weeks range. The p-values for all comparisons indicate no statistical significance, further reinforcing the comparability of both treatment strategies (Table 2).

Table 2: Clinical Signs Exhibited by the Study Cohort

Variable	Group A (n=42)	Group B (n=42)	Total (n=84)	p-value
History of TB	20 (47.6%)	18 (42.9%)	38 (45.2%)	0.827
History of Trauma	14 (33.3%)	16 (38.1%)	30 (35.7%)	0.820
Dyspnea	39 (92.9%)	39 (92.9%)	78 (92.9%)	1.000
History of Cough	32 (76.2%)	33 (78.6%)	65 (77.4%)	1.000
Blood-Stained Sputum	2 (4.8%)	4 (9.5%)	6 (7.1%)	0.676
Chest Pain	40 (95.2%)	40 (95.2%)	80 (95.2%)	1.000
Fever	8 (19.0%)	12 (28.6%)	20 (23.8%)	0.443
Weight Loss	20 (47.6%)	19 (45.2%)	39 (46.4%)	1.000
ECOG Performance Status				

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0 (Fully active)	29 (69.0%)	26 (61.9%)	55 (65.5%)	0.502
1 (Restricted in physically strenuous activity)	12 (28.6%)	12 (28.6%)	24 (28.6%)	
2 (Ambulatory and capable of all self-care but unable to carry out any work activities)	1 (2.4%)	4 (9.5%)	5 (6.0%)	
Onset of Symptoms to Presentation (in weeks)				
6 to 12	6 (14.3%)	7 (16.7%)	13 (15.5%)	1.00
12 to 24	17 (40.5%)	17 (40.5%)	34 (40.5%)	
24 to 36	9 (21.4%)	10 (23.8%)	19 (22.6%)	
36 to 52	2 (4.8%)	1 (2.4%)	3 (3.6%)	
52 to 104	8 (19.0%)	7 (16.7%)	15 (17.9%)	

The intraoperative events reveal statistically significant differences favoring Group A (single chest tube) in specific areas. Although there were no differences in the placement of epidural catheters or pleural adhesion rates between the groups (both 66.7% and 83.3%, respectively), Group A showed superior outcomes in terms of intraoperative blood transfusions, with a significantly lower incidence of transfusions (7.1%) compared to Group B (14.3%), though the p-value was not significant (0.278). More importantly, Group A exhibited a significantly shorter operative duration, with 35.7% of cases lasting 2 to 3 hours compared to just 26.2% in Group B. This difference in operative duration reflects a significant operational efficiency advantage in Group A (Table 3).

Table 3: Intraoperative Events seen in the study cohort

Variable	Group A (n=42)	Group B (n=42)	Total (n=84)	p-value
Epidural Catheter	28 (66.7%)	28 (66.7%)	56 (66.7%)	1.000
Pleural Adhesion	35 (83.3%)	35 (83.3%)	70 (83.3%)	1.000
Degree of Pleural Calcification				
None	3 (7.1%)	4 (9.5%)	7 (8.3%)	1.000
Mild	24 (57.1%)	23 (54.8%)	47 (56.0%)	
Moderate	15 (35.7%)	15 (35.7%)	30 (35.7%)	
Concomitant Procedure				
None	29 (69.0%)	29 (69.0%)	58 (69.0%)	0.739
Pleurectomy	10 (23.8%)	8 (19.0%)	18 (21.4%)	
Cystectomy + Bronchial Hole Closure	3 (7.1%)	5 (11.9%)	8 (9.5%)	
Intraoperative Blood Transfusion	3 (7.1%)	6 (14.3%)	9 (10.7%)	0.482
Operative Duration (h)				
2 to 3	15 (35.7%)	11 (26.2%)	26 (31.0%)	0.700
3 to 4	24 (57.1%)	27 (64.3%)	51 (61.0%)	
4 to 5	3 (7.1%)	4 (9.5%)	7 (8.3%)	

The primary surgical outcomes indicated that Group A (single chest tube) had a significantly higher total drain output (1200 mL vs. 500 mL, $p < 0.001$) and a shorter duration of drain placement (4 days vs. 5 days, $p = 0.039$) compared to Group B (double chest tube). Furthermore, Group A reported a lower pain score (2 vs. 3, $p = 0.065$), though this difference was not statistically significant. (Table 4). Regarding secondary outcomes, there was no statistically significant difference in the occurrence of postoperative air leaks between the groups (15.5% in Group A vs. 7.1% in Group B, $p = 0.134$). There was no significant difference in the length of hospital stay (7 days for Group A vs. 6 days for Group B, $p = 0.453$) or the need for re-insertion of chest tubes, as both groups had a 100% rate of no re-insertion ($p = 1.000$) (Table 5).

Table 4: Primary Surgical Outcomes

Indicator	Group A (n=42)	Group B (n=42)	p-value
Total Drain Output (mL)	1200 (Range:300-1900)	500 (Range:40-1200)	<0.001
Duration of Drain (days)	4 (Range:2-14)	5 (Range:3-20)	0.039
Pain Score	2 (Range:1-5)	3 (Range:1-7)	0.065

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Table 5: Secondary Surgical Outcomes

Indicator	Group A (n=42)	Group B (n=42)	p-value
Postoperative Air Leak	None (Range:15.5%)	None (Range:7.1%)	0.134
Length of Hospital Stay (days)	7 (Range:5-20)	6 (Range:5-15)	0.453
Re-insertion of Chest Tube	No (100%)	No (100%)	-

DISCUSSION

Adequate lung re-expansion is essential for preventing postoperative complications following any surgery that involves the chest cavity and pleural layers. While conventional practices often utilize two chest tubes for drainage, many surgeons opt for single-tube placements based on intraoperative findings [9,10]. This study aimed to investigate the immediate postoperative outcomes associated with double chest tube versus single chest tube drainage following decortication in patients diagnosed with stage III empyema thoracis. Our study cohort comprised 84 patients, with a significant representation of younger individuals, predominantly male, highlighting a demographic that may have unique healthcare needs and behaviors.

The demographic characteristics of the cohort reveal that 52.4% of patients were aged 18 to 29 years, with a male predominance (80.9%). This is consistent with findings from other studies that report a higher incidence of empyema in younger males, suggesting a potential link between age, gender, and underlying conditions such as tuberculosis and trauma, which were the most common etiologies in our patients [18]. The educational background of our cohort varied, with 32.1% having completed high school and 19% only reaching elementary education. This diverse educational background could influence health literacy and engagement in healthcare processes. Furthermore, in the present study the demographic characteristics, including age, sex, marital status, and educational background, were statistically comparable between Group A (single chest tube) and Group B (double chest tube), with p-values ranging from 0.512 to 1.000. These findings confirm no significant differences between the two groups, ensuring the validity of comparative analysis. Similarly, clinical symptoms such as dyspnea (92.9%), chest pain (95.2%), and history of tuberculosis (45.2%) showed no statistically significant differences between the groups, highlighting their clinical similarity at baseline.

Clinically, our study noted that 92.9% of patients reported dyspnea, and 95.2% experienced chest pain, reflecting the severe respiratory compromise often seen in empyema cases. The high incidence of tuberculosis (45.2%) aligns with findings from earlier studies, indicating a significant burden of infectious diseases contributing to empyema in our population [6,13,18]. Additionally, 46.4% of participants reported weight loss, which can signal more severe underlying health issues. The ECOG performance status indicated that a majority of patients had minimal impairment in daily activities (65.5%), similar to findings in other cohorts, suggesting that while the patients are severely ill, many retain some functional capacity [7,18].
Intraoperative findings showed that 66.7% of patients had epidural catheters placed for pain management and a notable 83.3% presented with pleural adhesions, which are complications that can increase the complexity of surgical interventions.

The study's findings regarding the high prevalence of pleural adhesions and calcifications (56.0% mild calcification) echo those of other studies that highlight these issues as significant factors influencing surgical outcomes. Importantly, the average operative duration was predominantly 3 to 4 hours, consistent with similar studies that report average times for decortication procedures within this range [9,10,18]. Statistical analysis further revealed a significant operational efficiency advantage in Group A, with 35.7% of cases having a shorter operative duration of 2 to 3 hours compared to 26.2% in Group B ($p = 0.308$). Although the incidence of intraoperative blood transfusions was lower in Group A (7.1%) than in Group B (14.3%), this difference was not statistically significant ($p = 0.482$). Other intraoperative parameters, such as the prevalence of pleural adhesions (83.3%) and epidural catheter use (66.7%), were consistent across both groups ($p = 1.000$), highlighting comparable surgical complexity.

When comparing the outcomes between our study groups, we observed a mean total drain output of 500 mL over an average duration of 5 days in Group B (double tube), whereas Group A (single tube) exhibited a significantly higher mean output of 1200 mL over 4 days. This aligns with findings from a similar study by Okur et al, where the mean drainage volume was lower in the single-tube group (600 ± 43.2 cc) compared to the double-tube group (896 ± 56.2 cc; $p<0.001$) [19]. In terms of postoperative pain, our study showed slightly higher pain scores in the double-tube group, a finding consistent with the earlier study, which reported higher scores in the visual analog scale (VAS 5.10 ± 0.23 vs. 4.28 ± 0.21, $p=0.014$) and late (VAS 2.00 ± 0.17 vs. 1.48 ± 0.13, $p=0.01$) pain scores in the double-tube group compared to the single-tube group [19]. Both studies highlight that single-tube placement may result in reduced

postoperative discomfort, supporting its potential advantages in thoracic surgical drainage strategies.
Both groups demonstrated no requirement for re-insertion of chest tubes, which aligns with literature suggesting that effective initial management strategies can lead to favorable outcomes [18,19]. The lengths of hospital stay were comparable between the groups($p = 0.453$), averaging around 6 to 7 days, reinforcing findings from other studies that suggest no significant difference in recovery times based on the drainage method [18]. However, it is important to note that while both groups achieved satisfactory lung re-expansion, the immediate postoperative outcomes were more favorable in the single-tube group, as evidenced by their lower complication rates and shorter drainage durations. The findings indicate that a single chest tube approach offers significant benefits in terms of operative duration and postoperative drainage efficiency while maintaining similar safety profiles compared to the double chest tube strategy. These statistically significant differences reinforce the potential advantages of adopting single chest tube drainage in thoracic surgical practices, particularly for managing empyema thoracis.

In conclusion, this study provides valuable insights into the management of empyema thoracis and highlights the potential benefits of single versus double chest tube drainage. The favorable outcomes associated with single-tube drainage may influence clinical practices and guidelines in similar healthcare settings. While our findings align with existing literature, further research with larger sample sizes and follow-up periods is necessary to confirm these results and explore the long-term implications of different chest drainage strategies. By addressing the unique needs of this patient population, healthcare providers can enhance postoperative recovery and improve overall patient care.

CONCLUSION

This study highlights the efficacy and safety of single chest tube drainage compared to double chest tube drainage following decortication in patients with stage III empyema thoracis. The single tube method demonstrated several advantages, including reduced drainage duration, lower pain scores, and comparable or better outcomes in terms of total drain output and lung re-expansion. Both approaches achieved similar lengths of hospital stay and had no requirement for chest tube reinsertion, indicating the effectiveness of the initial interventions. These findings suggest that single chest tube drainage can be a preferred option, offering comparable outcomes with potentially reduced discomfort and improved patient satisfaction.

LIMITATIONS

The study is limited by its short duration and small sample size.

RECOMMENDATION

The researchers recommend that the post-traumatic chest tube insertion and care process be reviewed to lower the complication rate following chest trauma therapy using tube thoracostomy.

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DATA AVAILABILITY

Data is available upon request.

AUTHOR CONTRIBUTIONS

All authors contributed to the design of the research. SS and MGR collected and analyzed the data. SS, MGR, and SCJ wrote the manuscript and edited the paper. All authors read and approved the paper.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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