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Efficacy of video-assisted thoracoscopic surgery versus intrapleural streptokinase for treatment of parapneumonic empyema with multiloculation and septation

Reza Ershadi, Matin Vahedi, Shahab Rafieian

Department of Thoracic Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

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Abstract

Introduction: Effective treatment of parapneumonic empyema with multiloculation and septation has been a challenge for clinicians for many years.

Aim: This study compared the clinical outcomes of video-assisted thoracoscopic surgery (VATS) and intrapleural streptokinase in patients with stage II empyema.

Material and methods: This is a retrospective study of 46 patients with parapneumonic empyema with multiloculation and septation in the pleural cavity treated with VATS or streptokinase in Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran, between January 2018 and January 2021. The main outcome measures of this study were hospital stay, febrile period, days with drainage, and treatment failure.

Results: A total of 46 patients were included in this study. Of these, 28 were treated with VATS deloculation, and 18 were treated with streptokinase. The average hospital stay was 2.8 ±1.7 days for the VATS group and 7.5 ±3.5 days for the streptokinase group ($p < 0.001$). The average days with fever were 1.9 ±0.7 days for the VATS group and 3.0 ±1.64 days for the streptokinase group ($p = 0.017$). The average days with drainage were 3.0 ±1.6 days for the VATS group and 7.5 ±4.4 days for the streptokinase group ($p < 0.001$). The success rate was 92.9% for the VATS group and 66.7% for the streptokinase group, which was significantly higher in the VATS group compared to the streptokinase group ($p = 0.042$). No cases of perioperative mortality occurred. The frequency of adverse events did not differ between study groups ($p > 0.05$).

Conclusions: Our results demonstrated that treatment of empyema with VATS is superior to streptokinase therapy.

Key words: streptokinase, empyema, video-assisted thoracoscopic surgery.

Introduction

Empyema, which is characterized by the collection of pus in the pleural cavity, is a challenging issue in medical settings [1]. It is a complex entity with multifactorial pathogenesis and etiology, while rapid, accurate diagnosis plays an important role in the management of the disease and survival of the patient [2]. The empyema is divided into three stages: stage I (exudative phase), stage II (fibrinopurulent phase), and stage III (organizing phase) [1]. Patients treated in the early stages have better outcomes. Repeated thoracentesis with antibiotic administration, chest tube drainage with or without intrapleural fibrinolytic and deoxyribonuclease (DNase), drainage using video-assisted thoracic surgery (VATS), and open surgery are treatment options for empyema [3–6]. VATS offers a shorter duration of pleural drainage and hospital stay and lower rates of mortality and morbidity compared to open surgery [7]. On the other hand, fibrin deposits may cause septations and multiloculation, which will result in longer hospitalization [8, 9].

Aim

In this retrospective study, we compare the efficacy of VATS and fibrinolytic treatment (streptokinase) in patients with stage II empyema.

Material and methods

This is a retrospective study of 46 patients with parapneumonic empyema with multiloculation and septation in the pleural cavity treated with VATS or streptokinase in Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran, between January 2018 and January 2021. Inclusion criteria were 1) parapneumonic empyema

Address for correspondence: Asst. Prof. Shahab Rafieian, Department of Thoracic Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran, e-mail: shrafieian@sina.tums.ac.ir

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with multiloculation and septation, 2) positive bacterial smear or culture, 3) pH < 7.2, glucose < 60 mg/dl or lactate dehydrogenase (LDH) > 1000 U/l. Exclusion criteria were 1) age less than 16 years, 2) empyema due to trauma, post-surgery (lung resection, esophageal surgery, etc.), 3) coagulopathy, 4) administration of streptokinase during the last 2 years, 5) anticoagulant agent administration, 6) pneumothorax before treatment, 7) severe trauma, 8) thrombocytopenia. The demographics, clinical, laboratory, treatment outcomes and complications of patients were collected via the hospital information system.

In the VATS group, under general anesthesia, patients were placed in the lateral decubitus position. By means of three ports, VATS surgery was implemented and drainage of purulent discharge, debridement, septum destruction, pleural space washing and if needed decortication were conducted. In the streptokinase group, patients received streptokinase 250000 U (dissolved in 100 ml normal saline) in the pleural space by means of a chest tube. The chest tube was clamped for 4 h; then it was connected to the suction with a pressure of –20 cm H_2O. This procedure was carried out for 4 consecutive days.

Illness duration before the intervention was the recorded number of days between the symptom presentation and chest tube insertion. Antibiotic therapy duration before the intervention was determined as the recorded number of days between the antibiotic therapy and the operation. Chest drainage after the intervention was the interval between the intervention and chest tube removal. Treatment failure refers to the need for decortication via thoracotomy due to insufficient pulmonary expansion.

Informed consent was obtained from all patients. The protocol of this study was in accordance with the ethical principles laid down in the Declaration of Helsinki and its later amendments. The protocol for this study was approved by the institutional review board and the ethics committee of Tehran University of Medical Sciences.

Statistical analysis

SPSS version 23 (IBM Corp., USA) was used to analyze the variables. Continuous variables are presented as mean (standard deviation) or median (IQR), and categorical variables are shown as frequency (percentage). Student's *t*-test (two-tailed) or the Mann-Whitney *U* test was used to compare continuous variables between study groups. The categorical variables were compared using the χ^2 test or Fisher's exact test. A *p*-value of < 0.05 was considered statistically significant.

Table I. Baseline characteristics of patients in VATS and streptokinase groups

Variable	VATS group (*n* = 28)	Streptokinase group (*n* = 18)	*P*-value
Age [years] mean ± SD	45.6 ±10.6	47.1 ±11.3	0.666[a]
Sex, *n* (%):			0.949[b]
Male	22 (78.6)	14 (77.8)	
Female	6 (21.4)	4 (22.2)	
Past medical history, *n* (%):			0.974[b]
HTN	3 (10.7)	3 (16.7)	
DM	4 (14.3)	3 (16.7)	
COPD	2 (7.1)	1 (5.6)	
IHD	4 (14.3)	2 (11.1)	

P-value of < 0.05 was considered statistically significant. SD – standard deviation, [a]Student *t*-test, [b]χ^2 test.

Results

Baseline characteristics of patients with empyema

A total of 46 patients with parapneumonic empyema with multiloculation and septation were included in this study. Of these, 28 were treated with VATS deloculation, and 18 were treated with streptokinase. Baseline characteristics of participants are detailed in Table I. The two study groups were comparable in terms of age, sex, and past medical history.

Laboratory and clinical parameters before intervention

The groups did not differ significantly in terms of composition and bacteriology of pleural fluid, duration of symptoms, and duration of antibiotic therapy before intervention (Tables II and III).

Clinical outcome after intervention

The average hospital stay was 2.8 ±1.7 days for the VATS group and 7.5 ±3.5 days for the streptokinase group. Hospi-

Table II. Comparison of laboratory findings before intervention between VATS and streptokinase groups

Variable	VATS group (*n* = 28)	Streptokinase group (*n* = 18)	*P*-value
Gram staining, *n* (%):			0.813[a]
Positive	13 (46.4)	9 (50)	
Negative	15 (53.6)	9 (50)	
Serum ESR [mm/h] median [IQR]	40 [25–52]	32.5 [18–45.2]	0.102[b]
Serum WBC [n/mm^3] median [IQR]	15317 [8206–17779]	12029 [7676–14198]	0.132[b]
Pleural LDH [U/l] median [IQR]	716 [361–876]	533 [264–1045]	0.736[b]
Pleural glucose [mg/dl] median [IQR]	57 [45–112]	86.5 [54.25–96.7]	0.727[b]

P-value of < 0.05 was considered statistically significant. [a]χ^2 test, [b]Mann-Whitney *U* test.

Table III. Comparison of clinical parameters before and after intervention between VATS and streptokinase groups

Variable	VATS group (n = 28)	Streptokinase group (n = 18)	P-value
Before intervention:			
Illness duration [days] mean ± SD	8.5 ±2.8	8.0 ±2.4	0.514[a]
AB therapy [days] mean ± SD	6.3 ±2.2	7.3 ±2.2	0.140[a]
After intervention			
Hospital stay [days] mean ± SD	2.8 ±1.7	7.5 ±3.5	< 0.001[a]
Days with fever [days] mean ± SD	1.9 ±0.7	3.0 ±1.6	0.017[a]
Days with drainage [days] mean ± SD	3.0 ±1.6	7.5 ±4.4	< 0.001[a]
Outcome, n (%):			0.042[b]
Success	26 (92.9)	12 (66.7)	
Failure	2 (7.1)	6 (33.3)	

P-value of < 0.05 was considered statistically significant. [a]Independent t test, [b]Fisher exact test.

Table IV. Comparison of side effects between VATS and streptokinase groups

Variable	VATS group (n = 28)	Streptokinase group (n = 18)	P-value
Air leak, n (%)	2 (7.1)	1 (5.6)	0.999[a]
Wound infection, n (%)	1 (3.6)	1 (5.6)	0.999[a]
Bleeding, n (%)	0 (0)	1 (5.6)	0.391[a]
Emphysema, n (%)	1 (3.6)	2 (11.1)	0.552[a]
Mortality, n (%)	0 (0)	0 (0)	0.999[a]

P-value of < 0.05 was considered statistically significant. [a]Fisher exact test.

tal stay was significantly shorter in the VATS compared to the streptokinase group (p < 0.001).

The average number of days with fever was 1.9 ±0.7 for the VATS group and 3.0 ±1.6 for the streptokinase group. Days with fever were significantly fewer in the VATS compared to the streptokinase group (p = 0.017).

The average number of days with drainage was 3.0 ±1.6 for the VATS group and 7.5 ±4.4 days for the streptokinase group. Days with drainage were significantly fewer in the VATS compared to the streptokinase group (p < 0.001).

Finally, the success rate was 92.9% for the VATS group and 66.7% for the streptokinase group, which was significantly higher in the VATS compared to the streptokinase group (p = 0.042).

Adverse events after intervention

No cases of perioperative mortality occurred. Two patients in the VATS and 1 patient in the streptokinase group developed an air leak, which were discharged with a Heimlich bag. The frequency of adverse events, including wound infection, bleeding, and emphysema, did not differ between study groups (p > 0.05) (Table IV).

Discussion

In this study, we compared the outcomes of VATS vs. streptokinase treatment for patients with parapneumonic empyema with multiloculation and septation. Our results demonstrated that treatment of empyema with VATS is superior to streptokinase therapy. In more detail, our experience from the minimally invasive treatment of parapneumonic empyema with multiloculation and septation showed that compared to fibrinolytic treatment (streptokinase), VATS is associated with a shorter hospital stay, shorter febrile period, and lower need for drainage. More importantly, VATS was associated with a lower need for decortication via thoracotomy and thus a greater success rate. Moreover, the complications of these two treatments showed no significant difference.

Pulmonary infection may cause pleural effusion, whereas complicated parapneumonic effusions are not absorbable and need interventions such as drainage [9]. In nearly 60% of patients with bacterial infection, pleural effusion is present, and in nearly 10%, empyema will develop [10]. Accumulation of fibrin deposits, bacterial and inflammatory products are characteristics of empyema, which will lead to longer hospitalization stay and a higher risk of mortality [9]. Fever, pain, allergic reactions, skin rash, and pleural hemorrhage could be detected in patients who underwent intrapleural fibrinolytic therapy [11, 12].

Several previous studies have investigated the superiority of minimally invasive treatment options for parapneumonic empyema. In a previous study, Marhuenda *et al*. randomly assigned children with empyema to two groups: thoracotomy and urokinase. Their results showed that median hospitalization stay and febrile days were not significantly different between the two groups. Treatment failure was 15% in the first group and 10% in the second group [13]. In another study by Cobanoglu *et al*., 54 cases with stage II or III of empyema were treated by fibrinolytic agent application or debridement by VATS. Their results showed that chest tube removal time, duration of hospitalization, and duration of symptoms after intervention were significantly higher for the streptokinase group, which is consistent with our findings [14]. In the study by Samancilar *et al.*, hospitalization stay was significantly higher in the streptokinase group while treatment success was not significantly different [15]. Forty patients were enrolled in the Hewidy *et al.* study and 20 were treated with medical thoracoscopy and the other group was treated by intrapleural instillation of streptokinase. Their results demonstrated that the duration of hospitalization was significantly higher in the second group while complications and mortality rates were similar in both groups [16], which is in accordance with our findings. In a randomized clinical trial by Maskell *et al*., intrapleural streptokinase administration was not associated with a higher mortality rate and longer hospitalization [17].

Froudarakis *et al.* found that intrapleural fibrinolytic therapy for empyema and pleural effusion was effective in 95% [11]. Shrestha *et al.* recommended VATS therapy for the treatment of early or advanced empyema stages [18]. Altogether, the current literature is not consistent regarding the effectiveness of VATS and streptokinase, with some studies showing that VATS is superior and other studies finding these two treatment options to be equally effective. Our experience is consistent with the narrative supporting the superiority of VATS for the treatment of parapneumonic empyema with multiloculation and septation.

This study had some limitations. First, the retrospective design of the study limits the generalizability of our results. Randomized clinical trials are better choices for this purpose. Secondly, this study was conducted in a single tertiary center. Thirdly, the sample size was limited, and thus, larger, multi-centric studies are recommended.

Conclusions

The results of this study show that treatment of empyema with VATS is superior to streptokinase therapy. VATS is associated with a shorter hospital stay, a shorter febrile period, and a lower need for drainage. More importantly, VATS was associated with a lower need for decortication via thoracotomy and thus a greater success rate.

Disclosure

The authors report no conflict of interest.

References

1. Shiraishi Y. Surgical treatment of chronic empyema. Gen Thorac Cardiovasc Surg 2010; 58: 311-6.
2. Reichert M, Hecker M, Witte B, Bodner J, Padberg W, Weigand MA, Hecker A. Stage-directed therapy of pleural empyema. Langenbecks Arch Surg 2017; 402: 15-26.
3. Subotic D, Lardinois D, Hojski A. Minimally invasive thoracic surgery for empyema. Breathe 2018; 14: 302-10.
4. Zahid I, Nagendran M, Routledge T, Scarci M. Comparison of video-assisted thoracoscopic surgery and open surgery in the management of primary empyema. Curr Opin Pulm Med 2011; 17: 255-9.
5. Light RW. Parapneumonic effusions and empyema. Proc Am Thorac Soc 2006; 3: 75-80.
6. Ozcelik C, Ulkü R, Onat S, Ozcelik Z, Inci I, Satici O. Management of postpneumonic empyemas in children. Eur J Cardiothorac Surg 2004; 25: 1072-8.
7. Chambers A, Routledge T, Dunning J, Scarci M. Is video-assisted thoracoscopic surgical decortication superior to open surgery in the management of adults with primary empyema? Interact Cardiovasc Thorac Surg 2010; 11: 171-7.
8. Wait MA, Sharma S, Hohn J, Dal Nogare A. A randomized trial of empyema therapy. Chest 1997; 111: 1548-51.
9. Okumus N, Karaosman S, Kıyan E. Efficacy of intrapleural streptokinase in complicated parapneumonic pleural effusions and empyema. Turk Thorac J 2010; 11: 10-3.
10. Light RW. A new classification of parapneumonic effusions and empyema. Chest 1995; 108: 299-301.
11. Froudarakis ME, Kouliatsis G, Steiropoulos P, Anevlavis S, Pataka A, Popidou M, Mikroulis D, Pneumatikos I, Bouros D. Recombinant tissue plasminogen activator in the treatment of pleural infections in adults. Respir Med 2008; 102: 1694-700.
12. Rahman NM, Maskell NA, West A, Teoh R, Arnold A, Mackinlay C, Peckham D, Davies CW, Ali N, Kinnear W. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. N Engl J Med 2011; 365: 518-26.
13. Marhuenda C, Barceló C, Fuentes I, Guillén G, Cano I, López M, Hernández F, Pérez-Yarza EG, Matute JA, García-Casillas MA. Urokinase versus VATS for treatment of empyema: a randomized multicenter clinical trial. Pediatrics 2014; 134: e1301-7.
14. Cobanoglu U, Sayir F, Bilici S, Melek M. Comparison of the methods of fibrinolysis by tube thoracostomy and thoracoscopic decortication in children with stage II and III empyema: a prospective randomized study. Pediatr Rep 2011; 3: e29.
15. Samancilar O, Akçam T, Kaya SO, Ozturk O, Akcay O, Ceylan KC. The efficacy of VATS and intrapleural fibrinolytic therapy in parapneumonic empyema treatment. Ann Thorac Cardiovasc Surg 2018; 24: 19-24.
16. Hewidy A, Elshafey M. Medical thoracoscopy versus intrapleural fibrinolytic therapy in complicated parapneumonic effusion and empyema. Egypt J Chest Dis Tuberc 2014; 63: 889-96.
17. Maskell NA, Davies CW, Nunn AJ, Hedley EL, Gleeson FV, Miller R, Gabe R, Rees GL, Peto TE, Woodhead MA. UK controlled trial of intrapleural streptokinase for pleural infection. N Engl J Med 2005; 352: 865-74.
18. Shrestha U, Thapa B, Baral R, Sapkota R, Sayami P. Video-thoracoscopic management of empyema thoracis in tertiary level thoracic unit. J Inst Med 2013; 35: 11-3.