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Systematic Review

Comparison of Video-assisted Thoracoscopic Surgery with Thoracotomy for Treatment of Chronic Empyema: A Systematic Review Study

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Abstract

Context: Empyema is a respiratory disease that has increased seriously in the past two decades. The usual treatments for stage III patients include thoracotomy and video-assisted thoracoscopic surgery. Hence, a systematic review of the literature was conducted to investigate the effectiveness and safety of the two procedures.

Methods: Electronic databases of PubMed, Cochrane Library, Scopus, NIHR HTA, Embase, Magiran, and SID were searched from 1990 until the end of June 2018. We used the Critical Appraisal Skills Programme (CASP) checklist for quality assessment. Data analysis was performed in Stata software. The pooled effectiveness results were demonstrated in Forest plats.

Results: Among 2,228 records initially retrieved, four studies entered the final stage of review, among which three were included in the meta-analysis. The findings showed no significant difference between the two methods of thoracoscopic surgery and thoracotomy in the treatment of organizational empyema in terms of duration of surgical operation (MD = 1.33, %95 CI: -0.66 - 3.31, P = 0.18). Postoperative hospital stay was not statistically different between the two surgical methods (MD = 1.68, %95 CI: -0.20 - 3.56, P = 0.08). In terms of safety, there was no particular risk for patients across the surgeries.

Conclusions: There is no statistically significant difference between video-assisted thoracoscopic surgery and thoracotomy in terms of effectiveness and safety. Nevertheless, the results should be considered cautiously due to the little number of included studies.

Keywords: Thoracotomy; Video-assisted Thoracoscopic Surgery; Empyema

1. Context

According to the World Health Organization, lung and respiratory diseases will be among the top three causes of mortality in the world by 2030 (1, 2). Empyema is one of the respiratory diseases that has increased seriously in the past two decades, according to epidemiological studies (3). Empyema is the infection of the pleural space, which is located between the lungs and the chest wall (4). Significant causes of empyema include pulmonary infections, surgical infections, trauma, spontaneous pneumothorax, sub-diaphragmatic infection, and esophageal perforation (5). Most cases of empyema are caused by pneumonia (4). Clinically, empyema is classified into three stages. The first stage or acute phase is exudative effusion, which is usually uncomplicated. The second stage is fibrinopurulent effusion, characterized by the accumulation of thick pus and highly sticky fibers and an abundance of cells. Finally, the third stage is the phase of chronic fibrosis or organizational phase in which the thickening of the peel and the limitation of the lung space occur (4, 6-8).

Therefore, empyema is one of the diseases of the pleural space that may lead to severe and debilitating complications (6). Its incidence is increasing throughout the world (9-13), especially in children, representing a severe illness with high mortality and chronic complications (14). Despite advances in medical care and availability of effective antibiotics, the disease is associated with high mortality (12, 13, 15-22). The high prevalence can be due to increased antibiotic-resistant infections, increased frequency of pneumonia, or weakened immune systems (15). There is also an increase in hospital costs due to illness (8) and delays in referral and surgical interventions, which can increase mortality rates (11).

The purpose of empyema treatment is to restore the lung

to normal functioning (23). During the triple stages of empyema, surgical treatments are usually performed in the third stage, in which there are chronic and debilitating complications, and there is no response to normal therapies (6). The choice of therapeutic methods in empyema depends on several factors, including the stage of disease, the patient's physical and clinical condition, the presence or absence of complications, and so on. Two basic steps must be taken in each method: Effective antibiotics and full fluid drainage of the pleural space. Several methods have been used to empty the pleural space (6), one of which is thoracotomy surgery. Postoperative complications are bleeding, large surgical wounds, wound infections, prolonged anesthesia, and hospital stay, diseases associated with thoracotomy wounds, high postoperativee pain, and a long period of post-surgical repair in open thoracotomy (4, 23-25). The success rate of thoracotomy therapy is more than 90%, but its high mortality rate is doubtful (6).

The technique of video-assisted thoracoscopic surgery (VATS) is associated with fewer complications compared to thoracotomy (26, 27). Thus, VATS is the most common method for empyema. Nevertheless, VATS may turn into thoracotomy if necessary (28). Besides, VATS is a surgical technique that can be performed by a small camera that enters the patient's chest (4). The use of thoracoscopy began in the mid-1990s (29), and its success rate varies from 68 to 93% (30). The advantages of VATS over thoracotomy are the reduction of ulcer opening and low risk of infection. In this method, the recovery time after surgery is shorter, and wound healing is also faster. The main advantage of VATS is that it is associated with open thoracotomy, loss of muscle, and bone fracture that is associated with less pain and a shorter time to return to activity (4). However, due to controversial results in the studies of effectiveness, safety, and side effects of VATS and thoracotomy in the treatment of chronic empyema (4, 25, 31-38), such as mortality, surgical duration, postoperativee bleeding, hospitalization time, chest tube duration, and response to antibiotic therapy, there is still no full assurance in the medical community in choosing one of these methods as the dominant method. However, some studies suggest that VATS can be an appropriate alternative for the treatment of chronic empyema (25, 31-35). But, in contrast to some studies, the superiority of thoracotomy to VATS is shown in the treatment of chronic empyema (36-38). Thus, it is necessary to choose the most appropriate option for the treatment of the disease. Considering the lack of strong evidence, the purpose of this study was to compare the effectiveness and safety of VATS with open thoracotomy in the treatment of organizational empyema.

2. Methods

2.1. Search Strategy

To determine the effectiveness and safety of VATS, the search was conducted in two steps: Electronic and manual search. The databases or major electronic search engines, such as PubMed, Cochrane Library, Scopus, NIHR HTA, Embase, Magiran, and SID, were searched from 1990 until the end of June 2018. The search strategy is attached in Appendix 1 in Supplementary File. The keywords included thoracotomy, video-assisted thoracoscopic surgery, thoracoscopy, and VATS, along with the most commonly used medical synonymous. To ensure that most articles are found, the bibliography of the included studies, along with recent issues of key journals, were handsearched. After completing the search, all the articles were entered into EndNote X8 software.

2.2. Inclusion and Exclusion Criteria

The research population of the study, which included studies of signs and symptoms of chronic empyema, was determined without age and gender restriction. Patients treated with VATS comprised the intervention group, and patients treated with thoracotomy surgery were identified as the comparison group. Linguistic restrictions were applied to select English and Persian studies. In terms of method, randomized clinical trials and cohort studies were included.

Exclusion criteria included studies without a human phase, studies that examined the first and second stages of the disease, studies in which the stage of the disease was unclear, studies in which VATS was converted to thoracotomy, studies with several parallel interventions, and studies that did not describe the methodology and outcomes. Articles in any form of case reports, merely available as abstracts, as well as conference papers and posters, were excluded from the study.

2.3. Data Extraction

For collecting and summarizing related information, a pre-designed preliminary data extraction form was used. Two authors independently extracted data from the full texts of the included articles. The data extraction form included specifying details related to the author's name, the title of the article, year of publication, country of study, type of study, sample size, number of men and women, the average age of the sample, intervention, mortality rate, number of hospital days, duration of antibiotics use, duration of surgery, air leakage, and postoperativee complications (wound infection and bleeding). For data synthesis and probabilistic sensitivity analysis, more information was extracted from the studies. All finally selected studies entered the stage of qualitative synthesis. Quality assessment of the studies was conducted by two researchers independently using the CASP checklist (39), and any dispute was resolved through discussion.

2.4. Statistical Analysis

The final studies that entered the meta-analysis were

used in the quantitative synthesis step, and a meta-analysis was performed to integrate the results and evaluate the effectiveness of the measurements of operating time and postoperative hospital stay using STATA software. Also, the I2 index was used quantitatively to examine heterogeneity. Due to the heterogeneity of the random model, a meta-analysis was used. A p value of less than 0.05 was considered significant. Safety-related information from the final studies was extracted and reported in the text.

3. Results

Based on PICO, inclusion and exclusion criteria, and search strategy, a total of 2,221 records were found, and seven records were added to the findings from the manual searching of journals and the search for sources of studies. Then, all records entered EndNote X8 software. A total of 2,228 records were obtained based on the search.

First, 893 duplicate articles were deleted, and then articles that were unrelated to the title of the study were deleted, with 886 articles removed at this stage. The abstracts of the remaining articles were reviewed, and 359 unrelated articles were removed. In the next step, the full texts of the articles were reviewed to match the PICO index and inclusion and exclusion criteria, and 86 articles were deleted at this stage. Finally, four articles by Reichert et al. (40), Waller et al. (25), Kadkhodaei et al. (4), and Shahin et al. (24) entered the final phase of quality assessment, among which three were included in the meta-analysis, and one article was reported due to the impossibility of combining and meta-analysis. The screening process and the choice of studies are shown according to the PRISMA standard (Figure 1).

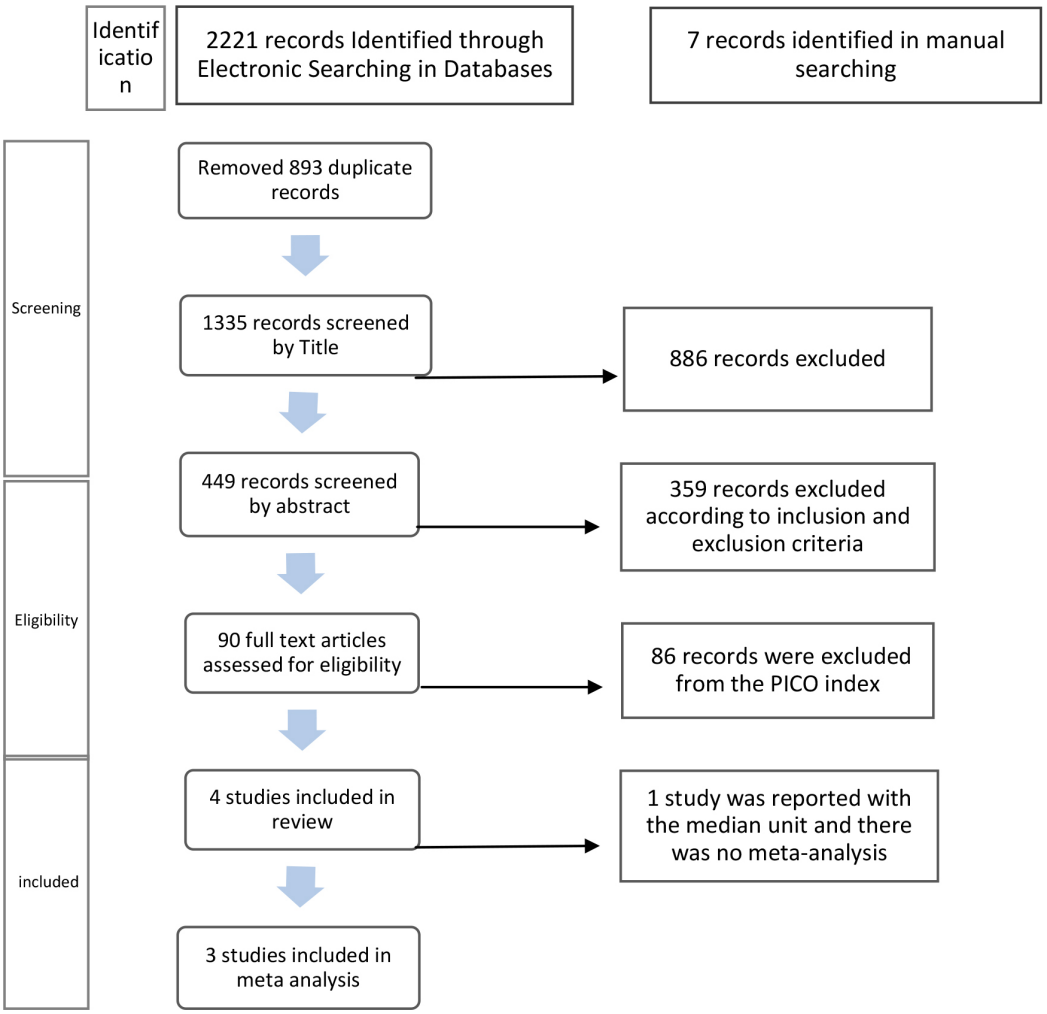

Figure 1. Process of screening articles according to the PRISMA standard

The characteristics of the included studies are summarized in Table 1. Studies were published between 2001 and 2018. The most recent study was Reichert et al.'s study from Germany (40) The studies by Waller et al. (25) and Shahin

et al. (24) were from the UK, and Kadkhodaei et al.'s study (4) was done in Iran. The total number of participants was 367, of whom 285 were men and 82 were women. The largest sample of 217 patients was in Reichert's study, and the lowest number of patients was 48 in Waller's study. A total of 167 patients were surgically treated with thoracotomy and 199 patients with VATS. In the VATS group, 166 patients had successful surgery, and 33 patients converted to thoracotomy.

Table 1. Characteristics of the Articles Entering the Study

Author Name	Reichert et al. (40)	Waller et al. (25)	Kadkhodaei et al. (4)	Shahin et al. (24)
Country of study	Germany	UK	Iran	UK
Publication year	2018	2001	2013	2010
Name of the journal	Surgical Endoscopy and Other Interventional Techniques	Annals of Thoracic Surgery	Razi Journal of Medical Sciences	Interactive Cardiovascular and Thoracic Surgery
Type of study	Retrospective cohort study	Prospective cohort study	Retrospective cross-sectional study	Retrospective
Sample size (Exit)	217 (5)	48 (15)	50	52 (1)
Men/Women	170/47	34/14	43/7	38/14
Age	54.2 ± 15.9 thoracotomy; 61.3 ± 15.6 VATS	43.5 ± 4.1 thoracotomy; 45.4 ± 4.1 VATS	37.6	52
Thoracotomy	107	12	29	19
VATS	110	36	21	32
Conversion to thoracotomy	5	15	7	6
Outcomes examined	Duration of surgery, duration of hospitalization, use of chest tube, duration of antibiotic use, mortality, bleeding, air leak	Duration of surgery, duration of hospitalization, mortality, re-surgery	Duration of surgery, duration of hospitalization, use of chest tube, duration of antibiotic use, mortality, re-surgery	Duration of hospitalization, mortality, bleeding, air leakage, wound infection, persistent space
Conclusion	VATS in late-stage (III) pleural empyema is safe and feasible. The decrease in postoperativee hospitalization demonstrated by adjusted multiple regression analysis may indicate the minimally-invasive approach being safe and more effective for patients.	VATS is a feasible new technique to achieve lung re-expansion in chronic post-pneumonic pleural empyema and has perioperative benefits over thoracotomy.	The therapeutic value of VATS and thoracotomy is the same in the treatment of organizational phase of empyema. However, a multicentric-randomized trial should be performed before VATS becomes the gold standard for the treatment of pleural empyema.	Patients treated with VATS spent less time in hospital and the conversion rate to open procedure for stage III empyema was only 19%, which encourages us to consider VATS as the first treatment choice.

Given that the selected studies were of a cohort type, based on the CASP checklist, two researchers independently evaluated them for quality assessment (39), and any dispute was resolved through discussion. The CASP checklist has no quantitative value, and we qualitatively completed it for each study. All studies received the grade of CASP initial questions. According to the approximate quality assessment, high to low-quality studies were Reichert et al. (40), Kadkhodaei et al. (4), Waller et al. (25), and Shahin et al. (24), respectively.

A meta-analysis was used to integrate the results of studies and evaluate the effectiveness of VATS. At this stage, three studies had the meta-analysis entry conditions, and the study by Shahin did not have the conditions for entering the meta-analysis due to the report on the median duration of hospitalization and a failure to report the surgical time. The meta-analysis results are as follows.

There was no significant difference between the two methods of VATS and thoracotomy in the treatment of organizational empyema in terms of operating time (MD = 1.33, %95 CI: -0.66 - 3.31, P = 0.18). On the other hand, considering that P = 0.00 is less than 0.1, the heterogeneity was statistically significant. The I2 coefficient for the surgical duration was 97.1%, which indicated a high degree of heterogeneity. Figure 2 shows the meta-analysis results for the operating time.

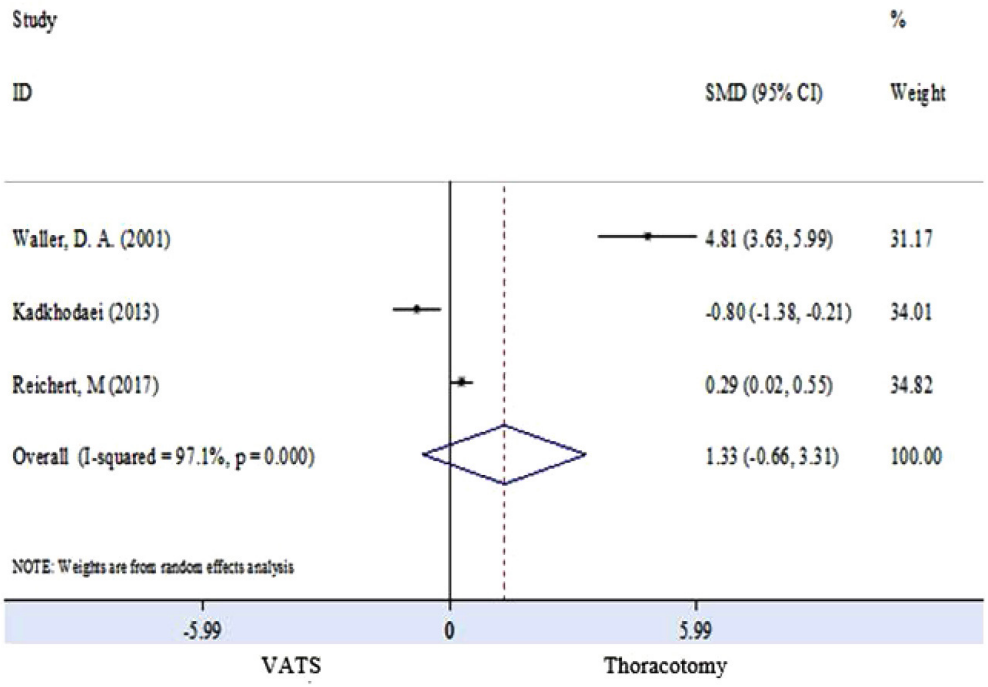

Figure 2. Meta-analysis of operating time in two methods of VATS and thoracotomy

There was no significant difference in terms of postoperative hospital stay between VATS and thoracotomy in the treatment of chronic empyema (MD = 1.68, %95 CI: -0.20 - 3.56, P = 0.08). The heterogeneity and I2 coefficient were 96.9% for the postoperative hospital stay. The result of P value showed heterogeneity in the postoperative hospital stay, and its value was statistically significant (P = 0.00), and due to the amount of I2, there was significant heterogeneity. Figure 3 shows the meta-analysis results for the duration of postoperative hospital stay.

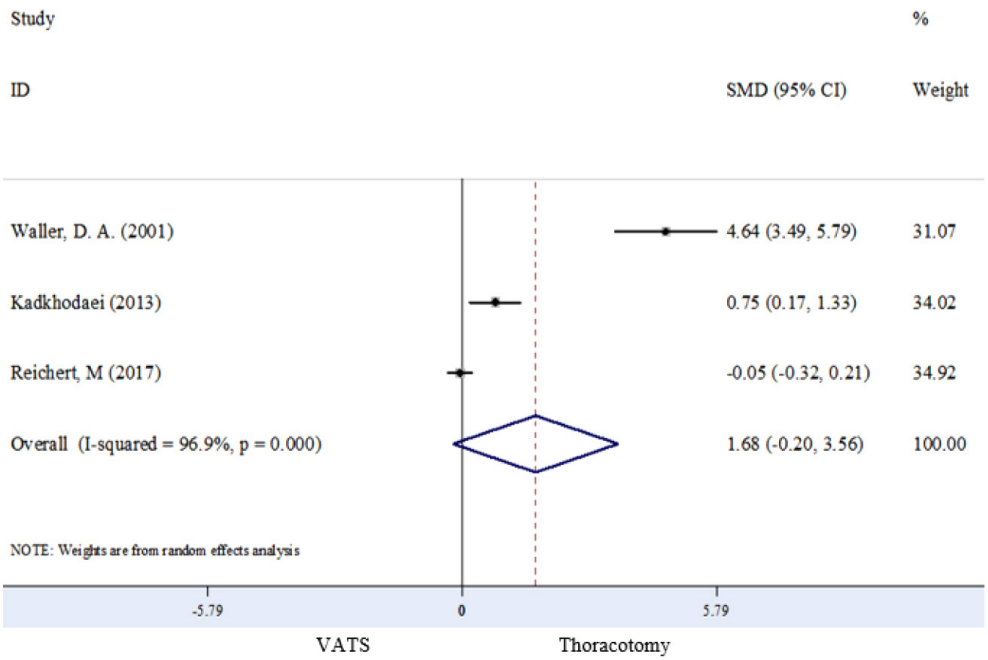

Figure 3. Meta-analysis of postoperative hospital stay in VATS and thoracotomy

In the study by Reichert et al. (40) with a sample of 217 persons, 107 patients were treated surgically with thoracotomy, and 110 patients were treated surgically with VATS. Among the VATS group, five patients converted to the thoracotomy method and were excluded from the study when evaluating the results. In the group converted to thoracotomy, only was surgical time reported as 241.8 ± 41.3 min, and we did not enter them into the meta-analysis. According to the results, the surgical time was shorter in the VATS group than in the thoracotomy group, and the longest duration in patients was when they turned from thoracoscopy to thoracotomy. The reason for the change was the lack of surgery progression in three cases and pulmonary artery bleeding in two cases. The duration of the chest tube was 6.6 ± 3.4 days in the thoracotomy group and 6.8 ± 4.2 days in the VATS group. The use of chest tube was after seven days of surgery in the thoracotomy group of 39 persons and in the VATS group was 37 persons and also the use of chest tube that is more than ten days, 16 in thoracotomy group and 18 in VATS group.

The duration of antibiotic use after thoracotomy and thoracoscopy was 10.2 ± 14.6 and 15.5 ± 28.8 days, respectively. The duration of postoperativee antibiotic treatment was significantly longer in the VATS group than in the thoracotomy group. The total duration of hospitalization was 28.6 ± 25.5 days in the thoracotomy group and 28.1 ± 30.7 days in the VATS group. The duration of intensive care unit stay after surgery was 114.6 ± 241.0 hours in the thoracotomy group and 238.4 ± 660.2 hours in the thoracoscopy group, which was considerably longer in the thoracoscopy group.

In the study by Waller et al. (25), 12 patients performed thoracotomy, and 36 patients performed VATS, of whom 21 patients were successfully treated and 15 patients converted to thoracotomy. The main reason for the conversion was the lack of access to the cavity. The results of this study were reported separately for 15 patients for whom the surgical time was 119.6 ± 13.5 min, and the duration of hospitalization was 8.5 ± 1.3 days, and none of the above-mentioned cases entered the meta-analysis. Surgical time and hospital stay were significantly longer in the thoracotomy group than in the VATS group. The Lung expansion after surgery was 98.8 ± 0.6% for the thoracotomy group, 98.6 ± 0.7% for the VATS group, and 98.5 ± 0.7% for the group turning into thoracotomy.

In the study by Kadkhodaie et al. (4), 29 patients were treated surgically with thoracotomy and 21 patients with VATS. Fourteen patients successfully completed VATS, and four patients converted to thoracotomy. The duration of chest tube use after surgery in the thoracotomy and VATS groups was 28 ± 8.6 and 20 ± 5.3 days, respectively, which was shorter in the thoracoscopy group. The duration of antibiotic use after thoracotomy and VATS was 27 ± 8.3 and 20 ± 51 days, respectively, which was shorter in the VATS group. The duration of antibiotic use and the need for drainage through the chest tube before and after operation was more in the thoracotomy group than in the VATS group, and the success rate in the two groups did not have a significant difference.

In the study by Shahin et al. (24), 19 patients had thoracotomy, and 32 patients had VATS, among whom six VATS patients converted to thoracotomy. The duration of hospitalization was eight and five days for the thoracotomy and VATS groups, respectively, indicating a shorter time of hospitalization in VATS. As the above cases were reported as median, it was not possible to combine them with other study results.

The safety results of VATS in comparison with thoracotomy are as follows. In the study by Reichert et al. (40), five cases of the VATS group converted to thoracotomy. Total complications were reported for 61 cases in the thoracotomy group and 55 cases in the VATS group. In the thoracotomy group, there were seven cases of mortality, and there were 10 cases in the VATS group. Three and five cases of recurrence and seven and 12 cases of air leak were reported, respectively. Mechanical ventilation was reported in 62 patients of the thoracotomy group for 71.4 ± 216.9 hours and 31 patients of the VATS group for 371.0 ± 1025 hours. The amounts of lost blood during surgery in the thoracotomy and thoracoscopy groups were reported to be 779.9 ± 837.4 and 494.3 ± 477.2 ml, respectively. Five cases in the thoracotomy group and six cases in the thoracoscopy group had bleeding. The total blood transfusion was 53 cases in the thoracotomy group and 46 cases in the VATS group. Antibiotic treatment after surgery was performed in 78 patients of the thoracotomy group and 86 patients of the thoracoscopy group. Two patients in the thoracotomy group and two patients in the VATS group had gastrointestinal infection and 13 and eight cases had pneumonia, respectively. Long-term drainage by chest tube after surgery lasting for more than 10 days was reported in 21 cases of the thoracotomy group and 20 patients of the thoracoscopy group. Re-drain occurred in 12 and eight people, respectively. Acute respiratory failure was reported in six patients of the thoracotomy group, and two patients of the VATS group and chronic respiratory failure was reported in nine and 12 patients and acute renal failure in three and four cases, respectively (40).

In the study by Waller et al. (25), there was no death in the thoracotomy group. One case of death was reported in the VATS group and one case of death in the converted group. There was no recurrence in any of the groups (25).

In the study by Kadkhodaei et al. (4), there were three cases of mortality in the thoracotomy group and two cases in the VATS group. Overall mortality was 6.5%, which was higher in the thoracotomy group than in the VATS group. The need for re-surgical treatment was reported in four cases of thoracotomy and four cases of VATS. The longer the hospital stay before surgery and the later the surgery, the lower the success rate and the higher the need for re-surgery and mortality (4).

In the study by Shahin et al. (24), there was no death

in any of the groups. There were three cases of air leak in the thoracotomy group. One case of wound infection was reported in the thoracotomy group and one case of bleeding in the VATS group. There was one case of persistent space in the thoracotomy group and two cases in the VATS group (24).

Most complications were reported in Reichert et al.'s article (40), which was due to the high number of patients and the study of various complications. The most common side effects were mortality that was reported in four studies.

4. Discussion

According to the World Health Organization, lung and respiratory diseases will be among the top three causes of mortality in the world by 2030 (1, 2). The fifth cause of death in Iran is now respiratory illness (41). Empyema is one of the respiratory diseases that has increased significantly in the past two decades, according to epidemiological studies (3). On the other hand, there is a need for significant resources for management and treatment (42), and rapid treatment reduces hospital costs, deaths, and side effects (42). Appropriate treatment of pleural empyema depends on the disease stage (43). It is undeniable that stage 3 empyema requires surgery to control disease; however, the choice of the most appropriate surgical method is still debatable (40).

With the introduction of video-assisted thoracoscopic surgery in the early 1990s, a less invasive alternative for decortication was proposed (44). Of course, the current standard surgical procedure is open thoracotomy. However, with the increasing experience with VATS, the management of the last stage of empyema is possible with minimally invasive surgery (43). Making decisions to choose a surgical procedure for treating these patients involves lightweight and heavyweight benefits and disadvantages of each method. In this secondary research (systematic review and meta-analysis), an analytical descriptive study with a health technology assessment approach was done to assess VATS in terms of effectiveness and safety compared with thoracotomy. It was given to provide sufficient information for decision making about choosing the most appropriate surgical method to use by policy makers and planners.

The systematic review and meta-analysis of the three studies to compare VATS and thoracotomy surgery in the treatment of organizational phase of empyema showed no significant differences in terms of the duration of postoperativee hospital stay and operating time, suggesting that VATS does not reduce the duration of surgery and hospitalization compared to thoracotomy. This can be due to the difference in experience and the use of VATS by surgeons. The main limitation of VATS is that it heavily depends on the surgeon's skill (45); however, in the meta-analysis performed by Pan et al. (46), the surgical duration of VATS was shorter than that of thoracotomy. This may be due to the reporting of the results as a combination of stages two and three of the disease, without splitting the two stages.

On the other hand, there was heterogeneity among the results of studies concerning the amount of postoperativee hospital stay and operating time, which may be due to the small number of articles obtained and samples in the study. This was due to the elimination of several studies because of a failure to identify the stage of the disease or reporting its outcomes as a combination of stages two and three, without splitting the two stages. Also, the duration of surgery was not precisely calculated in Kadkhodaei et al.'s study (4), and was reported to be approximate, which reduced the accuracy of the duration of surgery. However, the effectiveness of the VATS method in terms of mortality rate, survival rate, quality of life, duration of admission, duration of intensive care unit stay, duration of chest tube use, and the use of antibiotics after surgery is not known due to lack of evidence and studies in this field.

Investigating safety studies of the VATS technique showed that the complications reported in the studies may also occur with thoracotomy surgery, and all four studies confirmed the safety of the VATS technique. The only case reported with thoracoscopy was conversion to thoracotomy during surgery that cannot be due to the safety of the procedure. However, there was no specific information on the reasons for conversion in studies.

5. Conclusions

This review showed no difference between video-assisted thoracoscopic surgery and open thoracotomy in terms of effectiveness and safety. There was no difference in the operating time and postoperativee hospital stay in meta-analysis although, given the high heterogeneity, this cannot be relied upon. There is not enough evidence about mortality rate, survival rate, quality of life, duration of intensive care unit admission, duration of chest tube use, and the use of antibiotics after surgery. On the other hand, the examination of the evidence suggested the safety of video-assisted thoracoscopic surgery for patients. It is suggested that clinical trials be conducted on patients with organizational empyema, taking into account the mentioned outcomes and without conversion from thoracoscopy to thoracotomy to evaluate the effectiveness. Also, qualitative studies on patients' satisfaction with VATS and thoracotomy surgery and its role in patients' quality of life and ethical, social, organizational, and legal aspects of the video-assisted thoracoscopic surgery approach are suggested for making comparisons with thoracotomy surgery in the treatment of chronic empyema.

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