International Surgery

Lasers for Pulmonary Resections

--Manuscript Draft--

Manuscript Number:	INTSURG-D-22-00014R4
Full Title:	Lasers for Pulmonary Resections
Article Type:	Manuscript
Keywords:	Key words: Lasers; Mechanical staplers; Lobectomy
Corresponding Author:	Yi Zhang Xuanwu Hospital beijing, CHINA
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Xuanwu Hospital
Corresponding Author's Secondary Institution:	
First Author:	Yi Zhang
First Author Secondary Information:	
Order of Authors:	Yi Zhang
Order of Authors Secondary Information:	
Abstract:	Objective: To evaluate the effectiveness and safety of lasers compared with mechanical staplers in pulmonary resections using a qualitative and systematic study. Methods: Among randomized controlled trials (RCTs) published in the Medline, Web of Science, Cochrane Controlled Trials Register (CCTR), and clinical trial databases from June 1979 to October 2022, three studies were synthesized to compare the efficacy and safety of lasers and mechanical staplers in pulmonary resections. Results: The operation time in the laser group was longer than that in the staple group (weighted mean difference (WMD) = 12.00 min, 95% confidence interval (CI): -11.66 to 35.66 for McKenna, WMD = 39.00 min, 95% CI: 21.82 to 56.18 for Marulli, and WMD = 2.00 min, 95% CI: -15.10 to 19.10 for Scanagatta). However, the length of hospital stay in the laser group was comparable to that of the staple group (WMD = -2.00 days, 95% CI: -7.36 to 3.36 for McKenna, WMD = -3.00 days, 95% CI: -6.29 to 0.29 for Marulli, and WMD = 0.00 days, 95% CI: -1.69 to 1.69 for Scanagatta). The risk ratio (RR) for persistent air leaks in the laser group versus the staple group was RR = 0.68 (95% CI: 0.38 to 1.22) for McKenna, RR = 0.67 (95% CI: 0.12 to 3.61) for Marulli, and RR = 1.07 (95% CI: 0.53 to 2.16) for Scanagatta. Conclusion: The lasers have proven to be effective and comparable to the mechanical stapler technique in pulmonary resections, with the exception of an improved dyspnea index.

Lasers for Pulmonary Resections

Xingsheng Liu[1], Peilong Zhang[1], Yi Zhang[2]*

Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University Lung Cancer Center

*Correspondence author: Yi Zhang (zhangyixwhosp@xwh.ccmu.edu.cn)

Xingsheng Liu (M.D.), Peilong Zhang (M.D.), Yi Zhang (M.D.)

A shortened title

Lasers for Pulmonary Resections

Conflict of Interests

The authors declare no conflict of interests.

Acknowledgments

None

Funding

None

Lasers for Pulmonary Resections

Xingsheng Liu[1], Peilong Zhang[1], Yi Zhang[2]*

Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University Lung Cancer Center

*Correspondence author: Yi Zhang (zhangyixwhosp@xwh.ccmu.edu.cn)

Xingsheng Liu (M.D.), Peilong Zhang (M.D.), Yi Zhang (M.D.)

A shortened title

Lasers for Pulmonary Resections

Conflict of Interests

The authors declare no conflict of interests.

Acknowledgments

None

Abstract

Objective: Our goal is to evaluate the effectiveness and safety of lasers compared with mechanical staplers in pulmonary resections using a qualitative and systematic manner.

Summary of background data: Laser technique is effective in pulmonary resections among patients with pulmonary disease. However, systematic review of this technique need to be made to ascertain its key role in thoracosurgery domain.

Methods: For randomized controlled trials (RCTs) published in Medline, Web of Science, Cochrane Controlled Trials Register (CCTR), and clinical trial databases from June 1979 to October 2022, we identified and synthesized three studies to compare the efficacy and safety of lasers and mechanical staplers in pulmonary resections based on selection criteria. Two reviewers independently assessed trial bias and extracted data to make a using a qualitative systematic review.

Results: The three RCTs were obtained using surgery approach of video-assisted thoracoscopic surgery (VATS). The operating time of the laser group was longer than that of the staple group in Marulli study (WMD = 12.00 min, 95% CI -11.66 to 35.66 for McKenna, WMD = 39.00 min, 95% CI 21.82 to 56.18 for Marulli and WMD = 2.00 min, 95% CI -15.10 to 19.10 for Scanagatta), while the hospital stay of the laser group was comparative with that of the staple group (WMD = -2.00d, 95% CI -7.36 to 3.36 for McKenna, WMD = -3.00d, 95% CI -6.29 to 0.29 for Marulli and WMD = 0.00d 95% CI -1.69 to 1.69 for Scanagatta). Risk ratio (95%CI), expressed as the persistent air leaks of the laser group vs the staple group, was RR = 0.68 (95%CI 0.38 to 1.22) for McKenna, RR = 0.67 (95%CI 0.12 to 3.61) for Marulli, RR = 1.07 (95%CI 0.53 to 2.16) for Scanagatta, respectively and expressed as pneumothorax, RR = 7.09 (95%CI 0.90 to 55.95) for McKenna, RR = 0.33 (95%CI 0.01 to 7.76) for Marulli, RR = 6.28 (95%CI 0.34 to 117.39) for Scanagatta, respectively. At the 6th month follow-up, the mean postoperative forced expiratory volume in 1 second of the staple group was significantly improved compared with that of the laser group. The clinical symptoms and dyspnea index were improved by more than one grade 8 of 33 (24%) patients in the laser group and 26 of 39 (66%) patients in the staple group ($p = 0.003$).

Conclusions: The lasers are effective and comparable with mechanical stapler technique in pulmonary resections except for the improved for dyspnea index.

Key words: Lasers – Mechanical staplers –Lobectomy

The field of resection for patients with malignant lung diseases and some nonmalignant conditions (emphysema, pulmonary sequestrations, abscesses, bronchiectasis, and chronic pulmonary infections with localized parenchymal disruption) has attracted more and more attention. Electrocautery is widely used for pulmonary parenchymal resections, but persistent air leaks and pneumothorax often occur, and additional tools including mechanical staplers and lasers have been introduced to reduce these complications. In recent decades, more and more surgeons have generally accepted the mechanical staplers to cut and suture pulmonary tissues in anatomic lung resections [1]. Especially, in laparoscopic pulmonary resections, surgical staplers are fired in a staggered formation simultaneously to cut and ligate vessels and bronchus using a two-dimensional planar mode.

Since the 1960s, lasers defined as light amplification by stimulated emission of radiation have been considered a preferable choice for a variety of medical operations, including coagulation, evaporation and cutting of surgical tissues [2]. In 1980s, various types of lasers had been introduced to a range of thoracic surgical operations, especially most commonly presented in pulmonary metastasectomies [3,4]. In 1990s, laser bullectomy was employed by Wakabayashi and co-workers for patients with diffuse emphysema [5]. In the following years, the application of lasers (in particular 1318 nm neodymium-YAG lasers or 1908 nm Thulium lasers) has achieved illustrious haemostasis and airsealing effects on pulmonary resections [6]. On the other hand, lung parenchymal tissue contains 80 % of liquid components and few parenchymal tissue components, so these organs are suitable tissues for lasers [7].

Little information is available about the efficacy and safety of lasers used in the surgical treatment of pulmonary disease. The current published articles for laser used in pulmonary resections are mostly focused on case series and retrospective trials. It is not clear whether these patients who undergo pulmonary resections will benefit most from lasers, and the optimal patient selection criteria are unclear. Although several prospective studies have compared these different laser techniques with mechanical staplers in pulmonary resections, the wide heterogeneity of patient selection and assessment of outcomes in these published literatures results in a lack of sufficient evidences for their benefits and harms, which is the reason why we carried out this review. In addition, the efficacy and safety of these two kinds of pneumonectomy are still controversial. Based on these trials, we compared the current efficacy and safety of the two surgical applications through reviewing the RCTs in a narrative and systematic manner.

Material and Methods

Search Strategy

We attempted to identify publications of all relevant studies in Medline, Web of Science, CCTR, and clinical trial databases between June 1979 and october 2022 using the following search strategies: ((((lung[MeSH Terms]) OR (lung[Title/Abstract])) OR (lungs[Title/Abstract])) OR (pulmonary[Title/Abstract])) AND ((((lasers[MeSH Terms])) OR (laser[Title/Abstract])) OR (lasers[Title/Abstract])). The relevant articles were entered into the Science Citation Index (SCI) to retrieve reports citing them and the reference list of all the articles obtained were filtered.

Inclusion and Exclusion Criteria

The randomized controlled trials, cohort trials, and retrospective studies aiming to compare laser techniques vs mechanical staplers in pulmonary resections were included in our review. The surgical approach was thoracoscopy. Bilateral and unilateral procedures were considered, and only English articles were included for systematic review. We excluded studies if they exclusively focused on nonoperative management, nonthoracoscopic procedures, were performed using a less common approach: needlescopic approaches or single-incision approaches, and only a single arm study.

Selection of Studies

The title and abstract of literature considered to be potentially relevant were independently filtered by two reviewers (XS Liu and PL Zhang). After retrieving the full text of these articles, we filtered the studies using the inclusion and exclusion criteria. We resolved differences in study selection by consulting with the third reviewer (Y Zhang). We determined the excluded studies based on the above criteria and stated the reason. When selected studies were included in our research, we could use the following domains to assess their methodological quality and extract and analyze data.

Quality Assessment

Two reviewers (Liu and Qian) evaluated the methodology of included literatures independently based on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. Each participant had an equal chance of being allocated to a group by randomized method, indicating that the risk of bias in random allocation was low. If the investigators in charge of patient selection could not determine the next treatment in allocation (e.g. central central randomization; sealed, opaque, sequentially numbered assignment envelopes), the risk of bias in allocation concealment was considered low (e.g. central randomization; sealed, opaque and sequentially numbered assignment envelopes). If the patients were blind to the treatment assignment, the risk of bias of blinding of participants and personnel was considered low. If participants of the outcome assignment were blind to group assignment, the risk of bias of blinding of outcome assessors was considered low. The risk of incomplete outcome data caused by the use of intent-to-treat analysis in research was considered low. If researchers provided pre-specified published protocol available for comparison, the risk of bias of selective reporting was considered low. We categorized each item of bias as a low risk, a high risk, or unclear, and presented this information in a supplemental table 1. Disagreements in the bias assessment were resolved through discussions with a third expert (Y Zhang).

Outcome Measures

The pre-specified outcomes of our qualitative meta-analysis were as follows: efficacy outcomes (operating time, hospital stay and re-operation) and safety outcomes (mortality, prolonged air leak, pneumothorax, and other complications). Disability and health status, lung function, and analysis of costs were also included in our analysis.

Data Extraction

XS Liu extracted data on author, year of publication, patient characteristics (age, gender, BMI, history of smoking, and lung function), study design, criteria for the study, and clinical outcome from the trials using a standardized form (Table 1 and Table 2) and major clinical outcomes for qualitative analysis. PL Zhang or Y Zhang independently cross checked the extracted data. Any disagreement was resolved through discussion.

Statistical Analysis

RevMan 4.0.4 (The Cochrane Collaboration, Wintertree Software inc., Canada) was used to summarize relative risk (RR) and weight mean difference (WMD) which were expressed as point estimates in square brackets with a 95% confidence interval. Because only three articles were included in our research, we performed a qualitative systematic review without summarizing the results. When one was included in the 95% confidence interval of RR, there was no difference in outcomes between the two groups. When zero was included in the 95% confidence interval of the weighted mean difference, the difference between the two groups was considered not significant. We transformed median and range into mean and standard deviation according to the method of Hozo if necessary [8].

Results

Inclusion

The initial electronic searches identified titles from which abstracts were obtained to identify 799 potentially relevant studies of pulmonary resection comparing laser techniques with mechanical staplers from 1975 to 2022. After initially removing duplicated articles and screening titles and abstracts, 22 publications were included for full-text search. Due to the reasons below, 19 articles were excluded: lack of comparative trials (n = 10), lack of laser techniques (n =4), lack of mechanical staplers (n = 3) and low quality (n = 2). Only three studies appeared to meet the criteria for this review to qualitative analysis (Fig. 1). Two reviewers (XS Liu, K Qian) independently assessed the searching results and resolved the disagreements through discussion. The flow chart of the searching process is given, as shown in Fig. 1.

Author Verification

The author of this study submitted the data extraction sheets to verify the accuracy of information obtained from the paper and to provide other relevant information if necessary. But no reply was received.

Assessment of Quality

The risk of random sequence generation was low in one trial of Scanagatta and unclear in the other two trials. For all trials, the risks of allocation concealment, blinding of outcome assessment and selective reporting were considered unclear, while the risk of blinding of participants was considered high due to the nature of surgery procedure. The risk of incomplete outcome data was unclear in two trials and low in the trial of Scanagatta due to the intent-to-treat analysis (Fig. 2, Fig. 3, and supplemental table 1).

Characteristics of Participants

The participants were divided into the laser group and the staple group in all included studies. Participants in the study of McKenna had diffuse emphysema treated by bullectomy using VATS approach [9]. Participants in the study of Marulli had lung cancer scheduled for elective pulmonary lobectomy usingVATS approach [10]. Participants in the remaining study were immunocompetent adults scheduled for anatomic pulmonary resection using VATS approach [1]. Our study included 188 participants in total. The study population consisted mainly of 134 males (71%) with an average age of 67 years (Table 1).

Type of Intervention

In the laser group, a variety of types of lasers were used: a contact tip Nd:YAG laser (10 W) [9], a non-contact Thulium laser (40 W) [10], and a photocoagulation-mode Thulium laser [1]. Scanagatta did not report the laser power output. For the staple group, McKenna et al. used a 60 mm endoscopic stapler (ELC 60, Ethicon, Inc., Somerville, N.J.) with bovine pericardium (Peristrips, Biovascular, St. Paul, Minn.) to buttress the staples [9]; Marulli et al. applied standard staplers to complete pulmonary fissures [10]; and Scanagatta completed the division of fissures using staplers with sealants when needed [1] (Table 2).

Efficacy Outcomes

Operating Time

In general, the operating time is defined as the time from skin incision to skin closure. In both studies, the laser group and the staple group did not have significant difference in the operating time (WMD = 12.00 min, 95% CI -11.66 to 35.66) and WMD = 2.00 min, 95% CI -15.10 to 19.10). However, Marulli reported the mechanical staplers apparently decreased the operating time compared with the lasers (WMD = 39 min.00, 95% CI 21.82 to 56.18) (Fig. 4A).

Hospital Stay

In the three trials, there was no significant difference in MD between the two instruments (WMD = -2.00d, 95% CI -7.36 to 3.36 for McKenna; WMD = -3.00d, 95% CI -6.29 to 0.29 for Marulli, and WMD = 0.00d, 95% CI -1.69 to 1.69 for Scanagatta) (Fig. 4B).

Re-operation

RR (95%CI), expressed as the re-operation rate of the laser group vs the staple group, was RR = 1.18, 95% CI 0.08 to 18.17 for McKenna and RR =2.69, 95% CI 0.11 to 63.96 for Scanagatta. Marulli reported no patients required re-operation in both groups. (Fig. 4C).

Adverse Events

Mortality

McKenna reported no perioperative deaths in the laser group, and one death caused by contralateral tension pneumothorax in the staple group. No perioperative mortality was observed in both groups of Marulli and Scanagatta.

Persistent Air Leaks

The persistent air leaks were identified when air leaks lasted more than 7 days [11]. There was no significant difference in the incidence of persistent air leaks between the laser group and the staple group in the three studies (RR = 0.68, 95%: CI 0.38 to 1.22; RR = 0.67, 95% CI: 0.12 to 3.61; and RR =1.07, 95% CI: 0.53 to 2.16) (Fig. 4D).

Pneumothorax

McKenna reported six patients developed delayed pneumothorax in the laser group and one developed tension pneumothorax in the contralateral lung in the staple group (RR = 7.09, 95% CI: 0.90 to 55.95). Marulli reported pneumothorax in only one patient in the staple group (RR = 0.33, 95% CI 0.01 to 7.76). Scanagatta reported 3 cases of delayed pneumothorax in the laser group (RR = 6.28, 95% CI: 0.34 to 117.39) (Fig. 4E).

Other Complications

Our review indicated that there was no difference in the incidences of other complications included fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus in both groups (RR = 0.16, 95% CI: 0.01 to 3.13 for McKenna; RR = 0.42, 95% CI: 0.09 to 1.96 for Marulli and RR =1.11, 95% CI 0.41 to 3.03 for Scanagatta) (Fig. 4F).

Disability and Health Status

McKenna reported breathlessness probably measured using Medical Research Council or Rand Dyspnea scale, showing that 8/33 (24%) patients in the laser group had improved dyspnea by more than one grade ,compared with 26/39 (66%) patients in the staple group ($p = 0.003$). Marulli and Scanagatta did not report these information in their studies.

Lung Function

McKenna reported a mean improvement in FEV1 at six months of 13.4 ± 5.5% and 32.9 ± 4.8% in the laser group and the staple group respectively ($p < 0.01$). The increase in Forced Vital

Capacity (FVC) was similar: 6 ± 3% (the laser group) vs 21 ± 6% (the staple group) ($p = 0.07$). Marulli and Scanagatta did not report changes of lung function after pulmonary surgery.

Cost Analysis

Marulli found the hospitalization cost in the stapler group was significantly higher than that in the laser group: 5,650 ± 3,063 euros for the laser group vs 8,147±5,785 euros for the staple group ($P = 0.01$). Additionally, an equal significant result of Scanagatta reported the intraoperative cost of the two procedures: 807 ± 212 euros for the laser group vs 1,092 ± 274 euros for the staple group ($P < 0.0001$).

Discussion

The efficacy and safety of lasers and mechanical staplers for pulmonary surgery were compared through three RCT trials identified by systematically searching the literatures. Currently, the evaluation of various standard techniques widely applied in pulmonary resection involving surgical stapling, electrocautery and hand sewing, and their possible roles in thoracic surgical operations as surgical tools was performed. The effect of Nd:YAG laser on pulmonary parenchyma was first demonstrated by Minton in 1967, when it was used to precisely excise the tumor in an experimental model [12]. In the next few years, a new generation laser system, the 2,010-nm wavelength emitted by Cyber TM Thulium laser, was introduced into the field of thoracosurgery. Since the 1980s, the application of lasers in resections of pulmonary tissue was widely accepted and the effect on parenchyma-sparing surgery of various types of lasers was evaluated [13]. To our knowledge, there were no systematic reviews to compare the two procedures.

Considering the efficacy of the two methods, there was no significant difference in the operating time between the laser group and the staple group in two trials, while Marulli demonstrated that the use of mechanical staplers significantly decreased the operating time compared with lasers, which may be due to their application of a second Thulium laser irradiation at low power (20 W) in a defocused mode treating the dissected surface of the residual lobe, so as to achieve the ideal aero-haemostatic effect on lung parenchyma. In our systematic reviews, the overall hospital stay was shorter in the laser group, though without statistical significance, possibly due to the limited patients enrolled. Three RCTs regarding the occurrence of re-operation showed no difference in the re-operation rate between the two groups. In our clinical experience, the lasers had the same efficacy with the mechanical staplers.

Factors influencing post-operative persistent air leaks include underlying lung diseases such as emphysema, fibrosis, tuberculosis or malignancies, lymphangioleiomyomatosis, and intrathoracic adhesions, elderly patient (>75 years), and lower diffusion capacity for carbon monoxide [14]. In the case of pulmonary traumatization and dissection, persistent air leaks causes prolonged intercostal drainage, associated pain, increased immobility, and risk of further complications such as pneumonia, empyema, and pulmonary embolism [15]. Although many efforts have been made to reduce the occurrence of parenchymal air leaks after pneumonectomy, the desirable surgical techniques or tools to reduce or prevent this complication have not been determined, and in most cases, standard techniques cannot provide adequate sealing in patients. Mineo et al. reported three positive effects of laser irradiation (cutting, coagulation, and tissue shrinkage), leading to sealing through the progressive collapse of alveolar septa which produces a thick and multilayer air-proof membrane [16]. But we observed no significant difference in the incidence of persistent air leaks between the two groups, possibly because the sample sizes in these studies were small. However, the laser group showed a daily trend of reduction in the proportion of patients with persistent air leaks.

Additionally, pneumothorax and other complications, such as fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus were distributed equally in each group. Considering the high blood vessel density, it is necessary to remove the lung parenchyma with laser with a strong coagulation ability and excellent cutting performance. With respect to the mortality outcome, the results of three RCTs included concluded that the outcome of mortality was rare (<5% staple group event rate). These results can be explained by the features of laser, which can be strongly absorbed by water, resulting in excellent coagulation (low coagulation depth of only 0.2 mm) and aero-hemostatic effects, and maximal preservation of surrounding normal tissues.

Rogers and his colleagues found that removal of large bullae in isolated bullous disease and bullous emphysema may lead to improved expiratory flow and airway conductance, which may be due to the improved elastic recoil [17,18]. In 1996, a RCT containing two procedures (laser bullectomy and lung reduction surgery with staples) was conducted using VATS method, and the results strongly support the superiority of unilateral staple procedures over laser methods in terms of improved quality of life, pulmonary function and probably reduced oxygen dependence [9]. Although the study of Marulli and Scanagatta did not report these outcomes, they applied a new generation of laser (a Cyber TM Thulium surgical laser system) which may result in a better clinical status and pulmonary function in the laser group [1,10].

Above all, we summarized some advantages of laser mechanisms in pulmonary resections: (a) the minimal surrounding tissue damage and maximal preservation of normal parenchyma elasticity, (b) the aero-haemostatic effect, (c) the relative safety of major bronchi and vessels during the dissection, and (d) the system is cost-effective. Collectively, we concluded that laser may be an efficacy and safe alternative to the standard stapling technique except for the improved for dyspnea index.

The studies in this systematic review include many biases in terms of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. Long term health outcomes are unclear. It is hoped that further RCTs will be necessary to better define these issues establishing the advantages of the laser techniques over mechanical staplers.

Reference

1. Scanagatta P, Furia S, Bille A, Duranti L, Girelli L, Tavecchio LD *et al*. Thulium laser versus staplers for anatomic pulmonary resections with incomplete fissures: negative results of a randomized trial. *Tumori 2014*; **100** (3):259-64

2. Klämpfl F. Tissue Ablation and Laser Surgery. *J Biophotonics* 2017; **10** (10):1238-9

3. LoCicero J, 3rd, Hartz RS, Frederiksen JW, Michaelis LL. New applications of the laser in pulmonary surgery: hemostasis and sealing of air leaks. *Ann Thorac Surg* 1985; **40** (6):546-50

4. Moghissi K, Dench M, Goebells P. Experience in non-contact Nd YAG laser in pulmonary surgery. A pilot study. *Eur J Cardiothorac Surg* 1988; **2** (2):87-94

5. Wakabayashi A, Brenner M, Kayaleh RA, Berns MW, Barker SJ, Rice SJ *et al.* Thoracoscopic carbon dioxide laser treatment of bullous emphysema. *Lancet* 1991; **337** (8746):881-3

6. Stefani A, Oricchio F, Cinquepalmi A, Aramini B, Morandi U. Is laser-assisted resection preferable to lobectomy for pulmonary metastasectomy? *Lasers Med Sci* 2020; **35**(3):611-20

7. Panagiotopoulos N, Patrini D, Lawrence D, Scarci M, Mitsos S. Pulmonary metastasectomy and laser-assisted resection. *J Thorac Dis* 2018; **10** (Suppl 17):S1930-S1933

8. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005; **5**:13

9. McKenna RJ, Brenner M, Gelb AF, Mullin M, Singh N, Peters H *et al.* A randomized, prospective trial of stapled lung reduction versus laser bullectomy for diffuse emphysema. *J Thorac Cardiovasc Surg* 1996; **111**(2):317-21

10. Marulli G, Droghetti A, Di Chiara F, Calabrese F, Rebusso A, Perissinotto E *et al*. A prospective randomized trial comparing stapler and laser techniques for interlobar fissure completion during

pulmonary lobectomy. *Lasers Med Sci* **28** (2):505-11

11. Abu-Hijleh M, Styrvoky K, Anand V, Woll F, Yarmus L, Machuzak MS *et al.* Intrabronchial valves for air leaks after lobectomy, segmentectomy, and lung volume reduction surgery. Lung 2019; **197** (5):627-33

12. Minton JP, Andrews NC, Jesseph JE. Pulsed laser energy in the management of multiple pulmonary metastases. *J Thorac Cardiovasc Surg* 1967; **54** (5):707-13

13. da Cunha Moraes G, Vitoretti LB, de Brito AA, Alves CE, de Oliveira NCR, Dos Santos Dias A et al. Low-level laser therapy reduces lung inflammation in an experimental model of chronic obstructive pulmonary disease involving P2X7 receptor. *Oxid Med Cell Longev* 2018; **2018**:6798238

14. Shintani Y, Funaki S, Ose N, Kawamura T, Kanzaki R, Minami M *et al*. Air leak pattern shown by digital chest drainage system predict prolonged air leakage after pulmonary resection for patients with lung cancer. *J Thorac Dis* 2018; **10** (6):3714-21

15. Yeung C, Ghazel M, French D, Japkowicz N, Gottlieb B, Maziak D *et al*. Forecasting pulmonary air leak duration following lung surgery using transpleural airflow data from a digital pleural drainage device. *J Thorac Dis* **10** (Suppl 32):S3747-S3754

16. Mineo TC, Cristino B, Ambrogi V, Natali GL, Casciani CU. Usefulness of the Nd:YAG laser in parenchyma-sparing resection of pulmonary nodular lesions. *Tumori* **80** (5):365-9

17. Rogers RM, DuBois AB, Blakemore WS. Effect of removal of bullae on airway conductance and conductance volume ratios. J Clin Invest 1968; **47** (12):2569-79

18. Gelb AF, Gold WM, Nadel JA. Mechanisms limiting airflow in bullous lung disease. *Am Rev Respir Dis* 1973; 107 (4):571-8

Figure legend

Figure.1 PRISMA flowchart for literature searching.

Figure.2 A risk of bias graph.

Figure.3 A risk of bias summary (“+”low risk;“?”, unclear risk;“-”,high risk).

Figure.4 Forest plot of operation time (A), hospital stay (B), re-operation (C), persistent air leaks (D), pneumothorax (E), other complications (F).

Lasers for Pulmonary Resections: A Qualitative Systematic Review

Xingsheng Liu[1], Peilong Zhang[1], Yi Zhang[2]*

Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University Lung Cancer Center

*Correspondence author: Yi Zhang (zhangyixwhosp@xwh.ccmu.edu.cn)

Xingsheng Liu (M.D.), Peilong Zhang (M.D.), Yi Zhang (M.D.)

A shortened title

Lasers for Pulmonary Resections

Conflict of Interests

The authors declare no conflict of interests.

Acknowledgments

None

Funding

None

Lasers for Pulmonary Resections: A Qualitative Systematic Review

Xingsheng Liu[1], Peilong Zhang[1], Yi Zhang[2]*

Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University Lung Cancer Center

*Correspondence author: Yi Zhang (zhangyixwhosp@xwh.ccmu.edu.cn)

Xingsheng Liu (M.D.), Peilong Zhang (M.D.), Yi Zhang (M.D.)

A shortened title

Lasers for Pulmonary Resections

Conflict of Interests

The authors declare no conflict of interests.

Acknowledgments

None

Abstract

Objective: Our goal is to evaluate the effectiveness and safety of lasers compared with mechanical staplers in pulmonary resections using a qualitative and systematic manner.

Summary of background data: Laser technique is effective in pulmonary resections among patients with pulmonary disease. However, systematic review of this technique need to be made to ascertain its key role in thoracosurgery domain.

Methods: For RCTs published in Medline, Web of Science, Cochrane Controlled Trials Register (CCTR), and clinical trial databases from June 1979 to October 2022, we identified and synthesized three studies to compare the efficacy and safety of lasers and mechanical staplers in pulmonary resections based on selection criteria. Two reviewers independently assessed trial bias and extracted data to make a using a qualitative systematic review.

Results: The three RCTs were obtained using surgery approach of video-assisted thoracoscopic surgery (VATS). The operating time of the laser group was longer than that of the staple group in Marulli study (WMD = 12.00 min, 95% CI -11.66 to 35.66 for McKenna, WMD = 39.00 min, 95% CI 21.82 to 56.18 for Marulli and WMD = 2.00 min, 95% CI -15.10 to 19.10 for Scanagatta), while the hospital stay of the laser group was comparative with that of the staple group (WMD = -2.00d, 95% CI -7.36 to 3.36 for McKenna, WMD = -3.00d, 95% CI -6.29 to 0.29 for Marulli and WMD = 0.00d 95% CI -1.69 to 1.69 for Scanagatta). Risk ratio (95%CI), expressed as the persistent air leaks of the laser group vs the staple group, was RR = 0.68 (95%CI 0.38 to 1.22) for McKenna, RR = 0.67 (95%CI 0.12 to 3.61) for Marulli, RR = 1.07 (95%CI 0.53 to 2.16) for Scanagatta, respectively and expressed as pneumothorax, RR = 7.09 (95%CI 0.90 to 55.95) for McKenna, RR = 0.33 (95%CI 0.01 to 7.76) for Marulli, RR = 6.28 (95%CI 0.34 to 117.39) for Scanagatta, respectively. At the 6th month follow-up, the mean postoperative forced expiratory volume in 1 second of the staple group was significantly improved compared with that of the laser group. The clinical symptoms and dyspnea index were improved by more than one grade 8 of 33 (24%) patients in the laser group and 26 of 39 (66%) patients in the staple group (p = 0.003).

Conclusions: The lasers are effective and comparable with mechanical stapler technique in pulmonary resections.

Key words: Lasers – Mechanical staplers –Pulmonary resections

The field of resection for patients with malignant lung diseases and some nonmalignant conditions (emphysema, pulmonary sequestrations, abscesses, bronchiectasis, and chronic pulmonary infections with localized parenchymal disruption) has attracted more and more attention. Electrocautery is widely used for pulmonary parenchymal resections, but persistent air leaks and pneumothorax often occur, and additional tools including mechanical staplers and lasers have been introduced to reduce these complications. In recent decades, more and more surgeons have generally accepted the mechanical staplers to cut and suture pulmonary tissues in anatomic lung resections [1]. Especially, in laparoscopic pulmonary resections, surgical staplers are fired in a staggered formation simultaneously to cut and ligate vessels and bronchus using a two-dimensional planar mode.

Since the 1960s, lasers defined as light amplification by stimulated emission of radiation have been considered a preferable choice for a variety of medical operations, including coagulation, evaporation and cutting of surgical tissues [2]. In 1980s, various types of lasers had been introduced to a range of thoracic surgical operations, especially most commonly presented in pulmonary metastasectomies [3,4]. In 1990s, laser bullectomy was employed by Wakabayashi and co-workers for patients with diffuse emphysema [5]. In the following years, the application of lasers (in particular 1318 nm neodymium-YAG lasers or 1908 nm Thulium lasers) has achieved illustrious haemostasis and airsealing effects on pulmonary resections [6]. On the other hand, lung parenchymal tissue contains 80 % of liquid components and few parenchymal tissue components, so these organs are suitable tissues for lasers [7].

Little information is available about the efficacy and safety of lasers used in the surgical treatment of pulmonary disease. The current published articles for laser used in pulmonary resections are mostly focused on case series and retrospective trials. It is not clear whether these patients who undergo pulmonary resections will benefit most from lasers, and the optimal patient selection criteria are unclear. Although several prospective studies have compared these different laser techniques with mechanical staplers in pulmonary resections, the wide heterogeneity of patient selection and assessment of outcomes in these published literatures results in a lack of sufficient evidences for their benefits and harms, which is the reason why we carried out this review. In addition, the efficacy and safety of these two kinds of pneumonectomy are still controversial. Based on these trials, we compared the current efficacy and safety of the two surgical applications through reviewing the RCTs in a narrative and systematic manner.

Material and Methods

Search Strategy

We attempted to identify publications of all relevant studies in Medline, Web of Science, CCTR, and clinical trial databases between June 1979 and october 2022 using the following search strategies: ((((lung[MeSH Terms]) OR (lung[Title/Abstract])) OR (lungs[Title/Abstract])) OR (pulmonary[Title/Abstract])) AND ((((lasers[MeSH Terms])) OR (laser[Title/Abstract])) OR (lasers[Title/Abstract])). The relevant articles were entered into the Science Citation Index (SCI) to retrieve reports citing them and the reference list of all the articles obtained were filtered.

Inclusion and Exclusion Criteria

The randomized controlled trials, cohort trials, and retrospective studies aiming to compare laser techniques vs mechanical staplers in pulmonary resections were included in our review. The surgical approach was thoracoscopy. Bilateral and unilateral procedures were considered, and only English articles were included for systematic review. We excluded studies if they exclusively focused on nonoperative management, nonthoracoscopic procedures, or were performed using a less common approach: needlescopic approaches or single-incision approaches.

Selection of Studies

The title and abstract of literature considered to be potentially relevant were independently filtered by two reviewers (XS Liu and PL Zhang). After retrieving the full text of these articles, we filtered the studies using the inclusion and exclusion criteria. We resolved differences in study selection by consulting with the third reviewer (Y Zhang). We determined the excluded studies based on the above criteria and stated the reason. When selected studies were included in our research, we could use the following domains to assess their methodological quality and extract and analyze data.

Quality Assessment

Two reviewers (Liu and Qian) evaluated the methodology of included literatures independently based on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. Each participant had an equal chance of being allocated to a group by randomized method, indicating that the risk of bias in random allocation was low. If the investigators in charge of patient selection could not determine the next treatment in allocation (e.g. central central randomization; sealed, opaque, sequentially numbered assignment envelopes), the risk of bias in allocation concealment was considered low (e.g. central randomization; sealed, opaque and sequentially numbered assignment envelopes). If the patients were blind to the treatment assignment, the risk of bias of blinding of participants and personnel was considered low. If participants of the outcome assignment were blind to group assignment, the risk of bias of blinding of outcome assessors was considered low. The risk of incomplete outcome data caused by the use of intent-to-treat analysis in research was considered low. If researchers provided pre-specified published protocol available for comparison, the risk of bias of selective reporting was considered low. We categorized each item of bias as a low risk, a high risk, or unclear, and presented this information in a supplemental table 1. Disagreements in the bias assessment were resolved through discussions with a third expert (Y Zhang).

Outcome Measures

The pre-specified outcomes of our qualitative meta-analysis were as follows: efficacy outcomes (operating time, hospital stay and re-operation) and safety outcomes (mortality, prolonged air leak, pneumothorax, and other complications). Disability and health status, lung function, and analysis of costs were also included in our analysis.

Data Extraction

XS Liu extracted data on author, year of publication, patient characteristics (age, gender, BMI, history of smoking, and lung function), study design, criteria for the study, and clinical outcome from the trials using a standardized form (Table 1 and Table 2) and major clinical outcomes for qualitative analysis. PL Zhang or Y Zhang independently cross checked the extracted data. Any disagreement was resolved through discussion.

Statistical Analysis

RevMan 4.0.4 (The Cochrane Collaboration, Wintertree Software inc., Canada) was used to summarize relative risk (RR) and weight mean difference (WMD) which were expressed as point estimates in square brackets with a 95% confidence interval. Because only three articles were included in our research, we performed a qualitative systematic review without summarizing the results. When one was included in the 95% confidence interval of RR, there was no difference in outcomes between the two groups. When zero was included in the 95% confidence interval of the weighted mean difference, the difference between the two groups was considered not significant. We transformed median and range into mean and standard deviation according to the method of Hozo if necessary [8].

Results

Inclusion

The initial electronic searches identified titles from which abstracts were obtained to identify 799 potentially relevant studies of pulmonary resection comparing laser techniques with mechanical staplers from 1975 to 2022. After initially removing duplicated articles and screening titles and abstracts, 22 publications were included for full-text search. Due to the reasons below, 19 articles were excluded: lack of comparative trials (n = 10), lack of laser techniques (n =4), lack of mechanical staplers (n = 3) and low quality (n = 2). Only three studies appeared to meet the criteria for this review to qualitative analysis (Fig. 1). Two reviewers (XS Liu, K Qian) independently assessed the searching results and resolved the disagreements through discussion. The flow chart of the searching process is given, as shown in Fig. 1.

Author Verification

The author of this study submitted the data extraction sheets to verify the accuracy of information obtained from the paper and to provide other relevant information if necessary. But no reply was received.

Assessment of Quality

The risk of random sequence generation was low in one trial of Scanagatta and unclear in the other two trials. For all trials, the risks of allocation concealment, blinding of outcome assessment and selective reporting were considered unclear, while the risk of blinding of participants was considered high due to the nature of surgery procedure. The risk of incomplete outcome data was unclear in two trials and low in the trial of Scanagatta due to the intent-to-treat analysis (Fig. 2, Fig. 3, and supplemental table 1).

Characteristics of Participants

The participants were divided into the laser group and the staple group in all included studies. Participants in the study of McKenna had diffuse emphysema treated by bullectomy using VATS approach [9]. Participants in the study of Marulli had lung cancer scheduled for elective pulmonary lobectomy usingVATS approach [10]. Participants in the remaining study were immunocompetent adults scheduled for anatomic pulmonary resection using VATS approach [1]. Our study included 188 participants in total. The study population consisted mainly of 134 males (71%) with an average age of 67 years (Table 1).

Type of Intervention

In the laser group, a variety of types of lasers were used: a contact tip Nd:YAG laser (10 W) [9], a non-contact Thulium laser (40 W) [10], and a photocoagulation-mode Thulium laser [1]. Scanagatta did not report the laser power output. For the staple group, McKenna et al. used a 60 mm endoscopic stapler (ELC 60, Ethicon, Inc., Somerville, N.J.) with bovine pericardium (Peristrips, Biovascular, St. Paul, Minn.) to buttress the staples [9]; Marulli et al. applied standard staplers to complete pulmonary fissures [10]; and Scanagatta completed the division of fissures using staplers with sealants when needed [1] (Table 2).

Efficacy Outcomes

Operating Time

In general, the operating time is defined as the time from skin incision to skin closure. In both studies, the laser group and the staple group did not have significant difference in the operating time (WMD = 12.00 min, 95% CI -11.66 to 35.66) and WMD = 2.00 min, 95% CI -15.10 to 19.10). However, Marulli reported the mechanical staplers apparently decreased the operating time compared with the lasers (WMD = 39 min.00, 95% CI 21.82 to 56.18) (Fig. 4A).

Hospital Stay

In the three trials, there was no significant difference in MD between the two instruments (WMD = -2.00d, 95% CI -7.36 to 3.36 for McKenna; WMD = -3.00d, 95% CI -6.29 to 0.29 for Marulli, and WMD = 0.00d, 95% CI -1.69 to 1.69 for Scanagatta) (Fig. 4B).

Re-operation

RR (95%CI), expressed as the re-operation rate of the laser group vs the staple group, was RR = 1.18, 95% CI 0.08 to 18.17 for McKenna and RR =2.69, 95% CI 0.11 to 63.96 for Scanagatta. Marulli reported no patients required re-operation in both groups. (Fig. 4C).

Adverse Events

Mortality

McKenna reported no perioperative deaths in the laser group, and one death caused by contralateral tension pneumothorax in the staple group. No perioperative mortality was observed in both groups of Marulli and Scanagatta.

Persistent Air Leaks

The persistent air leaks were identified when air leaks lasted more than 7 days [11]. There was no significant difference in the incidence of persistent air leaks between the laser group and the staple group in the three studies (RR = 0.68, 95%: CI 0.38 to 1.22; RR = 0.67, 95% CI: 0.12 to 3.61; and RR =1.07, 95% CI: 0.53 to 2.16) (Fig. 4D).

Pneumothorax

McKenna reported six patients developed delayed pneumothorax in the laser group and one developed tension pneumothorax in the contralateral lung in the staple group (RR = 7.09, 95% CI: 0.90 to 55.95). Marulli reported pneumothorax in only one patient in the staple group (RR = 0.33, 95% CI 0.01 to 7.76). Scanagatta reported 3 cases of delayed pneumothorax in the laser group (RR = 6.28, 95% CI: 0.34 to 117.39) (Fig. 4E).

Other Complications

Our review indicated that there was no difference in the incidences of other complications included fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus in both groups (RR = 0.16, 95% CI: 0.01 to 3.13 for McKenna; RR = 0.42, 95% CI: 0.09 to 1.96 for Marulli and RR =1.11, 95% CI 0.41 to 3.03 for Scanagatta) (Fig. 4F).

Disability and Health Status

McKenna reported breathlessness probably measured using Medical Research Council or Rand Dyspnea scale, showing that 8/33 (24%) patients in the laser group had improved dyspnea by more than one grade ,compared with 26/39 (66%) patients in the staple group ($p = 0.003$). Marulli and Scanagatta did not report these information in their studies.

Lung Function

McKenna reported a mean improvement in FEV1 at six months of 13.4 ± 5.5% and 32.9 ± 4.8% in the laser group and the staple group respectively ($p < 0.01$). The increase in Forced Vital

Capacity (FVC) was similar: 6 ± 3% (the laser group) vs 21 ± 6% (the staple group) (p = 0.07). Marulli and Scanagatta did not report changes of lung function after pulmonary surgery.

Cost Analysis

Marulli found the hospitalization cost in the stapler group was significantly higher than that in the laser group: 5,650 ± 3,063 euros for the laser group vs 8,147±5,785 euros for the staple group (P = 0.01). Additionally, an equal significant result of Scanagatta reported the intraoperative cost of the two procedures: 807 ± 212 euros for the laser group vs 1,092 ± 274 euros for the staple group (P < 0.0001).

Discussion

The efficacy and safety of lasers and mechanical staplers for pulmonary surgery were compared through three RCT trials identified by systematically searching the literatures. Currently, the evaluation of various standard techniques widely applied in pulmonary resection involving surgical stapling, electrocautery and hand sewing, and their possible roles in thoracic surgical operations as surgical tools was performed. The effect of Nd:YAG laser on pulmonary parenchyma was first demonstrated by Minton in 1967, when it was used to precisely excise the tumor in an experimental model [12]. In the next few years, a new generation laser system, the 2,010-nm wavelength emitted by Cyber TM Thulium laser, was introduced into the field of thoracosurgery. Since the 1980s, the application of lasers in resections of pulmonary tissue was widely accepted and the effect on parenchyma-sparing surgery of various types of lasers was evaluated [13]. To our knowledge, there were no systematic reviews to compare the two procedures.

Considering the efficacy of the two methods, there was no significant difference in the operating time between the laser group and the staple group in two trials, while Marulli demonstrated that the use of mechanical staplers significantly decreased the operating time compared with lasers, which may be due to their application of a second Thulium laser irradiation at low power (20 W) in a defocused mode treating the dissected surface of the residual lobe, so as to achieve the ideal aero-haemostatic effect on lung parenchyma. In our systematic reviews, the overall hospital stay was shorter in the laser group, though without statistical significance, possibly due to the limited patients enrolled. Three RCTs regarding the occurrence of re-operation showed no difference in the re-operation rate between the two groups. In our clinical experience, the lasers had the same efficacy with the mechanical staplers.

Factors influencing post-operative persistent air leaks include underlying lung diseases such as emphysema, fibrosis, tuberculosis or malignancies, lymphangioleiomyomatosis, and intrathoracic adhesions, elderly patient (>75 years), and lower diffusion capacity for carbon monoxide [14]. In the case of pulmonary traumatization and dissection, persistent air leaks causes prolonged intercostal drainage, associated pain, increased immobility, and risk of further complications such as pneumonia, empyema, and pulmonary embolism [15]. Although many efforts have been made to reduce the occurrence of parenchymal air leaks after pneumonectomy, the desirable surgical techniques or tools to reduce or prevent this complication have not been determined, and in most cases, standard techniques cannot provide adequate sealing in patients. Mineo et al. reported three positive effects of laser irradiation (cutting, coagulation, and tissue shrinkage), leading to sealing through the progressive collapse of alveolar septa which produces a thick and multilayer air-proof membrane [16]. But we observed no significant difference in the incidence of persistent air leaks between the two groups, possibly because the sample sizes in these studies were small. However, the laser group showed a daily trend of reduction in the proportion of patients with persistent air leaks.

Additionally, pneumothorax and other complications, such as fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus were distributed equally in each group. Considering the high blood vessel density, it is necessary to remove the lung parenchyma with laser with a strong coagulation ability and excellent cutting performance. With respect to the mortality outcome, the results of three RCTs included concluded that the outcome of mortality was rare (<5% staple group event rate). These results can be explained by the features of laser, which can be strongly absorbed by water, resulting in excellent coagulation (low coagulation depth of only 0.2 mm) and aero-hemostatic effects, and maximal preservation of surrounding normal tissues.

Rogers and his colleagues found that removal of large bullae in isolated bullous disease and bullous emphysema may lead to improved expiratory flow and airway conductance, which may be due to the improved elastic recoil [17,18]. In 1996, a RCT containing two procedures (laser bullectomy and lung reduction surgery with staples) was conducted using VATS method, and the results strongly support the superiority of unilateral staple procedures over laser methods in terms of improved quality of life, pulmonary function and probably reduced oxygen dependence [9]. Although the study of Marulli and Scanagatta did not report these outcomes, they applied a new generation of laser (a Cyber TM Thulium surgical laser system) which may result in a better clinical status and pulmonary function in the laser group [1,10].

Above all, we summarized some advantages of laser mechanisms in pulmonary resections: (a) the minimal surrounding tissue damage and maximal preservation of normal parenchyma elasticity, (b) the aero-haemostatic effect, (c) the relative safety of major bronchi and vessels during the dissection, and (d) the system is cost-effective. Collectively, we concluded that laser may be an efficacy and safe alternative to the standard stapling technique in terms of operating time, hospital stay, re-operation, mortality, persistent air leaks, pneumothorax, post-operational complications, and cost.

The studies in this systematic review include many biases in terms of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. Long term health outcomes are unclear. It is hoped that further RCTs will be necessary to better define these issues establishing the advantages of the laser techniques over mechanical staplers.

Reference

1. Scanagatta P, Furia S, Bille A, Duranti L, Girelli L, Tavecchio LD *et al*. Thulium laser versus staplers for anatomic pulmonary resections with incomplete fissures: negative results of a randomized trial. *Tumori 2014*; **100** (3):259-64

2. Klämpfl F. Tissue Ablation and Laser Surgery. *J Biophotonics* 2017; **10** (10):1238-9

3. LoCicero J, 3rd, Hartz RS, Frederiksen JW, Michaelis LL. New applications of the laser in pulmonary surgery: hemostasis and sealing of air leaks. *Ann Thorac Surg* 1985; **40** (6):546-50

4. Moghissi K, Dench M, Goebells P. Experience in non-contact Nd YAG laser in pulmonary surgery. A pilot study. *Eur J Cardiothorac Surg* 1988; **2** (2):87-94

5. Wakabayashi A, Brenner M, Kayaleh RA, Berns MW, Barker SJ, Rice SJ *et al.* Thoracoscopic carbon dioxide laser treatment of bullous emphysema. *Lancet* 1991; **337** (8746):881-3

6. Stefani A, Oricchio F, Cinquepalmi A, Aramini B, Morandi U. Is laser-assisted resection preferable to lobectomy for pulmonary metastasectomy? *Lasers Med Sci* 2020; **35**(3):611-20

7. Panagiotopoulos N, Patrini D, Lawrence D, Scarci M, Mitsos S. Pulmonary metastasectomy and laser-assisted resection. *J Thorac Dis* 2018; **10** (Suppl 17):S1930-S1933

8. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005; **5**:13

9. McKenna RJ, Brenner M, Gelb AF, Mullin M, Singh N, Peters H *et al.* A randomized, prospective trial of stapled lung reduction versus laser bullectomy for diffuse emphysema. *J Thorac Cardiovasc Surg* 1996; **111**(2):317-21

10. Marulli G, Droghetti A, Di Chiara F, Calabrese F, Rebusso A, Perissinotto E *et al*. A prospective randomized trial comparing stapler and laser techniques for interlobar fissure completion during

pulmonary lobectomy. *Lasers Med Sci* **28** (2):505-11

11. Abu-Hijleh M, Styrvoky K, Anand V, Woll F, Yarmus L, Machuzak MS *et al.* Intrabronchial valves for air leaks after lobectomy, segmentectomy, and lung volume reduction surgery. Lung 2019; **197** (5):627-33

12. Minton JP, Andrews NC, Jesseph JE. Pulsed laser energy in the management of multiple pulmonary metastases. *J Thorac Cardiovasc Surg* 1967; **54** (5):707-13

13. da Cunha Moraes G, Vitoretti LB, de Brito AA, Alves CE, de Oliveira NCR, Dos Santos Dias A et al. Low-level laser therapy reduces lung inflammation in an experimental model of chronic obstructive pulmonary disease involving P2X7 receptor. *Oxid Med Cell Longev* 2018; **2018**:6798238

14. Shintani Y, Funaki S, Ose N, Kawamura T, Kanzaki R, Minami M *et al*. Air leak pattern shown by digital chest drainage system predict prolonged air leakage after pulmonary resection for patients with lung cancer. *J Thorac Dis* 2018; **10** (6):3714-21

15. Yeung C, Ghazel M, French D, Japkowicz N, Gottlieb B, Maziak D *et al*. Forecasting pulmonary air leak duration following lung surgery using transpleural airflow data from a digital pleural drainage device. *J Thorac Dis* **10** (Suppl 32):S3747-S3754

16. Mineo TC, Cristino B, Ambrogi V, Natali GL, Casciani CU. Usefulness of the Nd:YAG laser in parenchyma-sparing resection of pulmonary nodular lesions. *Tumori* **80** (5):365-9

17. Rogers RM, DuBois AB, Blakemore WS. Effect of removal of bullae on airway conductance and conductance volume ratios. J Clin Invest 1968; **47** (12):2569-79

18. Gelb AF, Gold WM, Nadel JA. Mechanisms limiting airflow in bullous lung disease. *Am Rev Respir Dis* 1973; 107 (4):571-8

Figure legend

Figure.1 PRISMA flowchart for literature searching.

Figure.2 A risk of bias graph.

Figure.3 A risk of bias summary (“+”low risk;“?”, unclear risk;“-”,high risk).

Figure.4 Forest plot of operation time (A), hospital stay (B), re-operation (C), persistent air leaks (D), pneumothorax (E), other complications (F).

Figure.1

Click here to access/download;Figure;Firgure.1.tif

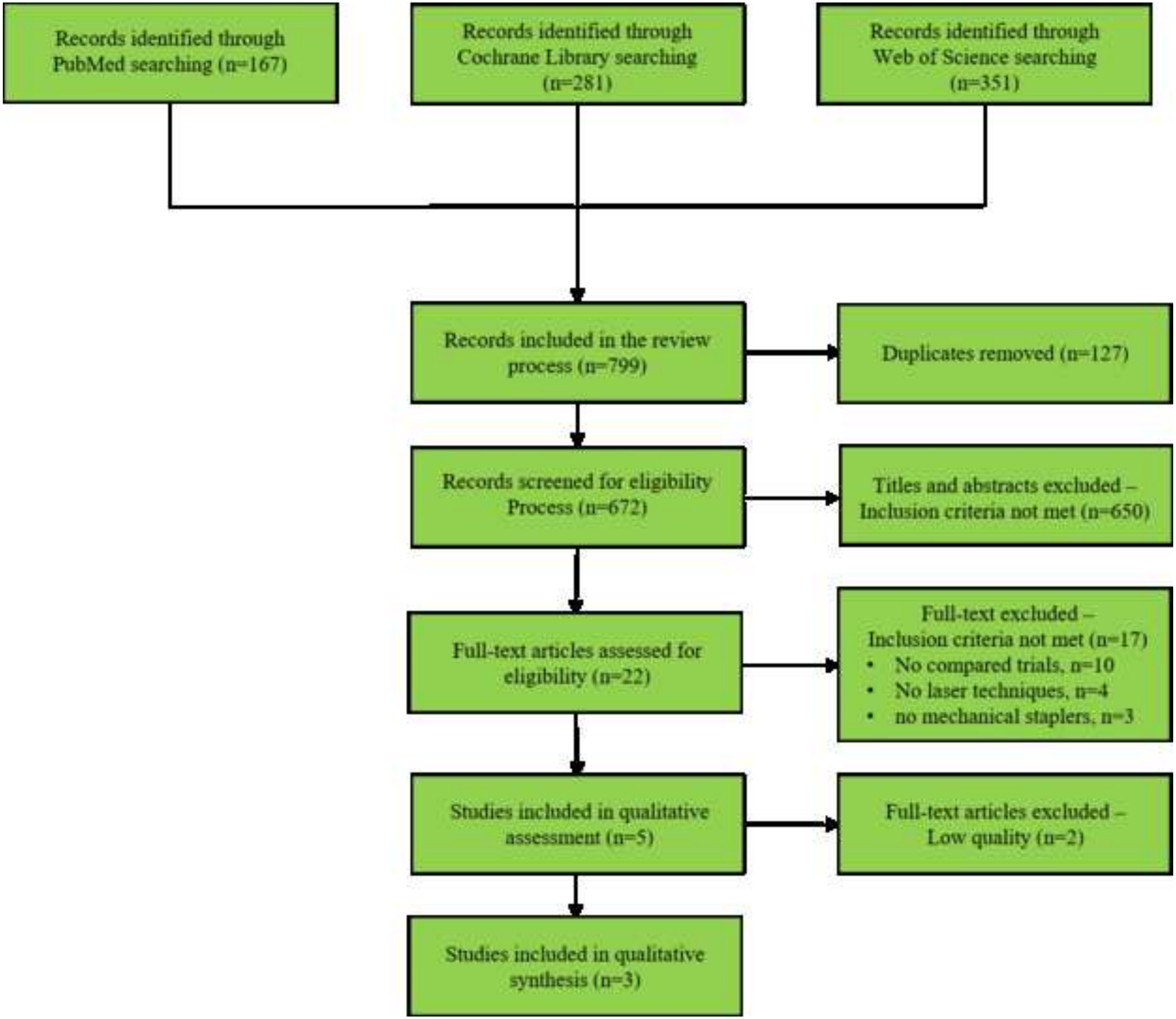


Figure.2

Click here to access/download;Figure;Figure.2.pdf

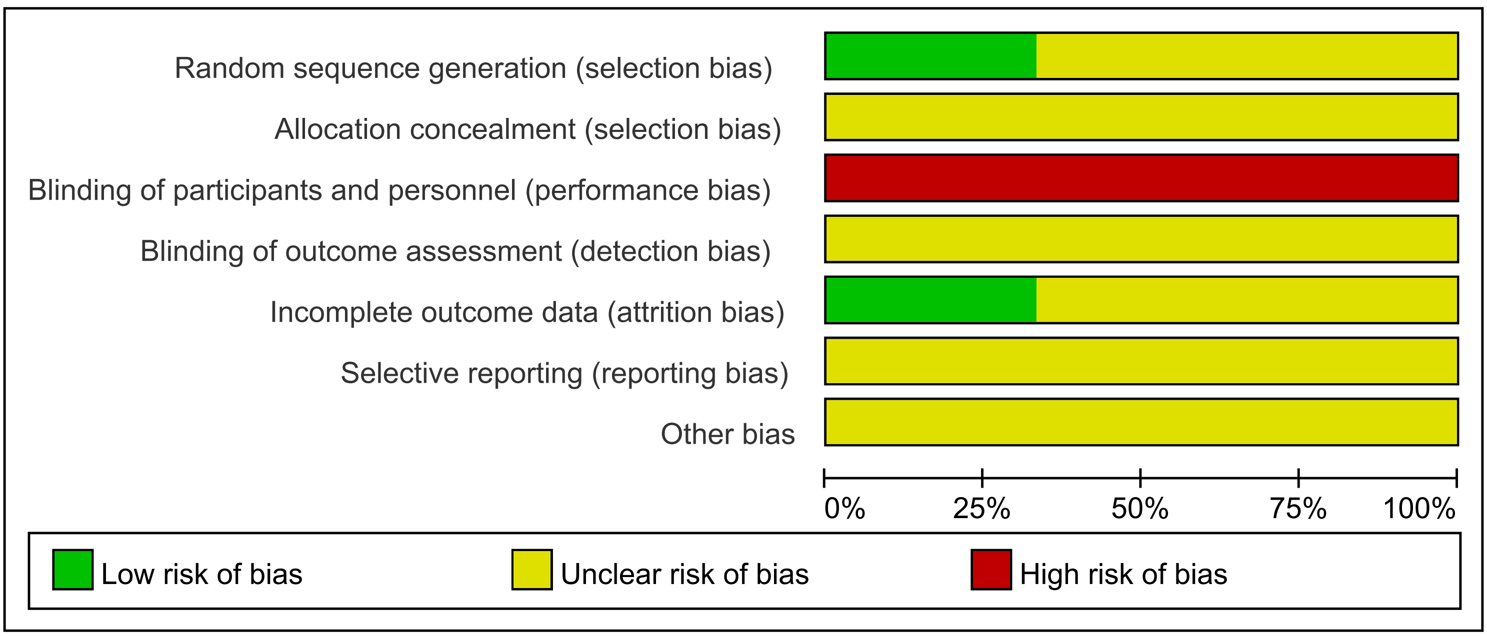
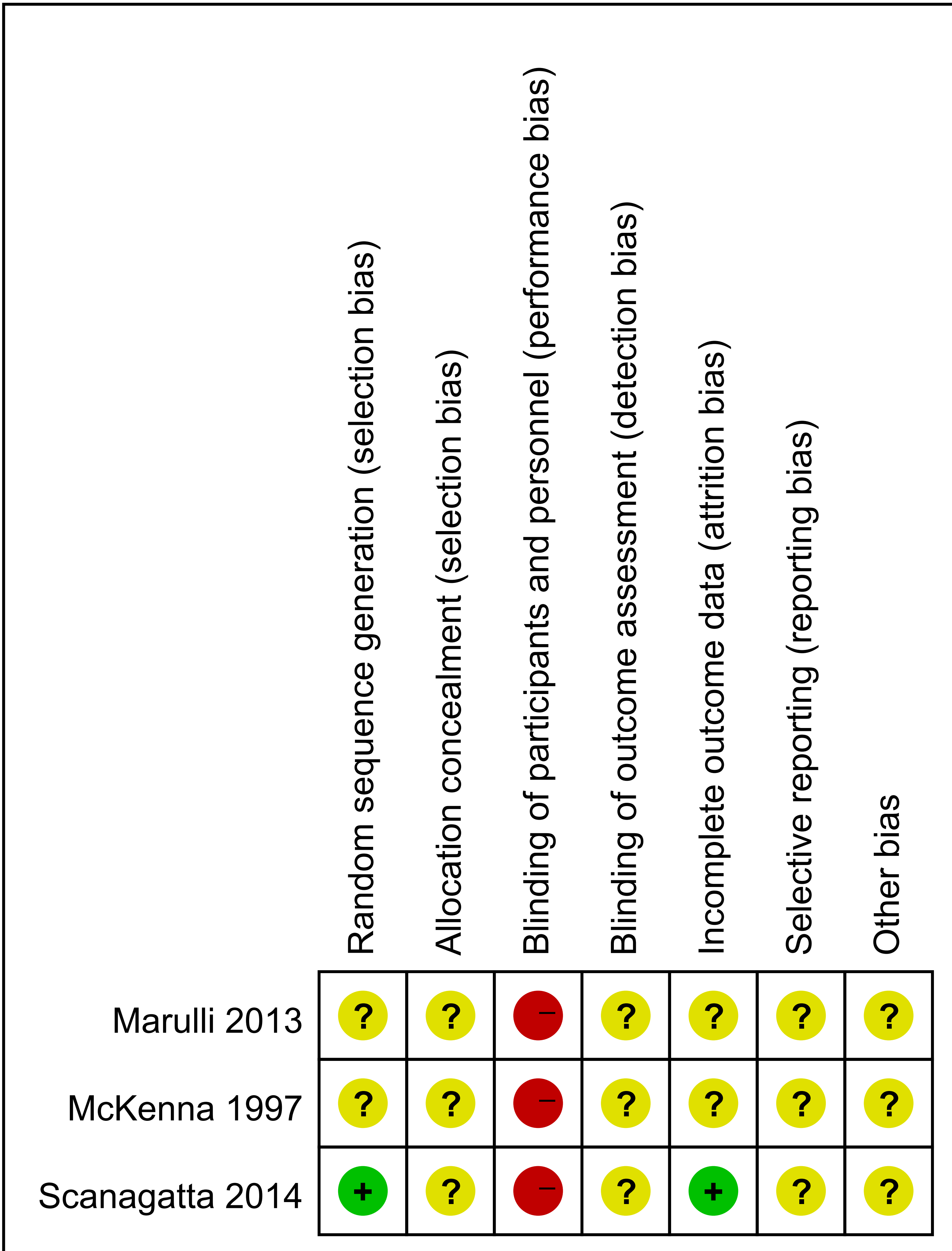


Figure.3

Click here to access/download;Figure;Figure.3.pdf



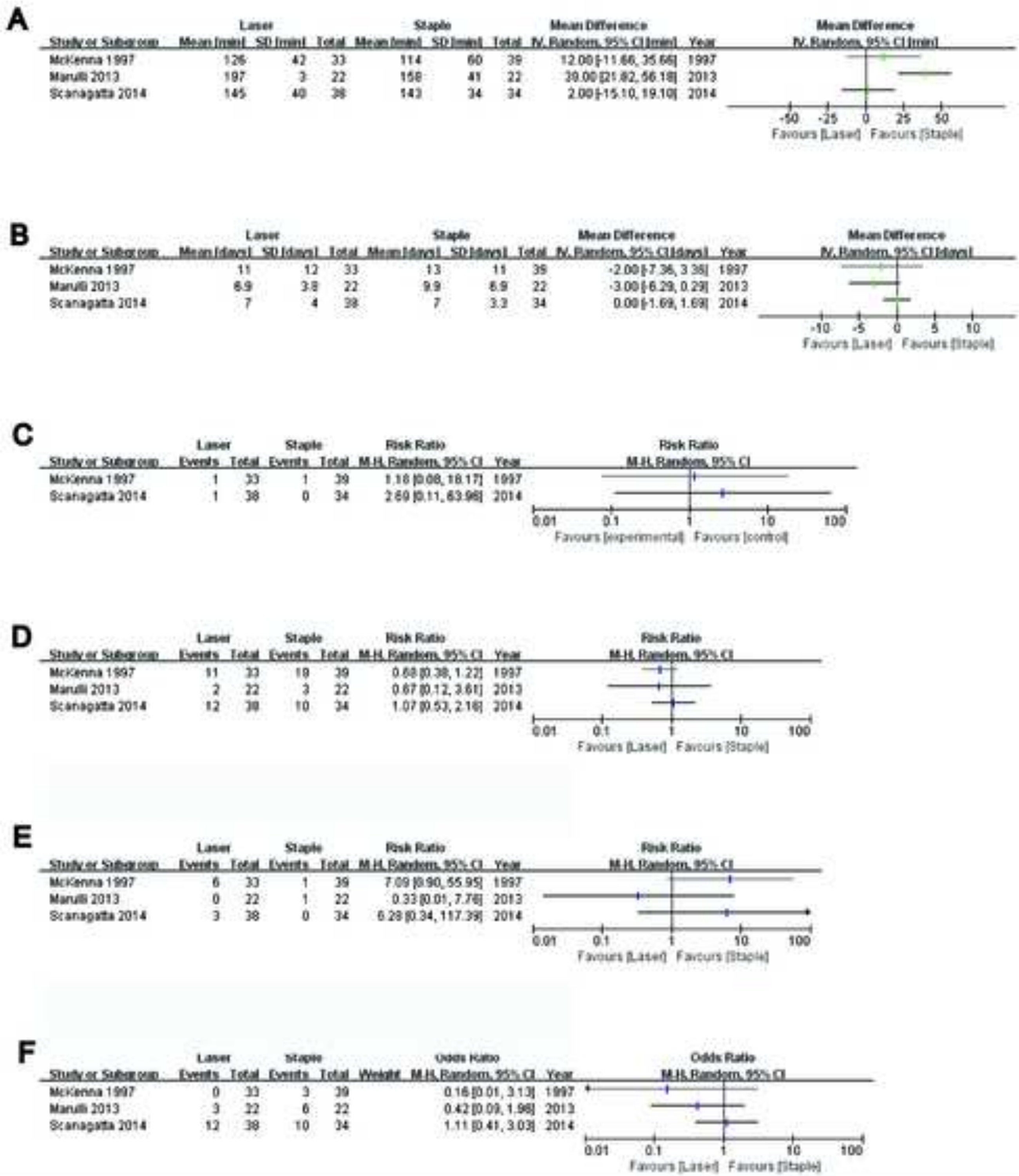

A
Laser
Staple
Mean Difference
Study or Subgroup Mean [min] SD [min] Total Mean [min] SD [min] Total IV, Random, 95% CI [min] Year
McKenna 1997 126 42 33 114 60 39 12.00 [-11.66, 35.66] 1997
Marulli 2013 197 3 22 158 41 22 39.00 [21.82, 56.18] 2013
Scanagatta 2014 145 40 38 143 34 34 2.00 [-15.10, 19.10] 2014
-50 -25 0 25 50
Favours [Laser] Favours [Staple]
B
Study or Subgroup Mean [days] SD [days] Total Mean [days] SD [days] Total IV, Random, 95% CI [days] Year
McKenna 1997 11 12 33 13 11 39 -2.00 [-7.36, 3.36] 1997
Marulli 2013 6.9 3.8 22 9.9 6.9 22 -3.00 [-6.29, 0.29] 2013
Scanagatta 2014 7 4 38 7 3.3 34 0.00 [-1.69, 1.69] 2014
-10 -5 0 5 10
Favours [Laser] Favours [Staple]
C
Risk Ratio
Study or Subgroup Events Total Events Total M-H, Random, 95% CI Year
McKenna 1997 1 33 1 39 1.18 [0.08, 18.17] 1997
Scanagatta 2014 1 38 0 34 2.69 [0.11, 63.96] 2014
0.01 0.1 1 10 100
Favours [experimental] Favours [control]
D
McKenna 1997 11 33 19 39 0.68 [0.38, 1.22] 1997
Marulli 2013 2 22 3 22 0.67 [0.12, 3.61] 2013
Scanagatta 2014 12 38 10 34 1.07 [0.53, 2.16] 2014
Favours [Laser] Favours [Staple]
E
McKenna 1997 6 33 1 39 7.09 [0.90, 55.95] 1997
Marulli 2013 0 22 1 22 0.33 [0.01, 7.76] 2013
Scanagatta 2014 3 38 0 34 6.28 [0.34, 117.39] 2014
F
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI Year
McKenna 1997 0 33 3 39 0.16 [0.01, 3.13] 1997
Marulli 2013 3 22 6 22 0.42 [0.09, 1.98] 2013
Scanagatta 2014 12 38 10 34 1.11 [0.41, 3.03] 2014
Favours [Laser] Favours [Staple]

Table 1

Table 1 Summary of participants' characteristics of included studies.

Baseline data	**McKenna 1996**		**Marulli 2013**		**Scanagatta 2014**	
	Laser (n = 33)	Staple (n = 39)	Laser (n = 22)	Staple (n = 22)	Laser (n = 38)	Staple (n = 34)
Age (yr)	69 ± 6	66 ± 8	68.7±9.9	63±16.7	68 (44-80) [a]	68 (48-83) [a]
Male (No.)	26	32	16	14	28	18
BMI	NR	NR	NR	NR	25.05 (19.30-34.84) [a]	25.10 (18.30-36.50) [a]
Never smoker	NR	NR	2	3	6	7
FEV1 (L)	0.7 ± 0.2	0.7± 0.2	2.3±0.5	2.3 ± 0.8	NR	NR
FVC (L)	2.1 ± 0.7	2.1 ± 0.7	2.9 ± 0.5	3±0.9	NR	NR

a: the data were expressed as mean and range. NR: not report.

Table 2 Characteristics of randomized controlled trials included in the qualitative meta-analysis.

Reference	Study design and sample size (n = sample size)	Criteria for entry to study		Intervention	Outcomes
		Inclusion	Exclusion		
McKenna 1996	A randomized controlled trial (n = 72)	All patients underwent surgery for emphysema.	Current cigarette smoking, age older than 75 years, carbon dioxide retention greater than 55 mm Hg, severe cardiac disease, history of cancer within the past 5 years, ventilator dependency, presence of	Neodymium: yttrium-aluminum-garnet contact laser. A 60 mm endoscopic stapler (ELC 60,	Operating time; Hospital days; Air leak; Delayed pneumothorax; Ileus; Deep vein thrombosis;

			a lung mass, prior thoracic surgery or a large bulla (>5 cm).	Ethicon, Inc., Somerville, N.J.).	Respiratory failure; Take back; Mortality.
Marulli 2013	A randomized controlled trial (n = 44)	Patients aged ≥18 years with lung cancer scheduled for elective pulmonary lobectomy with planned antero - or posterolateral incision and systematic lymphadenectomy. The fissure was of Craig's grade 3 or 4.	Previous lung surgery (on the same side), chemotherapy or radiotherapy (within the previous 3 or 4 weeks, respectively), preexisting advanced obstructive pulmonary disease [forced expiratory volume in 1 s (FEV1), <40 %], lobectomies as well as lobectomies for nonmalignant reasons, the need for adhesiolysis,	A Cyber TM Thulium surgical laser system. Routine surgical procedure with standard staplers.	Operating time; Hospital days; Daily amount of fluid leak; Air leak duration; Chest tube duration; Postoperative complications

			pneumonectomy, wedge or sleeve resection.		
Scanagatta 2014	A randomized controlled trial (n = 72)	immunocompetent adults aged 18 years or over who were scheduled for anatomic pulmonary resection other than pneumonectomy	Reoperations; the need for bronchoplasty or arterioplasty, thoracectomy or extended resections;	A Cyber TM Thulium surgical laser system Routine surgical procedure with standard staplers	Operating time; Hospital days; Prolonged air leaks; Chest tube duration; Postoperative complications

Lasers for Pulmonary Resections

Xingsheng Liu[1], Peilong Zhang[1], Yi Zhang[2]*

Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University Lung Cancer Center

*Correspondence author: Yi Zhang (zhangyixwhosp@xwh.ccmu.edu.cn)

Xingsheng Liu (M.D.), Peilong Zhang (M.D.), Yi Zhang (M.D.)

A shortened title

Lasers for Pulmonary Resections

Conflict of Interests

The authors declare no conflict of interests.

Acknowledgments

None

Abstract

Objective: To evaluate the effectiveness and safety of lasers compared with mechanical staplers in pulmonary resections using a qualitative and systematic study.

Summary of background data: Laser technique is effective in pulmonary resections among patients with pulmonary disease. However, a systematic review of this technique is necessary to determine its pivotal role in the field of thoracic surgery.

Methods: Among randomized controlled trials (RCTs) published in the Medline, Web of Science, Cochrane Controlled Trials Register (CCTR), and clinical trial databases from June 1979 to October 2022, three studies were identified and synthesized to compare the efficacy and safety of lasers and mechanical staplers in pulmonary resections based on selection criteria. Two reviewers independently assessed trial bias and extracted data to perform a qualitative systematic review.

Results: The three RCTs utilized the surgical approach of video-assisted thoracoscopic surgery (VATS). The operation time in the laser group was longer than that in the staple group (weighted mean difference (WMD) = 12.00 min, 95% confidence interval (CI): -11.66 to 35.66 for McKenna, WMD = 39.00 min, 95% CI: 21.82 to 56.18 for Marulli, and WMD = 2.00 min, 95% CI: -15.10 to 19.10 for Scanagatta). However, the length of hospital stay in the laser group was comparable to that of the staple group (WMD = -2.00 days, 95% CI: -7.36 to 3.36 for McKenna, WMD = -3.00 days, 95% CI: -6.29 to 0.29 for Marulli, and WMD = 0.00 days, 95% CI: -1.69 to 1.69 for Scanagatta). The risk ratio (RR) with 95% CI for persistent air leaks in the laser group versus the staple group was RR = 0.68 (95% CI: 0.38 to 1.22) for McKenna, RR = 0.67 (95% CI: 0.12 to 3.61) for Marulli, and RR = 1.07 (95% CI: 0.53 to 2.16) for Scanagatta. At the 6th month follow-up, the mean postoperative forced expiratory volume in 1 second of the staple group was significantly improved compared with that of the laser group. The clinical symptoms and dyspnea index were improved by more than one grade in 8 (24%) of 33 patients in the laser group and in 26 (66%) of 39 patients in the staple group (P = 0.003).

Conclusion: The lasers have proven to be effective and comparable to the mechanical stapler technique in pulmonary resections, with the exception of an improved dyspnea index.

Key words: Lasers; Mechanical staplers; Lobectomy

Introduction

The resection field for patients with malignant lung diseases and certain nonmalignant conditions (e.g., emphysema, pulmonary sequestrations, abscesses, bronchiectasis, and chronic pulmonary infections with localized parenchymal disruption) has remarkably attracted surgeons' attention. While electrocautery is frequently utilized for pulmonary parenchymal resections, it mainly leads to persistent air leaks and pneumothorax. To mitigate these complications, additional tools, such as mechanical staplers and lasers have been introduced. Over the last few decades, surgeons have widely embraced mechanical staplers for cutting and suturing pulmonary tissues in anatomic lung resections.[1] Particularly in laparoscopic pulmonary resections, surgical staplers are utilized in a staggered formation to simultaneously cut and ligate vessels and bronchi using a two-dimensional planar mode.

Since the 1960s, lasers, defined as light amplification by stimulated emission of radiation, have been recognized as a preferred option for various medical procedures, including coagulation, tissue evaporation, and cutting in surgical contexts.[2] In the 1980s, various types of lasers had been introduced for use in thoracic surgeries, notably appearing in pulmonary metastasectomies.[3,4] In the 1990s, laser bullectomy was employed by Wakabayashi and colleagues for patients with diffuse emphysema.[5] Subsequently, the application of lasers, particularly 1318 nm neodymium-YAG lasers or 1908 nm Thulium lasers, has demonstrated remarkable hemostasis and air-sealing effects in pulmonary resections.[6] Lung parenchymal tissue, containing 80% liquid components and few parenchymal tissue components, makes these organs appropriate candidates for laser use.[7]

There is a lack of information regarding the effectiveness and safety of lasers utilized in the surgical management of pulmonary diseases. Existing literature on laser use in pulmonary resections primarily comprises case series and retrospective trials. The optimal criteria for patient selection for pulmonary resections with lasers remain elusive, raising questions about whether these patients derive the greatest benefits from laser techniques. While several prospective studies have compared laser techniques with mechanical staplers in pulmonary resections, the wide variability in patient selection and outcome assessment across these published studies has resulted in insufficient evidence regarding their advantages and drawbacks. Moreover, the efficacy and safety of these two types of pneumonectomy continue to be subjects of debate. Hence, we conducted a comparative analysis of the efficacy and safety of lasers compared with mechanical staplers in pulmonary resections by systematically reviewing randomized controlled trials (RCTs).

Materials and Methods

Search Strategy

We aimed to identify all relevant studies by searching in Medline, Web of Science, CCTR, and clinical trial databases from June 1979 to October 2022. The following search strategies were used: ((lung [MeSH Terms]) OR (lung [Title/Abstract]) OR (lungs [Title/Abstract]) OR (pulmonary [Title/Abstract]) AND (lasers [MeSH Terms]) OR (laser [Title/Abstract]) OR (lasers [Title/Abstract])). Articles meeting our criteria were cross-referenced in the Science Citation Index (SCI) to retrieve reports citing them, and the reference lists of all obtained articles were filtered.

Inclusion and Exclusion Criteria

We included RCTs, cohort trials, and retrospective studies that compared laser techniques to mechanical staplers in pulmonary resections. The surgical approach was thoracoscopy. Both bilateral and unilateral procedures were considered, and only articles in English were included for systematic review. We excluded studies if they exclusively concentrated on nonoperative management, non-thoracoscopic procedures, utilized less common approaches such as needlescopic or single-incision approaches, or were single-arm studies.

Selection of Studies

The title and abstract of potentially relevant literature were independently reviewed by two reviewers (XS Liu and PL Zhang). After obtaining the full text of these articles, we applied the inclusion and exclusion criteria to filter the studies. Any discrepancies in study selection were resolved through consultation with a third reviewer (Y Zhang). Excluded studies were identified based on the specified criteria, and the reasons for exclusion were provided. Once selected studies were included in our research, we used the following domains to assess their methodological quality and extract and analyze data.

Quality Assessment

Two reviewers (Liu and Qian) independently evaluated the methodology of the included studies based on the following criteria: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. Each participant had an equal chance of being allocated to a group through a randomized method, indicating a low risk of bias in random allocation. If the investigators responsible for patient selection could not determine the next treatment allocation (e.g., central randomization, sealed, opaque, sequentially numbered assignment envelopes), the risk of bias in allocation concealment was considered low. When patients were blinded to the treatment assignment, the risk of bias in blinding of participants and personnel was considered low. Similarly, if the outcome assessors were blinded to the group assignment, the risk of bias in blinding of outcome assessors was considered low. The risk of incomplete outcome data, caused by the use of intent-to-treat analysis in the research, was considered low. Additionally, if researchers provided a pre-specified published protocol available for comparison, the risk of bias in selective reporting was considered low. We categorized each bias item as low-risk, high-risk, or unclear, and this information is presented in Supplemental Table 1. Any disagreements in bias assessment were resolved through discussions with a third expert (Y Zhang).

Outcome Measures

The predetermined outcomes for our qualitative meta-analysis were as follows: efficacy outcomes, including operating time, hospital stay, and re-operation rates; safety outcomes, such as mortality, prolonged air leak, pneumothorax, and other complications; as well as disability and health status, lung function, and cost analysis.

Data Extraction

XS Liu collected data on authorship, publication year, patients' characteristics (age, gender, body mass index (BMI), smoking history, and lung function), study design, inclusion criteria, and major clinical outcomes using a standardized form (Tables 1 and 2). The extracted data were then independently cross-checked by either PL Zhang or Y Zhang. Any discrepancies were resolved through discussion.

Statistical Analysis

RevMan 4.0.4 software was utilized for summarizing relative risks (RRs) and weighted mean differences (WMDs), which were presented as point estimates in square brackets along with 95% confidence intervals (CIs). Due to the limited number of studies (three articles) included in our analysis, a qualitative systematic review was conducted without meta-analysis. Median and range data were converted to mean and standard deviation using the method described by Hozo et al., if necessary.[8]

Results

Results of search strategy

The initial electronic searches identified titles, from which abstracts were retrieved to identify 799 potentially relevant studies on pulmonary resection comparing laser techniques with mechanical staplers from 1975 to 2022. After removing duplicate articles and screening titles and abstracts, 22 articles were selected for full-text review. However, 19 articles were subsequently excluded for the following reasons: lack of comparative trials (n = 10), absence of laser techniques (n = 4), absence of mechanical staplers (n = 3), and low quality (n = 2). Only three studies met the criteria for inclusion in this qualitative analysis (Fig. 1). Two reviewers (XS Liu, K Qian) independently assessed the search results and resolved any disagreements through discussion. The flowchart illustrating the search process is presented in Fig. 1.

Quality Assessment

The risk of random sequence generation was low in one trial conducted by Scanagatta et al. and unclear in the other two trials. For all trials, the risks of allocation concealment, blinding of outcome assessment, and selective reporting were considered unclear, while the risk of blinding of participants was high due to the nature of the surgical procedure. The risk of incomplete outcome data was unclear in two trials and low in Scanagatta et al.'s trial due to the intent-to-treat analysis (Figs. 2-3, and Supplementary Table 1).

Participants' Characteristics

The participants were divided into the laser group and the staple group in all included studies. Participants in McKenna et al.'s study had diffuse emphysema treated by bullectomy using the

VATS approach.[9] Participants in Marulli et al.'s study had lung cancer scheduled for elective pulmonary lobectomy using the VATS approach.[10] Participants in the remaining study were immunocompetent adults scheduled for anatomic pulmonary resection using the VATS approach.[11] The present study included a total of 188 participants. The study population mainly comprised 134 men (71%) with an average age of 67 years (Table 1).

Type of Intervention

In the laser group, a variety of types of lasers were used: a contact tip Nd:YAG laser (10 W),[9] a non-contact Thulium laser (40 W),[10] and a photocoagulation-mode Thulium laser.[11] Scanagatta et al. did not report the laser power output. For the staple group, McKenna et al. used a 60 mm endoscopic stapler (ELC 60, Ethicon, Inc., Somerville, NJ, USA) with bovine pericardium (Peristrips, Biovascular, St. Paul, MN, USA) to buttress the staples.[9] Marulli et al. applied standard staplers to complete pulmonary fissures.[10] Scanagatta et al. completed the division of fissures using staplers with sealants when needed (Table 2).[11]

Efficacy Outcomes

Operation Time

In general, the operation time is defined as the time from skin incision to skin closure. In both studies, the laser group and the staple group did not exhibit a significant difference in the operation time (WMD = 12.00 min, 95% CI -11.66 to 35.66; WMD = 2.00 min, 95% CI -15.10 to 19.10). However, Marulli et al. reported that mechanical staplers apparently decreased the operation time compared with the laser (WMD = 39 min.00, 95% CI 21.82 to 56.18) (Fig. 4A).

Length of Hospital Stay

In the three trials, there was no significant difference in the length of hospital stay between the two studies (WMD = -2.00d, 95% CI -7.36 to 3.36 for McKenna; WMD = -3.00d, 95% CI -6.29 to 0.29 for Marulli, and WMD = 0.00d, 95% CI -1.69 to 1.69 for Scanagatta) (Fig. 4B).

Re-operation

Assessment of re-operation rates (RR) with 95% CI revealed the following comparisons between the laser and staple groups: McKenna et al. reported RR of 1.18 (95% CI: 0.08 to 18.17), while Scanagatta et al. reported RR of 2.69 (95% CI: 0.11 to 63.96). Marulli et al. found no patients requiring re-operation in either group (Fig. 4C).

Adverse Events

Mortality

McKenna et al. reported no perioperative deaths in the laser group, and one death caused by contralateral tension pneumothorax was reported in the staple group. No perioperative mortality was identified in studies conducted by Marulli et al. and Scanagatta et al.

Persistent Air Leaks

The persistent air leaks were identified when air leaks lasted more than 7 days[12]. There was no significant difference in the incidence of persistent air leaks between the laser group and the staple group in the three studies (RR = 0.68, 95%: CI: 0.38 to 1.22; RR = 0.67, 95% CI: 0.12 to 3.61; and RR =1.07, 95% CI: 0.53 to 2.16) (Fig. 4D).

Pneumothorax

McKenna et al. reported 6 patients with delayed pneumothorax in the laser group and one with tension pneumothorax in the contralateral lung in the staple group (RR = 7.09, 95% CI: 0.90 to 55.95). Marulli et al. reported pneumothorax in only one patient in the staple group (RR = 0.33, 95%

CI 0.01 to 7.76). Scanagatta et al. reported 3 cases of delayed pneumothorax in the laser group (RR = 6.28, 95% CI: 0.34 to 117.39) (Fig. 4E).

Other Complications

It was revealed that there was no difference in the incidence rates of other complications, such as fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus between the two groups (RR = 0.16, 95% CI: 0.01 to 3.13 for McKenna; RR = 0.42, 95% CI: 0.09 to 1.96 for Marulli and RR =1.11, 95% CI: 0.41 to 3.03 for Scanagatta) (Fig. 4F).

Disability and Health Status

McKenna et al. demonstrated breathlessness, likely assessed using the Medical Research Council or Rand Dyspnea scale. Their findings revealed that 8 (24%) out of 33 patients in the laser group exhibited an improvement of more than one grade in dyspnea, contrasted with 26 (66%) out of 39 patients in the staple group ($P = 0.003$). In contrast, Marulli et al. and Scanagatta et al. did not provide data on this aspect in their studies.

Pulmonary Function

McKenna et al.'s study documented a mean improvement in FEV1 at six months of 13.4 ± 5.5% in the laser group and 32.9 ± 4.8% in the staple group ($P < 0.01$). The rise in the forced vital capacity (FVC) was also noted: 6 ± 3% in the laser group versus 21 ± 6% in the staple group ($P = 0.07$). Conversely, Marulli et al. and Scanagatta et al. did not provide data on changes in pulmonary function following pulmonary surgery.

Cost Analysis

Marulli et al. found the hospitalization cost in the stapler group was significantly higher than that in the laser group (5,650 ± 3,063 euros for the laser group vs. 8,147±5,785 euros for the staple group, P = 0.01). Additionally, Scanagatta et al. reported a significant difference in intraoperative costs (807 ± 212 euros for the laser group vs. 1,092 ± 274 euros for the staple group, P < 0.0001).

Discussion

The efficacy and safety of lasers and mechanical staplers for pulmonary surgery were compared through three RCT trials identified by systematically searching the literatures. Currently, the evaluation of various standard techniques widely applied in pulmonary resection involving surgical stapling, electrocautery and hand sewing, and their possible roles in thoracic surgical operations as surgical tools was performed. The effect of Nd:YAG laser on pulmonary parenchyma was first demonstrated by Minton in 1967, when it was used to precisely excise the tumor in an experimental model.[13] In the next few years, a new generation laser system, the 2,010-nm wavelength emitted by Cyber TM Thulium laser, was introduced into the field of thoracosurgery. Since the 1980s, the application of lasers in resections of pulmonary tissue was widely accepted and the effect on parenchyma-sparing surgery of various types of lasers was evaluated.[14] To our knowledge, there were no systematic reviews to compare the two procedures.

When considering the efficacy of the two methods, two trials found no significant difference in operating time between the laser and staple groups. However, Marulli et al.'s study demonstrated that the use of mechanical staplers significantly reduced operation time compared to lasers.[10] This could be attributed to their approach of applying a second Thulium laser irradiation at low power (20 W) in a defocused mode to treat the dissected surface of the residual lobe, aiming for an optimal aero-haemostatic effect on lung parenchyma. In this systematic review, we observed that the overall length of hospital stay was shorter in the laser group, although this difference did not reach statistical significance, likely due to the limited number of patients enrolled. Regarding the occurrence of re-operation, three RCTs exhibited no difference in the re-operation rate between the two groups. Based on our clinical experience, it was found that lasers were equally effective as mechanical staplers.

Factors influencing post-operative persistent air leaks include underlying lung diseases, such as emphysema, fibrosis, tuberculosis or malignancies, lymphangioleiomyomatosis, and intrathoracic adhesions, elderly patient (>75 years), and lower diffusion capacity for carbon monoxide.[15] In the case of pulmonary traumatization and dissection, persistent air leaks cause prolonged intercostal drainage, associated pain, increased immobility, and risk of further complications such as pneumonia, empyema, and pulmonary embolism.[16] Although many efforts have been made to reduce the occurrence of parenchymal air leaks after pneumonectomy, the desirable surgical techniques or tools to reduce or prevent this complication have not been determined, and in most cases, standard techniques cannot provide adequate sealing in patients. Darlong et al. reported three positive effects of laser irradiation (cutting, coagulation, and tissue shrinkage), leading to sealing through the progressive collapse of alveolar septa which produces a thick and multilayer air-proof membrane.[13] But we observed no significant difference in the incidence of persistent air leaks between the two groups, possibly because the sample sizes in these studies were small. However, the laser group showed a daily trend of reduction in the proportion of patients with persistent air leaks.

Additionally, pneumothorax and other complications, such as fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus were distributed equally in each group. Considering the high blood vessel density, it is necessary to remove the lung parenchyma with laser with a strong coagulation ability and excellent cutting performance. With respect to the mortality outcome, the results of three RCTs included concluded that the outcome of mortality was rare (<5% staple group event rate). These results can be explained by the features of laser, which can be strongly absorbed by water, resulting in excellent coagulation (low coagulation depth of only 0.2 mm) and aero-hemostatic effects, and maximal preservation of surrounding normal tissues.

Criner and his colleagues found that removal of large bullae in isolated bullous disease and bullous emphysema may lead to improved expiratory flow and airway conductance, which may be due to the improved elastic recoil.[17] In 1996, a RCT containing two procedures (laser bullectomy and lung reduction surgery with staples) was conducted using VATS method, and the results strongly support the superiority of unilateral staple procedures over laser methods in terms of improved quality of life, pulmonary function and probably reduced oxygen dependence.[9] Although the study of Marulli and Scanagatta did not report these outcomes, they applied a new generation of laser (a Cyber TM Thulium surgical laser system) which may result in a better clinical status and pulmonary function in the laser group.[10,11]

Despite these advantages, it is crucial to acknowledge the biases present in the studies included in this systematic review. Biases related to random sequence generation, allocation concealment, blinding of participants and personnel, outcome assessment blinding, incomplete outcome data, and selective reporting were noted. Additionally, the long-term health outcomes of using laser techniques in pulmonary resections remained elusive. To address these uncertainties and to better define the advantages of lasers over mechanical stapler, further RCTs are warranted. The future studies will play a vital role in promoting the efficacy, safety, and potential long-term benefits of laser mechanisms in pulmonary surgery.

In conclusion, laser mechanisms in pulmonary resections have demonstrated several notable advantages. These include the ability to minimize surrounding tissue damage and preserve normal parenchyma elasticity to a maximal extent. Additionally, lasers provide an aero-haemostatic effect during surgery, enhancing control over bleeding. They also offer a relative safety advantage when dissecting major bronchi and vessels, contributing to safer surgical procedures. Furthermore, the cost-effectiveness of laser techniques adds to their appeal as an alternative to the standard stapling method. These advantages collectively suggest that lasers can be an effective and safe option in pulmonary surgery, although their impact on improving dyspnea requires further investigation.

References

1. Marra A, Yankulov A. The role of new staplers in reducing the incidence of air leak. *J Thorac Dis* 2023;**15**(2):893-900

2. Park HJ, Cho YH, Goo H, Choi SH, Kim EY, Hong N et al. Treatment with Light-Emitting Diodes of Wavelength 863 nm Delays DMBA/TPA-Induced Skin Tumor Formation and Decreases Proinflammatory Cytokine Levels in ICR Mice. *Biomed Res Int* 2022;**2022**:4400276

3. Leivaditis V, Skevis K, Mulita F, Tsalikidis C, Mitsala A, Dahm M et al. Advancements in the Management of Postoperative Air Leak following Thoracic Surgery: From Traditional Practices to Innovative Therapies. *Medicina (Kaunas)* 2024;**60**(5):802

4. Mammana M, Baldi M, Melan L, Dell'Amore A, Rea F. Laser-assisted lung metastasectomy: a systematic review. *Updates Surg* 2023;**75**(7):1783-1793

5. Shalabi A, Ehab A, Shalabi SF, Kugler G, Schäfers HJ, Graeter T. Laser assisted pulmonary metastasectomy promises a low local recurrence rate. *Sci Rep* 2024;**14**(1):5988

6. Stefani A, Oricchio F, Cinquepalmi A, Aramini B, Morandi U. Is laser-assisted resection preferable to lobectomy for pulmonary metastasectomy? *Lasers Med Sci* 2020; **35**(3):611-20

7. Grapatsas K, Papaporfyriou A, Leivaditis V, Ehle B, Galanis M. Lung Metastatectomy: Can Laser-Assisted Surgery Make a Difference? *Curr Oncol* 2022;**29**(10):6968-6981

8. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;**5**:13

9. McKenna RJ, Brenner M, Gelb AF, Mullin M, Singh N, Peters H *et al.* A randomized, prospective trial of stapled lung reduction versus laser bullectomy for diffuse emphysema. *J Thorac Cardiovasc Surg* 1996;**111**(2):317-21

10. Marulli G, Droghetti A, Di Chiara F, Calabrese F, Rebusso A, Perissinotto E *et al*. A prospective randomized trial comparing stapler and laser techniques for interlobar fissure completion during pulmonary lobectomy. *Lasers Med Sci* 2013;**28** (2):505-511

11. Scanagatta P, Furia S, Bille A, Duranti L, Girelli L, Tavecchio LD et al. Thulium laser versus staplers for anatomic pulmonary resections with incomplete fissures: negative results of a randomized trial. *Tumori* 2014;**100** (3):259-264

12. Hua Q, Liu S, Shen L, Yang Z, Shen H. The safety and efficacy of additional chest tube placement in patients with prolonged air leaks after pulmonary resection: a propensity score-matched analysis. *Front Med (Lausanne)* 2024;**11**:1484327

13. Darlong L, Chakraborty A, Sharma P. Nd-YAG laser-assisted pulmonary metastasectomy: initial experience from a tertiary care cancer center in India. *Indian J Thorac Cardiovasc Surg* 2024;**40**(5):570-576

14. de Brito AA, da Silveira EC, Rigonato-Oliveira NC, Soares SS, Brandao-Rangel MAR, Soares CR et al. Low-level laser therapy attenuates lung inflammation and airway remodeling in a murine model of idiopathic pulmonary fibrosis: Relevance to cytokines secretion from lung structural cells. *J Photochem Photobiol B* 2020;**203**:111731

15. Ueda T, Takamochi K, Hattori A, Fukui M, Matsunaga T, Suzuki K. Postoperative management using a digital drainage system for massive air leakage after pulmonary resection. *Surg Today* 2024;**54**(2):130-137

16. Clark JM, Cooke DT, Brown LM. Management of Complications After Lung Resection: Prolonged Air Leak and Bronchopleural Fistula. *Thorac Surg Clin* 2020;**30**(3):347-358

17. Criner GJ. Surgical and Interventional Approaches in COPD. *Respir Care* 2023;**68**(7):939-960

Figure legend

Figure.1 PRISMA flowchart for literature searching.

Figure.2 A risk of bias graph.

Figure.3 A risk of bias summary (“+”low risk;“?”, unclear risk;“-”,high risk).

Figure.4 Forest plot of operation time (A), hospital stay (B), re-operation (C), persistent air leaks (D), pneumothorax (E), other complications (F).

Lasers for Pulmonary Resections

Xingsheng Liu[1], Peilong Zhang[1], Yi Zhang[2]*

Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University Lung Cancer Center

*Correspondence author: Yi Zhang (zhangyixwhosp@xwh.ccmu.edu.cn)

Xingsheng Liu (M.D.), Peilong Zhang (M.D.), Yi Zhang (M.D.)

A shortened title

Lasers for Pulmonary Resections

Conflict of Interests

The authors declare no conflict of interests.

Acknowledgments

None

Abstract

Objective: To evaluate the effectiveness and safety of lasers compared with mechanical staplers in pulmonary resections using a qualitative and systematic study.

Summary of background data: Laser technique is effective in pulmonary resections among patients with pulmonary disease. However, a systematic review of this technique is necessary to determine its pivotal role in the field of thoracic surgery.

Methods: Among randomized controlled trials (RCTs) published in the Medline, Web of Science, Cochrane Controlled Trials Register (CCTR), and clinical trial databases from June 1979 to October 2022, three studies were identified and synthesized to compare the efficacy and safety of lasers and mechanical staplers in pulmonary resections based on selection criteria. Two reviewers independently assessed trial bias and extracted data to perform a qualitative systematic review.

Results: The three RCTs utilized the surgical approach of video-assisted thoracoscopic surgery (VATS). The operation time in the laser group was longer than that in the staple group (weighted mean difference (WMD) = 12.00 min, 95% confidence interval (CI): -11.66 to 35.66 for McKenna, WMD = 39.00 min, 95% CI: 21.82 to 56.18 for Marulli, and WMD = 2.00 min, 95% CI: -15.10 to 19.10 for Scanagatta). However, the length of hospital stay in the laser group was comparable to that of the staple group (WMD = -2.00 days, 95% CI: -7.36 to 3.36 for McKenna, WMD = -3.00 days, 95% CI: -6.29 to 0.29 for Marulli, and WMD = 0.00 days, 95% CI: -1.69 to 1.69 for Scanagatta). The risk ratio (RR) with 95% CI for persistent air leaks in the laser group versus the staple group was RR = 0.68 (95% CI: 0.38 to 1.22) for McKenna, RR = 0.67 (95% CI: 0.12 to 3.61) for Marulli, and RR = 1.07 (95% CI: 0.53 to 2.16) for Scanagatta. At the 6th month follow-up, the mean postoperative forced expiratory volume in 1 second of the staple group was significantly improved compared with that of the laser group. The clinical symptoms and dyspnea index were improved by more than one grade in 8 (24%) of 33 patients in the laser group and in 26 (66%) of 39 patients in the staple group (P = 0.003).

Conclusion: The lasers have proven to be effective and comparable to the mechanical stapler technique in pulmonary resections, with the exception of an improved dyspnea index.

Key words: Lasers; Mechanical staplers; Lobectomy

Introduction

The resection field for patients with malignant lung diseases and certain nonmalignant conditions (e.g., emphysema, pulmonary sequestrations, abscesses, bronchiectasis, and chronic pulmonary infections with localized parenchymal disruption) has remarkably attracted surgeons' attention. While electrocautery is frequently utilized for pulmonary parenchymal resections, it mainly leads to persistent air leaks and pneumothorax. To mitigate these complications, additional tools, such as mechanical staplers and lasers have been introduced. Over the last few decades, surgeons have widely embraced mechanical staplers for cutting and suturing pulmonary tissues in anatomic lung resections.[1] Particularly in laparoscopic pulmonary resections, surgical staplers are utilized in a staggered formation to simultaneously cut and ligate vessels and bronchi using a two-dimensional planar mode.

Since the 1960s, lasers, defined as light amplification by stimulated emission of radiation, have been recognized as a preferred option for various medical procedures, including coagulation, tissue evaporation, and cutting in surgical contexts.[2] In the 1980s, various types of lasers had been introduced for use in thoracic surgeries, notably appearing in pulmonary metastasectomies.[3,4] In the 1990s, laser bullectomy was employed by Wakabayashi and colleagues for patients with diffuse emphysema.[5] Subsequently, the application of lasers, particularly 1318 nm neodymium-YAG lasers or 1908 nm Thulium lasers, has demonstrated remarkable hemostasis and air-sealing effects in pulmonary resections.[6] Lung parenchymal tissue, containing 80% liquid components and few parenchymal tissue components, makes these organs appropriate candidates for laser use.[7]

There is a lack of information regarding the effectiveness and safety of lasers utilized in the surgical management of pulmonary diseases. Existing literature on laser use in pulmonary resections primarily comprises case series and retrospective trials. The optimal criteria for patient selection for pulmonary resections with lasers remain elusive, raising questions about whether these patients derive the greatest benefits from laser techniques. While several prospective studies have compared laser techniques with mechanical staplers in pulmonary resections, the wide variability in patient selection and outcome assessment across these published studies has resulted in insufficient evidence regarding their advantages and drawbacks. Moreover, the efficacy and safety of these two types of pneumonectomy continue to be subjects of debate. Hence, we conducted a comparative analysis of the efficacy and safety of lasers compared with mechanical staplers in pulmonary resections by systematically reviewing randomized controlled trials (RCTs).

Materials and Methods

Search Strategy

We aimed to identify all relevant studies by searching in Medline, Web of Science, CCTR, and clinical trial databases from June 1979 to October 2022. The following search strategies were used: ((lung [MeSH Terms]) OR (lung [Title/Abstract]) OR (lungs [Title/Abstract]) OR (pulmonary [Title/Abstract]) AND (lasers [MeSH Terms]) OR (laser [Title/Abstract]) OR (lasers [Title/Abstract])). Articles meeting our criteria were cross-referenced in the Science Citation Index (SCI) to retrieve reports citing them, and the reference lists of all obtained articles were filtered.

Inclusion and Exclusion Criteria

We included RCTs, cohort trials, and retrospective studies that compared laser techniques to mechanical staplers in pulmonary resections. The surgical approach was thoracoscopy. Both bilateral and unilateral procedures were considered, and only articles in English were included for systematic review. We excluded studies if they exclusively concentrated on nonoperative management, non-thoracoscopic procedures, utilized less common approaches such as needlescopic or single-incision approaches, or were single-arm studies.

Selection of Studies

The title and abstract of potentially relevant literature were independently reviewed by two reviewers (XS Liu and PL Zhang). After obtaining the full text of these articles, we applied the inclusion and exclusion criteria to filter the studies. Any discrepancies in study selection were resolved through consultation with a third reviewer (Y Zhang). Excluded studies were identified based on the specified criteria, and the reasons for exclusion were provided. Once selected studies were included in our research, we used the following domains to assess their methodological quality and extract and analyze data.

Quality Assessment

Two reviewers (Liu and Qian) independently evaluated the methodology of the included studies based on the following criteria: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. Each participant had an equal chance of being allocated to a group through a randomized method, indicating a low risk of bias in random allocation. If the investigators responsible for patient selection could not determine the next treatment allocation (e.g., central randomization, sealed, opaque, sequentially numbered assignment envelopes), the risk of bias in allocation concealment was considered low. When patients were blinded to the treatment assignment, the risk of bias in blinding of participants and personnel was considered low. Similarly, if the outcome assessors were blinded to the group assignment, the risk of bias in blinding of outcome assessors was considered low. The risk of incomplete outcome data, caused by the use of intent-to-treat analysis in the research, was considered low. Additionally, if researchers provided a pre-specified published protocol available for comparison, the risk of bias in selective reporting was considered low. We categorized each bias item as low-risk, high-risk, or unclear, and this information is presented in Supplemental Table 1. Any disagreements in bias assessment were resolved through discussions with a third expert (Y Zhang).

Outcome Measures

The predetermined outcomes for our qualitative meta-analysis were as follows: efficacy outcomes, including operating time, hospital stay, and re-operation rates; safety outcomes, such as mortality, prolonged air leak, pneumothorax, and other complications; as well as disability and health status, lung function, and cost analysis.

Data Extraction

XS Liu collected data on authorship, publication year, patients' characteristics (age, gender, body mass index (BMI), smoking history, and lung function), study design, inclusion criteria, and major clinical outcomes using a standardized form (Tables 1 and 2). The extracted data were then independently cross-checked by either PL Zhang or Y Zhang. Any discrepancies were resolved through discussion.

Statistical Analysis

RevMan 4.0.4 software was utilized for summarizing relative risks (RRs) and weighted mean differences (WMDs), which were presented as point estimates in square brackets along with 95% confidence intervals (CIs). Due to the limited number of studies (three articles) included in our analysis, a qualitative systematic review was conducted without meta-analysis. Median and range data were converted to mean and standard deviation using the method described by Hozo et al., if necessary.[8]

Results

Results of search strategy

The initial electronic searches identified titles, from which abstracts were retrieved to identify 799 potentially relevant studies on pulmonary resection comparing laser techniques with mechanical staplers from 1975 to 2022. After removing duplicate articles and screening titles and abstracts, 22 articles were selected for full-text review. However, 19 articles were subsequently excluded for the following reasons: lack of comparative trials (n = 10), absence of laser techniques (n = 4), absence of mechanical staplers (n = 3), and low quality (n = 2). Only three studies met the criteria for inclusion in this qualitative analysis (Fig. 1). Two reviewers (XS Liu, K Qian) independently assessed the search results and resolved any disagreements through discussion. The flowchart illustrating the search process is presented in Fig. 1.

Quality Assessment

The risk of random sequence generation was low in one trial conducted by Scanagatta et al. and unclear in the other two trials. For all trials, the risks of allocation concealment, blinding of outcome assessment, and selective reporting were considered unclear, while the risk of blinding of participants was high due to the nature of the surgical procedure. The risk of incomplete outcome data was unclear in two trials and low in Scanagatta et al.'s trial due to the intent-to-treat analysis (Figs. 2-3, and Supplementary Table 1).

Participants' Characteristics

The participants were divided into the laser group and the staple group in all included studies. Participants in McKenna et al.'s study had diffuse emphysema treated by bullectomy using the

VATS approach.[9] Participants in Marulli et al.'s study had lung cancer scheduled for elective pulmonary lobectomy using the VATS approach.[10] Participants in the remaining study were immunocompetent adults scheduled for anatomic pulmonary resection using the VATS approach.[11] The present study included a total of 188 participants. The study population mainly comprised 134 men (71%) with an average age of 67 years (Table 1).

Type of Intervention

In the laser group, a variety of types of lasers were used: a contact tip Nd:YAG laser (10 W),[9] a non-contact Thulium laser (40 W),[10] and a photocoagulation-mode Thulium laser.[11] Scanagatta et al. did not report the laser power output. For the staple group, McKenna et al. used a 60 mm endoscopic stapler (ELC 60, Ethicon, Inc., Somerville, NJ, USA) with bovine pericardium (Peristrips, Biovascular, St. Paul, MN, USA) to buttress the staples.[9] Marulli et al. applied standard staplers to complete pulmonary fissures.[10] Scanagatta et al. completed the division of fissures using staplers with sealants when needed (Table 2).[11]

Efficacy Outcomes

Operation Time

In general, the operation time is defined as the time from skin incision to skin closure. In both studies, the laser group and the staple group did not exhibit a significant difference in the operation time (WMD = 12.00 min, 95% CI -11.66 to 35.66; WMD = 2.00 min, 95% CI -15.10 to 19.10). However, Marulli et al. reported that mechanical staplers apparently decreased the operation time compared with the laser (WMD = 39 min.00, 95% CI 21.82 to 56.18) (Fig. 4A).

Length of Hospital Stay

In the three trials, there was no significant difference in the length of hospital stay between the two studies (WMD = -2.00d, 95% CI -7.36 to 3.36 for McKenna; WMD = -3.00d, 95% CI -6.29 to 0.29 for Marulli, and WMD = 0.00d, 95% CI -1.69 to 1.69 for Scanagatta) (Fig. 4B).

Re-operation

Assessment of re-operation rates (RR) with 95% CI revealed the following comparisons between the laser and staple groups: McKenna et al. reported RR of 1.18 (95% CI: 0.08 to 18.17), while Scanagatta et al. reported RR of 2.69 (95% CI: 0.11 to 63.96). Marulli et al. found no patients requiring re-operation in either group (Fig. 4C).

Adverse Events

Mortality

McKenna et al. reported no perioperative deaths in the laser group, and one death caused by contralateral tension pneumothorax was reported in the staple group. No perioperative mortality was identified in studies conducted by Marulli et al. and Scanagatta et al.

Persistent Air Leaks

The persistent air leaks were identified when air leaks lasted more than 7 days[12]. There was no significant difference in the incidence of persistent air leaks between the laser group and the staple group in the three studies (RR = 0.68, 95%: CI: 0.38 to 1.22; RR = 0.67, 95% CI: 0.12 to 3.61; and RR =1.07, 95% CI: 0.53 to 2.16) (Fig. 4D).

Pneumothorax

McKenna et al. reported 6 patients with delayed pneumothorax in the laser group and one with tension pneumothorax in the contralateral lung in the staple group (RR = 7.09, 95% CI: 0.90 to 55.95). Marulli et al. reported pneumothorax in only one patient in the staple group (RR = 0.33, 95%

CI 0.01 to 7.76). Scanagatta et al. reported 3 cases of delayed pneumothorax in the laser group (RR = 6.28, 95% CI: 0.34 to 117.39) (Fig. 4E).

Other Complications

It was revealed that there was no difference in the incidence rates of other complications, such as fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus between the two groups (RR = 0.16, 95% CI: 0.01 to 3.13 for McKenna; RR = 0.42, 95% CI: 0.09 to 1.96 for Marulli and RR =1.11, 95% CI: 0.41 to 3.03 for Scanagatta) (Fig. 4F).

Disability and Health Status

McKenna et al. demonstrated breathlessness, likely assessed using the Medical Research Council or Rand Dyspnea scale. Their findings revealed that 8 (24%) out of 33 patients in the laser group exhibited an improvement of more than one grade in dyspnea, contrasted with 26 (66%) out of 39 patients in the staple group (P = 0.003). In contrast, Marulli et al. and Scanagatta et al. did not provide data on this aspect in their studies.

Pulmonary Function

McKenna et al.'s study documented a mean improvement in FEV1 at six months of 13.4 ± 5.5% in the laser group and 32.9 ± 4.8% in the staple group (P < 0.01). The rise in the forced vital capacity (FVC) was also noted: 6 ± 3% in the laser group versus 21 ± 6% in the staple group (P = 0.07). Conversely, Marulli et al. and Scanagatta et al. did not provide data on changes in pulmonary function following pulmonary surgery.

Cost Analysis

Marulli et al. found the hospitalization cost in the stapler group was significantly higher than that in the laser group (5,650 ± 3,063 euros for the laser group vs. 8,147±5,785 euros for the staple group, P = 0.01). Additionally, Scanagatta et al. reported a significant difference in intraoperative costs (807 ± 212 euros for the laser group vs. 1,092 ± 274 euros for the staple group, P < 0.0001).

Discussion

The efficacy and safety of lasers and mechanical staplers for pulmonary surgery were compared through three RCT trials identified by systematically searching the literatures. Currently, the evaluation of various standard techniques widely applied in pulmonary resection involving surgical stapling, electrocautery and hand sewing, and their possible roles in thoracic surgical operations as surgical tools was performed. The effect of Nd:YAG laser on pulmonary parenchyma was first demonstrated by Minton in 1967, when it was used to precisely excise the tumor in an experimental model.[13] In the next few years, a new generation laser system, the 2,010-nm wavelength emitted by Cyber TM Thulium laser, was introduced into the field of thoracosurgery. Since the 1980s, the application of lasers in resections of pulmonary tissue was widely accepted and the effect on parenchyma-sparing surgery of various types of lasers was evaluated.[14] To our knowledge, there were no systematic reviews to compare the two procedures.

When considering the efficacy of the two methods, two trials found no significant difference in operating time between the laser and staple groups. However, Marulli et al.'s study demonstrated that the use of mechanical staplers significantly reduced operation time compared to lasers.[10] This could be attributed to their approach of applying a second Thulium laser irradiation at low power (20 W) in a defocused mode to treat the dissected surface of the residual lobe, aiming for an optimal aero-haemostatic effect on lung parenchyma. In this systematic review, we observed that the overall length of hospital stay was shorter in the laser group, although this difference did not reach statistical significance, likely due to the limited number of patients enrolled. Regarding the occurrence of re-operation, three RCTs exhibited no difference in the re-operation rate between the two groups. Based on our clinical experience, it was found that lasers were equally effective as mechanical staplers.

Factors influencing post-operative persistent air leaks include underlying lung diseases, such as emphysema, fibrosis, tuberculosis or malignancies, lymphangioleiomyomatosis, and intrathoracic adhesions, elderly patient (>75 years), and lower diffusion capacity for carbon monoxide.[15] In the case of pulmonary traumatization and dissection, persistent air leaks cause prolonged intercostal drainage, associated pain, increased immobility, and risk of further complications such as pneumonia, empyema, and pulmonary embolism.[16] Although many efforts have been made to reduce the occurrence of parenchymal air leaks after pneumonectomy, the desirable surgical techniques or tools to reduce or prevent this complication have not been determined, and in most cases, standard techniques cannot provide adequate sealing in patients. Darlong et al. reported three positive effects of laser irradiation (cutting, coagulation, and tissue shrinkage), leading to sealing through the progressive collapse of alveolar septa which produces a thick and multilayer air-proof membrane.[13] But we observed no significant difference in the incidence of persistent air leaks between the two groups, possibly because the sample sizes in these studies were small. However, the laser group showed a daily trend of reduction in the proportion of patients with persistent air leaks.

Additionally, pneumothorax and other complications, such as fever, bleeding, pneumonia, chylothorax, respiratory failure, atrial fibrillation, deep vein thrombosis, transient cerebral ischemia, and ileus were distributed equally in each group. Considering the high blood vessel density, it is necessary to remove the lung parenchyma with laser with a strong coagulation ability and excellent cutting performance. With respect to the mortality outcome, the results of three RCTs included concluded that the outcome of mortality was rare (<5% staple group event rate). These results can be explained by the features of laser, which can be strongly absorbed by water, resulting in excellent coagulation (low coagulation depth of only 0.2 mm) and aero-hemostatic effects, and maximal preservation of surrounding normal tissues.

Criner and his colleagues found that removal of large bullae in isolated bullous disease and bullous emphysema may lead to improved expiratory flow and airway conductance, which may be due to the improved elastic recoil.[17] In 1996, a RCT containing two procedures (laser bullectomy and lung reduction surgery with staples) was conducted using VATS method, and the results strongly support the superiority of unilateral staple procedures over laser methods in terms of improved quality of life, pulmonary function and probably reduced oxygen dependence.[9] Although the study of Marulli and Scanagatta did not report these outcomes, they applied a new generation of laser (a Cyber TM Thulium surgical laser system) which may result in a better clinical status and pulmonary function in the laser group.[10,11]

Despite these advantages, it is crucial to acknowledge the biases present in the studies included in this systematic review. Biases related to random sequence generation, allocation concealment, blinding of participants and personnel, outcome assessment blinding, incomplete outcome data, and selective reporting were noted. Additionally, the long-term health outcomes of using laser techniques in pulmonary resections remained elusive. To address these uncertainties and to better define the advantages of lasers over mechanical stapler, further RCTs are warranted. The future studies will play a vital role in promoting the efficacy, safety, and potential long-term benefits of laser mechanisms in pulmonary surgery.

In conclusion, laser mechanisms in pulmonary resections have demonstrated several notable advantages. These include the ability to minimize surrounding tissue damage and preserve normal parenchyma elasticity to a maximal extent. Additionally, lasers provide an aero-haemostatic effect during surgery, enhancing control over bleeding. They also offer a relative safety advantage when dissecting major bronchi and vessels, contributing to safer surgical procedures. Furthermore, the cost-effectiveness of laser techniques adds to their appeal as an alternative to the standard stapling method. These advantages collectively suggest that lasers can be an effective and safe option in pulmonary surgery, although their impact on improving dyspnea requires further investigation.

References

1. Marra A, Yankulov A. The role of new staplers in reducing the incidence of air leak. *J Thorac Dis* 2023;**15**(2):893-900

2. Park HJ, Cho YH, Goo H *et al*. Treatment with Light-Emitting Diodes of Wavelength 863 nm Delays DMBA/TPA-Induced Skin Tumor Formation and Decreases Proinflammatory Cytokine Levels in ICR Mice. *Biomed Res Int* 2022;**2022**:4400276

3. Leivaditis V, Skevis K, Mulita F *et al*. Advancements in the Management of Postoperative Air Leak following Thoracic Surgery: From Traditional Practices to Innovative Therapies. *Medicina (Kaunas)* 2024;**60**(5):802

4. Mammana M, Baldi M, Melan L *et al*. Laser-assisted lung metastasectomy: a systematic review. *Updates Surg* 2023;**75**(7):1783-1793

5. Shalabi A, Ehab A, Shalabi SF *et al*. Laser assisted pulmonary metastasectomy promises a low local recurrence rate. *Sci Rep* 2024;**14**(1):5988

6. Stefani A, Oricchio F, Cinquepalmi A *et al*. Is laser-assisted resection preferable to lobectomy for pulmonary metastasectomy? *Lasers Med Sci* 2020; **35**(3):611-620

7. Grapatsas K, Papaporfyriou A, Leivaditis V *et al*. Lung Metastatectomy: Can Laser-Assisted Surgery Make a Difference? *Curr Oncol* 2022;**29**(10):6968-6981

8. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;**5**:13

9. McKenna RJ, Brenner M, Gelb AF *et al*. A randomized, prospective trial of stapled lung reduction versus laser bullectomy for diffuse emphysema. *J Thorac Cardiovasc Surg* 1996;**111**(2):317-321

10. Marulli G, Droghetti A, Di Chiara F *et al*. A prospective randomized trial comparing stapler and

laser techniques for interlobar fissure completion during pulmonary lobectomy. *Lasers Med Sci* 2013;**28** (2):505-511

11. Scanagatta P, Furia S, Bille A *et al*. Thulium laser versus staplers for anatomic pulmonary resections with incomplete fissures: negative results of a randomized trial. *Tumori* 2014;**100** (3):259-264

12. Hua Q, Liu S, Shen L *et al*. The safety and efficacy of additional chest tube placement in patients with prolonged air leaks after pulmonary resection: a propensity score-matched analysis. *Front Med (Lausanne)* 2024;**11**:1484327

13. Darlong L, Chakraborty A, Sharma P. Nd-YAG laser-assisted pulmonary metastasectomy: initial experience from a tertiary care cancer center in India. *Indian J Thorac Cardiovasc Surg* 2024;**40**(5):570-576

14. de Brito AA, da Silveira EC, Rigonato-Oliveira NC *et al*. Low-level laser therapy attenuates lung inflammation and airway remodeling in a murine model of idiopathic pulmonary fibrosis: Relevance to cytokines secretion from lung structural cells. *J Photochem Photobiol B* 2020;**203**:111731

15. Ueda T, Takamochi K, Hattori A *et al*. Postoperative management using a digital drainage system for massive air leakage after pulmonary resection. *Surg Today* 2024;**54**(2):130-137

16. Clark JM, Cooke DT, Brown LM. Management of Complications After Lung Resection: Prolonged Air Leak and Bronchopleural Fistula. *Thorac Surg Clin* 2020;**30**(3):347-358

17. Criner GJ. Surgical and Interventional Approaches in COPD. *Respir Care* 2023;**68**(7):939-960

Figure legend

Figure.1 PRISMA flowchart for literature searching.

Figure.2 A risk of bias graph.

Figure.3 A risk of bias summary (“+”low risk;“?”, unclear risk;“-”,high risk).

Figure.4 Forest plot of operation time (A), hospital stay (B), re-operation (C), persistent air leaks (D), pneumothorax (E), other complications (F).