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# 25 Years of Video-Assisted Thoracoscopic Surgery for Lobectomy in Early Stage Lung Cancer: A Review

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## Abstract

The development of video-assisted thoracoscopic surgery (VATS) was a landmark in thoracic surgery. Introduction of VATS for lobectomy was in 1992. During the last 25 years, the minimal invasive surgery for lobectomy in early stage lung cancer evolved gradually and nowadays VATS is the gold standard of treatment options for curative approach.

Despite the lack of evidence by large randomised trails, VATS is associated with a reduction of postoperative pain and a shorter duration of hospital stay. By the reduction of surgical trauma and better cosmetic results it got a high impact in patient's satisfaction. Additionally oncological efficiency of minimal invasive surgery seems to be at least comparable to open technique.

In recent years the minimal invasive technique was refined. Number of ports and the diameter of instruments were reduced. The latest developments in the field of VATS are arising of uniportal VATS and robotic assisted thoracoscopic surgery.

Fewer traumas should improve intensity of postoperative pain and shorten duration of hospital stay. Based on a literature review the main objective of this article is to discuss the superiority of minimal invasive surgery compared to thoracotomy and whether new developments of VATS result in benefits in short-term outcome or long-term results.

**Keywords: Video-assisted thoracoscopic surgery; Lobectomy; Lung cancer**

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## Introduction

Lung cancer is the most frequent cause of cancer-related deaths worldwide [1]. In case of primary lung cancer in early stage, surgical resection with video-assisted thoracoscopic surgery (VATS) is the gold standard of treatment options for curative approach [2].

First thoracoscopic interventions were described by Jacobaeus in 1912. He used a cystoscope to inspect the hemithorax to diagnose different types of pleurisy and creates a therapeutic lung collapse in patients with tuberculosis [3]. It is a coincidence that Davies published his first experiences about treatment of lung cancer by lobectomy in 1912 either [4].

In 1992 the conjunction succeeded, when Lewis et al. released the first publication about the pulmonary resection for malignant lung tumors with VATS. They described the feasibility of using VATS for lobectomy in 40 patients [5].

The rate of pulmonary resections performed by VATS increased from 8% in 2003 up to 44.7% in 2010 [6]. Databases of The Society of Thoracic Surgeons and the European Society of Thoracic Surgeons record a rate of pulmonary resections performed thoracoscopically of 61.5% and 21.8% in the period between 2010 and 2013 [7].

Although, using VATS for more than 20 years, there is no clear definition which is commonly used. Several attempts to clarify terminology where published. Migliore at al suggested the term, VATS' for surgery with a single skin incision of 5 cm to 6 cm and 2-4 ports, where the camera is separated from the other instruments [8]. The Cancer and Leukemia Group B (CALGB) 39802 trial established a definition of VATS lobectomy technique in 2007 which includes no use of rib-spreading; utility incision with a maximum length of 8 cm to deliver the specimen; vein, arteries and airway need to be dissected individually combined with standard lymph node sampling or dissection [9]. Presumably definition of the Cancer and Leukemia Group B is the most accepted.

However, VATS is associated with a reduction of morbidity and post operative pain, shorter hospitalization and faster recovery [10].

Still, there is a lack of evidence about superiority of VATS compared to open lobectomy. Few and small randomised controlled trails (RCT) were published, containing only one RCT including more than 100 patients [11-14]. Most evidence is given from meta-analyses of observational or matched studies.

During the last 20 years there where efforts to minimize the size and number of ports [15] to achieve benefits in patients treatment. Recent technical innovations are uniportal-VATS [8] and robot-assisted thoracic surgery (RATS) [16].

## VATS *vs.* OPEN – oncological results

VATS lobectomy is a common practice to resect lung cancer and it generates several advantages for patients compared to thoracotomy. It is widely accepted that VATS is less traumatic, there is less bleeding, less pain, the patients stay a shorter period in the hospital and they return earlier to normal activity [14].

Although, there is still a debate about the question if lobectomy via thoracotomy is oncological superior to VATS, especially whether open lobectomy might be more effective in the lymph node dissection.

In a meta-analysis of Zhang W et al. [17]. It is shown, that fewer total lymph nodes are dissected in VATS ($p < 0.00001$), despite a similar number of lymph node stations are removed, compared to thoracotomy. Most important statement of the meta-analysis is dissection of less N2 lymph nodes in VATS ($p < 0.0001$) and removal of fewer N1 lymph node stations ($p=0.04$). Disease-free and overall survivals are associated with the number of the dissected lymph nodes. In conclusion Zhang et al. reveal open surgery superior to VATS in oncological effectiveness.

However, there are several refutations for this statement. The meta-analysis of Zhang Z et al. [18]. Investigating results of lymph node dissection, survival rates and recurrence rates in different surgical techniques for early-stage non-small cell lung cancer (NSCLC), showed no significant difference in total number of dissected lymph nodes. Further, they present significantly lower systematic ($p < 0.01$) and regional ($p=0.04$) recurrence rates and higher survival rates ($p < 0.01$) in the VATS group compared to thoracotomy lobectomy.

A meta-analysis of Chen, including 20 studies with 3457 clinical stage I NSCLC patients, shows a significantly higher 5-year survival rate for patients operated with VATS, compared with open lobectomy ($p < 0.01$) [19].

In 2000 Sugi and colleagues published a study where they observed the effect of the surgical approach to the 5-year overall survival and the recurrence rate of clinical stage IA lung cancer [13]. Their survey compared two randomised groups. 52 patients were treated with open surgery and 48 patients were treated with VATS. Sugi showed no superior approach with regard to the incidence of recurrences (VATS 10%, open 19%) and the 5-year survival (VATS 90%, open 85%; $p=0.91$). They state VATS to be an adequate procedure for treatment of clinical stage IA lung cancer.

Several studies with propensity score analysis suggest that thoracoscopic approach for lobectomy does not result in worse long term results, compared to thoracotomy. The surgical technique does not influence the overall survival. Prognostic factors for improved survival are female gender ($p=0.006$), lower age ($p < 0.001$), histopathology ($p=0.008$) and low pathological TNM staging ($p < 0.001$) [20,21].

Summarized, oncological results of thoracoscopic approach are not worse in early stage lung cancer. Despite there might be a lower number of dissected lymph nodes in VATS, there is no difference in the number of resected lymph node stations, in the overall survival and the rate of recurrence, in contrast to open surgery.

An opportunity to improve N2-lymph node dissection in patients designated to be operated with VATS for NSCLC, might be the implementation of video-assisted mediastinoscopic lymphadenectomy before performing lobectomy.

## VATS *vs.* OPEN – pulmonary function and immunological changes

The sequence of functional evaluation of patients planned to undergo a pulmonary resection does not depent on the surgical technique. According to the proposal of Bollinger [22] most important factors of evaluation pulmonary function are FEV1, DLCO and $VO_{2max}$.Absolut contraindications for pulmonary resections are DLCO or FEV1 lower than 30% in patients destined for VATS lobectomy as well as for open approach.

In a prospective observational study of 195 patients who underwent pulmonary lobectomy Salati showed no superiority in functional recovery three months after operation, neither for VATS nor for open technique (23). There were no significant difference in the measured reduction of FEV1 (VATS= -7.2%, Open= -10%, $p=0.2$), DLCO (VATS= -10.6%, Open= -11.9, $p=0.7$) or $VO_{2max}$ (VATS= -6.9%, Open= -5.5%, $p=0.6$) in both groups [23].

Other publications focused on the issue of differences in pulmonary function after VATS- or open lobectomy are based on small case series and without matching procedure [23]. Although they see advantages for pulmonary resection performed with VATS, there remains a lack of evidence.

It is still to be clarified, whether there is of a potential benefit in postoperative pulmonary function depending on the surgical approach. Unfortunately, it is unlikely a RCT or large matched study covering this topic ever comes out.

Craig and colleagues compared the effects of open lobectomy and VATS lobectomy on acute phase responses [12]. It is well known, that acute phase response markers are associated with post-operative complications and inflammatory response leads to circulatory instability and organ dysfunction.

The RCT with a small group of patients (VATS n=19, Open n=16) showed a significantly lower CRP ($p=0.033$) and IL-6 ($P=0.002$) increase in patients treated by VATS. The authors suggest, that VATS surgery is less traumatic than open approach and that the choice of operative procedure might have implications for long-term survival of the patients.

## VATS *vs.* OPEN – complications, morbidity and mortality

The advantages of lobectomy by VATS compared to thoracotomy in regard to postoperative morbidity and mortality is the most indisputable issue. Many surveys, including meta-analysis and RCTs, were published covering this topic [11-14,19].

In a randomized controlled trail, including 55 patients, Kirby et al. stated no difference in the duration of hospital stay or chest tube ($p= >0.05$). Albeit, there was an increase of postoperative complications ($p < 0.05$), like prolonged air leak and pulmonary embolism in the thoracotomy group (n=30), compared to VATS group (n=25) [11].

A meta-analysis of Chen [19] compared 3457 patients in 20 studies, including 1759 patients in the VATS group and 1698 patients in the thoracotomy group. Chen reveals benefit in terms of intra-operative blood loss (p <0.01), drainage time (p=0.01), hospital stay (p <0.01) and incidence of complication (p <0.01) for patients in clinical stage I NSCLC after VATS. In regard to operation time, there were no differences in the two groups (p=0.14). Additionally, a higher 5 year survival rate is stated for the VATS group (p <0.01).

Evidence to prove superiority of VATS in terms of postoperative pain and quality of life was only given by non-randomised and observational studies until Bendixen and colleagues published their RCT in 2016. They investigated the effects of lobectomy via VATS or anterolateral thoracotomy for early stage lung cancer with 102 patients in the VATS group and 99 patients in the thoracotomy group [14]. They evaluated postoperative pain and self-reported quality of life during the first two days after operation and 2, 4, 8, 12, 26, 52 weeks after discharge from hospital. Pain was measured in the numeric rating scale and quality of life by standardized questionnaires. Patients treated by VATS experienced significantly less pain during the first 24 hours (P=0.0012) and had less episodes of moderate-to-severe pain during the 52 months of follow up (P <0.0001). Patients in the VATS group reported of a better quality of life, than the patients of the thoracotomy group (P=0.014).

Once the superiority of VATS in case of postoperative complications is assumed, a second step is to evaluate whether the subgroup of patients with lower performance status might benefit from a minimal invasive approach of operation.

Falcoz conducted a propensity-matched analysis from the ESTS database [24] and showed a lower incidence of complications after VATS lobectomy, especially major cardiopulmonary complications were less frequent (p=0.0094). Patients after VATS lobectomy required less often bronchoscopy for atelectasis (p <0.0001), had less wound infections (p=0.0218) and had a shorter duration of hospital stay (p=0.0003). Especially in the group of patients with an ASA-classification higher 2, VATS lobectomy showed better results than open surgery in regard to postoperative complications. Overall complications were less in the VATS group (p=0.0024), just like major cardiopulmonary complications (p <0.0001) and pneumonia (p=0.0024).

In a matched-case analysis from the ESTS database, Begum focused on the outcome after VATS and open pulmonary lobectomy in patients with low $VO_{2max}$ (< 15 ml/kg/min) [25]. The mortality after thoracotomy was significantly higher in the group with low $VO_{2max}$, compared to a group with higher $VO_{2max}$ (6.7% *vs.* 2.8%, p=0.008). In contrast to this results there were no significant differences in the mortality related to the $VO_{2max}$ in the patient treated via VATS (1.4% *vs.* 5.5%, p=0.4).The postoperative morbidity rate was similar in both groups for both types of surgical techniques. Begum states, patients with a lower $VO_{2max}$ might benefit from a minimal invasive approach for pulmonary resection.

In a propensity score matched analysis Agostini and colleagues investigated the effects of different approach for lobectomy on postoperative pulmonary complications, rehabilitation and physiotherapy requirements [26]. Their results were fewer demand of physiotherapy sessions (p <0.001) and reduced median therapy time per patient after VATS (p <0.001). They conclude that patient treated by VATS required half the physiotherapy resources, were more mobile earlier and experienced less pulmonary complications (p <0.001), compared to open surgery.

In summary, VATS lobectomy is associated with a lower occurrence of relevant postoperative pain and a shorter duration of hospital stay. Lower level of pain may be an explanation for faster rehabilitation, fewer requirements of physiotherapie resources and finally a lower rate of major cardiopulmonary complications. Interestingly, the shorter duration of hospital stay and less postoperative complications lead to increased costs of VATS, although the equipment needed for minimal invasive surgery is more expensive [27]. Particularly in patients with increased risk for cardiopulmonary complications or reduced pulmonary function a minimal invasive approach is favourable.

## Uniportal VATS and RATS - New developments in field of VATS

Since the first descriptions of VATS for pulmonary resections in patients with malignant lung tumors the procedure was refined. The number of ports and the diameter of camera and other instruments decreased to generate the minimal invasive surgery approach even less traumatic. Recent results of this process are the evolution of uniportal VATS and robotic-assisted thoracoscopic surgery (RATS).

Advocates of uniportal VATS claim an advantage for this technique in further reduction of postoperative pain with similar perioperative results, compared to the multi-port approach [28].

However, due to the lack of RCTs comparing uniportal VATS with thoracotomy or multiport VATS the feasibility and safety of uniportal VATS is shown in retrospective and observational studies so far [29]. Compared against thoracotomy uniportal VATS seem to be superior, regarding to the perioperative results.

In different retrospective surveys with propensity matched pair analysis Dai [30] and Shen [31] investigated the differences of perioperative results between uniportal- and multi portal VATS. Dai matched 63 pairs in his study. There was less blood loss (p=0.006), less postoperative pain (p=0.001) and a higher satisfaction rate (p=0.029) for patients treated by single-port VATS. No significant differences were shown in terms of postoperative complications (p=0.273), duration of hospital stay (p=0.703), duration of tube drainage (p=0.195) and surgery time (p=0.418).

In contrast to this Shen performed an analysis of 100 matched pairs and showed no difference in blood loss (p=0.22). Duration of hospital stay (p=0.05) and surgery time (p=0.13) where similar in both groups either. Postoperative pain was not mentioned in his survey.

Harris and colleagues published a meta-analysis [32] covering the topic of uniportal versus multi portal VATS. They selected eight retrospective studies, including three studies with matched pair analysis, in their survey and found statistically significant reduction of hospital stay (P <0.0001), duration of postoperative chest tube (p=0.0006) and reduction in the incidence of overall morbidities (p=0.009) for patients who underwent uniportal VATS lobectomy. Albeit, they state no more significant differences in duration of hospital stay, duration of chest tube, perioperative blood loss and overall morbidities when analysed the propensity matched data.

All in all uniportal VATS is a feasible and secure approach for lobectomy. To show up superiority of uniportal VATS over multiportal technique further studies, including RCTs, are

unavoidable. Additionally there need to be a focus on long-term follow up.

Another minimal invasive approach was the implementation of robotic-assisted surgery (RATS) in thoracic surgery, which came up at the beginning of the 20th century.

As a benefit of RATS towards conventional thoracoscopy, RATS enables a three dimensional imaging and instrumentarium with seven degrees of freedom [33].

Wie and colleagues [34] conducted a systematic review and meta-analysis of 12 retrospective cohort studies to assess the feasibility and short term surgical efficacy of RATS compared with VATS.

The mortality of patients undergoing VATS was higher than in the RATS group (p=0.003) However, after analysing matched studies only the were no statistically significant difference anymore (p=0.06). There were no significant differences in postoperative complications nor in comparison of blood loss or hospital stay. The authors conclude RATS to be a feasible and secure procedure with equivalent short-time efficacy compared to VATS.

In a retrospective review of 498 patients Kwon compared incidence of acute and chronic pain after RATS, VATS and thoracotomy for anatomic pulmonary resection [35]. There was no significant difference between RATS and VATS, but a decrease of acute pain after minimal invasive surgery compared to open approach (p=0.004). There were no differences between the techniques in regard of chronic pain, except the occurrence of chronic numbness, which was more often after open surgery (P=0.0269).

A retrospective study comparing the long term results after VATS, RATS and open surgery was published by Yang [36]. Three groups were matched by propensity score. Yang showed no significant difference in the overall survival between the matched groups (VATS *vs.* RATS, P=0.10; Open *vs.* RATS, P=0.53; VATS *vs.* Open, P=0.08).

These results match with the results of a multi-institutional review of Park [37,38], including 325 patients treated with RATS. The long term oncologic results after RATS lobectomy were equivalent to the stage- specific results after lobectomy for NSCLC performed with VATS or open thoracotomy.

In summary Robotic-assisted thoracoscopy is feasible and secure approach either. It is associated with a similar overall- survival compared to conventional VATS and thoracotomy.

## Conclusion

In case of primary lung cancer in early stage, surgical resection with video-assisted thoracoscopic surgery (VATS) is the gold standard of treatment options for curative approach [2]. The development and increasing implementation of VATS as an approach for lobectomy in early stage NSCLC in the last years, emerged benefit in patients treatment, particularly in reduction of postoperative pain and duration of hospital stay. The oncological results of minimal invasive surgery are equivalent to the results of open surgery, probably they are superior.

It is regardless whether multi portal VATS, uniportal VATS or RATS is used in the individual institution. In the recent literature all of these minimal invasive surgical approaches show similar results in overall survial, major postoperative complications, morbidity and duration of hospital stay.

Presumably the experiences of the surgical team are more important. They have to be familiar with the technique they perform in their center. The International VATS Lobectomy Consensus Group assumes that surgeons need to perform 50 VATS lobectomies to achieve technical proficiency and to maintain operative skills they should perform at 20 lobectomy a year [36]. Only a well-practised team is able to provide the best surgical result for their patients.

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