This item is the archived peer-reviewed author-version of:

Use of robotics in surgical treatment of non-small cell lung cancer

Reference:
Berzenji Lawek, Yogeswaran Suresh Krishnan, van Schil Paul, Lauwers Patrick, Hendriks Jeroen.- Use of robotics in surgical treatment of non-small cell lung cancer
Full text (Publisher's DOI): https://doi.org/10.1007/S11864-020-00778-0
To cite this reference: https://hdl.handle.net/10067/1708260151162165141
Use of robotics in surgical treatment of non-small cell lung cancer

Lawek Berzenji, MD; Krishan Yogeswaran, MD; Paul Van Schil, MD, PhD; Patrick Lauwers, MD; Jeroen M.H. Hendriks, MD, PhD

Institution: 1Antwerp University Hospital, Edegem, Belgium
Department of Thoracic and Vascular Surgery

*Correspondence: Jeroen M.H. Hendriks, MD, PhD, FEBTS
Department of Thoracic and Vascular Surgery
University Hospital of Antwerp & Antwerp University
Level 2, Route 146
Wilrijkstraat 10
B-2650 Edegem (Antwerp)
Belgium
Tel.: +32-3-8213785
Tel.: +32-3-8214361
E-mail: jeroen.hendriks@uza.be

Keywords: non-small cell lung cancer; minimally invasive surgery; da Vinci; robotic-assisted videothoracoscopic surgery (R-VATS); lobectomy; segmentectomy
Opinion statement

Robotic-assisted videothoracoscopic surgery (R-VATS) has become increasingly popular and widely-used since its introduction and is nowadays considered a standard treatment approach in many centres for the treatment of non-small cell lung cancer. R-VATS was initially developed to overcome the drawbacks of VATS by offering surgeons more flexibility and three-dimensional optics during thoracoscopic surgery. The effectiveness of R-VATS lobectomy regarding oncological outcomes, morbidity, mortality, and postoperative quality of life (QoL) has been shown in an increasingly number of studies. More recently, these results have also been corroborated for sublobar resections, more specifically for segmentectomy.

However, no well-powered, multi-centre randomised trials have been performed to demonstrate the superiority of R-VATS compared to open surgery or conventional types of VATS (total VATS, uniportal VATS, etc.). The majority of the evidence currently available is based on non-randomised studies and many studies report conflicting results when comparing R-VATS and conventional VATS. Moreover, there is a lack of data regarding the cost and the cost efficiency of robotic surgery compared to VATS and open surgery. Current evidence suggests that R-VATS costs are higher than VATS and that a deficit can only be prevented when up to 150-300 thoracic surgery procedures are performed annually. Finally, robotic-assisted laparoscopic surgery showed better ergonomics and reduced musculoskeletal disorders compared to non-robotic laparoscopic surgery.

Introduction

Lung cancer is the most common malignancy and one of the leading causes of cancer deaths worldwide [1]. Although worldwide rates of lung cancer vary, an overall increase in new cases of non-small cell lung cancer are seen, mainly due to rising incidences in developing countries [2]. In 2012, estimates have shown a total of 1.8 million new lung cancer diagnoses, comprising approximately 13% of all new cancer diagnoses. Furthermore, the five-year survival rate of lung cancer (17.8%) remains significantly lower than any of the other leading cancers [1]. To battle these odds, a large number of first world countries have implemented tobacco control policies over the last few decades, causing a decline in lung cancer death rates in men. However, despite these efforts, worldwide incidences of female lung cancer and overall lung cancer death rates are still rising, even in most developed nations [3, 4]. In the near future, rates of early stage lung cancer incidence may increase even more due to the implementation of lung cancer screening initiatives. The NELSON-trial and the NLST-trial are two major trials that have shown that low-dose screening with computed tomography scans (CT-scans) result in significantly lower mortality rates in high-risk groups [5, 6, 7].

For early-stage disease, surgical management of non-small cell lung cancer by means of lobectomy with hilar and mediastinal lymph node dissection remains the gold standard [8, 9]. Over the last three decades, the surgical landscape has changed towards minimally invasive surgery with video-assisted thoracoscopic surgery (VATS) as the standard of choice [10]. VATS has indeed proven to result in fewer perioperative complications, less pain and faster recoveries compared to the traditional thoracotomy approach [11]. However, despite these advantages, VATS has several limitations such as a steep learning curve, a lack of instrument flexibility, and poor depth perception and spatial coordination due to the two-dimensional optics [12]. More recently,
Robotic-assisted videothoracoscopic surgery (R-VATS) was developed and has been increasingly performed over the last 10 years due to its three-dimensional optics, more flexible and wrist-like instruments, and a counter-intuitive instrument control system [13]. Despite these advantages and the increasing popularity of R-VATS as a minimally invasive technique, there are still a number of controversial issues regarding R-VATS such as the high operating costs and a longer procedure time due to installation of the robotic system [14]. Furthermore, there is a lack of concrete data from large randomized controlled trials comparing short-term and long-term outcomes of open surgery with VATS and R-VATS. These studies are necessary to demonstrate the superiority of minimally invasive techniques regarding morbidity, mortality, postoperative physical recovery, cost-effectiveness, and long-term safety.

**Treatment**

**R-VATS lobectomy for early-stage lung cancer**

R-VATS is a relatively new minimally invasive technique that was developed to overcome the drawbacks of conventional VATS such as the steep learning curve, two-dimensional optics, lack of instrument flexibility, and difficult hand-eye coordination [15]. Although no well-powered randomized controlled trials are performed comparing R-VATS with open surgery for the treatment of early stage lung cancer, many studies have demonstrated a clear advantage of lobectomy by R-VATS over open surgery regarding perioperative blood loss, hospital length of stay (LOS), postoperative analgesia requirement, postoperative recovery, and 30-day mortality [16, 17, 18, 19]. Compared to conventional thoracoscopic surgery, earlier studies such as the Nationwide Inpatient Sample study in 2014 showed that R-VATS had higher risks of cardiovascular complications and iatrogenic bleeding [20]. However, more recent studies have not found any differences in short-term outcomes between VATS and R-VATS [21, 19]. In a recent meta-analysis by Liang et al. comparing R-VATS to VATS, a lower 30-day mortality and conversion rate to open surgery was seen in favour of R-VATS in 3239 patients [22•]. In addition, Emmert et al. showed an improved survival for R-VATS and Oh et al. demonstrated lower postoperative complication rates and shorter hospital stays for R-VATS compared to VATS. However, in the propensity-matched analysis performed by Oh et al, no difference in mortality between VATS and R-VATS was seen [23, 24]. Similarly, no significant difference between VATS and R-VATS was found regarding survival in the database analysis of the Society of Thoracic Surgeons (STS) which included 1220 R-VATS and 12378 VATS lobectomies [25]. All these data indicate that R-VATS is a safe and very effective minimal invasive technique for the surgical treatment of early stage lung cancer.

Only a limited number of studies have been published regarding the oncological outcomes and effectiveness of R-VATS surgery compared to open surgery or VATS. Wilson et al. showed an increased rate of nodal upstaging for robotic resection compared to VATS or open surgery in a retrospective study of 302 patients [26]. Another study by Yang et al. showed a higher number of nodal stations sampled by R-VATS as well [27]. However, data analysis of 64,676 patients from the National Cancer Database (NCDB) in the USA comparing R-VATS to conventional VATS and open surgery did not show superiority of R-VATS regarding lymph node yield or nodal upstaging of non-small cell lung cancers (NSCLC) [28]. The results of their database analysis suggested that both R-VATS and conventional VATS approaches are non-inferior to open surgery for intraoperative lymph node evaluation. Despite all these promising results, randomized controlled
trials are necessary to effectively demonstrate the superiority of minimally invasive techniques over open surgery without compromising oncologic outcomes. While no such study is started yet for R-VATS, the VIOLET study (NCT03521375) has commenced recruiting 500 patients to demonstrate improved patient-reported outcome measures after VATS when compared to open surgery in a randomized set-up.

**R-VATS segmentectomy for early stage lung cancer**

Currently, lobectomy with systematic mediastinal lymph node dissection is considered the gold standard for early-stage NSCLC [29, 30]. However, lobectomies result in a significant loss of lung tissue and worse quality of life (QoL) compared to less extensive resections. For elderly patients or patients with limited pulmonary reserve, sublobar resections, including wedge resection and anatomical segmentectomy, have been proposed as alternative surgical techniques [31, 30]. Several studies have been performed investigating oncological and survival outcomes of sublobar resections. However, there is no clear consensus on the noninferiority of sublobar resections compared to lobectomy. Both Khullar et al. and Subramanian et al. performed an analysis of the NCDB to investigate long-term results of sublobar resections [32, 33]. Khullar et al. concluded that overall survival was better after lobectomy and that sublobar resections resulted in higher rates of positive resection margins and inadequate lymph node dissection [33]. Subramanian et al. also found higher rates of positive resection margins and lower numbers of dissected lymph nodes in sublobar resections. Furthermore, in their study, sublobar resections were associated with higher risks of recurrence [32]. However, there is a growing amount of evidence from other studies that suggest that sublobar resection, and more specifically segmentectomy, has similar overall survival, disease-free survival, and oncological outcomes with improved QoL compared to lobectomy [34, 35]. Despite a growing number of studies suggesting that segmentectomy is a valuable alternative for lobectomy in selected cases, there is a lack of data regarding long-term results of robotic segmentectomy. A study performed by Dylewski et al. showed that robotic segmentectomy has lower complication rates than robotic lobectomy [36]. Other studies also found similar complication and mortality rates for robotic segmentectomy compared to VATS. In a recent study by Nguyen et al., oncological outcomes of robotic segmentectomy were investigated. The authors found a 14% upstage rate, 6% local or regional recurrence rate, and 73% lung cancer-specific survival for pathological stage I NSCLC. They concluded that robotic segmentectomy is a safe and feasible procedure for selected patients with limited pulmonary reserve [37]. In another recent study by Xie et al., a retrospective analysis was performed of 215 patients that underwent atypical or anatomical segmentectomy by either R-VATS or conventional VATS. The authors compared short-term outcomes between R-VATS and conventional thoracoscopic surgery. They concluded that robotic surgery was safe and resulted in higher rates of dissected lymph nodes compared to conventional VATS without increasing postoperative complication rates [38]. Despite these promising studies, the results of these studies have not been demonstrated in propensity-score matched series or randomized controlled trials (RCT). Currently, there are 2 ongoing RCTs that aim to investigate the oncological efficacy of sublobar resections compared to lobectomy: the Cancer and Leukemia Group B (CALGB) 140503 Phase III trial (NCT00499330) which aims to compare the outcomes of lobectomy with limited resection, and the JCOG0802/WJOG4607L trial which aims to evaluate the outcomes of lobectomy and segmentectomy [39, 40].
Costs/Cost-analysis

The use of robotic surgery for pulmonary resections has increased significantly in the last few years with an ever increasing amount of new robotic thoracic surgery programs being set up worldwide [41]. A recent analysis of the NCDB showed that R-VATS was used for approximately 9% of all lobectomies in the United States [42]. However, concerns have been raised regarding the high costs of acquiring and maintaining robotic systems as well as the additional learning curve for new robotic surgeons. A number of studies have attempted to perform cost analysis studies of R-VATS surgery, however, large discrepancies exist between these studies due to different definitions of cost [41]. A study by Paul et al. using the Nationwide Inpatient Sample (NIS) database found that median costs of R-VATS was significantly higher than conventional VATS [20]. Similar results were found in a study by Swanson et al. using the Premier registry database [43]. However, two single-institution analyses have shown that R-VATS lobectomy is comparable or less expensive than open lobectomy [44, 45]. This can be explained by the fact that R-VATS has reduced operation times and improved outcomes, especially in high-volume centres. However, most of the data from these studies is derived from early experiences with R-VATS and outdated cost analyses. More uniformity is necessary to delineate the exact costs associated with robotic surgery and to be able to perform cost-benefit studies in the near future. It is also expected that costs will decline as soon as more companies bring robotic systems to the market [41].

Ergonomics

Work-related musculoskeletal disorders (WMSDs) are prevalent among surgeons and often receive little attention in the daily practice of surgeons and surgical residents [46]. This is due to the fact that surgery often includes repetitive movements that require significant force on the trunk and upper extremities, and prolonged static body positioning [47]. However, these WMSDs can result in injuries such as carpal tunnel syndrome, wrist tendonitis, thoracic outlet syndrome, etc. if not prevented early on [48, 47]. Studies regarding ergonomics of robotic surgery and conventional laparoscopic surgery have shown that surgeons report overall less pain when using robotic surgery approaches [49, 50]. Furthermore, robotic surgery has also been associated with less wrist, elbow, shoulder, neck, back, hip, knee, ankle, and foot pain compared to conventional laparoscopy [51, 50, 49]. In addition, ergonomic training can significantly reduce pain among robotic surgeons. However, only a limited number of surgeons receive these training courses [47]. Current studies on ergonomics is often based on subjective data derived from non-validated assessment tools. Better and more objective tools are necessary to be able to clearly define surgical ergonomic risk factors and to implement interventions to prevent WMSDs in surgeons.

Local situation and refunding in Belgium

In Belgium refunding is limited for robotic procedures with exception of prostatectomy. In the case of R-VATS for anatomical lung resections, costs for the procedure and materials are refunded with a maximum of 1000 euro for the procedure and 1800 euro for stapling devices. In addition to this, no surplus in stapling costs can be charged to the patient. Due to these expenses, we do not use the custom da Vinci stapling devices anymore in our centre. During surgery, lung stapling is performed by the assisting surgeon at the operating table. In our case, we use automated stapling device with kits of cartridges that are within the refunded maximum cost in order to prevent
surplus costs. In our hospital, the robot is stationed in one operating room and used daily by several departments. The schedule is based on turn-over and re-examined every 4-6 months in order to guarantee its maximal use.

Before using the da Vinci robot for anatomical lung resections, we performed >200 VATS lobectomies and segmentectomies by a total thoracoscopic technique as described by Hansen [52]. When the da Vinci Xi was installed in 2016, we changed to R-VATS for these procedures. The learning curve was less than 10 procedures. So far, more than 150 R-VATS anatomical resections were performed. In total, only one patient died due to an aspiration pneumonia. We experienced 3 conversions, 2 due to intra-operative bleeding and one for a tear of the pars membranacea of the left main bronchus during stapling of the upper lobe bronchus. The R-VATS procedure is experienced as superior to VATS regarding dissection, view, handling (especially for lymph node dissection and more complex procedures such as segmentectomy), blood loss, and comfort for the surgeon. The total length of the procedure is longer but the real operating time (console time) is less. Similar to VATS, none of the R-VATS patients are hospitalised at the intensive care in contrast to thoracotomy patients in the past with similar stages. The length of stay in the hospital is equal to the conventional VATS series and mainly determined by time of drainage and need for iv antibiotics.

In addition to anatomical lung resections, we also use the Xi da Vinci robot for resection of mediastinal tumours such as thymomas and neurogenic tumours, first rib resections for thoracic outlet syndrome, selective postganglionic sympathectomy, hyperhidrosis and facial blushing, division of the arcuate ligament in case of median arcuate ligament syndrome, clipping of lumbar arteries in case of type II endoleak after EVAR if embolization fails, and for aorto-(bi)femoral bypasses when endovascular options fail.

Compliance with Ethics Guidelines

Conflict of Interest

The authors have no conflicts of interest to disclose.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance


Follow-up study on large nationwide lung cancer screening trial from the United States.


Large Dutch/Belgian randomized controlled trial regarding lung cancer screening with low-dose CT-scans.


One of the first large retrospective studies on the long-term results and surgical outcomes of robotic anatomical segmentectomy.


