Robotic thoracic surgery versus video-assisted thoracic surgery for lung cancer: a meta-analysis

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METHODS: We searched articles indexed in the PubMed and ScienceDirect databases that met our predefined criteria, published up to January 2015. A meta-analysis was performed by combining the results of reported incidences of perioperative morbidity and mortality. The relative risk (RR) was used as a summary statistic.

RESULTS: Eight eligible articles with 3379 subjects were considered in the analysis (8 articles for morbidity, while 4 articles for mortality). Overall, pooled analysis indicated that perioperative morbidity and mortality were similar between RTS and VATS (morbidity: RR, 1.02; 95% CI, 0.94–1.10; P = 0.605; mortality: RR, 0.28; 95% CI, 0.06–1.25; P = 0.095). No evidence of publication bias was observed.

CONCLUSIONS: This meta-analysis showed that RTS resulted in similar outcomes compared with VATS cases. RTS appears to be an appropriate alternative to VATS, which is associated with improved outcomes compared with open thoracotomy. RTS should be studied further in selected centres and compared with VATS in a randomized fashion to better define its potential advantages and disadvantages.

Keywords: Robotic thoracic surgery • Video-assisted thoracic surgery • Minimally invasive approach • Lung cancer • Meta-analysis

INTRODUCTION

Lung surgery for the purpose of diagnosis or treatment has evolved in the past 2 decades. There are several different minimally invasive approaches, such as robotic thoracic surgery (RTS) and video-assisted thoracic surgery (VATS), which are accepted treatment modalities for lung cancer [1, 2].

VATS is an evolving technique and is increasingly applied in situations where traditional open thoracotomy has long been used [3]. Compared with open thoracotomy, the purported benefits of VATS in lung surgery include smaller incisions, less blood loss, less pain, less complications, less respiratory compromise, faster recovery times and shorter lengths of stay [4]. Based on the systematic reviews of randomized and non-randomized clinical trials [5], and in comparative studies [6], there were fewer complications, shorter time and shorter length of stay in VATS patients than their open thoracotomy counterparts. In multivariate analysis, VATS was associated independently with a reduced risk of complications [6].

RTS, a robotic approach, has emerged as a viable minimally invasive surgery for lung cancer resection [7, 8]. Robotic lobectomy has been proposed as an alternative to VATS [9]. Advocates for RTS describe theoretical advantages of this technique over VATS, including 3D visualization of the operative field and greater articulation of the robotic instruments [7]. Several published studies have demonstrated that robotic resection is safe with equivalent clinical outcomes when compared with similar patients undergoing VATS or open resection [7, 10]. However, some clinical studies find that RTS results in similar outcomes compared with VATS cases [11–13].

There is no systematic review conducted so far to compare the perioperative outcomes of RTS with VATS for patients with lung cancer. Meta-analysis is a well-established statistical tool that serves for integration of data from independent studies in order to formulate more general conclusions. We therefore undertook a meta-analysis of studies to compare the morbidity and mortality of RTS with VATS for lung cancer resection.
MATERIALS AND METHODS

Search strategy

We performed a systematic search of the PubMed and ScienceDirect databases up to January 2015 using the searching strategy: ((robot-assisted OR robot OR robotic approaches) AND (video-assisted OR video)) AND (lung cancer or carcinoma). Emails were sent to the authors of identified studies for additional information if necessary. Reference lists of all eligible studies were screened to identify potentially eligible studies.

Selection criteria

Three authors conducted the search independently. Titles and abstracts were screened for subject relevance. Studies that could not be definitely excluded based on abstract information were also selected for full text screening. Two authors independently selected eligible studies for inclusion possibility. Where there was a disagreement for study inclusion, a discussion was held to reach a consensus. Eligible studies had to meet the following criteria: (i) human study; (ii) retrospective observational study, case-control study, cohort study or randomized clinical trial; (iii) studies providing data of perioperative morbidity or mortality for both RTS and VATS for lung cancer. The exclusion criteria included: (i) in vitro study; (ii) animal study, review or case report; (iii) studies providing neither morbidity nor mortality for either RTS or VATS; (iv) sample less than 20.

Data extraction and quality assessment

Two authors independently extracted data using a standard form. Discrepancies were resolved by discussion with a third investigator and by referencing the original report. The following information was extracted from each included study: country, first author’s family name, year of publication, study type, study period, demographics of subjects (number of subjects and age) and data of morbidity and mortality.

The qualities of all included studies were assessed using the Newcastle-Ottawa Scale. The assessment tool focused on three aspects, including participant selection, comparability and exposure. The studies would be assigned stars of 9 if all items were satisfied. Two authors assessed the quality independently.

Statistical analysis

Meta-analysis was performed by combining the results of reported incidences of perioperative morbidity and mortality. The relative risk (RR) was used as a summary statistic. The RRs were calculated using either fixed-effects models or, in the presence of heterogeneity, random-effects models. Heterogeneity between studies was tested through the $\chi^2$ and $I^2$ tests. If the $I^2$ value was greater than 50% and the $P$-value was less than 0.10, the meta-analysis was considered as homogeneous. In the presence of heterogeneity, subgroup analyses were used to identify the possible sources of heterogeneity. The stability of the study was detected by sensitivity analysis, through re-meta-analysis with one involved study excluded each time. Publication bias was measured using Begg’s tests and visualization of funnel plots. All $P$-values were two-sided. All statistical analyses were performed with Stata version 11.0 (Stata Corp, College Station, TX, USA).

RESULTS

Literature search

The systematic literature review identified 11 full articles for detailed assessment, among which 3 were excluded for reporting neither mortality nor morbidity for RTS and VATS. A manual search of the reference lists did not identify any additional relevant studies. Overall, 8 eligible articles with 3379 subjects from 9 retrospective observational studies were considered in the analysis, in which 8 articles were for morbidity, while 4 articles were for mortality [7, 8, 10–15]. A flow diagram of the study selection process is presented in Fig. 1.

Study characteristics and quality assessment

The detailed characteristics of the included studies and the results of the quality assessment are summarized in Table 1. All studies included for final analysis in the present meta-analysis were from retrospective observational studies. In these 9 retrospective observational studies, 3379 patients with lung cancer were compared, including 2110 patients who underwent VATS and 1269 patients who underwent RTS. The earliest study was published in 2011, and the latest in 2014. By geographic location, studies were conducted in four different countries (USA, Korea, Austria and Turkey). The number of subjects in each study ranged from 52 to 1644. The mean age of the population ranged from 57 to 77 years. The overall study quality averaged 6.5 stars (range 6–7) on a scale of 0–9.

The detailed characteristics of VATS and RTS are summarized in Table 2. Six of the included articles provided information about the ports used in VATS. Seven of the included articles reported about the surgical technique of RTS, six reported about the arms of the Da Vinci surgical system, and only four reported about the type of the Da Vinci surgical system. Only five of the included articles provided the number of surgeons on the RTS side, while four reported about the number of surgeons on the VATS side, and we had no

Figure 1: Flow diagram of screened and included papers.
idea about the number of surgeons in the other three articles. Unavailability of the robotic platform makes the procedure surgeon-dependent.

Assessment of perioperative morbidity

The fixed-effects meta-analysis results indicated that the overall perioperative morbidity rate was not significantly different between patients who underwent RTS when compared with patients who underwent VATS (RR, 1.02; 95% CI, 0.94–1.10; P = 0.605) (Fig. 2). The nine sets of results showed no significant amount of heterogeneity ($I^2 = 0$, $P = 0.892$) (Fig. 2).

Assessment of perioperative mortality

The present meta-analysis in the fixed-effects model showed that there was also no significant difference in the overall perioperative mortality rate between RTS and VATS (RR, 0.28; 95% CI, 0.06–1.25; $P = 0.095$) (Fig. 3). The four sets of results showed no significant amount of heterogeneity ($I^2 = 0$, $P = 0.849$) (Fig. 3).

### DISCUSSION

There are increased numbers of early-stage lung cancers in at-risk populations potentially best removed by minimally invasive surgical approaches. VATS has been shown to be safe and effective, with benefits in terms of reduced postoperative pain and better functional and aesthetic results compared with open lobectomy [16]. However, some randomized trials [17] indicate that the oncological results are equivalent to those of open surgery. Although VATS seems to be a safe and effective method for the treatment of early-stage lung cancer, it has not been widely adopted by the surgical community [18]. It has been estimated that only about 20% of potential patients with lung cancer receive this treatment.

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**Table 1:** Summary of relevant studies identified in the present meta-analysis on RTS versus VATS for lung cancer

<table>
<thead>
<tr>
<th>Studies</th>
<th>Country</th>
<th>Study type</th>
<th>Study period</th>
<th>RTS Mean age</th>
<th>No. Morbidity</th>
<th>Mortality</th>
<th>VATS Mean age</th>
<th>No. Morbidity</th>
<th>Mortality</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jang et al. [12]</td>
<td>Korea</td>
<td>ROS</td>
<td>2006–2009</td>
<td>64</td>
<td>40</td>
<td>4</td>
<td>60</td>
<td>40</td>
<td>7</td>
<td>NR</td>
</tr>
<tr>
<td>Louie et al. [10]</td>
<td>USA</td>
<td>ROS</td>
<td>2009–2011</td>
<td>65</td>
<td>46</td>
<td>20</td>
<td>66</td>
<td>34</td>
<td>12</td>
<td>NR</td>
</tr>
<tr>
<td>Augustin et al. [8]</td>
<td>Austria</td>
<td>ROS</td>
<td>2001–2009</td>
<td>65</td>
<td>26</td>
<td>11</td>
<td>65</td>
<td>26</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Swanson et al. [11]-1 ROS</td>
<td>USA</td>
<td>ROS</td>
<td>2009–2011</td>
<td>66</td>
<td>295</td>
<td>159</td>
<td>66</td>
<td>295</td>
<td>151</td>
<td>NR</td>
</tr>
<tr>
<td>Swanson et al. [11]-2 ROS</td>
<td>USA</td>
<td>ROS</td>
<td>2009–2011</td>
<td>61</td>
<td>325</td>
<td>179</td>
<td>61</td>
<td>325</td>
<td>165</td>
<td>NR</td>
</tr>
<tr>
<td>Demir et al. [14]</td>
<td>Turkey</td>
<td>ROS</td>
<td>2007–2014</td>
<td>61</td>
<td>34</td>
<td>8</td>
<td>57</td>
<td>65</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>Lee et al. [15]</td>
<td>USA</td>
<td>ROS</td>
<td>2011–2012</td>
<td>71</td>
<td>35</td>
<td>4</td>
<td>77</td>
<td>34</td>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

RTS: robotic thoracic surgery; VATS: video-assisted thoracic surgery; ROS: retrospective observational study; NR: not reported.

**Table 2:** The characteristics of VATS and RTS

<table>
<thead>
<tr>
<th>Studies</th>
<th>Type of Da Vinci system</th>
<th>Surgical technique</th>
<th>Arms</th>
<th>No. of surgeons</th>
<th>Ports</th>
<th>No. of surgeons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jang et al. [12]</td>
<td>S</td>
<td>Robot-assisted lobectomy</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>1*</td>
</tr>
<tr>
<td>Louie et al. [10]</td>
<td>NR</td>
<td>Completely portal robotic lobectomy</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>4*</td>
</tr>
<tr>
<td>Augustin et al. [8]</td>
<td>NR</td>
<td>Robot-assisted lobectomy</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Swanson et al. [11]-1 ROS</td>
<td>NR</td>
<td>Robot-assisted lobectomy</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Swanson et al. [11]-2 ROS</td>
<td>NR</td>
<td>Robot-assisted lobectomy</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Deen et al. [13]</td>
<td>Si</td>
<td>Completely portal robotic lobectomy</td>
<td>3</td>
<td>NR</td>
<td>4</td>
<td>NR</td>
</tr>
<tr>
<td>Kent et al. [7]</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Demir et al. [14]</td>
<td>Both S and Si</td>
<td>Completely portal robotic segmentectomy</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>NR</td>
</tr>
<tr>
<td>Lee et al. [15]</td>
<td>S</td>
<td>Completely portal robotic lobectomy</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>1*</td>
</tr>
</tbody>
</table>

RTS: robotic thoracic surgery; VATS: video-assisted thoracic surgery; NR: not reported.

*RTS and VATS were performed by the same surgeons.*

Publication bias and sensitivity analysis

Publication bias was determined by Begg’s test and visualization of the funnel plot. There was no evidence of publication bias for morbidity ($P = 0.251$) (Fig. 4) and mortality ($P = 0.296$) (Fig. 5). Sensitivity analysis showed that excluding any one study from the pooled analysis did not vary the results substantially (Table 3).
Figure 2: Forest plot of the RR of perioperative morbidity after RTS versus VATS for lung cancer. RR: relative risk; RTS: robotic thoracic surgery; VATS: video-assisted thoracic surgery.

Figure 3: Forest plot of the RR of perioperative mortality after RTS versus VATS for lung cancer. RR: relative risk; RTS: robotic thoracic surgery; VATS: video-assisted thoracic surgery.

Figure 4: Funnel plot of the RR of perioperative morbidity after RTS versus VATS for lung cancer. RR: relative risk; RTS: robotic thoracic surgery; VATS: video-assisted thoracic surgery; logor: logarithm of RR to base 10; s.e.; standard error of the logarithm of RR to base 10.

Figure 5: Funnel plot of the RR of perioperative mortality after RTS versus VATS for lung cancer. RR: relative risk; RTS: robotic thoracic surgery; VATS: video-assisted thoracic surgery; logor: logarithm of RR to base 10; s.e.; standard error of the logarithm of RR to base 10.
As we know, successful thoracoscopic surgery is likely surgeon-dependent and requires patience and acquisition of new technical skills. Because the learning curve for VATS is steep, assessments of trainee progress and operator competency are important aspects of quality assurance [19]. In addition, the uncomfortable position of the surgeon, the lack of instrument flexibility and the 2D view make VATS cumbersome, resulting in a long learning curve of approximately 40–50 cases, and for some surgeons, the use of VATS may compromise the oncological quality of the surgical treatment [20].

However, RTS may address many of the shortcomings of VATS [12]. Gains have been made in other cancer-related disease processes for prostate cancer, kidney cancer, colorectal cancer, gastric cancer and uterine cancer [21]. Robotic surgery in humans was first reported that RTS for lung cancer is feasible and safe [10]. VATS showed a steep learning curve, whereas RTS showed more favourable results beginning with the initial case and had a less steep learning curve, demonstrating its better adaptability [24]. Because of its easier manoeuvrability, the robotic surgical system can enable the rapid acquisition of dexterity and accuracy in a short time [25].

In the present study, our systematic review of over 3300 participants from 9 retrospective observational studies found that perioperative morbidity and mortality were similar between patients with lung cancer who underwent RTS and those who underwent VATS. Thus, we suggest that RTS is an appropriate alternative to VATS, which is associated with improved outcomes compared with open thoracotomy for lung cancer.

To the best of our knowledge, this is the most comprehensive meta-analysis to compare the perioperative outcomes of RTS with VATS for patients with lung cancer. We made sure to minimize the bias by means of study procedure. Not only did we search the PubMed and ScienceDirect databases to identify potential studies, but we also manually examined all reference lists from relevant studies. Sensitivity analysis showed that excluding any one study from the pooled analysis did not vary the results substantially. Publication bias was also absent, as determined by Begg’s test. However, the possible limitations of our study must be considered. Firstly, including only 3379 participants from 9 retrospective observational studies with no randomized clinical trial included in the meta-analysis might weaken the quality of the results. Secondly, patients’ baseline characteristics differed between studies, and there was inevitably some variability in the surgical techniques and skills of surgeons. Thirdly, the present study demonstrated a large number of old-version Da Vinci robotic systems (five of eight articles included demonstrated the three-arm robotic system, which are summarized in Table 2), thus, this meta-analysis may ignore the possible benefits of upgrading the technology. Fourthly, we could only compare the perioperative outcomes of RTS with VATS for patients with lung cancer in the present meta-analysis, but failed to establish a real assessment of outcomes for each technique. Despite these limitations, our findings point out a new direction for future research. We suggest that further study in a randomized fashion should be conducted to compare RTS with VATS to better define the potential advantages and disadvantages of both of the minimally invasive approaches for lung cancer, and that further study should also focus on a real assessment of outcomes for each technique.

In conclusion, the present meta-analysis indicated that RTS resulted in similar perioperative morbidity and mortality compared with VATS cases. Thus, we suggest that RTS is an appropriate alternative to VATS for lung cancer resection. In the absence of randomized, controlled trials for comparing RTS with VATS, our findings represent the highest level of clinical evidence in the current literature on this issue.

Conflict of interest: none declared.

REFERENCES


