Do minimally invasive approaches increase the survival of patients with early-stage lung cancer undergoing lobectomy

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The recent study "Long-term survival based on the surgical approach to lobectomy for clinical stage I nonsmall cell lung cancer: comparison of robotic, video-assisted thoracic surgery, and thoracotomy lobectomy" by Yang *et al*. sheds light on the benefits but also on the limits of minimally-invasive (MI) lobectomy (1).

In the 90', thoracoscopy evolved with great enthusiasm. In 1993, Thomas J. Kirby proved the safety of video-assisted thoracic surgery (VATS) lobectomy with his initial experience of 44 lobectomies (2). With the description of complete tumor resection with lymph node sampling by Robert McKenna in 1994, VATS lobectomy became more acceptable in the treatment of lung cancer (3). Furthermore, major advances in thoracoscopy imaging and instrumentation facilitated more complex procedures, such as segmentectomy, pneumonectomy or sleeve-resections. In parallel, in the early 90', the first master-slave robot was created by *SRI International*. In 1995, *Intuitive Surgical* acquired *SRI*'s intellectual property and created the da Vinci® Surgical System, approved by the FDA in 2000. Robot-assisted surgery is considered the most important surgical development of the last 15 years and created great enthusiasm. Compared to conventional thoracoscopy, the da Vinci® system created an immersive operating environment. Four interactive robotic arms permitted an enhanced dexterity with three degrees of freedom wrist inside the patient and a 3D display provided an intuitive manipulation. The first robot-assisted thoracic surgery (RATS) lobectomy was performed in 2002 (4).

The benefits of MI lobectomy suffer from little high-quality evidence. In fact, only two randomized control trials (RCTs) comparing surgical outcomes of VATS lobectomy to thoracotomy were performed in 1995 and 2000 (5,6). These RCTs did not show a better outcome with VATS approach but they had a number of limitations and used a rib-spreading procedure for VATS. In 2001, a RCT showed lower surgical stress after VATS (7). Over time, thanks to published meta-analyses of randomized and non-randomized trials with clear benefits of VATS over thoracotomy, VATS lobectomy was used increasingly as an alternative to thoracotomy lobectomy. These benefits included decreased postoperative pain and length of hospital stay and fewer complications (8). Moreover, a recent RCT published in the *Lancet* compared postoperative pain and quality of life after lobectomy using VATS or thoracotomy (N=206). It demonstrated that VATS was associated with less postoperative pain and a better quality of life during the first year after surgery. However, postoperative complications (prolonged air leak, re-operation for bleeding, twisted middle lobe, arrhythmia and neurological events) didn't differ between the two groups (9). The cost-effectiveness benefit of VATS compared to open lobectomy was demonstrated by two previous studies (10,11).

In regards to robot-assisted surgery, a recent propensity-matched analysis with 69 pairs showed comparable post-operative outcomes and similar oncologic results for lung cancer between RATS and VATS (12). Furthermore, RATS approach achieved a more accurate nodal staging due to the 3D display and the flexible instrumentation (1,13). However, RATS had higher hospital costs and longer operative time than VATS (12). To be adopted, the clinical benefit of RATS, such as for nodal staging, must

be considerable. According to clinicaltrials.gov, the current RCT (NCT02617186) comparing VATS and RATS lobectomy should answer these questions.

For the first time, Yang *et al*. matched three surgical approaches (open, VATS, RATS) to lobectomy for early-stage cancer and compared long-term overall survival (OS) and the disease-free survival (DFS) (N=470). This study revealed similar complication rates among the three groups but the length of stay in hospital was shorter for MI approaches. At 10 years (median =52.1 months), comparable DFS and OS were demonstrated in the three groups (1). So, the surgical approaches for lobectomy had no impact in the long-term survival in patients with early-stage lung cancer. This study corroborates previous retrospective studies by Higuchi *et al*. (N=160) and Flores *et al*. (N=741), suggesting an equivalent 5-year survival between VATS and thoracotomy (14,15).

Despite the benefits of VATS lobectomy, traditional thoracotomy approach remains the most common procedure in the United States and in Europe (16,17). According to the European Society of Thoracic Surgery registry, only 11.3% of lobectomies were performed by VATS between 2010 and 2012 with a large variation in practice across different European countries (17). For example, in France, 11% of lobectomies were performed by VATS between 2011 and 2012, while 55% were performed by VATS in Denmark at the same time (17,18). In our unit, VATS lobectomy program only started in 2012 but with a rapid increase; in 2015, 81% of lobectomies for non-small cell lung cancer were performed by VATS. Few thoracic centers use RATS lobectomy. Its widespread utilization seems compromised by the high cost of the system (around $2 millions) and the higher cost per-procedure. However, 3'660 da Vinci® system have been sold worldwide as of March 2016: 2,431 in the United States, 616 in Europe, 441 in Asia, and 172 in the rest of the world (19).

This slow widespread of MI approaches however is not inherent to thoracic surgery. Despite multiple RCTs in favor of MI surgery, there is a wide geographic variation in the utilization of laparoscopic approach for colon cancer in the United States, varying from 0% to 67% (20). Surgical innovations follow a natural evolution rather than a revolution. Experience, habits, teaching and educational resources for patients play a major role in the development of MI approaches. Furthermore, technological assessment is a long and difficult process because it is related to evidence-based medicine and cost-effectiveness analysis. Furthermore, the formulation and dissemination of recommendations followed by quality control takes considerable time.

In conclusion, the study by Yang *et al*. suggests that the surgical approaches (open, VATS, RATS) for lobectomy have no impact on the long-term survival in patients with early-stage lung cancer. The rate of complications among the different approaches remains contradictory. While VATS lobectomy can now be considered validated, RATS lobectomy must pass through the same technology assessment. Finally, because there are some clear benefits for the patients, MI lobectomy must be enforced to become the standard approach. This will ensure the implementation of new technologies for the benefit of the patients.

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