

Nonintubated thoracic surgery: a lead role or just a walk on part?

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With the advent of the patient-centered health care concept, thoracic surgeons of the modern era are called to minimize at most the overall invasiveness of their performances, while increasing safety and effectiveness as much as possible. This need has driven an outstanding development of minimally-invasive surgical approaches, which are now the standard to perform a broad spectrum of thoracic operations. A recent and fascinating evolution in this field is represented by the increasing interest toward the use of so-called “non-intubated” anesthesia protocol, which are expected to provide a further improvement in postsurgical outcomes (1-8).

My colleagues and I started to perform this kind of operation in the early 2000's. The basic idea of this emerging surgical practice was that the patients would remarkably benefit from the avoidance of general anesthesia and double-lumen ventilation. This convincement is founded solidly on a large body of observations that the latter method, which is since long time the standard one in thoracic surgery, may cause a series of complex inflammatory changes on the ventilated lung, and even on distant organs (1,7-14). The avoidance of these effects is expected to translate into a lesser morbidity rate and a faster perioperative recovery, especially in the subgroup of patients with chronic respiratory failure. Another theoretical pro was that non-intubated surgery could offer some benefits in terms of oncological outcome, as the reduction in ventilator-related stress and the lesser need of opioids are believed to preserve perioperative anticancer immunosurveillance (15-18).

Therefore, in our early experience, we started to adopt non-intubated videothoracoscopy for removing peripheral lung lesions, mostly metastases and stage I non-small cell lung cancer, in fully awake patients with increased risk for general anesthesia (1). After having taken familiarity with the

basic technique, we came to some interesting observations. First, we noted that the collapse of the operated lung (that is, surgical pneumothorax) was well tolerated by almost all patients. Indeed, changes in basic vital parameters were irrelevant, and adequate arterial oxygenation could be maintained with just oxygen administration via a facial mask. The increase in arterial CO₂ was of mild extent, almost always asymptomatic, and usually below the so-called permissive limit (60-70 mmHg). Furthermore, we noted that, despite the preservation of diaphragm contractility, breathing movements of the operated lung were minimal, and even lacking in some instances, without any relevant disturbance to the surgical maneuvers. These observations prompted us to go on with this surgical method, and subsequently we extended the indication to other conditions. These included fibrinopurulent pleural empyema (6) and advanced pulmonary emphysema (7). The latter was deemed to be particularly challenging, due to the extremely severe respiratory impairment, the higher likelihood of pleural adhesions, and the presence of a redundant, hyperinflated lung which could jeopardize the technical feasibility. Even in this field, however, we reported encouraging results. In particular, the employ of a non-resectional lung reduction technique allowed us to fasten the operating time and perform the “awake” operation in an easier and safer way.

At that time, our standard anesthetic protocol was a combination of thoracic epidural anesthesia and the avoidance of intraoperative sedation. This was due to the need of maintaining an effective spontaneous ventilation throughout the operation, while offering an optimal analgesic coverage. When we and other groups felt that the time was right to start performing non-intubated major lung surgeries, however, new concerns came out.

First, this kind of operations takes longer, hence the need of having the patient “comfortably numb” throughout the operation while preserving central airway patency. Second, the surgical maneuvers in proximity of the hilar structures can trigger cough reflex. This was not a concern for minor operation, but could instead negatively affect both the safety and feasibility when performing anatomical resection. The most remarkable improvements in this field, were the introduction of vagal blockade, and the employ of bi-spectral index monitoring during the operation. Both these techniques enormously facilitated non-intubated major lung resections, as they can help prevent cough, and allow to titrate the level of sedation under a real-time measurement. We could never figure out that reaching the goal of performing non-intubated, video-assisted pulmonary lobectomies and segmentectomies would have taken a so short time span.

This said, what about the level of evidence on these topics? Unfortunately, we all are far from the opportunity of recommending against or in favor the routine use of non-intubated thoracic surgery in daily clinical practice. One should never forget what is the basic principle of our profession, that is, patients’ safety come first. Is non-intubated thoracic surgery safe enough to be performed electively? And even when assuming an optimistic answer, another question can come out: are non-intubated thoracic operations actually safer than the equivalent procedures performed with general anesthesia? Many published studies so far have reported, at least, a non-superior rate of complications of non-intubated thoracic surgeries versus their conventional counterparts (1,19). Furthermore, it appear that in patients at high-risk for general anesthesia, a certain reduction of some specific complications can be attained (19,20). However, the vast majority of these studies are based on observational or retrospective case series, usually including a small number of patients.

These is an urgent need of more robust studies in this regard. Just to give an idea, when considering the estimated rate of postsurgical death after lung cancer resection in an over 65 patient with low comorbidity status (2.3%), a sample of more than 600 subjects would be necessary to detect, with a sufficient reliability, whether a given surgical or anesthesiological method can attain a 3-fold risk reduction. This simple consideration get amplified when taking into the account minor videothoroscopic operations, such as talc pleurodesis for pleural effusion (21) or bullectomy/pleuroabrasion for pneumothorax. Indeed, these procedures are much less likely to give any relevant

intra- or postsurgical complication, regardless of the kind of anesthesia adopted (21,22). The same reasoning applies when considering other primary outcome measures. These may include patient satisfaction, hospital stay, oncologic results, and cost saving issues. In this regard, some studies showed a certain economical benefit for non-intubated thoracic surgery (21), which was likely attributable to a faster discharge, a shorter operating room time, and a lesser morbidity rate. But are all these advantages reproducible in the real-world scenario? For example, non-intubated thoracic surgery needs adequately trained staff with exposure to a large number of videothoroscopic operations, so that costs allotted for planning and maintaining a standardized skill level should be included in the future analyses. Dry and wet labs, simulator-based training, increased need of having disposable devices ready for immediate use in the operating theater, are all examples of possible sources of economic expense for a non-intubated thoracic surgery facility.

In this issue of *Surgical Innovation*, a prospective randomized trial of non-intubated major resection for stage I lung cancer is published (23). We are grateful to the authors and the Editor for providing a high-quality study like this. The authors analyzed a series of primary and secondary outcome measures, and found definitively a better performance of non-intubated thoracic surgery in terms of postoperative hospital-stay and some surrogate measures of recovery quality, including feeding time and need of postoperative antibiotics. I also have found to be particularly interesting that, in this study, level of TNF-alpha in the broncho-alveolar lavage fluid was significantly lesser than in patients who underwent conventional surgery. Plasma level of C-reactive protein was also remarkably lower, a finding which is in keeping with our previous report on this topic (17). We hope that this paper will serve as a benchmark for future publications on these topics, and its focus on biological markers of surgical traumatism merits a great consideration.

We are also aware of at least other two randomized controlled trials of non-intubated videothoracoscopy versus conventional operations which are currently underway. One is that from the Taiwan University group, which is one of the leading institutions in this setting. This trial (NCT01533233) is aimed at evaluating safety and oncological outcome after non-intubated videothoroscopic lobectomy plus mediastinal lymph node dissection in clinical stage I non-small cell lung cancer. The other trial (NCT02109510) is from the Korea University and aims at evaluating several outcomes, including overall perioperative

well-being, intraoperative gas exchange, and costs, in the specific subgroup of patients undergoing bullectomy-pleurodesis for spontaneous pneumothorax by either general or non-intubated anesthesia with intercostal nerve block and dexmetomidine/ketamine administration. We are awaiting with enthusiasm the results of both these studies, which will hopefully provide a lot to the current knowledge on these topics.

Some other questions should also be addressed. Which is the best anesthesia regimen to be used for non-intubated operations? Different methods have been proposed in this regard, but there is no definitive consensus on pros and cons profiles between the available techniques. Thoracic epidural anesthesia seems to be the more accepted one (24), as it can provide an effective and broad analgesic coverage as well as a series of non-analgesic advantages (25). Other available options are paravertebral block and intercostal nerve block (26). We hope that appropriate randomized, controlled studies will be shortly undertaken to evaluate comparatively the performances of all these techniques and their peculiar features in the specific setting of non-intubated thoracic surgery. For example, the effect of these techniques on respiratory function should be considered. Indeed, low-grade bronchial constriction, a mild cardiovascular impairment or a slight reduction in auxiliary ventilation due to neural block (25,27-29) may have remarkable effect when performing thoracic surgeries on non-intubated subjects, despite being substantially irrelevant when tested in the conventional scenario.

To conclude, perhaps, the question which role should non-intubated thoracic surgery be given is too premature. At the present time, we all have still to think a lot about the movie itself, and have yet to define what the story should tell about. It will be just only when we will be corroborated by the strength of scientific evidence that we will be able to walk on the red carpet of thoracic surgery excellence and innovation.

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