

## Peer Review File

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### Reviewer A

You present some kind of "How I do it"-article, which should be specified in the title.

For the purpose of a teaching article, pictures would be helpful.

Other comments:

- The way you use the English language is unacceptable. Suggest to have an English-editing by native.
- Your technical advice are sensible, but they are not the only correct way; they should be presented as "one" way, not "the" way. Furthermore, a lot of your advice are not specific for NITS, they apply to VATS in general. In a NITS-paper, you should specify which manoeuvres are advantageous particularly for NITS, and why.
- You do not - at least shortly - explain the pathomechanisms of intubated versus non-intubated VATS, the actual advantages and disadvantages, the risk of barotrauma, delirium, ARDS, etc.

### Reply

1/ The subtitle is added to the title of the contribution

Essentials in Spontaneous Ventilation Video-assisted Thoracoscopic Surgery. How we do it. 2/ Figures 1, 2, 3 will be incorporated into the article

- Fig 1 Internal intercostal block
- Fig 2 Vagal block from the right side
- Fig 3 Vagal block from the left side

3/ English native proofreading of the text was obtained.

4/ There is, as you exactly said, not only one correct way to implement NITS procedure. In our experience the technical difference are represented especially by intercostal block and vagal block. After exact implementation of these we do not see any technical contrast between intubated and non-intubated procedure. But you are right! There is a bad need to underline that the success of these manoeuvres comprises in the closest cooperation between surgeon and anesthetist in the course of the regional intrathoracic anaesthesia.

5/ Remind the pathomechanisms of intubated (versus non-intubated) VATS, which were reviewed by Tommaso Claudio Mineo and Federico Tacconi of Rom (10), in particular:

- a) Ventilator associate lung injury (VALI) entails a compartmental inflammatory status which leads, in turn, to interstitial edema, loss of surfactant, ventilation-to-perfusion mismatch, and decreased compliance. In patients with preexisting lung disease, VALI can evolve into a frank acute lung injury. Subclinical VALI possibly leading to minor respiratory impairment can still occur in healthy lungs, and independently on extent of surgical trauma
- b) One-lung ventilation related injury (OLV) at the dependent lung, OLV induces ventilation-to-perfusion mismatch, and promotes further inflammatory changes. Hypoxic environment establishing at the non-dependent (non-ventilated) lung causes tissue acidosis, alveolar edema, vascular congestion, cytokine release, and an increased malondialdehyde level. These changes can

occur early after minor operations and even in the absence of surgical trauma. At re-ventilation, high oxygen fraction triggers oxidative burst, leading to neutrophil recruitment and macrophage activation.

c) Extrapulmonary side effects of general anesthesia (GA) and OLV are mediated by the spillover of cytokines toward the systemic circulation, and may include liver injury, natural-killer cell impairment and arrhythmias. The latter also include transient QT-tract prolongation, which has been shown to occur in up to 80% of patients with possible evolution to torsade de pointe

d) Hypoxemia defined as  $SaO_2 < 90\%$ , with an inspired oxygen fraction of 0.5. It occurs in 10% of thoracic operations, mostly during right procedures, in the supine position, and in heavy smokers. Double-lumen tube dislodgement is also a frequent cause.

e) Tracheobronchial rupture

Although its estimated rate is quite low (1/20.000), tracheobronchial rupture may carry a mortality rate as high as 22%. Women seem to be at a higher risk, probably as a result of their smaller airway caliber. Deteriorated clinical conditions and radiotherapy also significantly increase the risk; Injury to the hypopharynx, esophagus, and vocal cords may also rarely occur, although a reliable incidence estimate is not available.

All these represent an wide field for the future programmes of the NITS research.

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#### Reviewer B

The manuscript is interesting and very well written, describing a novel operative technique in Europe. I only suggest that the authors may add some key operation pictures or images for a better demonstration of this novel technique.

I also want to congratulate the great works made by the authors.

#### Reply

Your kind expression pleased us. Thanks!

Three crucial figures will be added to the manuscript

- Fig 1 Internal intercostal block
  - Fig 2 Vagal block from the right side
  - Fig 3 Vagal block from the left side
- 

#### Reviewer C

This manuscript submits the key points concise and detail about spontaneous ventilation video-assisted thoracoscopic surgery, including the most important part, i.e. the collaboration between anesthesia and operations. Delicate anesthetic and surgical management were demonstrated to achieve the art of simplicity. The safety of regional anesthesia including dosage of local anesthetics and operational skills were specific addressed in this article.

However, some minor revision is recommended for our readers with better understanding.

#### Abstract

Line 6, it would be better to replace “between 40-60” instead of “about 40”. BIS levels between 40-60 indicates the standard general anesthesia state. However, it is a good idea to start the artificial pneumothorax under the anesthetic depth with BIS level near 40 rather than 60.

#### The procedure

##### Point 5

The requirement of intravenous general anesthetics will be reduced after complete onset of intercostal nerve blocks (usually several minutes later). Careful adjustment of anesthetic depth goaled with similar BIS levels is essential cause too deep anesthesia may follow with an effort respiration.

##### Point 6

Line 5, after intercostal nerve blocks, wait for several minutes and observe the smoothness of ventilation before performing vagal nerve blocks.

#### Reply

Let us acknowledge your keen insight into "the art of simplicity" and kind assistance.

Get down to business:

1

#### Abstract

In the line 6 of the abstract will be replaced “between 40-60” instead of “about 40”.

2

#### The Procedure

a) To the Point 5 is added according your bright recommendation: The requirement of intravenous general anesthetics will be reduced after complete onset of intercostal nerve blocks (usually several minutes later). Careful adjustment of anesthetic depth goaled with similar BIS levels is essential cause too deep anesthesia may follow with an effort respiration.

b)

Point 6, Line 5 is expanded by: after intercostal nerve blocks, wait for several minutes and observe the smoothness of ventilation before performing vagal nerve blocks.

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