

## 2022 European Society of Cardiology guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery: which impact to lung cancer resection?

In August 2022, the European Society of Cardiology, with endorsement of the European Society of Anesthesiology and Intensive Care, issued the updated guidelines regarding overall management of patients scheduled for non-cardiac surgery (1). The document contains a massive amount of new concepts, updates and revisions, and - first of all - the surgical community should express gratitude to all the colleagues who contributed to this challenging task.

The ESC guidelines embrace several points, each one representing a daily challenge in decision-making processes, especially when dealing with patients with cardiovascular risk factors. The topics touched deal with preoperative assessment of cardiac function, management of blood thinners, risk reduction strategies, and many others points.

While issued recommendations are not meant to be oriented to a specific surgical field, their connection to the main key points of lung cancer surgery is very strict. Indeed, compared to other surgical subspecialties, lung resections carry myriads of cardiac and vascular implications. First of all, lung cancer patients are very often current or former smokers, which implies a higher risk of coronary artery disease and other cardiovascular comorbidities. Furthermore, thoracic surgery exposes patients to postoperative cardiovascular complications also due to its specific pathophysiologic changes and anatomical relationships. Possible specific mechanisms of cardiac involvement during and after lung surgery are (but not limited to): increased right ventricular dysfunction secondary to lung tissue removal (2, 3), induction of arrhythmias due to vagus nerve injury (4, 5), induction of postoperative hypoxia due to chest pain and phlegm retention, and reduced blood venous return in case of massive mediastinal shift. Several recommendations from updated ESC guidelines intimately deal with all these points and deserve a focused comment.

For example, in the new recommendations section, it is mentioned that minimally-invasive accesses can be adopted as a risk-reduction strategy. In lung cancer surgery, this means that video-assisted procedures (VATS) in lieu of open thoracotomy should be strongly considered as the best option for performing lung resection, especially to patients with high

cardiovascular risk. However, the class of recommendation is regarded as IIa, meaning that – even though VATS should be considered as the best choice - the indication is still not compulsory. The recommendation seems reasonable, by virtue on the current knowledge on this topic. Certainly, in the last two decades, VATS has become the standard method to perform lung resection in an increasing number of surgical centers all around the world. The rationale of this revolution is that patients are assumed to benefit from the reduced surgical traumatism and reduced postoperative chest pain. Both these factors should lead to a faster recovery and less inflammatory perturbation, ultimately translating into lesser mortality and morbidity. However, it should be highlighted that a very strong evidence in favor of VATS versus open surgery was not available until recently. Indeed, despite of the exponential increase of patients undergoing VATS resections and the large amount of literature reporting excellent results, many studies on this topic were retrospective in nature. Furthermore, the few available randomized-controlled trials (RCTs) either did not have cardiovascular complications rate as the main endpoint (5), or they were not double-blinded with a potential for expectance bias (6). In August 2021, the early results of a large, multicenter RCT VIOLET study become available. This is probably the largest study so far on this topic, as it involved 9 teaching hospitals in the United Kingdom (7). Interestingly, the study was blinded to both patients and non-operating medical and nurse staff. The VIOLET trial showed that, compared to open thoracotomy, VATS lobectomy can achieve a significant reduction of postoperative morbidity.

In particular, readmission rate and incidence of serious events after discharge were both significantly lesser after VATS, thus suggesting that the benefits of a minimally-invasive approach can extend themselves beyond the immediate perioperative phase.

The landscape for the next future is that benefits of minimally-invasive approaches in major lung resections may become even more evident, thanks to implementation of technical refinements such as single-port access, use of robotics, non-intubated anesthesia protocols and others.

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Yet another relatively new point that was rightfully addressed in the ESC guidelines is assessment of frailty. Frailty status is a multifactorial concept that can be loosely defined as a generalized functional insufficiency related to age-related changes such as sarcopenia, even though it is also remarkably affected by concomitant organ diseases as well. Unfortunately, there are different ways and criteria to measure and classify frailty. Some methods are mainly based on patients' ability to execute common daily life tasks. Some others include more specific factors, such as presence of chronic illness and nutritional status. It is clear that different "frailty score" systems lie in a spurious context in between "performance status scales" (resembling the ones in use in clinical oncology) and disease-specific "symptom severity" staging systems. While it is welcome that thoracic surgeons familiarize with the concept of frailty, there is an urgent need for harmonized criteria for assessing and staging frailty. As well, fine-tuned workup algorithms in some particular scenarios should be the subject of future investigations. For example, research might evaluate whether it would be useful to extend VO<sub>2</sub>max estimation by means of cardio-pulmonary exercise test to lung cancer patients with a frail status and normal or nearly-normal respiratory function tests, in order to optimize surgical risk stratification in these delicate subjects.

In the section of ESC guidelines regarding patient blood management, two concepts come out to thoracic surgeons' attention. The first one is the grade-I recommendation in favor of washed-cells salvage in case of heavy blood loss. The other one is the use of tranexamic acid to prevent major postoperative bleeding. Regarding intraoperative blood salvage, we found extremely important that the ESC is supporting this practice. Indeed, for many years, thoracic surgeons have been reluctant to adopt intraoperative cells salvage, due to the fear of possible tumor cell dissemination favoring cancer metastatization. It must be highlighted that this assumption should be downgraded to mere conjecture. In fact, the only literature finding showing early metastatization following lung cancer resection with application of autologous blood salvage is just a single case report, dating back more than 40 years ago. Since then, no other study was able to find any substantial difference in oncologic outcomes between patients who received allogenic blood transfusion (8) or no transfusion at all. Furthermore, even though cancer cells were found into salvaged blood in some studies, it is difficult to discern whether they were already present into circulation. For these reasons, the recommendation of considering intraoperative blood salvage in patients with heavy intraoperative bleeding seems acceptable in lung cancer surgery, even though there are no randomized controlled trials available in this regard. This is particularly true when considering that, instead, allogenic blood transfusion carries a well-known risk of undesired events, including anaphylaxis, transfusion-associated lung injury, and induction of transient loss of anticancer defense mechanisms. On the other hand, it should be reminded that heavy bleeding calling for intra-

or perioperative blood transfusion is a relatively uncommon event in major lung resections, unlike other surgical fields. Therefore, the economic impact of having a blood salvage unit always equipped in the operating room seems questionable. Certainly, it may be clearly advantageous when relevant blood loss can be anticipated, such as in traumatic or postoperative hemothorax after lung resection. A similar reasoning may apply as well to the prophylactic use of tranexamic acid to reduce blood loss and need for transfusions. The latter strategy might be considered in rare circumstances, such as patients with vascularized pleural adhesions that may lead to serious intra- or postoperative blood loss.

To conclude, we again renew our acknowledgements to the colleagues involved in the development of new ESC guidelines. In this regard, we are confident that more and more thoracic surgeons worldwide will embrace an evidence-based mentality, in order to improve at most the safety and quality standards of our practice. We also hope that attention to extra-clinical skills and concepts such as team working, alongside a dynamic approach to surgical practice with easier acceptance of changes, will remarkably improve this process.

New era surgeons have no more chance to say "we always did in this way"!

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