Review Article on Thoracic Surgery

Enhanced recovery after surgery (ERAS) and fast-track in video-assisted thoracic surgery (VATS) lobectomy: preoperative optimisation and care-plans

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Abstract: Main specific interventions for preoperative clinical optimisation of patients undergoing lung cancer surgery include assessment and treatment of comorbidities, minimizing preoperative hospitalization, minimizing preoperative fasting, and optimisation of antibiotic and thrombo-embolic prophylaxis. Preoperative patient optimisation is considered a crucial part of enhanced recovery after thoracic surgery pathways. Potentially, advantages of this fast-track management could be even higher when considering video-assisted thoracic surgery (VATS) major lung resection, because reduced trauma related to minimally invasive techniques is one of the main factors improving postoperative outcome. Literature data and clinical evidences in this setting are reported and discussed.

Keywords: Video-assisted thoracic surgery (VATS); lobectomy; fast-track surgery

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Introduction

Enhanced recovery and fast-track protocols have been developed in thoracic surgery, as in other surgical areas, to reduce factors of delayed postoperative recovery, and to achieve faster mobilization and resumption of regular activities (1,2). Reduction of perioperative complication rate is one of the primary goals to be reached to decrease length of hospital stay and related costs.

Decreased surgical trauma related to minimally invasive techniques is one of the main factors improving postoperative outcome. Therefore, advantages of a fast-track management could be potentially higher when considering video-assisted thoracic surgery (VATS) lobectomy, especially in the setting of major lung resections (3,4).

Multidisciplinary approach is a fundamental aspect of enhanced recovery after surgery (ERAS) since initial diagnosis of tumor has been achieved and treatment plan has been established. The primary goal for all patients undergoing lung cancer surgery is always the optimisation of perioperative and intraoperative management on the basis of evidence-based best medical practice.

Currently, published data have largely proven the benefits of the ERAS approach in main areas of general surgery (5-7). Increasing evidences have been provided showing that preoperative optimization of patient clinical status may allow to reduce the physical and psychological stress related to the operation and to promote restoration of function. However, there is still paucity of similar reports in thoracic surgery, and specifically in lung cancer surgery. In particular, no published data are available concerning ERAS specifically in VATS lobectomy.

ERAS protocols require a preoperative general assessment of all patients who are undergoing elective surgery in order to establish if they are fit for the planned intervention.

Especially for patients with poor performance status, accurate preoperative evaluation should start soon after the initial diagnosis, and should include detailed patient history and clinical assessment, blood exams including basic metabolic panel and complete blood count, and measurements of pulmonary and cardiac function. Patient risk factors have to be identified adequately in advance before surgery, in order to allow specific interventions for possible preoperative optimisation.

Patient clinical optimisation in the preoperative setting should mainly include the following interventions: (I) identification, evaluation and treatment of comorbidities with particular interest for those that can be modified in a limited interval of time while awaiting surgery; (II) minimizing preoperative hospitalization; (III) optimisation of antibiotic and thrombo-embolic prophylaxis; (IV) minimizing perioperative fasting.

Other very important interventions in preoperative management for patient optimisation include physiotherapy and counseling which are not among the purposes of this article.

Comorbidities and risk factors

It is mandatory to assess patient comorbidities and risk factors in the preoperative phase to plan adequate management before the intervention. Current literature data show that the presence of significant comorbidities increases the risk of post-operative complications, and that preoperative optimisation of comorbidities is able to reduce morbidity rate after surgery. However, only some comorbidities can be optimised in the limited interval of time between diagnosis and surgical treatment (generally few weeks). Most clinical arrangements in the preoperative phase should be directed to the treatment of such diseases. Main pathologic conditions related to increased perioperative risk which can be treated and optimised whilst awaiting surgery include: anaemia, malnutrition, chronic obstructive pulmonary disease (COPD) and active smoking. These conditions and their specific management will be discussed in the present article. Other frequent comorbidities such as diabetes and hypertension may only require adjustment of therapeutic plan, but the disease status cannot be substantially modified before surgery. Additional comorbidities that significantly increase the surgical risk, such as obesity and alcohol abuse, have to be identified and considered when estimating the surgical risk, although their effective treatment is not possible in a short period of time before the operation.

Anaemia is defined as the deficiency of red cells in blood with hemoglobin concentration <13 g/dL in males or <12 g/dL in females. It is a frequent finding in patients with lung cancer, as in all the oncologic patients. The presence of anaemia has been reported to be related with increased postoperative complication and mortality rate in all areas of surgery (8). Therefore, it is mandatory that anaemic patients are identified, investigated and treated before elective surgery. Blood transfusion is the most common method to improve hemoglobin levels in anaemic surgical patients. However, it carries a higher risk of complications including acute transfusion reactions, immunosuppression, post-operative infections that may cause prolonged hospitalization (9). Therefore, in the preoperative period, transfusion is usually used only for patients with severe anaemia (hemoglobin concentration <8 g/dL). Main alternative strategies to treat minor degrees of anaemia are iron supplementation and erythropoietin. These therapies are associated with significantly lower complication rate and allow to reduce the need for transfusion. To date the benefits of preoperative anaemia correction have been clearly reported, but so far published studies have only assessed the impact of such treatment on the outcome of lung cancer patients undergoing adjuvant chemo- or radiotherapy (10), and there are still limited data in the surgical setting. Based on the above-mentioned evidences, ERAS pathways recommend preoperative treatment of anemia with iron supplementation or erythropoietin for all patients with haemoglobin level <10 g/dL.

Malnutrition is another frequent condition in lung cancer patients. Some studies have found preoperatively a severe malnutritional status in over 20% of patients with operable lung cancer (11). The presence of malnutrition can be responsible of a number of postoperative problems including impaired wound healing, immune dysfunction and muscle wasting with respiratory fatigue. These complications usually result in delayed patient recovery and longer hospital stay. Preoperative screening for malnutrition is therefore strongly recommended for all patients undergoing oncologic surgery. There is currently a grade A evidence supporting the administration of nutritional support for at least 2 weeks before major surgery to all patients with severe preoperative nutritional risk (12).

Severe nutritional risk is defined as the presence of at least 3 of the following conditions: weight loss >10–15% within last 6 months, body mass index (BMI) <18.5 kg/m^2, Subjective Global Assessment Grade C, and serum

albumin level <30 g/L without coexisting hepatic or renal dysfunction.

A French multicenter study has evaluated the impact of malnutrition on the postoperative outcome of almost 20,000 patients who received major lung resection. Patients with preoperative BMI< 18.5 kg/m^2 showed a significantly increased operative death rate, surgical complication rate, respiratory complication rate and infectious complication rate (13).

At present there are still no definitive evidences to indicate the best nutritional support which should be administered before the intervention. In the literature, there are only some small prospective studies evaluating the impact of preoperative nutritional support on the outcome of patients with normal nutritional status who underwent major surgery for lung cancer. Differently, there is lack of reports examining the benefits of preoperative treatment of poor nutritional status in patients with operable lung cancer. In a small prospective randomized trial, a combination of alpha-ketoglutaric acid and 5-hydroxymethylfurfural administered preoperatively not only improved exercise capacity and reduced oxidative stress, but also resulted in a significant reduction in intensive care unit stay and postoperative hospitalization of patients with normal BMI who received resection for lung cancer (14).

Another recent prospective randomized study has analysed the postoperative outcome after resection for non-small cell lung cancer (NSCLC) comparing 31 patients who received preoperatively a protein-rich nutrition support (arginine, omega-3-fatty acids and nucleotides) for 10 days with 27 patients who had only normal diet. The operation was performed in VATS in 35% of patients in the experimental group and in 40% in the control group. There was a significant advantage for patients who received preoperative nutrition who showed decreased complication rate (19% *vs.* 44%) and mean chest tube removal time (4 *vs.* 6 days) (15).

COPD is frequently found in patients with lung cancer who are candidates to surgical resection, and is related with higher risk of pulmonary complications. A large body of literature data shows that the preoperative optimisation of the pharmacological therapy is effective in improving respiratory function and reducing the risk of pulmonary complications. There is evidence from prospective studies that COPD patients with untreated functional airway obstruction achieve a significant improvement in global pulmonary function after the administration of a long acting brochodilator treatment before surgery (16). The addition of inhaled steroid to long acting bronchodilator in patients with previously untreated COPD has been found related with improved preoperative FEV1 and lower postoperative pulmonary complication rate compared to long acting bronchodilator alone (17). The association of respiratory physiotherapy before surgery has been also proven to provide significant functional improvement allowing the operation in patients previously considered unfit for the pulmonary resection (18).

Active smoking is another frequent perioperative risk factor for patients with lung cancer which has a negative impact on complication and mortality rate after major lung surgery (19). Smoking cessation has been reported to reduce perioperative morbidity and mortality (19,20). In a study from the Society of Thoracic Surgeons Database the prevalence of major pulmonary complications after lung resection was 6.2 % in current smokers and 2.5% in non-current smokers (20). However, there is also evidence that benefits of smoking cessation are as higher as longer is the time of cessation before surgery. Some studies report that smoking cessation at least 1 year before major surgery abolishes the increased risk of postoperative mortality and of arterial and respiratory complications generally found in current smokers (19,21).

Therefore, current guidelines for management of lung cancer patients recommend that smoking cessation should be always encouraged as soon as possible before surgery, but the operation should not be postponed to allow this (22). Nicotine replacement and other therapies to help stop smoking are also recommended (23).

Preoperative hospitalization

Prolonged hospitalization has a negative psychologic impact on patient with potential detrimental influence on immune defence. Accurate preoperative assessment is mandatory to identify main risk factors and to establish appropriate treatment for patient optimisation. This approach may allow to reduce surgery delay or cancellation rate making prolonged preoperative hospitalization unnecessary and increases patient satisfaction. As a consequence, same-day admission or admission the night before surgery for patients undergoing operation early in the morning can become the rule. This type of management, associated with detailed explanation of the intended perioperative pathway, contributes to decrease patient anxiety with a favourable impact on postoperative outcome, thus reducing perioperative costs (1).

Antibiotic prophylaxis

Appropriate perioperative antibiotic prophylaxis is mandatory to reduce infectious complication rate in patients undergoing pulmonary resection (24). The choice of prophylactic antibiotics is based on the most common pathogens likely to result in infections of the surgical site. In pulmonary resection bacteria from skin and respiratory flora are the most common cause of infection. Staphylococcus Aureus is the most frequently identified pathogen. Other common bacteria responsible for postoperative lung infection include *S. Aureus*, coagulase negative staphylococci, *Streptococcus Pneumomiae* and gram-negative bacilli (25). Main literature evidences show that first-generation cephalosporins, such as cefazolin, offer adequate coverage for the most common pulmonary surgical site infections and are appropriate for antibiotic prophylaxis in this setting. The suggested dosage for cefazolin is 1–2 g I.V. before surgery (26). Current guidelines recommend to administer the preoperative antibiotic 60 minutes or less before surgical incision. Ideal time is 30 minutes or less before the operation (27). At present there is no special indication for VATS lobectomy and for ERAS protocols.

Preoperative airway colonization with pathogens is a significant risk factor for the occurrence of lung infections after thoracic surgery. Therefore, patients with abundant bronchial secretions, and especially those with COPD, should be managed with particular care. The latter condition may have previously required repeated antibiotic treatments which could be responsible of changes in usual pattern of flora and potential development of antibiotic resistance.

Second-generation cephalosporins are generally indicated as a second-choice option. If the patient has history of methicillin-resistant *S. Aureus* or penicillin allergy, then vancomycin or macrolides (clindamycin) can be used in place of cephalosporins.

Thromboembolic prophylaxis

The majority of patients who undergo lung cancer surgery should be considered at least at moderate risk for postoperative venous thromboembolism (VTE). In a large study including 706 thoracic surgery patients, pulmonary embolism (PE) occurred in 7% of patients who did not receive prophylaxis, but there were no episodes of PE in patients receiving mechanical prophylaxis (28). VATS lobectomy is classified as a non-high bleeding risk operation. Therefore, at present, general VTE prophylaxis guidelines are recommended for non-high bleeding risk patients undergoing minimally invasive major lung resection, especially in the context of fast-track protocols. According to the American College of Chest Physicians (ACCP) guidelines, no prophylaxis or mechanical prophylaxis only (anti-embolism stockings, intermittent pneumatic compression devices or foot impulse devices) should be performed for patients with low risk for VTE. Patients with moderate VTE risk (Caprini score 3–4) should receive pharmacological prophylaxis with low molecular weight heparin (LMWH) for 7–10 days or until discharge. Association of mechanical prophylaxis is optional. Patients with high VTE risk (Caprini score ≥5) should be treated with pharmacological prophylaxis with LMWH associated with mechanical prophylaxis (anti-embolic stockings or intermittent pneumatic compression devices) for 7–10 days or until discharge.

Preoperative fasting

Prolonged preoperative fasting is related to metabolic and psychological stress. Fasting from the midnight before lung surgery has been largely employed in the past, and is still in use in many thoracic surgery units with the aim of reducing the risk of bronchial inhalation during general anaesthesia and immediately after surgery.

There is currently a high level of evidence showing that shorter preoperative fasting is not related with increased perioperative complication rate. Studies appeared in the last decades have proven that gastric volume is not increased after a light breakfast of tea and buttered toast consumed 2–4 hours before elective surgery (29-31) and that abstaining from fluids for a prolonged time before the operation is detrimental for patients. It is therefore important to encourage patients to drink until 2 hours before surgery. This reduces their discomfort and improves their well-being (31,32)

Guidelines from the European Society of Anaesthesiology (33) recommend that all patients undergoing lung cancer surgery without specific risk factors for inhalation should be encouraged to drink clear fluids (water, pulp-free fruit juice, tea and coffee without milk) up to 2 hours before elective surgery. Tea and coffee with milk added up to about one third of the total volume can be still considered clear fluids. Solid food should not be prohibited up to 6 hours before elective surgery. In general, a light meal with toasted bread and liquids can be allowed up to 6 hours preoperatively,

while a regular meal including fried or fatty food can be allowed up to 8 hours before surgery.

Some prospective randomized trials have shown that preoperative oral intake of carbohydrates has to be considered beneficial and safe up to 2 hours before elective surgery (34).

Conclusions

Preoperative optimisation of the patient who is candidate to major surgery is a crucial part of enhanced recovery after Thoracic Surgery pathways. This approach may allow to significantly reduce postoperative complication rate. Data from future prospective studies will show if the application of such principles could provide increased advantage in the perioperative outcome of patients undergoing VATS lobectomy, given that reduced trauma associated with minimally invasive technique is one of the main factors improving surgical outcome.

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