

Anaesthesia during oesophagectomy

Denise P. Veelo, Bart F. Geerts

Department of Anaesthesiology, Academic Medical Center, Amsterdam, The Netherlands

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Correspondence to: Denise P. Veelo, MD, PhD. Department of Anaesthesiology, Academic Medical Center, Amsterdam, Meibergdreef 9, 1105 AZ, The Netherlands. Email: d.p.veelo@amc.uva.nl.

Abstract: In this review, we will provide an overview of the current state of the art of perioperative practices for open and laparoscopic oesophagus surgery from the anaesthetist's perspective. Morbidity and mortality after oesophagectomy is still high despite multidisciplinary and enhanced recovery pathways showing promising results. The anaesthetist has an important role in the complex care of the oesophageal cancer patient. Minimizing unnecessary fluid administration, adequate pain management, hypotension, and protective lung ventilation are examples of proven strategies that can improve outcome after this high-risk surgery.

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Introduction

Oesophageal surgery is high-risk. Despite innovations in surgical techniques (open vs. laparo-thoracoscopic) and the addition of neo-adjuvant chemo-radiotherapy, major morbidity still can be up to 65% and 30-day mortality rate as high as 4% (1,2). Pulmonary infections and anastomotic dehiscence make up for the majority of reported complications. To reduce complications minimally invasive techniques were introduced and some studies report a more favourable outcome (1). This especially translates into a reduction in pulmonary complications, which are reported to decrease by 60% (2). However, outcome seems especially related to patient and tumour characteristics, surgical experience and hospital volume (3,4). Over the years, it has become clear that a multimodal, multispecialty and dedicated-team approach is essential for these patients, including strict patient selection, work-up, and enhanced recovery after surgery (ERAS) protocols (5). The anaesthetist is an essential member of the multidisciplinary team. Pain and stress, fluid, hemodynamic, and ventilation management can influence outcome significantly. Best practices may differ

depending on the surgical techniques used.

In this review, we will provide an overview of the current state of the art perioperative practices for open and laparoscopic surgery from the anaesthetist's perspective.

Preoperative screening and optimisation

Patients with oesophageal cancer often have comorbidities, suffer from significant weight loss, poor nutritional state and are more fragile (6,7). An overweight patient will have a higher chance of wound infections while an underweight patient has odds of death go up 5-fold (8). Timely screening of the preoperative patient will allow the possibility to improve the health status of the patient and to reduce chances of adverse outcome (9). The anaesthetist should be involved early in a multidisciplinary evaluation that also includes a debate whether or not to proceed to surgery based on expected perioperative morbidity.

To assess the perioperative risk of morbidity and mortality some general and some oesophagectomy specific risk scoring systems exist. Warnell and co-workers reviewed ten of these models that were externally validated (3). The

accuracy of these scoring varies widely with overestimation of mortality occurring frequently (5–200% of cases) and a reported area under the curve between 0.58 and 0.78. Common risk factors are age, comorbidities (cardiopulmonary, diabetes, renal insufficiency, liver dysfunction), preoperative treatment (neoadjuvant chemotherapy), tumor staging and hospital characteristics (hospital volume of oesophagectomies) (3).

More elaborate general preoperative risk scores have also recently been developed from large databases of over one million patients. The **POSPOM scoring** system is such a scoring system (10). Unfortunately, it fails to consider the patient comorbidities completely neither does it reflect the full scope of the oesophagectomy (both abdominal and thoracic surgery). However, this score does provide the patient and all specialists involved in the care with a more reliable (albeit likely underestimation) of what would happen if oesophageal surgery were performed.

A structured preoperative screening in an anaesthesia outpatient clinic has become the standard for anaesthesia care in most countries. During the pre-assessment cardiac function should be evaluated by assessing functional disabilities and the MET score. An EKG can provide information about dysrhythmias, conduction delays, previous myocardial infarction, and hypertrophic development of atrium and/or ventricle. When wall motion or valvular issues are suspected, an echocardiography can provide new insights. Most patients will receive **chemoradiation**, which may **impact cardiac function**. Lund *et al.* found that **baseline cardiac output can be decreased** by as **much as 15% due to chemo-radiotherapy** during rest (11). Although the impact has been described as mild, anaesthetic drugs, surgery, **one lung ventilation** (shunting), and laparo-thoracoscopy may further influence heart function.

Additional work-up should include blood testing for renal and liver function, haematology, irregular antibodies and clotting upon indication. When oesophagectomy is to be performed, functional assessment of the lungs needs to be performed. The patients need to be able to undergo one-lung ventilation (**OLV**). As most patients in this population have been or are smokers, the incidence of significant emphysema is higher. Exact cut-offs to perform one-lung ventilation have not been clearly determined. **Acute lung injury after oesophagectomy** has been reported in as many **as 25% of** all cases after surgery (12). Risk factors are low pre-operative body mass index, smoking, the experience of the surgeon, the duration of surgery and OLV, post-operative anastomotic leak, peri-operative hypoxaemia,

hemodynamic instability requiring additional fluids or vasoactive support (12).

Weight loss is often pathognomonic for poor outcome after surgery and albumin levels can be a marker of very poor nutritional state (13). A dietician should be consulted to optimize weight, fat and protein status. Sometimes it is warranted to delay surgery to supplement proteins as this might improve wound healing and prevent infections or anastomotic breakdown. Early involvement of physiotherapist to improve physical or cardiopulmonary fitness and a dietician for a good nutritional state seems rational but studies into the effect on outcome are contradictory (14–17).

Best anaesthetic practices

Type of anaesthesia

The discussion of the advantages over the use of one anaesthetic over the other has led to a number of studies to be performed. However, this discussion is complicated by the small number of studies available, small number of patients included and the differences in endpoints and methodology, which makes them difficult to compare.

Some studies have described immune-modulatory benefits and reduced ischemia-reperfusion injury markers of volatile anaesthetics during one lung ventilation. However, after thoracic surgery there seems to be **no clear relation** between **inflammatory** markers and **pulmonary morbidity** as the results of clinical studies are **conflicting** (18–22).

During one lung ventilation hypoxic pulmonary vasoconstriction (**HPV**) influences intrapulmonary shunting and oxygenation. **Volatile anaesthetics** have been shown to **impair HPV in** a dose dependent matter in contrast to propofol in animal models (23). However, when titrate to effect the influence of volatile anaesthetics on intrapulmonary shunting may be **equal to that of propofol** (24).

Thoracic epidural analgesia

There seems to be no benefit of using either volatile anaesthetics or propofol on the occurrence and severity of post-operative pain (25). But the evidence on the use of multimodal treatment regimes during oesophagectomy and especially the **thoracic epidural analgesia (TEA)** seems clear. This **benefit** has been shown for both **open as minimally invasive** oesophagectomy. TEA provides superior analgesia, **reduces** respiratory **complications**, need for postoperative mechanical ventilation, rehabilitations and hospital length

of stay (26-30). Most studies show mainly an effect on pulmonary morbidity although a reduction in the incidence of anastomotic leakage has also been suggested (31). TEA has no clear anti-inflammatory effects (32).

Ventilatory management

Ventilatory management during transthoracic oesophagectomy is usually managed with OLV by means of a double-lumen tube (DLT). This technique enables easy separation of both lungs but has also been associated with complications such as hoarseness and damage to the vocal cords, and tracheo-bronchial lacerations. Confirmation of position requires fiber-optic bronchoscopy. Recently the video DLT has been introduced. This DLT has an integrated high-resolution camera, which would remove the need for fiber-optic confirmation (33). Although the first reports with this technique are promising, conclusive studies are needed to confirm added safety, utility and cost-effectiveness of this device. An alternative technique for separated lung ventilation is the use of a bronchus blocker. This device is thought to be similar in terms of performance for patients with normal airways. In patients with airway abnormalities and difficult intubation bronchus blockers may be preferred (34). During minimally invasive transthoracic and trans-hiatal surgery the use of one lung ventilation may not be obligatory. One Chinese group reported the use of single lumen intubation for thoracoscopy as feasible and safe (35). Indeed, the need for OLV might also depend on the position of the anastomosis and the need for optimal surgical views. Challenges for the anaesthesiologist during OLV are deoxygenation and hypercapnia due to shunting and atelectasis. The latter may especially be difficult to manage during thoracoscopy, which may take place in the left lateral or prone position (36,37). Laparoscopic surgery in the prone position is described to be associated with better oxygenation due to lower shunt fractions and better ventilation/perfusion matching (38,39). In addition, it may decrease blood loss and improve surgical ergonomics.

The incidence of acute respiratory distress syndrome (ARDS) or acute lung injury (ALI) after oesophagectomy is high with a reported incidence of 16% up to 33% (40). Important etiologic factors are fluid overload, vascular leakage, damage of lung lymphatics and pulmonary endothelium. These are induced by peripheral and alveolar inflammatory mediator production and cellular infiltration. Patient and procedure related risk factors for ALI have been discussed earlier. The severity of the inflammatory response

may be a predictive factor in postoperative pulmonary morbidity (41). The use of OLV may aggravate this process. The use of lung protective ventilation strategies during one lung ventilation such as the use of smaller tidal volumes (5 mL/kg), plateau pressures below 35 cmH₂O and the application of PEEP has been shown to decrease the inflammatory response and improve oxygenation and resulted in shorter times until extubation and pulmonary complications (41,42). Although no large outcome studies have been done for patients after oesophagectomy, the benefits of the use of lung protective ventilation in the prevention and treatment of ARDS/ALI in critically ill patients and the general surgical population are well established (43).

Fluid management

Intravenous fluids and outcome

Both hypervolemia and hypovolemia may be associated with increased morbidity (44). Fluid management in this patient group has until recently focused on restricting fluid administration to prevent pulmonary and cardiac complications (40). The majority of studies focus on patients after lung surgery and only a few small retrospective studies are available on oesophageal surgery showing a reduction in pulmonary complications with fluid restriction (45,46). However, it remains unclear whether a reduction in anastomotic leakage can be achieved by fluid restriction as surgical and anatomical factors may play a more important etiologic role. This can also be concluded from the data of Wei *et al.* (45). A relationship between fluid balance and anastomotic leakage was not found. Indeed, a too restrictive approach may also increase the possibility of post-operative complications, such as cardiac ischemia, and kidney failure (44). A review of Ishikawa *et al.* on the development of acute lung injury after lung surgery highlights this fact (47). They state that although the incidence of renal injury in thoracic surgical patients has been estimated to be 1.4%, outcome was mainly based on incidence of patients requiring renal replacement therapy. If other criteria would be used the incidence of kidney injury may be much higher varying between 6% and 33%.

Goal directed therapy

Perioperative goal-directed fluid therapy (PGDT) aims to

optimize fluid administration by using objective parameters predicting fluid responsiveness such as pulse pressure and stroke volume variation, stroke volume or cardiac output. Its application has been shown to improve outcome in high risk surgery patients and may either reduce or increase the amount of infused fluids depending on the population studied, pre-PGDT fluid habits, the hemodynamic algorithm and type of fluid used (48). However, most studies have focused on abdominal and vascular surgery patients and outcome data is lacking on those for thoracic surgery, especially those receiving open and laparothoracoscopic oesophagectomy. Minimally invasive technologies currently available to guide goal-directed fluid therapy include oesophageal Doppler, arterial waveform analysis, photoplethysmography, and bioimpedance. Some experiences in thoracic surgery have been made using arterial waveform analysis targeting dynamic markers of preload responsiveness such as stroke volume variation (SVV), pulse pressure variation (PPV) and stroke volume index (SVI) (49-51). The accuracy of SVV and PPV are influenced by the tidal volume given and chest compliance, which is affected during open chest surgery. The use of this marker in these patients remains controversial (40). EVLW has been used as a predictor for the development of acute lung injury in patients after thoracotomy. Recently, Haas *et al.* showed that a GDFT algorithm using SVV did not increase extravascular lung water (EVLW) in patients undergoing thoracotomy for lung resection and oesophagectomy suggesting the safety of use of such protocols (49). Unfortunately no large prospective outcome studies have been done as yet and especially the utility of these markers with surgery by means of thoracoscopy is unknown.

Presently restrictive fluid regimes are most advocated based on the evidence available. However, one can make the argument for goal directed approaches generated from experience in the general surgical population, especially for patients with pre-existent kidney disorders.

Haemodynamics vs. integrity of the anastomosis

During oesophagectomy multiple arteries are ligated. The newly formed gastric tube depends only on the right gastro-epiploic artery leaving the fundus (and future anastomosis) dependent on passive diffusion of blood. Poor local perfusion is thought to be the main etiologic factor in development of anastomotic leakage (52). Optimally, local perfusion pressure and flow would be monitored during the operation and

during the first postoperative days. However, until now this has only been done in experimental settings (53-58).

Monitoring techniques

Standard intraoperative haemodynamic monitoring includes EKG, (continuous) arterial blood pressure, and central venous pressure. Some experimental perfusion or microcirculation monitor techniques have been described in oesophagus surgery (53-59). Examples are Laser Doppler Flowmetry, Near Infrared Spectroscopy (NIRS), Laser Speckle (Contrast) Imaging (LSI), Fluorescence Imaging (FI), Sidestream Darkfield Microscopy (SDF) and Optical Coherence Tomography (OCT). Although these techniques are very promising most are not yet validated and may be difficult to use and interpret at the bedside. Intraoperatively a real-time widefield overview of the flow of the gastric tube may be preferable, such as LSI (59). The surgeon may then be able to adjust location of the anastomosis based on flow parameters and determining borders between vital and less vital (ischemic) tissue regions. Furthermore anaesthesiologists may adjust hemodynamic and fluid management and titrate on effect. Postoperatively other techniques, measuring oxygenation or flow may be more useful. Previous studies researched by Miyazaki, Ikeda and Pierie *et al.* reported that anastomotic leakage was more common in patients with lower local flow values (52,56,57). However, large prospective clinical studies are needed to show the usefulness of these techniques in influencing outcome.

Pressure and/or flow?

For the anaesthesiologist it is important to consider whether to optimize perfusion pressure, flow or both in order to improve outcome, especially anastomotic dehiscence. The evidence on this topic is scarce. One recent observational study studied the effect of hypotensive episodes (systolic pressure decline of >30% of baseline value for more than 5 minutes) during oesophagectomy and the occurrence of anastomotic leak in 84 patients (60). They found that more anastomotic leakages were seen in patients with hypotensive episodes and high vasopressor use. Interestingly, hypotensive episodes seemed more frequent in patients in prone positioning and with the use of epidural catheters. Although this was a small study the results are in line with recent large studies in the general surgical population showing the correlation between low blood pressures and adverse

outcome (61). As discussed above little evidence is available on the influence of flow parameters and outcome. The usefulness of monitoring SVI in relation to outcome has also been suggested in a small study of Sugawara *et al.* (51). They showed that those patients that had a SVI <35 mL/m² at the end of oesophagectomy had a higher chance of developing acute kidney injury.

Some efforts have been made to investigate whether the anaesthesiologist can influence perfusion of the gastric tube directly. Most studies confirm that the presence of systemic hypotension negatively affects flow over the gastric tube (52,54,56,58,62). However, increasing MAP above normal levels likely has no additional benefits. Venous congestion may be an additional factor in decreasing flow over the gastric tube. The local application of nitroglycerin is recommended by some investigators under those circumstances (53,55).

Enhanced recovery

Enhanced recovery programs have gained traction in all areas of surgery. The goal is to achieve independence from medical treatment, decrease complication rates and achieve early discharge. Length of stay has been reduced with the help of ERAS protocols in oesophagectomy patients (63). Although most topics mentioned above are part of the ERAS protocol, other items that should be named are early extubation, preoperative carbohydrate loading up to two hours prior to surgery, and early and adequate postoperative feeding (5).

It is unclear if oesophagectomy patients should be transferred to a post-anaesthesia care unit, intensive care unit or normal recovery after surgery. Patient allocation differs between hospitals and is often based on historical choices. It seems rational to have patients stay in a high-care environment to spot early neo-oesophagus breakdown, sepsis, inadequate pain management, and persistent hemodynamic instability. Experience with the protocols and specificities of post-operative care of oesophagectomy is essential.

Aside from achieving early and adequate feeding, diligent fluid titration in the post-operative setting and ward seems a rational approach. Studies on this topic are lacking. Finally, we would like to point out that for the longest periods of their hospital stay oesophagectomy patients are not monitored for their vital signs. Miniaturisation and wireless techniques now allow heart rate, temperature and respiratory rate monitoring with the application of a small patch (64,65). Data is not yet available on the value in

spotting the morbid patient by means of these devices but this may be an important possibility to improve care for these patients. With ICU outreach teams and MEWS on one end and wireless monitoring tools on the other, the gap for failure to rescue seems to be closing.

Conclusions

Morbidity and mortality after oesophagectomy is still high despite multidisciplinary and enhanced recovery pathways showing promising results. The anaesthetist has an important role in the care of the complex care of the oesophageal cancer patient. Minimising unnecessary fluid administration, adequate pain management, hypotension, and protective lung ventilation are examples of proven strategies that can improve outcome after this high-risk surgery. Future possibilities for improvement may especially lie in the early rescue of deteriorating patients in the postoperative surgical wards.

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Footnote

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