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New Fast-Track Concepts in Thoracic Surgery: Anesthetic Implications

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Abstract Fast-track anesthesia has become the standard of care for many surgical procedures, especially for colectomy. Its practice in cardiac surgery has been extensive mainly for economic reasons. On the other hand, fast-track is less practiced after lung surgery probably because of continuous debate on pleural drainage.

Keywords Fast-track · Lung surgery · Cardiac surgery

Introduction

Kehlet and Wilmore introduced the concept of fast-track surgery, also known as enhanced recovery after surgery (ERAS) in 1990 [1, 2]. From this date, many institutions have modified their patients' care to follow these multimodal recommendations concerning every period of the surgical pathway. The concept aims for the patient's early recovery and discharge from hospital thanks to a reduction in surgical stress response, and also in postoperative organ dysfunction or complications. Colorectal surgery is the most frequent model to implement this program. The key points of this clinical pathway are as follows:

- *Preoperative preparation* optimization of comorbidities (cardiac disease, chronic obstructive pulmonary disease, diabetes mellitus, …), cessation of smoking and alcohol, education of patients.
- *Anesthesia* restriction of fasting period before anesthesia, preoperative carbohydrate intake, use of short acting anesthetic drugs, local or regional anesthesia/analgesia or neuraxial blockade according to the case, maintenance of normothermia, limitation of fluid or goal-directed fluid therapy.
- *Surgery* minimally invasive surgical techniques, limitation of use or early removal of nasogastric tubes, catheters, and drains.
- *Postoperative course* prevention of nausea and vomiting, early enteral nutrition and postoperative mobilization, adequate multimodal analgesia using preferentially local, regional or epidural analgesia, opioid-free analgesia.

In addition, each type of procedure has specific features.

Fast-Track in Thoracic Surgery

The Pioneering Work of Cerfolio

Cerfolio et al. [3] were pioneers in the application of the fast-track concept in thoracic surgery. Their protocol is characterized by

- an extensive information given to the patient and family with explicit mention of the expected discharge date (D3 or D4),

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- an epidural catheter with infusion as soon as the surgery starts,
- a posterolateral thoracotomy sparing the serratus anterior muscle,
- an active rehabilitation as soon as D1: chest physical therapy every 8 h, respiratory nebulizers every 4 h, chest tube placed to water seal, ambulation four times daily, feeding with aspiration precautions,
- removal of all tubes at D2: discontinuation of central line, epidural catheter (start of oral pain medication), and of urinary catheter, removal of the single chest tube (if wedge resection) or of one of the chest tubes if no air leak and if drainage is <400 mL for last 24 h,
- preparation for discharge at D3: discontinuation of the second chest tube if no air leak and output <400 mL for 24 h, discharge to home in the afternoon or on D4 depending on patient's wishes and level of pain control. A Heimlich valve is placed in case of persistent air leak.

Impressive results have been published on 500 patients (39 % lobectomy) by Cerfolio et al. [3]: Median discharge at D4 (range 2–119 days) with 65 % of the patients leaving before D5, and a low 1.8 % readmission rate (pneumonia in five patients, weakness and poor pain control in four patients).

New Insights

Several points at every step of the pathway have been outlined since Cerfolio's 2001 publication.

Preoperative Period

Pulmonary rehabilitation must be distinguished from prehabilitation, which is a broader program.

Pulmonary Rehabilitation Pulmonary rehabilitation programs for patients with chronic lung disease are well established [4]. The National Emphysema Treatment Trial (NETT) study had provided a significant demonstration of the effectiveness of pulmonary rehabilitation in a large cohort of patients with advanced emphysema [5]. Recently Coats et al. [6] showed in a short series of patients awaiting lung resection surgery that a home-based exercise-training program is feasible and improved exercise tolerance and muscle strength. This improvement in pulmonary function is also of interest for patients undergoing chemo-radiotherapy prior to lung resection, particularly in the highest risk patients (smokers, respiratory impairment) as demonstrated by Tarumi et al. [7] but the 10-week duration of this program appears hardly feasible. A randomized clinical trial has terminated but, due to the low recruitment rate, the study design was changed to a feasibility study: the Perioperative Rehabilitation in Operation for Lung Cancer (PROLUCA) (NCT01893580) [8]. The intervention program consisted of exercise before surgery (individually designed home-based exercise program performed for at least 30 min every day until surgery) and/or after surgery (12 weeks' rehabilitation program combined with three individual counseling sessions). No result of this trial has been published. A randomized clinical trial from the Mayo Clinic is still enrolling participants to determine if length of hospital stay is decreased after rehabilitation versus usual care. Patients will undergo ten sessions of mindfulness-based pulmonary rehabilitation prior to surgery. Each session is about two hours long and consists of upper/lower extremity training, breathing exercises, and education (NCT01682850).

Prehabilitation Prehabilitation consists generally of a four-week preoperative multimodal program: exercise training (anaerobic and aerobic), nutritional and psychological support, with the goal of increasing the physiologic reserve and muscle mass [9••]. It is associated, if necessary, with other facets like treatment of medical comorbidities, smoking and alcohol cessation, all aspects particularly important in patients with lung cancer. Furthermore, some patients had to undergo chemo-radiotherapy regimens before surgery for lung cancer with a negative impact on surgical recovery. West et al. [10] have recently confirmed that neoadjuvant chemo-radiotherapy before rectal cancer surgery reduces physical fitness and that a structured and personalized exercise intervention is feasible in the period between this therapy and surgery and permits the return of fitness to baseline levels. Today, there is no published trial of prehabilitation before lung resection.

Intraoperative Phase

Inflammation Response to One-Lung Ventilation (OLV) and Choice of Hypnotic Agent Inflammatory cytokines are released during OLV [11] and can trigger a local or systemic inflammatory response. De Conno et al. [12] demonstrated in a prospective, randomized study that sevoflurane has an immunomodulatory role with significant reduction of inflammatory mediators, in comparison to propofol. However, clinical impact of the choice of the hypnotic agent remains controversial. Modolo et al. [13] reviewed 20 studies that enrolled 850 participants and concluded that there is very little evidence for a difference between agents. On the other hand, Sun et al. [14] reported contradictory results; they analyzed eight randomized controlled trials that included 365 patients and reported significant differences in the concentration of alveolar inflammatory mediators between the volatile group and

intravenous group, in which the volatile group had lower levels of TNF-α, IL-6, and IL-8. They also reported that the overall number of pulmonary complications was lower in the volatile group (RR 0.42; 95 % CI 0.23–0.77; $p = 0.005$) and that patients in that group had significantly shorter hospitalization stay (−3.59 days; 95 % CI 5.70 to −1.48 days; $p = 0.001$). A randomized study has recently been completed by Beck Schimmer from Zurich (Switzerland) that compared desflurane and propofol; its primary outcome measure was major postoperative complications (≥grade IIIa, according to the classification of surgical complications from Dindo and Clavien) but no results have so far been published (NCT01452256).

Inflammation Response to OLV and Mode of Ventilation Lung protective ventilation can prevent postoperative complications [15] as demonstrated in abdominal surgery [16]. Two reviews have recently been published on the risk of acute lung injury due to OLV [17, 18•]. Current recommendations suggest to limit duration of OLV and to provide protective ventilation with a low FiO2, low tidal volumes of 4–5 mL/kg predicted body weight during OLV, and low ventilatory pressures. Contralateral lung recruitment before OLV and lung recruitment thereafter are also recommended. The level of positive end-expiratory pressure applied to the dependent lung during OLV is still under debate: a standardized level of 5–10 cm H_2O or an individualized PEEP level determined for example after a PEEP decrement trial [19].

Intravenous Fluid Management Fluid administration is an essential part of intraoperative management and one of the "pillars" of fast-track surgery [20]. Indeed, fluid is a medication that can be beneficial or harmful according to the given dose [21]. Insufficient volume will result in extracellular dehydration, low cardiac output and reduced tissue perfusion with a risk of organ dysfunction, or even organ failure if hypoperfusion persists. However, excessive administration of fluids will generate congestion and subsequent tissue edema with a decrease in oxygen delivery. The diffusion of oxygen from the red blood cells to the mitochondria is hampered by the accumulation of fluids in the interstitial space. The consequences of excessively positive fluid balance are also an increased post-operative morbidity and mortality [22]. Several studies involving high-risk surgical patients have shown that "blind" fluid administration results in poorer outcome when compared to "clever" fluid therapy. Two "clever" strategies achieving the same goal have been described. One (called "the restrictive" approach) uses a precise estimation of the patient losses to replace them and avoid congestion [23, 24]. The other (called "the goal-directed" approach) uses the measurement of stroke volume to guide fluid titration: small aliquots of fluids are given as long as stroke volume increases, indicating an improvement in tissue perfusion, and (more importantly) any fluid administration is interrupted when stroke volume no longer increases, indicating that the threshold for congestion has been reached. The benefit of goal-directed fluid administration has been established in various surgical settings including, digestive, orthopedic, and cardiac surgery [25, 26]. To the best of our knowledge, no report on lung surgery has been published yet. However, due to the poor tolerance of lung edema, it appears very reasonable to use a quantitative rather than a "blind" approach to administer fluids in patients undergoing lung surgery. The National Institute for Health and Clinical Excellence recommends the use of esophageal Doppler (CardioQ-ODM) in patients undergoing major or high-risk surgery or other surgical patients for whom a clinician would consider using invasive cardiovascular monitoring (http://www.nice.org.uk/guidance/mtg3/chapter/1-Recommendations).

Surgical Procedure and Drainage The use of a minimally invasive surgical technique is a key-point for fast-track surgery. The change from the traditional posterolateral thoracotomy to minimally invasive video-assisted thoracoscopy (VATS) is a major improvement. Several authors have reported less morbidity and a shorter hospital stay on thousands of patients undergoing VATS [27–29]. However, Cao et al. [30] reported that patients who underwent VATS lobectomy or open lobectomy had similar long-term survival and the literature lacks from randomized trials between both techniques.

Chest tube management is usually determined by department policy, or the individual surgeon's choice. Thoracic surgeons seldom follow Cerfolio's protocol. According to this author, the chest tube can be removed when there is no air leak and when drainage output is less than 400 mL for 24 h [3]. In case of air leaks, this protocol recommends passive suction (water seal) or active suction at night with water seal during the day followed by home discharge with a Heimlich valve, and tube removal after 2–3 weeks [31]. Chest tube withdrawal has been reported to be safe after VATS lobectomy for a fluid production around 500 mL/day [32]. Recently, others proposed removal of chest tubes regardless of fluid output, as long as it was neither blood or chyle and if the air leak was less than 20 mL/min for more than 6 h [33]. Regarding the number of chest tubes, Bertholet et al. [34•] retrospectively analyzed 133 patients who underwent pulmonary lobectomy. They suggested that placement of a single chest tube and early conversion to water seal decreases the duration of air leak and of chest tube drainage, and the length of hospital stay after lobectomy. Finally, analysis of current practice shows that most surgeons place one chest tube for

minimally invasive lobectomy and two for open lobectomy and that chest tube management is variable depending especially on the surgeon's experience and on the volume of surgical procedures performed in each center [35].

Postoperative Period

Analgesic Technique The choice of the analgesic technique is also an old dispute between two "lobbies": anesthesiologists who favor thoracic epidural analgesia and those who favor paravertebral analgesia. Norum and Breivik [36] reported that randomized trials indicate that pain after thoracotomy is more effectively relieved by thoracic epidural analgesia than by paravertebral blocks. In contrast, Baidya et al. [37] stated in a systematic review and meta-analysis that thoracic paravertebral block may be as effective as thoracic epidural analgesia for post-thoracotomy pain relief and is also associated with fewer complications. In fact, most fast-track lung surgery programs included thoracic epidural analgesia and not paravertebral block [3, 38, 39]. Moreover, most of the anesthesiologists are unaware of several beneficial effects of thoracic epidural analgesia such as modulation of the neuroendocrine and stress response, modulation of the immune function and inflammation [40], and favorable properties on blood clotting [41, 42].

Our policy is to prefer thoracic epidural analgesia for patients scheduled for a postero-lateral thoracotomy because of the irregularity of pain relief obtained by the paravertebral block.

Increasing use of VATS poses a problem: do we continue to favor thoracic epidural analgesia or not? It seems logical to choose thoracic epidural analgesia if there is a reasonable risk for conversion to a thoracotomy and a less invasive technique in other cases. This technique can be a single-injection thoracic paravertebral block [43], an intercostal block, an intrapleural analgesia [44], all of these combined with multimodal analgesia [45, 46].

Recent innovations may change the management:

- insertion of a multiholed catheter between the pericostal sutures and the serratus muscle, connection to an elastomeric pump with a local anesthetic solution, infusion during 48 h [47],
- use of liposomal bupivacaine which offers the potential to provide prolonged blockade of intercostal nerves (72–96 h) [48].

Length of Stay A fast-track program is only effective if it allows a rapid discharge from the hospital without excessive readmission rates. But what are the "right numbers" of postoperative days after surgery? First of all, we have to remind that patients treated by Cerfolio at the beginning of the century had a median day of discharge at postoperative day 4 (range 2–119 days), 65 % of them leaving the hospital on postoperative day 4 or sooner, with a 1.8 % readmission rate, although they had a conventional thoracotomy [3]. Such a median postoperative length of stay of 4 days has been calculated from the analysis of the 2011 to 2014 General Thoracic Surgery Database (20,657 lobectomy patients from 231 participating centers) [49]. This shows that most services seek to reduce the length of stay whether through a formalized program of fast-track or not. Some authors described the impressive results of a fast-track procedure with a median length of stay of 2 days [50] while others, like our group [39], reported longer lengths of stay. Sociological, economic and regulatory aspects can explain the differences observed. Bertholet et al. [34•] insist on non-medical reasons which explain a longer length of stay: "hesitance of patients (or relatives) to leave the hospital early, problems with nursing home placement or lack of home health care." The other key point regarding discharge was the management of chest tubes as described above.

The next step is to perform some procedures such as outpatient procedures. This has already been reported for open lung biopsy in selected patients [51] and even for thoracoscopic resection of lung nodules [52].

Finally, Salati et al. [53] reported that the fast-tracking management did not increase the readmission rate. However, Assi et al. [54] reported a less optimistic view: 13 % readmission to the hospital within 30 days of discharge or early unplanned return to the clinic. These authors found that unplanned transfer to the intensive care unit during the initial hospital stay (odds ratio, 10.4; 95 % CI 1.1–103.5; $p = 0.04$) and Charlson comorbidity index higher than 0 (odds ratio, 1.5; 95 % CI 1.04–2.03; $p = 0.03$) are predictors of readmission. A simplistic view can be drawn from the data published by Freeman et al. [55•]: too early is dangerous and too late is symptomatic for a very high-risk patient.

Breaking News…

Some surgeons considered that fast-track is outdated. Awake thoracic surgery was reported by Pompeo et al. in 2004 when they published awake thoracoscopic resection of solitary pulmonary nodules [56]. This group published several papers relating their experiences in a text book: Awake Thoracic Surgery (Bentham Science Publishers 2012). They claim that "Thoracic surgeons of the third millennium must accept the challenge of this dynamic and rapidly evolving scenario without losing the right root, which probably lays just between well-established conventional surgery techniques and newly available advanced

technology tools. Awake thoracic surgery will benefit from evidence-based data that are progressively accumulating" [57]. But few groups follow this recommendation [58]. Kiss and Castillo [59] described that awake video-assisted thoracic surgery can be performed after wound infiltration and lidocaine administration in the pleural space or with more invasive techniques such as thoracic wall blocks, selective intercostal nerve blockade, thoracic paravertebral blockade and thoracic epidural analgesia.

Fast-Track in Cardiac Surgery

The management of patients undergoing cardiac surgery has evolved considerably from mandatory prolonged postoperative sedation [60] to rapidly reversible anesthesia with a brief stay in the Intensive Care Unit (ICU). This has occurred despite the fact that older patients are operated on, and that coronary artery bypass graft (CABG) surgery is now considered for the most complex cases, others being treated percutaneously. Many elements have contributed to this change but the cost factor has probably been the main determinant. One of the major studies on this subject showed that early tracheal extubation reduces total costs per CABG procedure by 25 %, predominantly through nursing and cardiovascular intensive care unit cost reduction. This is accomplished by decreasing the high costs of intensive care by transferring patients to the less expensive ward without increasing the rate of complications [61]. To optimize the use of ICU beds, a risk prediction model of fast-track failure was proposed. This model has been validated in a group of 1597 patients including 175 (11 %) with failed fast-track management [62]. There are a few dissonant voices. Guenther discussed the economic impact of early extubation (during the 6 first postoperative hours) versus extubation in the morning of postoperative day 1 explaining that a lot of costs are not related directly to the timing of extubation [63]. Lahey et al. warns about frequent readmissions outside the hospital where the cardiac surgical procedure has been performed [64].

A major point must also be outlined: there are several types of organization. Patients are transferred from the operating room to a dedicated ICU or to a conventional ICU or even to a specialized or conventional PACU, and then later to a high dependency unit or to the surgical ward with or without telemetry. A recent study has shown that postoperative transfer to a specialized PACU rather than to an ICU leads to earlier extubation and quicker discharge to a step down unit, without compromising patient safety [65]. Furthermore, each country has its mode(s) of facturation.

In fact, reducing stay in ICU and early discharge from hospital are currently standard care. However, a word of caution comes from the meta-analysis published in 2012 by the Cochrane group which confirms that fast-track strategy carries similar postoperative morbidity and mortality to the conventional approach in patients at low or moderate risk, reduces the length of stay in the intensive care unit but not the length of stay in the hospital [66••].

Choice of Anesthetic Drugs

Regardless of the intravenous or inhaled anesthetic agent, monitors of depth of anesthesia are used to facilitate their administration throughout the procedure avoiding overdosing that can promote hypotension, and underdosage with the risk of intraoperative awareness which was dreaded during morphine anesthesia [67]. This risk still occurs especially when anesthesia is lightened during an episode of hemodynamic disorder and during the postoperative sedation.

Propofol is easier to administer during cardio-pulmonary bypass than volatile anesthetics and can be used for postoperative sedation. Sevoflurane preserves myocardial function in patients with CABG surgery [68, 69] and can be also used for postoperative sedation [70] using new delivery systems such as Anaconda® (ACD; Sedana Medical AB, Uppsala, Sweden) [71]. Remifentanil and sufentanil are mainly used. They differ especially by their context-sensitive half-time (i.e. the time required for the drug's plasma concentration to decrease by 50 % after cessation of the infusion): ultra-short for remifentanil (approximately 3 min, even after prolonged infusion) [72] and 10 times longer for sufentanil after 4 h infusion [73]. Choice of remifentanil is fully justified if extubation is anticipated in the operating room (ultra fast-track) but it requires early and optimal management of postoperative pain due to the lack of residual analgesia. Choice of sufentanil is logical if extubation is anticipated in the ICU. In the same way, use of rocuronium is justified for ultra fast-track since reversal can be provided by neostigmine or sugammadex.

Choice of Analgesic Techniques

The use of thoracic epidural analgesia in cardiac anesthesia is also a subject of debate. The study published by Svircevic et al. [74], showed that there was no clinically relevant benefit of this technique. On the other hand, Jakobsen et al. [75] recommend using it. Hemmerling et al. [76] have reviewed the literature from 1966 to 2012 and found that the risk of catheter-related epidural hematoma is 1 in 5493 with a 95 % confidence interval (CI) of 1/970–1/31114 and that the risk of catheter-related epidural hematoma in cardiac surgery is similar to the risk in the general surgery population (1 in 6628; 95 % CI 1/1170–1/37552). However, the recommendations for epidural anesthesia are

so stringent that only a few teams continue to use thoracic epidural analgesia prior to cardiac surgery. The requirements include: normal coagulation tests, discontinuation of antiplatelet agents 5–7 days before, epidural catheter placed the day before (or at least 4 h before surgery), deferral of intervention 24 h if bleeding puncture, normalization of coagulation tests before removing the epidural catheter.

Intrathecal injection of morphine, usually 500 μg, is a less invasive technique which facilitates ultra fast-track and provides up to 24 h of analgesia [77].

Extubation in the Operating Room or in the ICU

There are two concepts in cardiac surgery: the concept of fast-track, the most common, which pursues the goal of rapid ventilator weaning and an accelerated postoperative recovery and the most controversial concept of ultra fast-track which requires modifications of the anesthetic and surgical techniques to allow the patient's extubation in the operating room.

Quick extubation in the ICU has become the standard of care although Cheng et al. [78] showed in a randomized, controlled clinical trial published in 1996 that early extubation, in the "window of opportunity" which is comprised between 1 and 6 h) and prolonged sedation and extubation (12–22 h) in patients after coronary artery bypass grafting were similar especially in regard to myocardial ischemia. Use of agents with short elimination half-time or with dexmedetomidine [79] ensures adequate sedation until the criteria for extubation are present (i.e.: stable hemodynamic status, temperature >36.5 °C without shivering, no active bleeding). This strategy can be used even if patients are not specifically selected for fast-track procedures. However, several authors have defined populations which are clearly not eligible for fast-track. Wong et al. [80] have shown that risk factors of delayed extubation after CABG surgery are older age, female gender, postoperative use of intra-aortic balloon pump, inotropes infusion, bleeding, and atrial arrhythmia. In addition, risk factors of prolonged ICU stay are delayed extubation, preoperative myocardial infarction, and postoperative renal failure. Risk factors for mortality were: female gender, emergency surgery, and poor left ventricular function.

Ultra fast-track has gained popularity with the increasing practice of off-pump CABG [81] but cardiac surgery carries a high-risk of postoperative hemorrhage requiring urgent re-exploration, sometimes for acute tamponade.

Fast-track strategy also includes the rapid transfer of the patient to the surgical ward after 6–8 h when several criteria are present. These criteria include a well oriented patient without pain, a stable hemodynamic status without drugs, a sinus rhythm without signs of ischemia, oxygen saturation (SpO2) >94 % with oxygen <5 L/min, PaCO2 <50 mmHg, no bleeding (drainage <50 mL/h), diuresis >0.5 mL/kg/h, and normothermia [82]. Failure of the protocol has been reported in 16 % of the selected patients; two characteristics were found to be related to the failure: older age and left ventricular dysfunction [82].

Breaking News…

Introduction of off-pump coronary artery bypass graft procedure was a significant evolution facilitating fast-track strategies. But changes are ongoing with especially transfemoral transcatheter aortic valve implantation (TAVI), percutaneous interventional mitral regurgitation treatment using the Mitra-Clip® system. As there is no barrier for "progress," awake CABG has been proposed [83] with the recent introduction of robot-assisted cardiac surgery [84].

Conclusion

While fast-track anesthesia is now routinely used in cardiac surgery (thanks to a multidisciplinary collaboration amongst anesthesiologists, surgeons, surgical nurses, and physiotherapists), much work is still necessary to develop this practice after lung surgery. The work is ongoing but careful attention must be paid to late postoperative results.

Compliance with Ethics Guidelines

Conflict of Interest Morgan Le Guen, Bernard Cholley, and Marc Fischler declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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