We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

186,000

200M

Download

154
Countries delivered to

Our authors are among the

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us? Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.

For more information visit www.intechopen.com



Chapter

ERAS in General Thoracic Surgery

Domenico Viggiano, Leonardo Politi, Alessandro Gonfiotti and Andrea Droghetti



Enhanced recovery after surgery (ERAS®) is a strategy that seeks to reduce patients' perioperative stress response, thereby reducing potential complications, decreasing hospital length of stay and enabling patients to return more quickly to their baseline functional status. This programme results from the union of several perioperative clinical elements that have individually proved to be beneficial to the patient and have showed, when used together, a synergy that results in a significant outcome improvement. The term was coined at the end of the 1990s and originally used to refer to a complex fast-track programme in open colorectal surgery. Subsequently, the practice has spread to other surgical specialties centralising the interest of clinicians and researchers. The objective of this chapter is to analyse the key elements of an ERAS protocol applicable to minimally invasive thoracic surgery.

Keywords: ERAS, fast track, VATS lobectomy, lung cancer, surgical recovery

1. Introduction

ERAS is the acronym of enhanced recovery after surgery: a multimodal perioperative approach based on the best medical evidence [1]. This programme results from the union of several perioperative clinical elements that have individually proved to be beneficial to the patient and have showed, when used together, a synergy that results in a significant outcomes improvement.

The key elements of each ERAS protocol include preoperative counselling and nutrition, avoidance of perioperative fasting and carbohydrate loading up to 2 h preoperatively, standardised anaesthetic and analgesic regimens (epidural and non-opioid analgesia) and early mobilisation (**Figure 1**) [2]. A meta-analysis showed that ERAS programmes in major surgery reduce hospitalisation by 2–3 days and complications by 30–50% [3].

From its introduction at the start of 1990s, ERAS has improved perioperative approach of many specialities: general surgery (colon resection) [4], vascular surgery [5], thoracic surgery [6, 7] and recently urology (cystectomy) [8, 9]. The aim of such programmes is to try to change the physiological and psychological responses to major surgery [1]: the experiences collected until now have shown a reduction in complications and hospital stay, improvements in cardiopulmonary function, earlier return of bowel function and earlier resumption of normal activities [10, 11].

There are relatively few reports on the use of ERAS in thoracic surgery; the aim of our paper is to focus on the key elements of an ERAS protocol, evaluating their applicability in thoracic surgery oncology, particularly in the field of minimally invasive surgery.

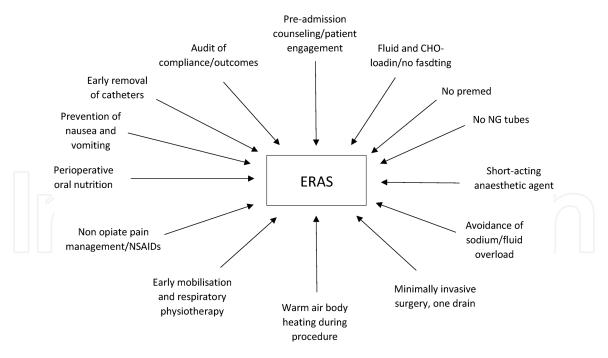


Figure 1.
The key elements of ERAS protocol.

2. Principles of ERAS

Response to major surgery is inevitable: for many years, this was a postulate in conventional perioperative metabolic care. This concept has recently been challenged with the view that a substantial element of the stress response can be avoided with the appropriate application of modern anaesthetic, analgesic and metabolic support techniques. Another referral point in conventional post-operative care was the patient's prolonged bed rest: this concept is now under revision also [12]. In the catabolic patient, medium-term functional decline will ensue if active steps are not taken to return the patient to full function as soon as possible. Based on these two concepts, a new view of peri-operative surgical care has been created, based on the principles of stress reduction and promotion of return to baseline after surgery, avoiding medium term sequelae of conventional post-operative care (e.g. loss in

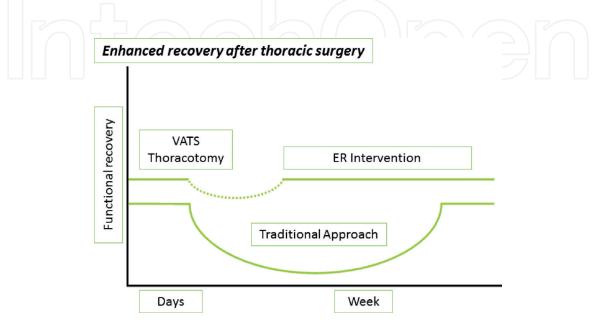


Figure 2. *Multidisciplinary approach to the ERAS protocol.*

nutritional status and fatigue) [13]. So, the ERAS programme results in a clinical pathway with the aim of attenuate surgical stress, maintain physiological function and expedite return to normal function; a cornerstone of each ERAS protocol is a real multidisciplinary approach, avoiding the so-called silo mentality, defined as 'an attitude found in some organisations that occurs when several departments or groups do not want to share information or knowledge with other individuals in the same company' [14] (**Figure 2**).

3. ERAS key elements

3.1 Preadmission counselling and patient information

It is well known that an exhaustive preoperative patient information can enhance post-operative recovery and pain relief, particularly in patients who show most denial and the highest levels of anxiety [15, 16] **Figure 1**. A clear and comprehensible explanation of what is to happen during a patient's hospital stay can also facilitate adherence to the care pathway and allows timely recovery and an early discharge: patients should receive oral and written preadmission information forms describing what will happen during their hospital stay, what they have to expect, and what will be their role during their recovery. In addition, at the first meeting, the patient should also be given a specific role with clear tasks to perform during the post-operative period [17]. These include targets for food intakes and oral nutritional supplements (ONS) and targets for staying out of bed.

3.2 Preoperative fasting and metabolic condition

Fasting after midnight has been the standard in elective surgery to avoid pulmonary aspiration without obtaining scientific support: a recent review [18] has shown that this practice is not only not useful but, in some cases, even negative for the patient's metabolism. Current recommendations from leading national anaesthesia society suggest clear fluid intake up to 2 h from anaesthesia induction and a 6-h fast for solid foods [19–21]. Some works in the literature, which analysed the effects of preoperative fasting on patients, concluded by proposing that patients arrive in the operating theatre fed. Examples of preoperative nutrition are the use of clear carbohydrate-rich beverages (12.6%) at a dose of 800 ml before midnight and 400 ml 2–3 h before surgery: this leads to a reduction in thirst, hunger and anxiety in patients awaiting surgery [22] and to a significant reduction in post-operative insulin resistance [23]. In this way, the patients' metabolism benefits more from post-operative nutrition [24] with a lower risk of hyperglycaemia [25]. This approach, validated for different major surgery, is easy to apply also for thoracic surgery.

3.3 Anaesthetic protocol and multimodal pain relief

According to ERAS principles, the efforts of anaesthetic procedure has to be made to minimise the impact of anaesthetic agents and techniques on organ function and also to ensure appropriate depth of anaesthesia and avoidance of awareness but also avoiding overdose: it is rational, therefore, to use agents with short pharmacodynamic duration (propofol and remifentanil) [26], thereby allowing pro-active recovery to start on the day of surgery. Thus, opioids with longer-lasting effect (morphine and fentanyl) should be avoided. Short acting inhalation anaesthesia is a reasonable alternative to total intravenous anaesthesia. Although the protective role

of epidural analgesia before the beginning of surgery, by limiting the production of stress hormones and post-operative insulin resistance, has been sufficiently clarified, its effect on post-operative outcome is still debated [27]. Epidural analgesia has been identified for usual post-operative analgesia because of its optimal pain relief capacity and the benefits on post-operative [28]. However, a recent large single study [29] has questioned the benefits of epidural analgesia in terms of postoperative morbidity and mortality. Moreover, it is necessary to take into account the risks associated with the procedure: epidural hematomas, abscesses or neurological damage are in the order of 0.01-0.6 [30]. The catheter is positioned in the awake patient to establish the effectiveness of the block. During surgery, the block can be maintained by continuous infusion of local anaesthetic (e.g. bupivacaine 0.1%) plus a low-dose opiate (e.g. 2 mg/ml fentanyl) at 4–10 ml/h. Epidural opioids in small does synergise with epidural local anaesthetics in providing analgesia, allowing a reduced dosage of both agents. Furthermore, low-dose epidural opioids improve the analgesic effects without major systemic effects [31]. Finally, it has been demonstrated that the addition of a small dose of adrenaline to epidural infusion of local anaesthetic and opioid enhances the analgesic effect of these drugs avoiding systemic opioid related side-effects [32–34].

Analysing the data presented in the literature of recent controlled studies and a Cochrane review, several studies [35] highlight how early mobilisation is effectively obtained using continuous epidural local anaesthetic or local anaesthetic-opioid techniques. Epidural local anaesthetic techniques provide a more effective analgesia than patient controlled analgesia (PCA), allowing greater physiological benefits on surgical stress responses; achieving the randomised studies have demonstrated that continuous epidural analgesia has positive effects on the reduction of pulmonary morbidity, but not on other types of morbidity or on hospital stay and convalescence [36]. This probably for unimodal intervention that does not take advantage of the efficient analgesia: the use of non-steroid anti-inflammatory drugs (NSAIDs) may provide some additional analgesia [37]. The principal objective for postoperative analgesia is eliminating opioid with their opioid-related side effects and improving quality of recovery [38]. An optimal deadline for post-operative continuous epidural analgesia has not been established; however, 2 days is the period identified from several large case series and normally used in clinical practice. It should also be emphasised that there is no evidence for the use of NSAIDs to improve analgesia in addition to a well-functioning epidural: this practice should be avoided.

There are several papers in the literature that have demonstrated the efficacy of these analgesic principles also for thoracic surgery; for example: the use of epidural analgesia that reduces post-operative morbidity or the use of lower doses of opioid to reduce their adverse effects and promote early mobilisation [39].

3.4 Surgical aspects

Minimally invasive surgery is a central point of any fast-track programme: when applied it has shown its effectiveness in terms of reduction of hospital stay, post-operative complications and pain both in the comparison of VATS surgery vs. open surgery [40] and for standard multiportal VATS vs. uniportal [41]. The comparison between multiportal VATS and uniportal has showed many advantages in favour of the latter: less trauma tissue, less blood loss and less complication. This can potentially be translated into a reduction in post-operative hospitalisation and faster recovery of the daily activities of patients, which is the goal of the ERAS programme. A recent meta-analysis published by Harris and The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia, compares eight observational studies published over the past two years comparing the outcome

of oncologic patients [41] treated with conventional VATS lobectomy (multiport) vs. uniportal VATS. The results (1850 patients, of which 627 treated with uniportal VATS and 1223 with multiportal VATS), show statistically significant differences in favour of the single-port in terms of length of stay (6.2 \pm 2.6 vs. 6.7 \pm 3.4 days, P < 0.0001), duration of thoracic drainage (4.5 \pm 2.2 vs. 5.4 \pm 2.9 days, P = 0.0006), post-operative complications (12.0 vs. 13.7%, P = 0.009). Post-operative pain also appeared to be minor in monoportal procedures although with non-statistically significant values. However, taking into account VATS interventions for minor surgery, further work confirms a reduction in post-operative pain using a smaller number of thoracoscopic accesses [42, 43]: in this way appear to be clear a rationale link behind the fewer accesses to the chest and hence fewer intercostal nerves that can be traumatised during surgical procedures.

3.4.1 Minimal invasiveness of VATS approach

The minimal invasiveness of VATS procedures is based on the lower impact of its surgical trauma compared to traditional open procedures by thoracotomy. However, several VATS techniques have been described over the years, differing mainly on the number of ports and their location. The number of ports can be discussed as a factor affecting the invasiveness of the surgical procedure and consequently influencing the post-operative functional recovery. Several authors have highlighted how the transition from VATS multiportal approach to a monoportal approach is effective in optimising post-surgical results by reducing pain, complications and the length of hospital stay. Hence the idea that, in order to optimise surgery within an ERAS programme, monoportal VATS can facilitate a faster recovery of the patient, an early discharge and a promptly return to daily life. Tamura recent study [44] has shown how single-port technique reduces post-operative pain and increases quality of life in the peri-operative period. In two subsequent publications, Rocco and others [42] and Gonfiotti et al. [43] showed that a monoportal VATS approach is less associated with residual pain and post-operative paraesthesia. With the limits of non-randomised observational studies, we believe that these data can allow us to hypothesise that a lesser surgical trauma on the chest wall can result in a faster functional recovery, even when we talk about minimally invasive surgery.

3.4.2 Prevention of post-operative air leak

The air passage from the lung parenchyma into the pleural space after pulmonary resection is called air leak. In the literature, we can find the definition of prolonged air loss (PAL) as an air passage beyond the five post-operative days. Different studies show that the effects of this complication on the post-operative course significantly impacts on the risk of other complications (e.g. pleural empyema), post-operative hospitalisation and increased hospital costs and, more generally, a worse post-operative course.

Prolonged air leak appears to be a rather frequent complication after VATS lobectomy. In the reports of the Italian VATS group the incidence of PAL after a pulmonary lobectomy is equal to 7.2%, similar to the data present in the literature. Therefore, the prevention of a PAL is a fundamental element in ERAS perspective [45, 46]. In addition to this, Brunelli [47] reported a higher rate of pleural empyema in patients with PAL and Varela [48, 49] showed an increased incidence of pneumonia, atelectasis due to sputum retention and pleural effusion, demonstrating how PAL is associated with an increased risk of post-operative complications.

Therefore, it is fundamental to prevent the onset of PAL, mainly by adopting two different strategies:

- a. Reduction of residual pleural space
- b. Reinforcing/protecting suture line

In a recent paper [50] which considers five selected studies, in four of these, the fissureless technique used in pulmonary lobectomy has shown itself superior to the standard approach for PAL prevention and the reduction of the cessation of air loss time, concluding that, based on the current data, we can consider the fissureless technique better than the standard one [51]. Criticisms of this conclusion are mainly made when considering lower lobectomies: although the fissureless technique is accepted in upper or middle lobectomies, it is not considered as valid for lower lobectomies, mainly for oncological reasons as it could reduce the effectiveness of VATS lymph node dissection of stations N1 [52].

3.4.3 Number of pleural drainages

According to fast-tracking, could be indicated the positioning of just one pleural drainage (28/30 Fr) for all surgical procedure, instead of two used for example after a pulmonary lobectomy; a second drainage tube may be useful when a significant post-operative air leak is expected or in case of a bi-lobectomy [53]. The advantages of positioning a single thoracic drain reside in the reduction of post-operative pain that allows early patient mobilisation and therefore faster recovery [54, 55].

3.5 Promotion of early oral intake

One of the key objectives in the post-operative period for normally fed patients is the restoration of normal Gastro Intestinal (GI) function that allows an adequate food intake and a rapid recovery. A recent meta-analysis of controlled trials about early enteral or oral feeding versus 'nil by mouth' after major surgery showed no clear advantage in keeping patients fasting after elective surgery [56]. Early nourish reduced both the risk of any kind of infection and the mean hospitalisation. However, the risk of vomiting is increased in patients early fed and, in the absence of a multimodal anti-emetic therapy, early enteral feeding has been associated with intestinal swelling, impaired mobilisation and reduced pulmonary function [57]; for these reasons, it is essential to adopt a targeted strategy for post-operative nausea and vomiting (PONV).

The use of emetogenic drugs (neostigmine, opioids, certain gaseous anaesthetic agents, etc.) should be avoided, favouring agents that are less emetogenic. Patients at risk for PONV should receive prophylactic treatment (e.g. ondansetron, dexamethasone or droperidol) [58].

For malnourished patients, the use of oral nutritional supplements (ONS) in the post-operative period and for 8 weeks after discharge, demonstrated effective benefits in terms of recovery of nutritional status, protein balance and quality of life [47]. Positive effects on clinical outcomes from ONS have also been documented also in series of elective surgical patients who were not screened specifically for malnutrition [59]. The difference between these studies, which used traditional nutrition protocols, and ERAS programmes is that oral integration in the first started 4–5 days after surgery, in the second is commenced the day before surgery and continued for at least the first four post-operative days, in order to achieve recommended intakes of energy and protein [60, 61]. This point of ERAS programme is crucial also for patients undergoing minimally invasive thoracic surgery: in fact, we need not to forget the aim of 'a more quickly return to their baseline functional status' and we know from several authors that when used in combination,

preoperative oral carbohydrate loading, epidural analgesia and early enteral nutrition, they improved the maintenance of nutritional status following surgery [25].

3.6 Early mobilisation and discharged criteria

Several factors are negatively influenced by bed rest: tissue oxygenation, pulmonary function, muscle strength, insulin resistance, muscle loss and risk of thromboembolism.

To minimise bed rest, the ERAS protocol should provide an organisation suitable for a plan of assistance with daily mobilisation targets and the patient should be nursed in an environment that stimulates mobilisation.

A useful stimulus can come, for example, from the compilation of a 'hospitalisation diary' in which the patient documents the activities performed on a daily basis; in this way, we can set more easily achievable goals such as, for example, that the patient remains out of bed at least 2 h on the day of surgery, increasing up to 6 h a day until discharge. As mentioned in the first part of the work, the ERAS project depends on the interaction of different professional figures: at this stage, the role of the nurse maintaining close and constant contact with the patient is crucial, and achieving decisive results also through the application of specific and innovative programmes such as 'nursing care map and programme'.

Patients can be discharged when they meet the following criteria:

- Good pain control with oral analgesia
- Taking solid food, no intravenous fluids
- Independently mobile or same level as prior to admission
- All of the above and willing to go home

The discharge process starts at the preadmission counselling session when it is determined if the patient lives alone and has any special needs (e.g. transport, social support, etc.). Problems that will delay discharge must be addressed at this time rather than once the patient has been admitted. Furthermore, it is crucial to set up a close follow-up on telephone monitoring of patient conditions followed by outpatient visits at predetermined times, the first of which generally falls to 15 and 30 days after discharge: to this, the key role played by a dedicated figure, the 'case manager', is of significant importance.

IntechOpen

Author details

Domenico Viggiano^{1*}, Leonardo Politi², Alessandro Gonfiotti² and Andrea Droghetti¹

- 1 Thoracic Surgery Unit, ASST, Mantova, Italy
- 2 Thoracic Surgery Unit, Careggi University Hospital, Florence, Italy
- *Address all correspondence to: viggiano.md@gmail.com

IntechOpen

© 2020 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. (CC) BY

References

- [1] Fearon KC, Ljungqvist O, Von Meyenfeldt M, et al. Enhanced recovery after surgery: A consensus review of clinical care for patients undergoing colonic resection. Clinical Nutrition. 2005;24(3):466-477
- [2] Weimann A, Braga M, Harsanyi L, et al. ESPEN guidelines on enteral nutrition: Surgery including organ transplantation. Clinical Nutrition. 2006;25:224-244
- [3] Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: A meta-analysis of randomized controlled trials. Diseases of the Colon and Rectum. 2013;56(5):667-678
- [4] Wind J, Polle SW, Fung Kon Jin PH, et al. Systematic review of enhanced recovery programmes in colonic surgery. The British Journal of Surgery. 2006;**93**:800-809
- [5] Podore PC, Throop EB. Infrarenal aortic surgery with a 3-day hospital stay: A report on success with a clinical pathway. Journal of Vascular Surgery. 1999;29:787-792
- [6] Gonfiotti A, Viggiano D, Droghetti A, et al. Enhanced recovery after surgery and video-assisted thoracic surgery lobectomy: The Italian VATS Group surgical protocol. Journal of Thoracic Disease. 2018;**10** (Suppl 4): S564-S570
- [7] Gonfiotti A, Viggiano D, Bongiolatti S, et al. Enhanced recovery after surgery (ERAS®) in thoracic surgical oncology. Future Oncology. 2018;**14**(6s):33-40
- [8] Willemsen PJ, Appeltans BM. Hospital stay of 2 days after open sigmoidectomy with a multimodal

- rehabilitation programme. British Journal of Surgery. 1999;**86**(7):968-969
- [9] Koupparis A, Dunn J, Gillatt D, et al. Improvement of an enhanced recovery protocol for radical cystecomy. British Journal of Medical and Surgical Urology. 2010;3:237-240
- [10] Eskicioglu C, Forbes SS, Aarts MA, Okrainec A, McLeod RS. Enhanced recovery after surgery (ERAS) programs for patients having colorectal surgery: A meta-analysis of randomized trials. Journal of Gastrointestinal Surgery. 2009;13:2321-2329
- [11] Lassen K, Soop M, Nygren J, et al. Consensus review of optimal perioperative care in colorectal surgery: Enhanced recovery after surgery (ERAS) group recommendations. Archives of Surgery. 2009;**144**:961-969
- [12] Kehlet H, Mogensen T. Hospital stay of 2 days after open sigmoidectomy with a multimodal rehabilitation programme. The British Journal of Surgery. 1999;86(2):227-230
- [13] Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. British Journal of Anaesthesia. 1997;78:606-617
- [14] Ensor P. The functional silo syndrome. AME Target. 1988; **Spring**:16
- [15] Egbert LD, Battit GE, Welch CE, Bartlett MK. Reduction of postoperative pain by encouragement and instruction of patients. A study of doctor–patient rapport. The New England Journal of Medicine. 1964;270:825-827
- [16] Kiecolt-Glaser JK, Page GG, MacCallum RC, Glaser R. Psychological influences on surgical recovery. Perspectives from psychoneuroimmunology.

- The American Psychologist. 1998;53(11):1209-1218
- [17] Disbrow EA, Bennett HL, Owings JT. Effect of preoperative suggestion on postoperative gastrointestinal motility. The Western Journal of Medicine. 1993;**158**(5):488-492
- [18] Ljungqvist O, Soreide E. Preoperative fasting. The British Journal of Surgery. 2003;**90**(4):400-406
- [19] Eriksson LI, Sandin R. Fasting guidelines in different countries. Acta Anaesthesiologica Scandinavica. 1996;40(8 Part 2):971-974
- [20] Soreide E, Fasting S, Raeder J. New preoperative fasting guidelines in Norway. Acta Anaesthesiologica Scandinavica. 1997;41(6):799
- [21] Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: A report by the American Society of Anesthesiologist Task Force on Preoperative Fasting. Anesthesiology. 1999;**90**(3):896-905
- [22] Hausel J, Nygren J, Lagerkranser M, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. Anesthesia and Analgesia. 2001;**93**(5):1344-1350
- [23] Soop M, Nygren J, Myrenfors P, Thorell A, Ljungqvist O. Preoperative oral carbohydrate treatment attenuates immediate postoperative insulin resistance. American Journal of Physiology. Endocrinology and Metabolism. 2001;**280**(4):E576-E583
- [24] Yuill KA, Richardson RA, Davidson HI, Garden OJ, Parks RW. The administration of an oral carbohydratecontaining fluid prior to major

- elective upper-gastrointestinal surgery preserves skeletal muscle mass postoperatievely—A randomised clinical trial. Clinical Nutrition. 2005;24(1):32-37
- [25] Soop M, Carlson GL, Hopkinson J, et al. Randomized clinical trial of the effects of immediate enteral nutrition on metabolic responses to major colorectal surgery in an enhanced recovery protocol. The British Journal of Surgery. 2004;**91**(9):1138-1145
- [26] British National Formulary. Oxford, UK: Pharmaceutical Press; 2003
- [27] Uchida I, Asoh T, Shirasaka C, Tsuji H. Effect of epidural analgesia on postoperative insulin resistance as evaluated by insulin clamp technique. The British Journal of Surgery. 1988;75(6):557-562
- [28] Scimia P, Basso Ricci E, Droghetti A, Fusco P. The ultrasoundguided continuous erector spinae plane block for postoperative analgesia in video-assisted thoracoscopic lobectomy. Regional Anesthesia and Pain Medicine. 2017;42(4):537
- [29] Rigg JR, Jamrozik K, Myles PS, et al. Epidural anaesthesia and analgesia and outcome of major surgery:
 A randomised trial. Lancet.
 2002;359(9314):1276-1282
- [30] Holte K, Kehlet H. Epidural anaesthesia and analgesia—Effects on surgical stress responses and implications for postoperative nutrition. Clinical Nutrition. 2002;**21**(3):199-206
- [31] Liu SS, Carpenter RL, Mackey DC, et al. Effects of perioperative analysis technique on rate of recovery after colon surgery. Anesthesiology. 1995;83(4):757-765
- [32] Niemi G, Breivik H. Adrenaline markedly improves thoracic epidural

- analgesia produced by a low-dose infusion of bupivacaine, fentanyl and adrenaline after major surgery. A randomised, double-blind, cross-over study with and without adrenaline. Acta Anaesthesiologica Scandinavica. 1998;42(8):897-909
- [33] Niemi G, Breivik H. Epinephrine markedly improves thoracic epidural analgesia produced by a small-dose infusion of ropivacaine, fentanyl, and epinephrine after major thoracic or abdominal surgery: A randomized, double-blinded crossover study with and without epinephrine. Anesthesia and Analgesia. 2002;94(6):1598-1605
- [34] Niemi G, Breivik H. The minimally effective concentration of adrenaline in a low-concentration thoracic epidural analgesic infusion of bupivacaine, fentanyl and adrenaline after major surgery. A randomized, double-blind, dose-finding study. Acta Anaesthesiologica Scandinavica. 2003;47(4):439-450
- [35] Jorgensen H, Wetterslev J, Moiniche S, Dahl JB. Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. Cochrane Database of Systematic Reviews. 2000;4:CD001893
- [36] Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: Cumulative meta-analyses of randomized, controlled trials. Anesthesia and Analgesia. 1998;86(3):598-612
- [37] Power I, Barratt S. Analgesic agents for the postoperative period. Nonopioids. Surgical Clinics of North America. 1999;79(2):275-295
- [38] Kehlet H, Holte K. Effect of postoperative analgesia on surgical

- outcome. British Journal of Anaesthesia. 2001;87(1):62-72
- [39] Das-Neves-Pereira JC, Bagan P, Coimbra-Israel AP, et al. Fast-track rehabilitation for lung cancer lobectomy: A five-year experience. European Journal of Cardio-Thoracic Surgery. 2009;36(2):383-391
- [40] McKenna RJ Jr, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: Experience with 1,100 cases. The Annals of Thoracic Surgery. 2006;81(2):421-425
- [41] Harris CG, James RS, Tian DH, et al. Systematic review and meta-analysis of uniportal versus multiportal video-assisted thoracoscopic lobectomy for lung cancer. Annals of Cardiothoracic Surgery. 2016;5(2):76-84
- [42] Jutley RS, Khalil MW, Rocco G. Uniportal vs standard three-port VATS technique for spontaneous pneumothorax: Comparison of post-operative pain and residual paraesthesia. European Journal of Cardio-Thoracic Surgery. 2005;28(1):43-46
- [43] Gonfiotti A, Jaus MO, Viggiano D, et al. Uniportal videothoracoscopic surgery: Our indications and limits. Innovations (Phila). 2015;**10**(5):309-313
- [44] Tamura M, Shimizu Y, Hashizume Y. Pain following thoracoscopic surgery: Retrospective analysis between single-incision and three-port video-assisted thoracoscopic surgery. Journal of Cardiothoracic Surgery. 2013;8:153
- [45] Crisci R, Droghetti A, Migliore M, et al. Video-assisted thoracic lobectomy for lung cancer in Italy: The 'VATS Group' Project. Future Oncology. 2016;12:9-11
- [46] Singhal S, Ferraris VA, Bridges CR, et al. Management of

- alveolar air leaks after pulmonary resection. The Annals of Thoracic Surgery. 2010;**89**:1327-1335
- [47] Brunelli A, Xiume F, Al Refai M, et al. Air leaks after lobectomy increase the risk of empyema but not of cardiopulmonary complications: A case-matched analysis. Chest. 2006;**130**:1150-1156
- [48] Varela G, Jimenez MF, Novoa N, et al. Estimating hospital costs attributable to prolonged air leak in pulmonary lobectomy. European Journal of Cardio-Thoracic Surgery. 2005;27:329-333
- [49] Temes RT, Willms CD, Endara SA, et al. Fissureless lobectomy. The Annals of Thoracic Surgery. 1998;65:282-284
- [50] Dunning J, Prendergast B, Mackway-Jones K. Towards evidence-based medicine in cardiothoracic surgery: Best BETS. Interactive Cardiovascular and Thoracic Surgery. 2003;2:405-409
- [51] Li S, Lv W, Zhou K, et al. Does the fissureless technique decrease the incidence of prolonged air leak after pulmonary lobectomy? Interactive Cardiovascular and Thoracic Surgery. 2017;25:122-124
- [52] Nosotti M, Droghetti A, Luzzi L, et al. First Italian consensus conference on VATS lobectomy for NSCLC. Tumori. 2017;**103**:124-135
- [53] Bjerregaard LS, Jensen K, Petersen RH, et al. Early chest tube removal after video-assisted thoracic surgery lobectomy with serous fluid production up to 500 ml/day. European Journal of Cardio-Thoracic Surgery. 2014;45:241-246
- [54] Miyazaki T, Sakai T, Yamasaki N, et al. Chest tube insertion is one important factor leading to intercostal nerve impairment in thoracic surgery.

- General Thoracic and Cardiovascular Surgery. 2014;**62**:58-63
- [55] Zhang X, Lv D, Li M, et al. The single chest tube versus double chest tube application after pulmonary lobectomy: A systematic review and meta-analysis. Journal of Cancer Research & Therapy. 2016;**12**:309-316
- [56] Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: Systematic review and meta-analysis of controlled trials. British Medical Journal. 2001;323(7316):773-776
- [57] Watters JM, Kirkpatrick SM, Norris SB, Shamji FM, Wells GA. Immediate postoperative enteral feeding results in impaired respiratory mechanics and decreased mobility. Annals of Surgery. 1997;226(3):369-377. Discussion 377-380
- [58] Gan TJ, Meyer T, Apfel CC, et al. Consensus guidelines for managing postoperative nausea and vomiting. Anesthesia and Analgesia. 2003;97(1):62-71
- [59] Beattie AH, Prach AT, Baxter JP, Pennington CR. A randomised controlled trial evaluating the use of enteral nutritional supplements postoperatively in malnourished surgical patients. Gut. 2000;46(6):813-818
- [60] Smedley F, Bowling T, James M, et al. Randomized clinical trial of the effects of preoperative and postoperative oral nutritional supplements on clinical course and cost of care. The British Journal of Surgery. 2004;**91**(8):983-990
- [61] Fearon KC, Luff R. The nutritional management of surgical patients: Enhanced recovery after surgery. The Proceedings of the Nutrition Society. 2003;62(4):807-811