

Enhanced Recovery After Surgery (ERAS) Protocols and Perioperative Lung Protection

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ABSTRACT

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Aim of review: Patients are at risk for lung injury in the perioperative period. The enhanced recovery after surgery (ERAS) has been associated with a reduction in duration of hospital stay, readmissions, and reoperations, together with decreased mortality and morbidity, improved pain control, better cost containment, and improved patient satisfaction.

Method: we review the recent literatures on ERAS for prevention of perioperative pulmonary complications (PPCs).

Recent findings: Current ERAS protocols include >20 elements. Many elements in ERAS protocol can prevent perioperative lung injury, therefore reduce complications, enhance recovery, reduce length of stay, and lower the cost. Preadmission information, education and counseling, preoperative optimization, prophylaxis against thromboembolism, standard anesthetic protocol, laparoscopy and modifications of surgical access, perioperative fluid management, postoperative analgesia, and early mobilization impact directly on perioperative lung protection. Minimization of preoperative fasting, early resumption of oral intake, avoidance of bowel preparation can reduce the volume of intravenous fluid requirement, indirectly prevent lung injury.

Summary: ERAS elements can prevent lung injury, reduce complications, enhance recovery, reduce length of stay, and lower the cost.

Enhanced Recovery After Surgery (ERAS) is a standard, coordinated interdisciplinary perioperative surgical care program that incorporates evidence-based interventions to minimize surgical stress, improve physiological and functional recovery, reduce complications, and facilitate earlier discharge from the hospital (1). ERAS has been associated with a reduction in duration of hospital stay, readmissions, and reoperations, together with decreased mortality and morbidity, im-

proved pain control, better cost containment, and improved patient satisfaction (2-5). ERAS can achieve result on three dimensions of the Triple Aim: better health care, better patient experience, and lower cost. Therefore ERAS should be widely applied to optimize the quality and effectiveness of health care. Since the early 1990s, the ERAS has gradually evolved to become the standard of care in colorectal surgery (6). The benefits of ERAS have been also demonstrated in patients undergoing urological, gynecological, and orthopedic surgery.

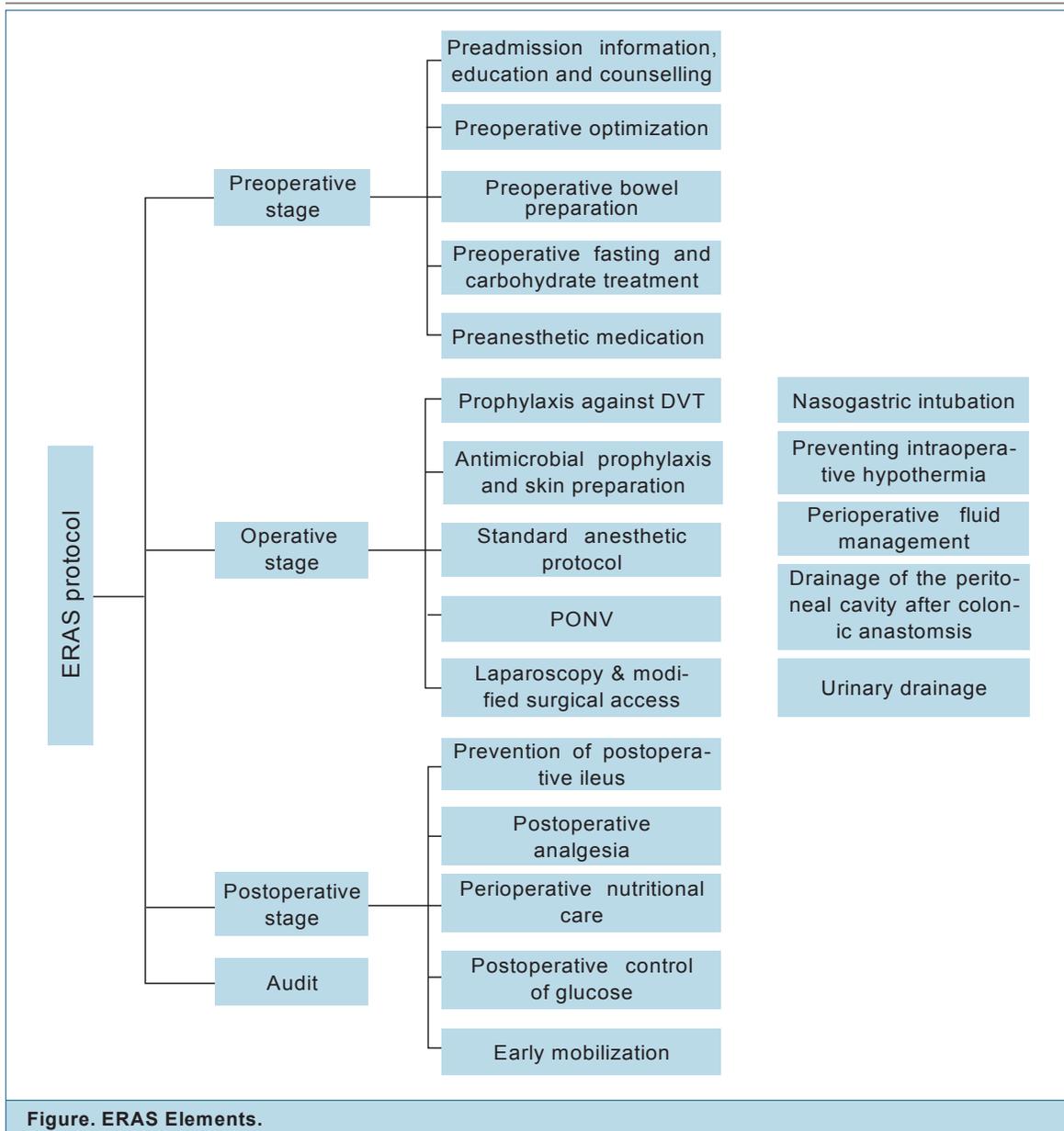


Figure. ERAS Elements.

cological, orthopedic, upper gastrointestinal, hepatobiliary, cardiac and vascular surgery.

Current ERAS protocols include >20 elements (Figure).

Patients are at risk for several types of lung injury in the perioperative period including atelectasis, pneumonia, pneumothorax, acute lung injury, and acute respiratory distress syndrome (7). Therefore, normal lungs need protection from multiple potentially injurious factors, including, but not limited to, cardiopulmonary bypass (CPB), sepsis, trauma, lung ischemia – reperfusion, and blood product transfusion (7). Injured

lungs need protection from ongoing injury.

Many elements in ERAS protocol can prevent perioperative lung injury, or influence the extent and course of perioperative lung injury. These elements are reviewed and discussed as follows.

Preadmission Information, Education and Counseling

Personal counseling, leaflets or multimedia information containing explanations of the procedure along with tasks that the patient should be encouraged to fulfill may improve perioperative feeding,

early postoperative mobilization, pain control, and respiratory physiotherapy; and hence reduce the prevalence of complications (8-10).

Patient education in lung maneuvers initiated preoperatively is more effective in reducing pulmonary complications versus education initiated postoperatively (11,12). Lung expansion maneuvers include incentive spirometry and chest physical therapy consisting of various combinations of the following: deep breathing exercises, postural drainage, percussion and vibration, cough, suctioning, and mobilization (13). Therefore, preoperative education can improve pulmonary function, then reduce postoperative pulmonary complications.

Preoperative Optimization

Patients with pre-existing organ dysfunction [ischemic heart disease, chronic obstructive pulmonary disease (COPD) and renal insufficiency] are more likely to develop an acute coronary syndrome, heart failure, bronchopneumonia or respiratory failure following major interventions (14). Exacerbation of bronchial inflammation with airway instrumentation, preoperative bacterial airway colonization, surgery-induced immunosuppression and increased muscular work of breathing may all promote the onset of lung injury [postoperative pulmonary complications (PPCs)] (15).

PPCs may be manifested as mild hypoventilation or as fulminate pulmonary edema due to adult respiratory distress syndrome. It is true that pulmonary diseases affect oxygen uptake, carbon dioxide removal, and cardiac output (16). A recent review discussed patient-related risk factors that may lead to risk for PPCs (17). Important patient-related risk factors include smoking, poor general health, age 70 years or older, and COPD (17).

Use of bronchodilators and glucocorticoid agents, and cessation of smoking are principal treatments to optimize COPD patients. Preoperative inhaled beta-2 adrenergic agonists (i.e., salbutamol) and anticholinergic agents (i.e., ipratropium) should be continued up to the day of surgery in all symptomatic asthmatics and in COPD patients with bronchial hyperreactivity (18). Short-term treatment with systemic or inhaled corticosteroids has been shown to "tune up" the

lung function and to decrease the incidence of wheezing following endotracheal intubation without increasing the risk of infection or wound dehiscence (18). Antibiotics should be prescribed only if there is evidence of pulmonary infection. Optimization of COPD patients reduced PPCs.

Smoking is another patient factor that has a negative influence on recovery. Current smokers have an increased risk for postoperative pulmonary and wound complications (19). Cigarette-smoke contains more than 1,000 components with wide-ranging effects on pulmonary, cardiovascular and immune functions, healing of wounds, homeostasis, drug metabolism and patient mental status, all of which may influence the postoperative outcome (20,21). Smoking status is a consistent univariate risk factor for adverse cardiac events and a variety of pulmonary adverse events such as bronchospasm, laryngospasm, cough and hypoxemia requiring intensive care unit (ICU) admission (15). Hence it is recommended that clinicians should advise complete cessation of smoking for at least 4 weeks before major elective surgery. Cessation of smoking can reduce incidence of lung injury.

Patients with well-controlled asthmatic disease present similar risk for PPCs as those patients without asthma, regardless of the type of anesthesia (22). The keys to an uncomplicated perioperative course are assiduous attention to detail in preoperative assessment, and maintenance of the anti-inflammatory and bronchodilatory regimens through the perioperative period. Potential trigger agents should be identified and avoided (23).

Sleep apnea may predispose to increased rate of PPCs. Preoperative recognition of obstructive sleep apnea (OSA), constant control of the airway, titration of analgesic and sedative drugs, and careful monitoring could avoid many unexpected complications after surgery (24).

Ventilation-associated pneumonia (VAP) is one of the most important risk factors for hospital mortality in cardiac surgery patients (25). Oronasopharyngeal decontamination with chlorhexidine has proven to be an effective method to reduce the VAP rate in these patients (26) and should be a routine practice (27).

Alcohol abusers have a two-to-threefold in-

crease in postoperative morbidity, the most frequent complications being bleeding, wound and cardiopulmonary complications (10). Experimental data indicate that ethanol causes depletion of pulmonary antioxidant glutathione which in turn leads to decreased surfactant production, impaired alveolar liquid clearance and alterations in epithelial cell permeability (28). One month of preoperative abstinence reduces postoperative morbidity by improving pulmonary and other organ function (29,30).

Low preoperative hemoglobin (Hb) levels are well known as major predicting factors in requiring perioperative blood transfusion in orthopedic surgery (31,32). Transfusion-related acute lung injury (TRALI) is defined clinically as the development of acute lung injury (ALI) during or within 6 hours after the transfusion of any blood product (33,34). TRALI has been the leading cause of transfusion-related mortality for many years (35).

A recent study (36) showed that preoperative iron deficiency (ID) was treated with iron and erythropoiesis-stimulating agent (ESA). Substituted anemic patients showed a distinctly higher preoperative and postoperative hemoglobin levels. Red blood cell (RBC) units requirement were reduced by 44% (36). Preoperative optimization of hemoglobin level can reduce transfusion requirement, and prevent acute lung injury.

Preoperative medical optimization (COPD, asthma, sleep apnea), cessation of smoking, abstinence alcohol, anemia correction can reduce PPCs.

Prophylaxis Against Thromboembolism

Deep Vein Thrombosis (DVT), with the associated risk of pulmonary embolism (PE), occurs in 45 to 75 % of patients who undergo orthopedic procedures on lower extremities (37). PE can result in serious lung injury.

The incidence of asymptomatic DVT in colorectal surgical patients without thromboprophylaxis is 30%, with fatal pulmonary embolus (PE) occurring in 1% of subjects (10). Patients with malignant disease, previous pelvic surgery, taking corticosteroids preoperatively, extensive comorbidity and hypercoagulable states are at increased risk (38, 10). Mechanical thromboprophylaxis with well-fitted compression stockings

significantly reduced the prevalence of DVT in-hospitalized patients (39).

The addition of intermittent pneumatic compression should also be considered, particularly in patients with malignant disease or who have undergone pelvic surgery (40, 10). There is extensive evidence supporting the use of pharmacological thromboprophylaxis with low-molecular-weight-heparin (LMWH) or unfractionated heparin (10). A recent study of 4195 colorectal patients demonstrated that pharmacological prophylaxis reduced the prevalence of symptomatic venous thromboembolism (VTE) from 1.8% to 1.1% and also reduced overall colorectal cancer mortality (41,10). Therefore, prophylaxis against thromboembolism can prevent pulmonary embolism.

Standard Anesthetic Protocol

The anesthesiologist is responsible for three key elements in affecting outcome after surgery: stress reactions to the surgery, fluid therapy, and analgesia. Recognition of the importance of these ERAS components has led to the description of a "trimodal approach" for optimizing outcomes in laparoscopic surgery for anesthesiologists (42,10).

Mechanical ventilation is frequently requirement in patients under general anesthesia for surgery. Ventilation can cause so called ventilator-associated lung injury via overdistension of alveoli in aerated lung tissue, or repetitive opening and closing of atelectatic lung parts, or both (7).

Two meta-analyses of observational studies and randomized controlled trials of intra-operative ventilation concluded that lung-protective ventilation with lower tidal volumes and/or higher levels of positive end expiratory pressure (PEEP) could prevent ventilator-associated lung injury and postoperative complications (43, 44). Two randomized controlled trials support this by demonstrating that the combined use of lower tidal volumes and higher levels of PEEP protects against PPCs (45, 46).

One randomized controlled trial (47) and a recent meta-analysis (43) support lower tidal volume to be beneficial also in patients without acute respiratory distress syndrome (ARDS). Several smaller studies and trials (45,46) and two re-

cent meta-analyses (43, 44) support that protective ventilation is also beneficial in short-term ventilation for patients during general surgery.

Laparoscopy and Modifications of Surgical Access

Laparoscopy in colonic resection improves recovery if judged by the prevalence of postoperative complications, pain and hospital stay (10).

During laparoscopy surgery, the use of the steep Trendelenburg position causes abdominal contents to push the diaphragm cephalad along with all of the mediastinal structures (48). This cephalad movement reduces the lung's functional reserve capacity (FRC), decreases pulmonary compliance, and predisposes to atelectasis (48).

This potential risk might be lowered by reducing tidal volume, increasing respiratory rate, and allowing permissive hypercarbia (49). In the pressure control- volume guaranteed ventilation (PC-VG) mode the ventilator functions as a pressure control ventilator, but tidal volume is also set (49). The advantage of this mode is the combination of the decelerating inspiratory flow pattern of the pressure-control mode and control of arterial CO₂ via guarantee of tidal volume and ultimately minute volume (50). Therefore PC-VG mode can improve pulmonary function and reduce incidence of atelectasis.

Perioperative Fluid Management

Administering too much fluid can lead to increased interstitial lung water, pulmonary edema and pneumonia, which can lead to pulmonary complications (lung injury)(51, 10).

A randomized controlled trial revealed that low intraoperative fluid regimens were associated with lower transfusion and fluid replacement requirements, and subsequently better clinical outcomes (52).

Avoidance of fluid excess is the first goal in perioperative fluid management. Goal directed fluid therapy can improve postoperative outcomes in moderate, and high risk patients (53). Minimization of preoperative fasting, early resumption of oral intake, avoidance of bowel preparation can reduce the volume of intravenous fluid requirement.

Postoperative Analgesia

Many meta-analyses have demonstrated improved outcomes with thoracic epidural analgesia (TEA) compared with opioid-based analgesia, including pain, complications, post-operative nausea and vomiting (PONV) and insulin resistance (54-58).

A randomized, controlled trial showed that thoracic epidural analgesia yielded significant improvement in pulmonary function, most likely due to a more profound postoperative analgesia (59). Higher forced expiratory volume in 1 s (FEV1.0) and peak expiratory flow rate (PEFR) were reported on postoperative days 2 and 3 in the thoracic epidural group than in the control group (59). Oxygen delivery and mixed venous oxygen saturation were higher in the epidural group (59). Another prospective, randomized, controlled trial demonstrated that high TEA decreases postoperative pain and atelectasis and improves pulmonary function in patients undergoing coronary artery bypass grafting (CABG) surgery (60).

Early Mobilization

Combining forced mobilization with nutritional support results in improved muscle strength but only during the early postoperative phase (61, 10). Early mobilization has been postulated to reduce chest complications and may counteract insulin resistance from immobilization (62, 10).

Early mobilization was shown to improve forced vital capacity, maximum voluntary ventilation, and arterial oxygenation (63). Mobilization results in increased tidal volumes which may assist the reversal of atelectasis leading to improve gas exchange (64). Another observation study showed that early mobilization resulted in significant increase in minute ventilation, and tidal volume (65). Early mobilization also significantly increases inspiratory flow rates and rib cage displacement (65). Therefore, early mobilization can improve pulmonary function, reduce postoperative pulmonary complications.

In conclusion, eight out of 21 ERAS elements play very important roles in preventing lung injury, reducing postoperative pulmonary compli-

cations. Three other elements can reduce the volume of intravenous fluid requirement; indirectly prevent pulmonary edema. These ERAS elements can prevent lung injury, reduce complications, enhance recovery, reduce length of stay,

and lower the cost.

Declaration of Interests

No potential conflict of interest relevant to this review was reported.

References

- Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg* 2002; 183: 630-41.
- Khoor CK, Vickery CJ, Forsyth N, Vinall NS, Eyre-Brook IA. A prospective randomized controlled trial of multimodal perioperative management protocol in patients undergoing elective colorectal resection for cancer. *Ann Surg* 2007; 245: 867-72.
- Kehlet H, Dahl JB. Anaesthesia, surgery, and challenges in postoperative recovery. *Lancet* 2003; 362: 1921-8.
- Wind J, Polle SW, Fung Kon Jin PH, von Meyenfeldt MF, Ubbink DT, Gouma DJ, et al. Laparoscopy and/or Fast Track Multimodal Management Versus Standard Care (LAFA) Study Group; Enhanced Recovery after Surgery (ERAS) Group. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg* 2006; 93: 800-9.
- Gouvas N, Tan E, Windsor A, Xynos E, Tekkis PP. Fasttrack vs standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis* 2009; 24: 1119-31.
- Kehlet H, Slim K. The future of fast-track surgery. *Br J Surg* 2012; 99: 1025-6.
- Kilpatrick B, Slinger P. Lung protective strategies in anesthesia. *Br J Anaesth* 2010; 105 (Suppl. 1): i108-16.
- Halaszynski TM, Juda R, Silverman DG. Optimizing postoperative outcomes with efficient preoperative assessment and management. *Crit Care Med* 2004; 32: S76-86.
- Disbrow EA, Bennett HL, Owings JT. Effect of preoperative suggestion on postoperative gastrointestinal motility. *West J Med* 1993; 158: 488-92.
- Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, et al. Enhanced Recovery After Surgery Society. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Clin Nutr* 2012; 31: 783-800.
- Fagevik Olsen M, Hahn I, Nordgren S, Lönnroth H, Lundholm K. Randomized controlled trial of prophylactic chest physiotherapy in major abdominal surgery. *Br J Surg* 1997; 84: 1535-8.
- Chumillas S, Ponce JL, Delgado F, Viciano V, Mateu M. Prevention of postoperative pulmonary complications through respiratory rehabilitation: a controlled clinical study. *Arch Phys Med Rehabil* 1998; 79: 5-9.
- Arozullah A, Conde M, Lawrence V. Preoperative evaluation for postoperative pulmonary complications. *Med Clin N Am* 2003; 87: 153-73.
- Kaafarani HM, Itani KM, Thornby J, Berger DH. Thirty-day and one-year predictors of death in non-cardiac major surgical procedures. *Am J Surg* 2004; 188: 495-9.
- Licker M, Schweizer A, Ellenberger C, Tschopp JM, Diaper J, Clergue F. Perioperative medical management of patients with COPD. *Int J Chron Obstruct Pulmon Dis* 2007; 2: 493-515.
- Rassias A, Procopio M. Stress response and optimization of perioperative care. *Dis Mon* 2003; 49: 517-54.
- Smetana GW. Preoperative pulmonary evaluation. *N Engl J Med* 1999; 340: 937-44.
- Silvanus MT, Groeben H, Peters J. Corticosteroids and inhaled salbutamol in patients with reversible airway obstruction markedly decrease the incidence of bronchospasm after tracheal intubation. *Anesthesiology* 2004; 100: 1052-7.
- Sorensen LI, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection: a randomized controlled trial. *Ann Surg* 2003; 238: 1-5.
- Moller AM, Villebro N, Pedersen T, Tønnesen H. Effect of preoperative smoking intervention on postoperative complications: a randomized clinical trial. *Lancet* 2002; 359: 114-7.
- Warner DO. Perioperative abstinence from cigarettes: physiologic and clinical consequences. *Anesthesiology* 2006; 104: 356-67.
- Tirumalasetty J, Grammer LC. Asthma, surgery, and general anesthesia: a review. *J Asthma* 2006; 43: 251-4.
- Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth* 2009; 103 (Suppl. 1): i57-i65.
- Jain SS, Dhand R. Perioperative treatment of patients with obstructive sleep apnea. *Curr Opin Pulm Med* 2004; 10: 482-8.
- Tamayo E, Alvarez FJ, Martínez-Rafael B, Bustamante J, Bermejo-Martin JF, Fierro I, et al. Ventilator-associated pneumonia is an important risk factor for mortality after major cardiac surgery. *J Crit Care* 2012; 27: 18-22.
- Segers P, Speekenbrink RG, Ubbink DT, van Ogtrop ML, de Mol BA. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: a randomized controlled trial. *J Am Med Assoc* 2006; 296: 2460-6.
- García-Delgado M, Navarrete-Sánchez I, Colmenero M. Preventing and managing perioperative pulmonary complications following cardiac surgery. *Curr Opin Anesthesiol* 2014; 27: 146-52.
- Burnham EL, Moss M, Harris F, Brown LA. Elevated plasma and lung endothelial selectin levels in patients with acute respiratory distress syndrome and a history of chronic alcohol abuse. *Crit Care Med* 2004; 32: 675-9.
- Tønnesen H, Kehlet H. Preoperative alcoholism and postoperative morbidity. *Br J Surg* 1999; 86: 869-74.
- Tønnesen H, Rosenberg J, Nielsen HJ, Rasmussen V, Hauge C, Pedersen IK, et al. Effect of preoperative abstinence on poor postoperative outcome in alcohol misusers: randomised controlled trial. *BMJ* 1999; 318: 1311-6.
- Munoz M, Garcia-Erce JA, Cuenca J, Bisbe E, Naveira E. AWGE (Spanish Anaemia Working Group). On the role of iron therapy for reducing allogenic blood transfusion in orthopaedic surgery. *Blood Transfus* 2012; 10: 8-22.
- Muñoz M, Breyman C, García-Erce JA, Gómez-Ramírez S, Comin J, Bisbe E. Efficacy and safety of intravenous iron therapy as an alternative/adjunct to allogenic blood transfusion. *Vox Sang* 2008; 94: 172-83.
- Toy P, Popovsky MA, Abraham E, Ambruso DR, Holness LG, Kopko PM, et al. Transfusion-related acute lung injury: Definition and review. *Crit Care Med* 2005; 33: 721-26.
- Kleinman S, Caulfield T, Chan P, Davenport R, McFarland J, McPhedran S, et al. Toward an understanding of transfusion-related acute lung injury: Statement of a consensus panel. *Transfus* 2004; 44: 1774-89.
- Fatalities reported to FDA following blood collection and transfusion: Annual summary for fiscal year 2012. Available at: <http://www.fda.gov/Biologics-BloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/ucm346639.htm>. Accessed June 7, 2014.
- Enko D, Wallner F, von-Goedecke A, Hirschmugl C, Auersperg V, Halwachs-Baumann G. The impact of an algorithm-guided management of preoperative anemia in perioperative hemoglobin level and transfusion of major orthopedic surgery patients. *Anemia* 2013; 2013: 641876.
- Consensus conference. Prevention of venous thrombosis and pulmonary embolism. *JAMA* 1986; 256: 744-49.
- Fleming FJ, Kim MJ, Salloum RM, Young KC, Monson JR. How much do we need to worry about venous thromboembolism after hospital discharge? A study of colorectal surgery patients using the National Surgical Quality Improvement Program database. *Dis Colon Rectum* 2010; 53: 1355-60.
- Amaragiri SV, Lees TA. Elastic compression stockings for prevention of deep vein thrombosis. *Cochrane Database Syst Rev* 2000; CD001484.
- Hill J, Treasure T. Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital: summary of the NICE guideline. *Heart* 2010; 96: 879-82.
- Kwon S, Meissner M, Symons R, Steele S, Thirlby R, Billingham R, et al. Surgical Care and Outcomes Assessment Program Collaborative. Perioperative pharmacologic prophylaxis for venous thromboembolism in colorectal surgery. *J Am Coll Surg* 2011; 213: 596-603.
- Levy BF, Scott MJ, Fawcett WJ, Day A, Rockall TA. Optimizing patient outcomes in laparoscopic surgery. *Colorectal Dis* 2011; 13(Suppl. 7): 8-11.
- Serpa Neto A, Cardoso SO, Manetta JA, Pereira VG, Espósito DC, Pasqualucci Mde O, et al. Association of use of lung protective ventilation with lower tidal volumes and clinical outcomes among patients without acute respiratory distress syndrome: a meta-analysis. *JAMA* 2012; 308: 1651-9.
- Hemmes SN, Serpa Neto A, Schultz MJ. Intraoperative ventilatory strategies to prevent postoperative pulmonary complications: a meta-analysis. *Curr Opin Anaesthesiol* 2013; 26: 126-33.
- Futier E, Constantin JM, Paugam-Burtz C, Pascal

- J, Eurin M, Neuschwander A, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N Engl J Med* 2013; 369: 428-37.
46. Severgnini P, Selmo G, Lanza C, Chiesa A, Frigerio A, Bacuzzi A, et al. Protective mechanical ventilation during general anesthesia for open abdominal surgery improves postoperative pulmonary function. *Anesthesiology* 2013; 118: 1307-21.
47. Determann RM, Royakkers A, Wolthuis EK, Vlaar AP, Choi G, Paulus F, et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: a preventive randomized controlled trial. *Crit Care* 2010; 14: R1.
48. Baltayan S. A brief review: anesthesia for robotic surgery. *J Robotic Surg* 2008; 2: 59-66.
49. Slutsky AS. ACCP consensus conference: mechanical ventilation. *Chest* 1993; 104: 1833-59.
50. Gainsburg DM. Anesthetic concerns for robotic-assisted laparoscopic radical prostatectomy. *Minerva Anesthesiol* 2012; 78: 596-604.
51. Varadhan KK, Lobo DN. A meta-analysis of randomized controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right. *Proc Nutr Soc* 2010; 69: 488-98.
52. Wuethrich PY, Studer UE, Thalman G, Burkhard F. Intraoperative continuous norepinephrine infusion combined with restrictive deferred hydration significantly reduces the need for blood transfusion in patients undergoing open radical cystectomy: results of a prospective randomized trial. *Eur Urol* 2013; pii: S0302-2838(13)00874-9.
53. Hamilton MA, Cecconi M, Rhodes A. A system review and meta analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. *Anesth Analg* 2011; 112: 1392-402.
54. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: a meta-analysis. *JAMA* 2003; 290: 2455-63.
55. Werawatganon T, Charuluxanun S. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. *Cochrane Database Syst Rev* 2005; CD004088.
56. Jorgensen H, Wetterslev J, Moïniche S, Dahl JB. Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. *Cochrane Database Syst Rev* 2000; CD001893.
57. Popping DM, Elia N, Marret E, Remy C, Tramèr MR. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. *Arch Surg* 2008; 143: 990-9.
58. Uchida I, Asoh T, Shirasaka C, Tsuji H. Effect of epidural analgesia on postoperative insulin resistance as evaluated by insulin clamp technique. *Br J Surg* 1988; 75: 557-62.
59. Stenseth R, Bjella L, Berg EM, Christensen O, Levang OW, Gisvold SE. Effects of thoracic epidural analgesia on pulmonary function after coronary artery bypass surgery. *Eur J Cardiothorac Surg* 1996; 10: 859-65.
60. Tenenbein PK, Debrouwere R, Maguire D, Duke PC, Muirhead B, Enns J, et al. Thoracic epidural analgesia improves pulmonary function in patients undergoing cardiac surgery. *Can J Anaesth* 2008; 55: 344-50.
61. Lassen K, Soop M, Nygren J, Cox PB, Hendry PO, Spies C, et al. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg* 2009; 144: 961-9.
62. Henriksen MG, Jensen MB, Hansen HV, Jespersen TW, Hessov I. Enforced mobilization, early oral feeding, and balanced analgesia improve convalescence after colorectal surgery. *Nutrition* 2002; 18: 147-52.
63. Scheidegger D, Bentz L, Piolino G, Pusterla C, Gigon JP. Influence of early mobilisation on pulmonary function in surgical patients. *Eur J Intensive Care Med* 1976; 2: 35-40.
64. The effects of positioning and mobilisation on oxygen transport. In Pryor JA and Prasad SA (Eds): *Physiotherapy for Respiratory and Cardiac Problems: Adults and Pediatrics* (3rd ed.) Edinburgh: Churchill Livingstone, pp. 121-36.
65. Zafiropoulos B, Alison JA and McCarren B. Physiological responses to the early mobilisation of the intubated, ventilated abdominal surgery patient. *Aust J Physiother* 2004; 50: 95-100.