3 Difficulties in Anesthesia for Urologic Laparoscopy

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Laparoscopic techniques have rapidly increased in popularity because of multiple advantages: smaller incisions compared with traditional open techniques, reduction in the postoperative pain, lower postoperative pulmonary complications, lower incidence of postoperative ileus, and early ambulation. All of these aspects carry substantial medico-economic advantages [1].

Urologic laparoscopy techniques are minimally invasive and have rapidly gained acceptance [2]. Laparoscopic procedures performed in urology include diagnostic procedures for evaluating undescended testis, orchiopexy, varicocelectomy, bladder suspension, pelvic lymphadenectomy, nephrectomy, partial nephrectomy, nephroureterectomy, adrenalectomy, prostatectomy, and cystectomy. The physiological consequences of laparoscopy are related to the combined effects of elevated intraperitoneal pressure following carbon dioxide (CO_2) insufflation to create a pneumoperitoneum, effects of systemic absorption of carbon dioxide, and alteration of patient position [3]. The lengthy operative duration, unsuspected visceral injury, and the difficulty in evaluating the amount of blood loss are additional factors that contribute in the complexity of anesthetic practice for laparoscopic surgery. Understanding of the pathophysiologic consequences of elevated intra-abdominal pressure (IAP) is crucial for the anesthesiologist in order to prevent or adequately respond to changes in the perioperative period [4].

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Pulmonary Changes in Laparoscopy

Pneumoperitoneum is created by insufflation of carbon dioxide (CO_2) – which is currently the routine gas used for laparoscopy – results in ventilatory and respiratory changes. Changes in pulmonary function during abdominal insufflation include reduction in lung volumes, decrease in pulmonary compliance, and increase in peak airway pressure [5].

Reduction in functional residual capacity (FRC) and lung compliance associated with supine positioning and induction of anesthesia would be aggravated by CO_2 insufflation and cephalad shift of the diaphragm during head-down tilt [6].

Hypoxemia because of reduction in FRC is uncommon in healthy patients during laparoscopy. However, reduction in FRC may result in significant hypoxemia because of ventilation-perfusion mismatch and intrapulmonary shunting in obese patients or in patients with preexisting pulmonary diseases such as those in the American Society of Anesthesiologists (ASA) classes III and IV (Table 3.1) [7].

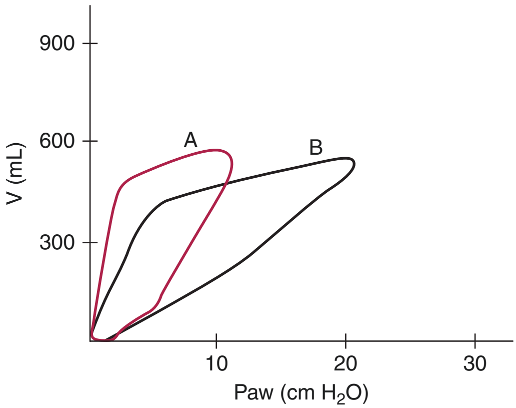
Carbon dioxide is the gas of choice for laparoscopic surgery. It does not support combustion as nitrous oxide (N_2O), and therefore can be used safely with diathermy. Compared with helium, the high blood solubility of CO_2 and its capability for pulmonary excretion reduces the risk of gas embolism. CO_2 insufflation into the peritoneal cavity increases arterial carbon dioxide tension ($PaCO_2$), which is anesthetically managed by increasing minute ventilation. Absorption of carbon dioxide depends on vascularity and the surface area, making absorption greater in pelvic extraperitoneal laparoscopic procedures than abdominal intraperitoneal ones. Mullet and colleagues examined end-tidal CO_2 ($EtCO_2$) and pulmonary CO_2 elimination during CO_2 insufflation for laparoscopic cholecystectomy and pelviscopy. CO_2 absorption reached a plateau within 10 min after initiation of intraperitoneal insufflation, but continued to increase slowly throughout extraperitoneal insufflation. The resulting rise in $PaCO_2$ is unpredictable, particularly in patients with severe pulmonary disease (Fig. 3.1) [8].

Cardiovascular Changes in Laparoscopy

The hemodynamic response to peritoneal insufflation depends on the interaction between many factors including the degree of IAP achieved [9], patient positioning, [10] neurohumoral response, [11] cardiorespiratory status of the patients and

Table 3.1 Pulmonary changes associated with laparoscopy (Adapted from Schellpfeffer and Crino [42])

Increased	Decreased	No significant change
Peak inspiratory pressure	Vital capacity	PaO_2 (in healthy patients)
Intrathoracic pressure	Functional residual capacity (FRC)	
Respiratory resistance	Respiratory compliance	
$PaCO_2$		



	TV	Ppeak	Pplat	C	PETCO2
A	522	12	9	56	31
B	525	21	19	27	39

Fig. 3.1 Change in total respiratory compliance during pneumoperitoneum for laparoscopic procedure. The intra-abdominal pressure was 14 mm Hg, and the head-up tilt was 10°. The airway pressure (Paw) versus volume (V) curves and data were obtained from the screen of a Datex Ultima monitoring device. Curves are generated before insufflation (**A**) and 30 min after insufflation (**B**). Values are given for tidal volume (TV, in mL); peak airway pressure (Ppeak, in cm H_2O); plateau airway pressure (Pplat, in cm H_2O); total respiratory compliance (**C**, in mL/cm H_2O); and end-tidal carbon dioxide tension ($PETCO_2$, in mmHg) (Adapted from Joris [4])

the intravascular volume status [6]. Principally, the physiologic responses include an elevation in systemic vascular resistance (SVR), mean arterial blood pressure (MAP), and myocardial filling pressures, accompanied by an initial fall in cardiac index (CI), with little change in heart rate. The rise in the IAP that occurs with pneumoperitoneum compresses vessels of the venous system, causing initially an increase in the venous return, which is then followed by a sustained decrease [12]. The decrease in cardiac output is a multifactorial phenomena, related to the decline in venous return [13] followed by a reduction in left ventricular end-diastolic volume when measured using transesophageal echocardiography (TEE) (Fig. 3.2) [14].

The compression of the arterial vasculature increases afterload and hence the SVR [15]. Using flow-directed pulmonary artery catheters in healthy patients, Joris and colleagues [16] observed a significant (35–40%) reduction in CI with induction of anesthesia, which was further decreased to 50% of baseline following peritoneal insufflation. Branche and colleagues observed a similar phasic hemodynamic response to pneumoperitoneum [12]. These hemodynamic changes would carry a detrimental effect on patients with depressed ejection fractions. Pulmonary edema, perioperative myocardial ischemia, and arrhythmias could manifest during lengthy laparoscopic surgery. Ishizaki et al. reported that IAP $\leq$ 12 mm Hg had minimal hemodynamic effects, and recommend this pressure value to avoid cardiovascular compromise during CO_2 insufflation (Table 3.2) [10].

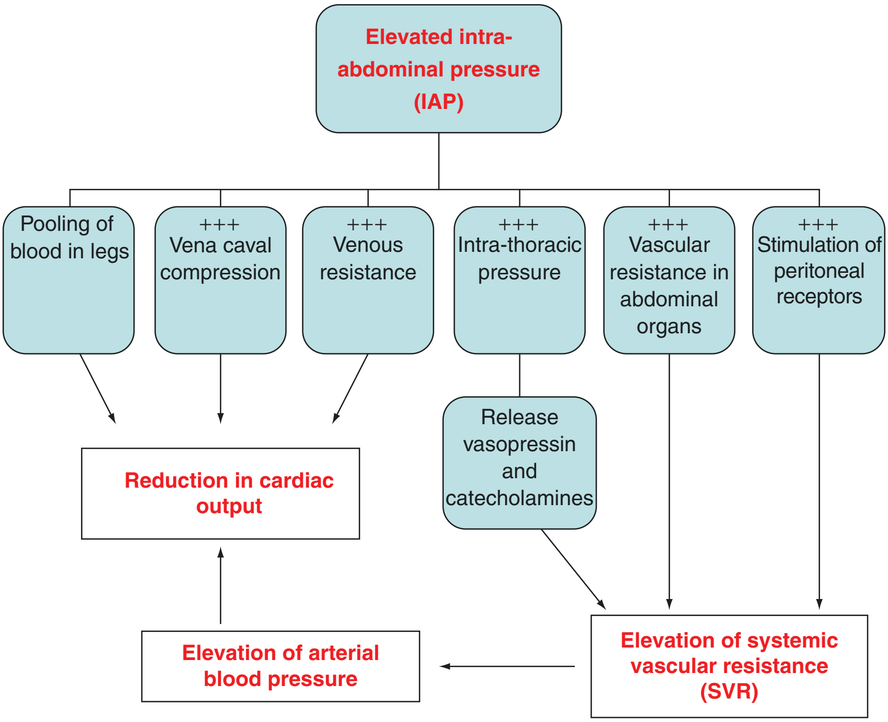


Fig. 3.2 Schematic representation of the different mechanisms leading to decreased cardiac output during pneumoperitoneum for laparoscopy (Adapted from Joris [4])

Table 3.2 Hemodynamic changes during laparoscopy (Adapted from Schellpfeffer and Crino [42])

Increased	Decreased	No change
SVR MAP CVP	CO (initially, then increases) Venous return (at IAP > 10)	Heart rate (may increase due to hypercapnia or catecholamine release)
PAOP		
Left ventricular wall stress		
Venous return (at IAP < 10)		

SVR systemic vascular resistance, *MAP* mean arterial pressure, *CVP* central venous pressure, *PAOP* pulmonary artery occlusion pressure, *IAP* intra-abdominal pressure

Neurohumoral Response

Vasopressin and catecholamines are mediators activating the sympathetic nervous system. Joris and colleagues observed a marked increase in plasma vasopressin immediately after peritoneal insufflation in healthy patients and the profile of vasopressin release paralleled the time course of changes in SVR [16].

Patient Positioning

The patient's positioning may have significant effects on the hemodynamic consequences of pneumoperitoneum. By using transesophageal echo (TEE), Cunningham and colleagues reported a significant reduction in left ventricular end-diastolic area on assumption of the reverse Trendelenburg position, indicating reduced venous return. Left ventricular ejection fraction was maintained throughout in otherwise healthy patients. However, such changes in left ventricular loading conditions might have adverse consequences in patients with cardiovascular disease [11].

Miscellaneous Changes

Renal System

The renal system is affected by the mechanical compressive effects of pneumoperitoneum that accounts for almost 50% reduction in glomerular filtration rate, renal plasma flow, and urine output during laparoscopic interventions [17]. Urine output increases significantly following pneumoperitoneum deflation. Oliguria has been associated with prolonged duration of pneumoperitoneum during laparoscopic nephrectomy [18]. A possible mechanism for intraoperative oliguria during laparoscopic surgery is an increase in stress hormone levels, such as antidiuretic hormone (ADH) [19]. Thus, oliguria during prolonged laparoscopic procedures does not reflect depletion in the intravascular volume.

Cerebral Circulation

Cerebral blood flow velocity and intracranial pressure both increase during CO_2 pneumoperitoneum, with implications for patients with intracranial mass lesions [20].

Splanchnic Circulation

The splanchnic circulation flow is reduced, but it is counterbalanced by the splanchnic vasodilating effects of carbon dioxide. The effects of pneumoperitoneum on the splanchnic circulation are not clinically significant [20].

Intra-operative Complications Throughout Laparoscopic Urologic Procedures

Various complications may possibly occur in laparoscopic procedures:

- *Pulmonary* complications include pneumothorax, pneumomediastinum, hypoxemia, hypercapnia, and pulmonary aspiration.

- *Cardiovascular* involvement could be in the form of dysrhythmias, hypotension, hypertension, venous gas embolus, and venous thrombosis.
- *Miscellaneous* complications include vascular injury, visceral perforation, oliguria, hypothermia, peripheral nerve injury, and surgical emphysema [21].

Anesthesia for Patients Undergoing Urologic Laparoscopic Surgery

The number of patients presenting for laparoscopic surgery is increasing, with a great percentage of them having cardiac, respiratory, or renal dysfunctions and other system affections. The changes that occur during abdominal insufflation prior to laparoscopic surgery and the hemodynamic consequences that take place turn these situations into great challenges anesthetically. The challenging aspect is that preoperative dysfunctions will still exist after the operation, needing further postoperative care; furthermore perioperative myocardial ischemia, infarction, and arrhythmias are the most common cause of morbidities following anesthesia and surgery for cardiac patients undergoing noncardiac surgery. In patients with severe pulmonary dysfunction, prolonged postoperative mechanical ventilation could delay the discharge of the patient from the operating room and may prolong the intensive care unit (ICU) stay. Elevated blood urea nitrogen (BUN), serum creatinine, history of renal dysfunction, left ventricular dysfunction, advanced age, jaundice, and diabetes mellitus are predictive of postoperative renal dysfunction.

Challenges in Cardiac Patients Undergoing Laparoscopic Surgery

The role of anesthetist in the preoperative period is divided into three stages: (1) the patient's risk assessment, (2) evaluation of functional capacity, and (3) determination of surgical risk; this is to help in patient selection for surgery and optimization of medical status.

Risk Assessment

In 2007, the American College of Cardiology and the American Heart Association (ACC/AHA) produced updated guidelines for perioperative evaluation for noncardiac surgery. These guidelines differentiate clinical predictors of increased perioperative cardiac risk into three categories (major, intermediate, and minor). For patients with major clinical risk predictors, their elective nonurgent surgical procedures, whether open or laparoscopic, should be postponed till they undergo preoperative evaluation and treatment, if needed (Table 3.3).

Table 3.3 Active cardiac conditions (major clinical risk predictors) for which patients should undergo evaluation and treatment before noncardiac surgery (class I, level of evidence: B) (Adapted from Fleisher et al. [22])

Medical disorder
Unstable coronary syndrome
Unstable severe angina (CSS class III or IV)
Recent M.I. (recent MI as more than 7 days and less than or equal to 30 days)
Decompensated heart failure (HF)
NYHA class IV worsening or new onset HF
Significant arrhythmias
Mobitz II
Third degree A-V block
Symptomatic ventricular arrhythmias
Supraventricular tachyarrhythmias (SVTs)
Atrial fibrillation (A.F.) with uncontrolled ventricular rate
Severe valvular lesions
Severe stenotic lesions

Functional Capacity

The patient's exercise tolerance is assessed by history and is expressed as metabolic equivalents (1 MET = 3.5 mL O_2/kg/min) on a scale defined by the Duke Activity Status Index that estimate patient's maximal oxygen consumption capacity. METs greater than 10 are classified as excellent, 7–10 METs are good, 4–7 METs moderate, and, lastly, METs less than 4 is a poor functional capacity. Activities that require more than 4 METs include moderate cycling, climbing two flights of stairs, and jogging.

Surgical Risk Factors

The type of surgery and the resultant degree of hemodynamic stress influences the risk to the patient. Some procedures previously counted as high risk are now categorized as intermediate risk, owing to improved perioperative management. The risks of not performing the surgery should be taken into account, and the experience and skill of the surgeon and anesthetist. Endoscopic and laparoscopic procedure ranges from low risk to intermediate risk surgery where reported cardiac risk generally less than 1% [22].

Preoperative Therapy

For patients undergoing laparoscopic urologic procedures, most cardiac medications should be continued preoperatively. There is evidence that continuation of angiotensin-converting enzyme (ACE) inhibitors may increase the incidence of hypotension and some physicians have recommended withholding them for 24 h preoperatively.

In goal-directed optimization, patients with high risk factors should be admitted preoperatively to a high-dependency or intensive care unit for invasive monitoring (including pulmonary artery catheter), manipulation of fluid, and inotropic therapy in order to achieve the optimal cardiac index, oxygen delivery, and consumption. Patients receiving antiplatelets present a challenge in management. Dual-antiplatelet therapy using aspirin and clopidogrel carries a 0.4–1.0% increased absolute risk of major bleeding compared with aspirin alone [23]. Increased blood loss in patients taking aspirin has been reported in noncardiac surgery, including general surgical, gynecologic, urologic operations, and in dermatologic surgery. Merritt and Bhatt concluded that monotherapy with aspirin need not be routinely discontinued for elective noncardiac surgery [24]. Burger et al. reviewed the surgical literature with regard to the risks of stopping low-dose aspirin versus the risks of bleeding and found that, in the majority of surgeries, low-dose aspirin may result in increased frequency of procedural bleeding (relative risk 1.5), but not an increase in the severity of bleeding complications or perioperative mortality due to bleeding complications [25].

Intraoperative Monitoring

Standard intraoperative monitoring is recommended for all patients undergoing minimal-access procedures. There may be hemodynamic consequences to the rise in the intra-abdominal pressure during laparoscopic interventions; invasive monitoring by arterial and pulmonary artery catheters may be useful in patients at high risk, especially if they have had a recent myocardial infarction with cardiac failure, provided that the anesthetist has the experience to insert them and interpret the data. The pulmonary artery catheter is most useful in monitoring volume status and cardiac performance, such as cardiac output/index, mixed venous oxygen saturation, systemic and pulmonary vascular resistances. Transesophageal echocardiography may be used to assess volume status and valvular disease and is the best way to detect ischemia early (segmental wall motion abnormalities), but requires expertise to interpret [26]. $EtCO_2$ is most commonly used as a noninvasive indicator of $PaCO_2$ in assessing the adequacy of ventilation during laparoscopic procedures. Temperature should be monitored throughout laparoscopic surgery.

Intraoperative Management

The oxygen supply/demand ratio must be maintained to avoid ischemia in coronary artery disease patients. During pneumoperitoneum, the rise of the systemic vascular resistance would impair oxygen supply/demand ratio. The maintenance of arterial blood pressure and reduction of heart rate should reduce the risk of ischemia [26].

Anesthetic Agents

In laparoscopic surgery, general anesthesia is the technique of choice, owing to the lengthy procedure and the diaphragmatic cephalad migration. The choice of anesthetic agents does not significantly affect the risks of perioperative complications, provided that hypertension, tachycardia, and hypotension are avoided. Anesthetic agent choice should be governed by the experience and skill of the anesthetist and their familiarity with the techniques and drugs. Etomidate has the fewest cardiovascular effects, but most people are more familiar with thiopentone or propofol, both of which should be titrated carefully to effect. Pretreatment with a dose of opioid (fentanyl and sufentanil, 1.5–5 and 0.25–1 μg/kg, respectively) reduces the required dose of induction agent and attenuates the hemodynamic response to intubation. Remifentanil is a new, potent, ultra-short-acting opioid, in a dose 0.05–2 μg/kg/min has great ability to produce hemodynamic stability and suppress the stress response. Concerns were previously raised that isoflurane might cause a "coronary steal" situation, but these have subsided. The concerns regarding the use of N_2O during laparoscopy, as it might lead to bowel distension and postoperative nausea and vomiting, has been a controversial issue. Clinically there is no significant difference in bowel distention and postoperative nausea and vomiting when N_2O-oxygen was compared to air-oxygen and no conclusive evidence suggesting N_2O cannot be used during laparoscopy [27]. The rise in the SVR that accompanies peritoneal insufflation leads to afterload elevation and increase in the left ventricular workload, adding more stress to the coronary circulation disrupting the oxygen supply/demand ratio. At this stage a vasodilator agent is of value in reducing the elevated SVR; inhalational anesthetic agents, especially isoflurane and sevoflurane, are the agents of choice, as the hemodynamic profile of sevoflurane resembles that of isoflurane [28]. In cardiac patients, sevoflurane had a cardiovascular outcome data equivalent to that of isoflurane [29]. When intravenous vasodilator agent is warranted, hydralazine is recommended for perioperative hypertension in a dose of 5–20 mg in a titrated intravenous (IV) boluses every 15–20 min until the desired blood pressure is reached. Fenoldopam mesylate is a selectively D_1-dopamine receptor agonist with moderate affinity for α(alpha)$_2$-adrenoceptors (infusion rates studied in clinical trials range from 0.01 to 1.6 μg/kg/min) reduces systolic and diastolic blood pressure in patients with malignant hypertension. It offers advantages in the acute resolution of severe hypertension compared to sodium nitroprusside, particularly in patient with preexisting renal impairment [30]. Esmolol is an ultra-short-acting selective β(beta)$_1$-antagonist that reduces heart rate and to a lesser extent blood pressure. Successfully used to prevent tachycardia and hypertension in response to perioperative stimuli such as intubation, surgical stimulation, and emergence from general anesthesia, esmolol is given by infusion in a dose 50–300 μg/kg/min. Labetalol α(alpha)- and β(beta)-blocker for treatment of hypertension can be used as a bolus; the initial dose is 0.1–0.25 mg/kg IV over 2 min, then repeated every 10 min to a total of 300 mg. When used as a continuous infusion, it is usually started at 2 mg/min and titrated to effect [31]. Owing to their systemic vasodilatory effects, intravenous isradipine and nicardipine have been shown to be effective in the treatment of postoperative hypertension in cardiac surgical patients, with minimal side effects [32].

Challenges in Patients with Pulmonary Disease Undergoing Laparoscopic Surgery

Six risk factors predispose patients to postoperative pulmonary complications:

- Preexisting pulmonary disease
- Thoracic or upper abdominal surgery
- Smoking
- Obesity
- Age (>60 years)
- Prolonged general anesthesia (>3 h)

Chronic obstructive pulmonary disease (COPD) is the most common pulmonary disorder encountered in anesthetic practice. During preoperative assessment using a pulmonary function test, patients with a forced expiratory volume in the first second (FEV_1) less than 50% of predicted (1.2–1.5 L) usually have dyspnea on exertion, whereas those with an FEV_1 less than 25% (< 1 L for men) typically have dyspnea with minimal activity. The latter patients often exhibit CO_2 retention and pulmonary hypertension. Many patients have concomitant cardiac disease and should also receive a careful cardiovascular evaluation. Laparoscopic procedures commonly lead to elevation of $PaCO_2$; mechanical ventilation should be adjusted through manipulation of tidal volume and respiratory rate to achieve normocapnia and avoid hypercarpia. The use of arterial blood gas sampling and capnogram are helpful monitoring devices is such situations [33].

Challenges in Patients with Perioperative Renal Dysfunction and Renal Failure

Preoperative preparation is of benefit for patients with renal disease undergoing urologic laparoscopic procedures. Hemodynamic instability is common, especially on a lengthy laparoscopic extensive surgery such as laparoscopic nephrectomy. From the standpoint of renal dysfunction, there may be a varying degree of decreased ability to concentrate urine, decreased ability to regulate extracellular fluid and sodium, impaired handling of acid loads, hyperkalemia, and impaired excretion of medications as in end stage renal disease (ESRD). Renal impairment is confounded by anemia, uremic platelet dysfunction, arrhythmias, pericardial effusions, myocardial dysfunction, chronic hypertension, neuropathies, malnutrition, and susceptibility to infection. If a contrast study is definitely indicated, the patient should be well hydrated and the contrast dose limited to the minimum needed, plus the addition of *N*-acetylcysteine, which acts as a nephroprotective agent to prevent contrast-induced nephropathy [34].

Preoperatively patients must be euvolemic, normotensive, normonatremic, and normokalemic. Patients should not be acidotic or severely anemic, or without significant platelet dysfunction as this would carry deleterious bleeding consequences in a laparoscopic urologic procedure. Dialysis usually corrects uremic platelet dysfunction and is best performed within the 24 h before surgery, though 1-deamino-8-d-arginine vasopressin (DDAVP) may also be administered to correct platelet dysfunction.

Patients with ESRD who have left ventricular dysfunction undergoing laparoscopic urologic procedures would need invasive monitoring in the form of invasive blood pressure, pulmonary artery catheter (PAC) to measure pulmonary capillary wedge pressure (PCWP) and left ventricular functions. A sterile technique should be strictly followed when inserting any catheters to reduce risk of infection. Hyperkalemia should be considered in patients with ESRD who develop ventricular arrhythmias or cardiac arrest. Rapid administration of calcium chloride temporizes the cardiac effects of hyperkalemia until further measures (administration of glucose and insulin, hyperventilation, administration of sodium bicarbonate and potassium-binding resins, and dialysis) can be taken to shift potassium intracellularly and to decrease total body potassium [35].

Contraindications for Laparoscopic Procedures

Relative contraindications for laparoscopy include increased intracranial pressure, patients with ventriculoperitoneal or peritoneojugular shunts, hypovolemia, congestive heart failure or severe cardiopulmonary disease, and coagulopathy. Morbid obesity, pregnancy, and prior abdominal surgery were previously considered contraindications to laparoscopic surgery; however, with improved surgical techniques and technology, most patients with these conditions can safely undergo laparoscopic surgery [36].

Postoperative Pain Management in Laparoscopic Urologic Surgeries

Pain is a form of stress and produces an elevation in stress hormones and catecholamines. Good pain management results in shorter hospital stay, reduced morbidities (especially in patients with less physiologic reserve, such as those in the intensive care unit), and better immune function, less catabolism and endocrinal derangements, and fewer thrombo-embolic complications. Recent studies have shown the value of preemptive analgesia in some surgical situations. The blockade of the pathways involved in pain transmission before surgical stimulation may decrease the patient's postoperative pain. Balanced (multimodal) analgesia is the term applied for using two or more analgesic agents that act by different mechanisms to achieve a superior analgesic effect without increasing adverse events compared with increased doses of single agents. For example, epidural opioids can be administered in combination with epidural local anaesthetics; intravenous opioids can be administered in combination with NSAIDs, which have a dose sparing effect for systemically administered opioids.

Pharmacological Options for Pain Management

Postoperative pain management should be stepwise and balanced as mentioned before. Laparoscopic surgery is a minimally invasive surgery, hence producing mild intensity pain. Postoperative pain can be controlled by simple noncomplicated techniques, which adds to the list of advantages to laparoscopic procedures.

Non-opioid analgesics: Paracetamol, NSAIDs, including COX-2 inhibitors are considered an effective choice for postoperative pain, especially in low-intensity pain procedures.

Weak opioid analgesics: Including tramadol alone or in combination with paracetamol.

Strong opioids: Are useful in moderate to severe postoperative pain control, including morphine, meperidine, and oxycodone.

Adjunctive analgesics: Ketamine, clonidine, gabapentine, pregabaline [37].

Patient-Controlled Analgesia

Advances in computer technology have allowed the development of patient-controlled analgesia (PCA). By pushing a button, patients are able to self-administer precise doses of opioids intravenously (or intraspinally) on an as needed (PRN) basis. The physician programs the infusion pump to deliver a specific dose, the minimum interval between doses (lockout period), and the maximum amount of opioid that can be administered in a given period, and a basal infusion can be simultaneously delivered (Table 3.4).

Studies show that PCA is a cost-effective technique that produces superior analgesia with very high patient satisfaction with reduced total drug consumption. Patients additionally like the control that is given to them; they are able to adjust the analgesia according to their pain severity, which varies with activity and the time of day. PCA therefore requires the understanding and cooperation of the patient; this limits its use in very young or confused patients. The routine use of a basal ("background") infusion is controversial.

Table 3.4 General guidelines for patient-controlled intravenous analgesia (PCIA) orders for the average adult (Adapted from Morgan et al. [37])

Opioid	Bolus dose	Lockout (min)	Infusion rate
Morphine	1–3 mg	10–20	0–1 mg/h
Meperidine (Demerol)	10–15 mg	5–15	0–20 mg/h
Fentanyl (Sublimaze)	15–25 μg	10–20	0–50 μg/h
Hydromorphone (Dilaudid)	0.1–0.3 mg	10–20	0–0.5 mg/h

Central Neuraxial Blockade

Epidural administration of local anesthetic–opioid mixtures is an excellent technique for managing postoperative pain following abdominal, pelvic, open, and laparoscopic surgical procedures. Patients often have better preservation of pulmonary function and are able to ambulate early, with the added benefit of early physical therapy and lower risk for postoperative venous thrombosis. In lengthy extensive laparoscopic urologic surgery such as cystectomy, nephrectomy, and prostatectomy, the preoperative insertion of epidural catheter provides titratable analgesia with extendable duration and level. The tip of the catheter should be placed as close as possible to the surgical dermatomes: T6–T10 for major intra-abdominal surgery, and L2–L4 for lower limb surgery. Diluted local anesthetic solutions combined with opioids shows synergistic effect. Bupivacaine 0.0625–0.125% (or ropivacaine 0.1–0.2%) combined with fentanyl 2–5 μg/mL provides excellent postoperative analgesia with lower drug requirements and fewer side effects. Patient controlled epidural analgesia (PCEA) is a term describing the patient-controlled administration of analgesic medications in the epidural space, to cover periods of increased discomfort.

Dosage of PCEA: A mixture of Bupivacaine 0.0625–0.125% (or ropivacaine 0.1–0.2%) combined with fentanyl 2–5 μg/mL

- Background infusion of 4–6 mL/h
- Controlled infusion bolus dose: 2 mL (2–4 mL) lumbar or thoracic
- Minimum lockout interval 10 min (10–30 min)

Epidurally administered, preservative-free morphine allows lumbar injection to provide proper analgesia in both thoracic and upper abdominal procedures, which is attributed to the rostral spread phenomena of hydrophilic opioids. Epidural clonidine in a dose of 3–5 μg/kg is an effective analgesic, but it can be associated with hypotension and bradycardia [37].

Ketamine

Ketamine is a noncompetitive, use-dependent antagonist of *N*-methyl-D-aspartate (NMDA) receptors; it reduces the postoperative pain in opioid tolerant patients, and postoperative nausea and vomiting. At a serum level of 0.1 μg/mL or higher, pain threshold is elevated [38]. Ketamine reduces opiate requirements by 30% postoperatively [39]. An intravenous dose of 0.1–0.2 mg/kg followed by a continuous infusion of 5–7 μg/kg/min is considered a sub-anesthetic dose effective in reducing morphine requirements in the first 24 h after surgery [40]. Central nervous system (CNS) excitatory effects included sensory illusions, sympathoneuronal release of norepinephrine, elevated blood pressure, tachycardia, elevated intracranial pressure (ICP), blurred vision, and altered hearing [41].

References

1. Morgan GE Jr, Mikhail MS, Murray MJ. Laparoscopic surgery. In: Foltin J, Lebowitz H, Boyle PJ, eds. *Clinical Anesthesiology*. 4th ed. New York: McGraw-Hill; 2006:522-523.
2. Clayman RV, Kavoussi LR. Endosurgical techniques for the diagnosis and treatment of noncalculus disease of the ureter and kidney. In: Walsh P, Retik A, Stamey T, et al., eds. *Campbell's Urology*. 6th ed. Philadelphia, PA: W.B. Saunders; 1992:2231.
3. Cunningham AJ, Nolan C. Anesthesia for minimally invasive procedures. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:2204-2220.
4. Joris JL. Anesthesia for laparoscopy. In: Fleisher LA, Johns RA, Savarese JJ, Wiener-Kronish JP, Young WL, eds. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2005:2285-2300.
5. Walder AD, Aitkenhead AR. Role of vasopressin in the haemodynamic response to laparoscopic cholecystectomy. *Br J Anaesth*. 1997;78:264-266.
6. Safran D, Sgambati S, Orlando R. Laparoscopy in high-risk cardiac patients. *Surg Gynecol Obstet*. 1993;176(6):548-554.
7. Holzman M, Sharp K, Richards W. Hypercarbia during carbon dioxide gas insufflation for therapeutic laparoscopy: a note of caution. *Surg Laparosc Endosc*. 1992;2(1):11-14.
8. Bardoczky GI, Engelman E, Levarlet M, Simon P. Ventilatory effects of pneumoperitoneum monitored with continuous spirometry. *Anaesthesia*. 1993;48(4):309-311.
9. Eldar S, Sabo E, Nash E, Abrahamson J, Matter I. Laparoscopic cholecystectomy for acute cholecystitis. *Prospective trial World J Surg*. 1997;21(5):540-545.
10. Ishizaki Y, Bandai Y, Shimomura K, Abe H, Ohtomo Y, Idezuki Y. Safe intraabdominal pressure of pneumoperitoneum during laparoscopic surgery. *Surgery*. 1993;114(3):549-554.
11. Cunningham AJ, Turner J, Rosenbaum S, Rafferty T. Transoesophageal assessment of haemodynamic function during laparoscopic cholecystectomy. *Br J Anaesth*. 1993;70(6):621-625.
12. Branche PE, Duperret SL, Sagnard PE, Boulez JL, Petit PL, Viale JP. Left ventricular loading modifications induced by pneumoperitoneum: a time course echocardiographic study. *Anesth Analg*. 1998;86(3):482-487.
13. Richardson JD, Trinkle JK. Hemodynamic and respiratory alterations with increased intra-abdominal pressure. *J Surg Res*. 1976;20(5):401-404.
14. Dorsay DA, Green FL, Baysinger CL. Hemodynamic changes during laparoscopic cholecystectomy monitored with transesophageal echocardiography. *Surg Endosc*. 1995;9(2):128-133.
15. Wahba RW, Béïque F, Kleiman SJ. Cardiopulmonary function and laparoscopic cholecystectomy. *Can J Anaesth*. 1995;42(1):51-63.
16. Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholecystectomy. *Anesth Analg*. 1993;76(5):1067-1071.
17. Puri GD, Singh H. Ventilatory effects of laparoscopy under general anaesthesia. *Br J Anaesth*. 1992;68(2):211-213.
18. Kerbl K, Clayman RV, McDougall EM, Kavoussi LR. Laparoscopic nephrectomy: the Washington University experience. *Br J Urol*. 1994;73(3):231-236.
19. Ortega AE, Peters JH, Incarbone R, et al. A prospective randomized comparison of the metabolic and stress hormonal responses of laparoscopic and open cholecystectomy. *J Am Coll Surg*. 1996;183(3):249-256.
20. Wolf JS Jr, Carrier S, Stoller ML. Gas embolism: helium is more lethal than carbon dioxide. *J Laparoendosc Surg*. 1994;4(3):173-177.
21. Barash PG, Cullen B, Stoelting RK. Anesthesia for minimally invasive procedures. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1066-1068.
22. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *Circulation*. 2007;116(17):e418-e499.
23. Eikelboom JW, Hirsch J. Bleeding and management of bleeding. *Eur Heart J*. 2006;8:G38-G45.
24. Merritt JC, Bhatt DL. The efficacy and safety of perioperative antiplatelet therapy. *J Thromb Thrombolysis*. 2004;17(1):21-27.

25. Burger W, Chemnitius JM, Kneissl GD, Rücker G. Low-dose aspirin for secondary cardiovascular prevention: cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation – review and meta-analysis. *J Intern Med*. 2005;257(5):399-414.
26. Poldermans D, Bax JJ, Boersma E, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery: The Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). *Eur J Anaesthesiol*. 2010;27:92-137.
27. Taylor E, Feinstein R, White PF, Soper N. Anesthesia for laparoscopic cholecystectomy: is nitrous oxide contraindicated? *Anesthesiology*. 1992;76:541-543.
28. Graf BM, Vicenzi MN, Bosnjak ZJ, Stowe DF. The comparative effects of equimolar sevoflurane and isoflurane in isolated hearts. *Anesth Analg*. 1995;81(5):1026-1032.
29. Searle N, Martineau RJ, Conzen P, et al. Comparison of sevoflurane/fentanyl and isoflurane/fentanyl during elective coronary artery bypass surgery. *Can J Anaesth*. 1996;43(9):890-899.
30. Kien ND, Moore PG, Jaffe RS. Cardiovascular function during induced hypotension by fenoldopam or sodium nitroprusside in anesthetized dogs. *Anesth Analg*. 1992;74(1):72-78.
31. Morgan GE Jr, Mikhail MS, Murray MJ. Adrenergic agonists and antagonists. In: Foltin J, Lebowitz H, Boyle PJ, eds. *Clinical Anesthesiology*. 4th ed. New York: McGraw-Hill; 2006:212-223.
32. Kaplan J. Clinical considerations for the use of intravenous nicardipine in the treatment of postoperative hypertension. *Am Heart J*. 1990;119(2):443-446.
33. Morgan GE Jr, Mikhail MS, Murray MJ. Anesthesia for patients with respiratory disease. In: Foltin J, Lebowitz H, Boyle PJ, eds. *Clinical Anesthesiology*. 4th ed. New York: McGraw-Hill; 2006:511-524.
34. Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med*. 2000;343(3):180-184.
35. Playford HR, Sladen RN. What is the best means of preventing perioperative renal dysfunction. In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. Philadelphia, PA: Saunders; 2004:181-190.
36. Curet MJ. Special problems in laparoscopic surgery. Previous abdominal surgery, obesity, and pregnancy. *Surg Clin North Am*. 2000;80(4):1093-1110.
37. Morgan GE Jr, Mikhail MS, Murray MJ. Postoperative pain. In: Foltin J, Lebowitz H, Boyle PJ, eds. *Clinical Anesthesiology*. 4th ed. New York: McGraw-Hill; 2006:346-374.
38. Nimmo W, Clements J, Ketamine. In: Prys-Robert CH, ed. *Pharmacokinetics of Anesthesia*. Boston, MA: Blackwell; 1984:235.
39. Guignard B, Coste C, Costes H, et al. Supplementing desflurane-remifentanil anesthesia with small-dose ketamine reduces perioperative opioid analgesic requirements. *Anesth Analg*. 2002;95:103-108.
40. Bell RF, Dahl JB, Moore RA, Kalso EA. Perioperative ketamine for acute postoperative pain. *Cochrane Database Syst Rev* 2006;(1):CD004603. doi:10.1002/14651858.CD004603.pub2.
41. Grabow T. Special techniques in pain management. In: Wallace MS, Staats PS, eds. *Pain Medicine and Management: Just the Facts*. New York: McGraw-Hill; 2005:255-363.
42. Schellpfeffer RS, Crino DG. Anesthesia for minimally invasive surgery. In: Duke J, ed. *Anesthesia Secrets*. 3rd ed. Philadelphia, PA: Mosby Elsevier; 2006:494-499.