ROBOTIC LAPAROSCOPIC RADICAL CYSTECTOMY
INHALATIONAL VERSUS TOTAL INTRAVENOUS
ANESTHESIA: A PILOT STUDY

MOHAMED M. ATALLAH* AND MAHMOUD M. OTHMAN**

Summary

Background: Robotic assistance may refine laparoscopic radical cystectomy. Steep Trendelenburg tilt (TT) and pneumoperitoneum (PP) are challenging anesthesia maneuvers. In view of those maneuvers, would inhalational anesthesia or total intravenous anesthesia (TIVA) be the more appropriate anesthetic management for this kind of surgery? This issue is under consideration in this clinical trial.

Methods: 15 patients scheduled for robotic laparoscopic radical cystectomy (RLRC) were randomly allocated into two groups to be anesthetized by either isoflurane anesthesia (ISO n = 8) or ketamine-midazolam-fentanyl total intravenous anesthesia (TIVA n = 7). The hemo-respiratory dynamics, oxygenation and biochemical variables were monitored taking into consideration the system organ function as primary outcomes, and operative conditions and recovery profile as secondary outcomes.

Results: The PP and TT increased the mean arterial and airway pressures and decreased lung compliance, and were associated with respiratory acidemia, while changes in heart rate remained within normal range. The duration of PP was shorter in TIVA patients but mean arterial pressure was higher than ISO group. ISO was associated with increased plasma concentrations of prothrombin, fibrinogen and aspartate aminotransferase.

Conclusions: Though the number of patients is small in this study (n = 15), it nevertheless brings to light the advantages of TIVA during the robotic laparoscopic radical cystectomy (RLRC), by shortening the duration of PP without an increase in prothrombin and fibrinogen concentrations. A larger number of clinical trial are needed to further clarify this issue.

Keywords: anesthesia, inhalation, isoflurane; anesthesia, intravenous, ketamine, midazolam, fentanyl; surgery, radical cystectomy.

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On the morning of surgery, patients were premedicated with 7.5 mg midazolam and 300 μg clonidine given orally two and one hour respectively, before transfer to the operative suite. These doses were reduced by 50% to patients ≥60 years old. Patients were allocated by computer generated random numbers to receive either isoflurane anesthesia (ISO n = 8) or ketamine-midazolam-fentanyl total intravenous anesthesia (TIVA n = 7).

Age-adjusted single dose upper lumbar extradural analgesia was performed in the sitting position in both groups before induction using bupivacaine 0.5% mixed with morphine. Arterial and central venous cannulation were secured.

The ISO group was induced with 1 μg/kg⁻¹ fentanyl, 0.1 mg/kg⁻¹ midazolam and sleeping dose of thiopentone and maintained by isoflurane at end-tidal concentrations adjusted to help minimizing changes in HR and arterial BP. The TIVA group was induced with fentanyl 1 μg/kg⁻¹, midazolam 100 μg/kg⁻¹ and ketamine 2 mg/kg⁻¹ and maintained by separate infusion of the three drugs (Table 1). Before creation of PP, ketamine dose was reduced by 25%, and midazolam and fentanyl doses were reduced by 50%. These were normalized following the creation of PP. Pipecuronium was used to facilitate tracheal intubation in both groups to maintain adequate surgical muscle relaxation and was replaced by vecuronium when repeated serum creatinine level was >1.5 mg/dL⁻¹. The lungs were ventilated with oxygen enriched air (FIO₂ = 0.35) and ventilation was manipulated to minimize excessive increases in end-tidal CO₂ concentrations.

After induction, the patients were placed in an extended lithotomy position with a 45º TT. Sufficient padding was applied around the shoulder and pressure points and the arms were tucked in.

Following RLRC, the resected bladder specimen was removed though a mini-subumbilical laparotomy incision. A neobladder was then fashioned from the terminal ileum. The ureters were re-implanted to the neobladder. The latter was relocated into the pelvis. The wound was then closed. Finally, the neobladder was then anastomosed to the urethral stump via laparoscopic approach.
from the basal values, Wilcoxon-matched pairs signed ranks test was used. P-value <0.05 was considered statistically significant.

**Results**

This prospective randomized clinical trial was performed with 15 patients who underwent RLRC and open surgery neobladder creation. Patient demographic data and durations of operative interventions are displayed in Table 2.

The median durations of PP and RLRC were shorter during TIVA by 32% and 36% respectively.

HR changes did not display any significant difference between both groups (Fig. 1). PP and TT increased MBP in both groups, with more higher values in TIVA patients. Following PP deflation, MBP returned to within normal range in both groups (Fig. 1). Stepping up anesthetic doses prevented excessive increases in BP in five and two patients in ISO and TIVA respectively. Nitroglycerine infusion (0.5-10 μg/kg\(^{-1}\) min\(^{-1}\)) was needed in the rest of the patients. Two patients in TIVA needed additional sodium nitroprusside (0.5-2 μg/kg\(^{-1}\) min\(^{-1}\)).

<table>
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<tr>
<th>valeurs</th>
<th>Isoflurane</th>
<th>TIVA</th>
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<tbody>
<tr>
<td>Demographic data</td>
<td></td>
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</tr>
<tr>
<td>Age (y)</td>
<td>58 ± 7 (47-66)</td>
<td>56 ± 5 (50-63)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>71 ± 10 (54-80)</td>
<td>80 ± 14 (58-95)</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>167 ± 24 (105-181)</td>
<td>170 ± 4 (165-175)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>6/2</td>
<td>7/0</td>
</tr>
<tr>
<td>Duration of intervention (h)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trendelenburg tilt</td>
<td>4.4 ± 0.7 (2.8-5.2)</td>
<td>3.8 ± 0.5 (3.0-4.5)</td>
</tr>
<tr>
<td>Pneumoperitoneum</td>
<td>4.0 ± 0.8 (2.4-4.8)</td>
<td>2.7 ± 0.8 (1.9-4.0)*</td>
</tr>
<tr>
<td>Robotic cystectomy</td>
<td>3.6 ± 0.8 (2.1-4.5)</td>
<td>2.3 ± 0.8 (1.5-3.8)*</td>
</tr>
<tr>
<td>Open surgery</td>
<td>3.5 ± 1.0 (1.8-4.5)</td>
<td>4.0 ± 0.6 (3.0-4.5)</td>
</tr>
<tr>
<td>Total anesthetic duration</td>
<td>8.8 ± 0.8 (8.0-10.0)</td>
<td>8.0 ± 0.5 (7.3-8.8)*</td>
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</table>

* Significant intergroup difference (P <0.05)

Preoperative condition: 3 hypertensives in TIVA group, 1 diabetes mellitus in TIVA group, 6 C-virus hepatitis, 4 in isoflurane group and 2 in TIVA group.
Mean airway pressure was increased, and lung compliance was decreased following PP creation and TT. However, following deflation, TIVA patients showed higher lung compliance values (Fig. 1).

PP produced respiratory acidemia which gradually resolved postoperatively (Fig. 2). Plasma albumin decreased in all patients during the 7 days study period, while prothrombin and fibrinogen increased only following ISO (Fig. 3). Serum aspartate aminotransferase (AST) increased on the third postoperative day following ISO, but serum bilirubin and alanine aminotransferase were within normal values (Fig. 4). Serum sodium, potassium, and creatinine were within normal ranges during the study period.

Growth hormone and cortisol increased in all patients during operative intervention (Table 3). By the end of surgery, growth hormone returned to normal values in TIVA patients, but remained high following ISO. Cortisol levels remained high in both groups. Intraoperative blood loss was minimal in 13 patients. One patient in each group needed two units of blood.

Recovery was delayed for 60 min in one patient following ISO and for 45-150 min in 5 patients following TIVA. The latter needed pressure support ventilation. Surgical emphysema affecting the medial aspects of the thighs and lower abdomen was observed in 4 and 3 patients following ISO and TIVA respectively. This extended to the face in one patient in each group. Periorbital edema was observed. Patients did not complain of pain from the surgical incisions and postoperative analgesics were needed for patients with extended surgical emphysema. There was no incidence of pneumothorax, pneumomediastinum, pulmonary edema or any other system organ affection during the postoperative period.

**Discussion**

RLRC was performed with limited number of patients anesthetized by either ISO or TIVA. The creation of PP and TT increased mean arterial and airway pressures and decreased lung compliance, and was associated with respiratory acidemia, while changes in HR remained within normal range. The duration of PP was shorter in TIVA patients but MBP was higher than ISO group. ISO was associated with increased plasma concentrations of prothrombin, fibrinogen and AST. Recovery was more delayed following TIVA.

Peritoneal insufflation with carbon dioxide and modification in patient position with 45º TT were applied to provide adequate visual and operative conditions. PP induces widespread changes in cardiovascular system. Experimental data demonstrated a decrease in cardiac output and MBP. Elevated preload and afterload and decreased cardiac output and ejection fraction were reported in clinical studies. Head

<table>
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<tr>
<th>Table 3</th>
<th>Serum growth hormone and cortisol following isoflurane anesthesia (ISO, n = 8) and ketamine-midazolam-fentanyl total intravenous anaesthesia (TIVA, n = 7) Values are median ± SD (range)</th>
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<tr>
<td></td>
<td>Growth hormone (mg/ml(^1))</td>
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<tr>
<td>ISO</td>
<td>TIVA</td>
</tr>
<tr>
<td>Basal</td>
<td>0.1 ± 0.3 (0.1-1.0)</td>
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<tr>
<td>End of:</td>
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<tr>
<td>Robotic cystectomy</td>
<td>8.0 ± 7.1(^*) (0.8-21.0)</td>
</tr>
<tr>
<td>Open surgery</td>
<td>1.2 ± 1.3(^*) (0.4-3.6)</td>
</tr>
<tr>
<td>Postoperative (2h)</td>
<td>0.5 ± 0.9 (0.1-2.2)</td>
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\(^*\) Significant difference (P<0.05) from basal value.
Fig. 1
Perioperative median values of mean blood pressure (MBP, mmHg), heart rate (HR, bpm), compliance (Comp., ml/cm H$_2$O), and mean air way pressure (Paw, CmH$_2$O) during isoflurane anesthesia (ISO) and TIVA.

Fig. 2
Perioperative median values of pH, arterial carbon dioxide tension (PaCO$_2$, mmHg), and serum bicarbonate (HCO$_3$-, mmol/L) during isoflurane anesthesia (ISO) and TIVA.

Fig. 3
Postoperative median serum concentrations of prothrombin, Fibrinogen, and albumin after isoflurane anesthesia (ISO) and TIVA.

Fig. 4
Postoperative median serum concentrations of bilirubin, Aspartate aminotransferase (AST), and Alanine aminotransferase (ALT) after isoflurane anesthesia (ISO) and TIVA.
down position either increased these changes or had no more effect, but none of these clinical studies had adopted this steep TT.

Respiratory acidosis and decreased lung mechanics together with transient reduction of the pulmonary shunt were demonstrated after PP in clinical settings.

The cerebral blood flow velocity increased and the cerebral vascular resistance decreased, while maintaining the vasoreactivity unaffected.

During pneumoperitoneum, the blood flow to the abdominal organs is variably affected. Hollow viscous organs are less disturbed than solid organs. Experimental data demonstrated a decrease in total hepatic blood flow, mostly through a decrease in portal vein blood flow, with contradictory reports on hepatic artery buffer response. Cirrhotic liver showed a similar decrease in total hepatic blood flow. Clinical studies reported a decrease in hepatic blood flow and increase in hepatic enzymes, being more following cholecystectomy than after colectomy, suggesting impairment of hepatic function specially in elderly patients. PP and hypovolemia markedly alter renal blood flow. In our study, abdominal organ function was not affected apart from mild increase in AST following ISO.

Most experimental studies investigating the effects of PP on “organ function” have been conducted mostly on small animals without organ disease, while the majority of the clinical reports were young adults and mostly with healthy system organs. With RLRC, the denominator is different. Patients are likely to be elderly adult or older, sicker and with significant underlying disease demonstrating lower threshold for physiologic decompensation. Perioperative risk factors include preexisting system organ dysfunction, hypovolemia and possibly any other iatrogenic intervention. Risk-adjusted strategy should be adopted. Preexisting disease have to be optimally managed. Perioperative optimization of vital functions and minimization of postoperative pain avoid further deterioration of preexisting diseases. PP pressure and the degree of head down have to be the least compatible with good surgical conditions. Adequate anesthesia and prompt replacement of fluid and blood loss minimize the surgical stress response.

Inhalational anesthetics have a cardioprotective effect. This has been reported in vitro studies and clinically in coronary surgery patients. In this pilot study, ISO anesthesia was followed by increased plasma concentrations of prothrombin, fibrinogen and AST suggesting incomplete stress and hepatic protection. The clinical advantages of TIVA during radical cystectomy has been recommended. It provided better operating conditions and a more acceptable recovery profile. The absence of significant changes in plasma concentrations of prothrombin, fibrinogen and AST following TIVA suggests a satisfactory stress and hepatic protection.

Which of the two techniques is more favourable for RLRC is still speculative. The results of this limited-number clinical trial do not equate to that coming from reasonably powered study. Although the duration of PP was shorter in TIVA patients and the measured plasma concentrations of the coagulation factors were within normal range, yet a definite advantage for TIVA would be claimed following a clinical trial with adequate number of patients.

In conclusion, the study is limited in number and the patients were carefully chosen from cancer bladder population to be of appropriate age and body weight with minimal organ system dysfunction. While this study refers to an advantage of TIVA during RLRC, yet a large number clinical trial are needed to confirm these advantages.

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References


