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ORIGINAL ARTICLE

Lower Incidence of Prolonged Extubation in Propofol-Based Total Intravenous Anesthesia Compared with Desflurane Anesthesia in Laparoscopic Cholecystectomy: A Retrospective Study

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Background: Reducing anesthesia-controlled time (ACT) such as extubation time may improve operating room (OR) efficiency result from different anesthetic techniques. However, the information about the difference in ACT between desflurane (DES) anesthesia and propofol-based total intravenous anesthesia (TIVA) techniques for laparoscopic cholecystectomy (LC) under general anesthesia (GA) is not available in the literature. **Methods:** This retrospective study uses our hospital database to analyze the ACT of elective LC after either DES anesthesia or TIVA via target-controlled infusion (TCI) with propofol from January 2010 to December 2011. The various time intervals including waiting for anesthesia time, anesthesia time, surgical time, extubation time, exit from OR after extubation, total OR time, postanesthetic care unit (PACU) stay time, and percentage of prolonged extubation (≥15 min) were compared between the two anesthetic techniques. **Results:** We included data from 622 patients undergoing LC, with 286 patients receiving TIVA and 336 patients receiving DES anesthesia. The extubation time was faster (7.8 ± 0.4 vs. 10.9 ± 0.4 min; $P < 0.001$) and the exit from OR after extubation was faster (6.8 ± 0.5 vs. 9.3 ± 0.5 min, $P < 0.001$) in the TIVA group than that in the DES group. Besides, the incidence of prolonged extubation was lower (4.5% vs. 10.1%, $P = 0.014$) in the TIVA group than that in the DES group. The prolonged extubation was associated with age, sex, anesthetic technique, and anesthesia time. **Conclusions:** In our hospital, propofol-based TIVA by TCI provided faster extubation time, faster exit from OR after extubation, and lower prolonged extubation rate compared with DES anesthesia in LC. Besides, older age, female, DES anesthesia, and lengthy anesthesia time were factors affecting prolonged extubation.

Key words: Propofol, desflurane, target-controlled infusion, anesthesia-controlled time, laparoscopic cholecystectomy

INTRODUCTION

Anesthesia-controlled time (ACT) is one of the most important factors that regulate operating room efficiency.[1] Extubation time is of special interest because it could be affected by different anesthetic agents or techniques.[2-4] Evidence showed that prolonged extubation decreases operating room (OR) efficiency and slows workflow due to the surgeon and OR staff staying idly waiting for extubation.[5] Accordingly, an appropriate anesthetic technique to provide faster extubation time from GA is essential for anesthesiologists in order to improve the efficiency of OR. Agoliati *et al*.[6] defined that prolonged extubation was equal or longer than 15 min. Dexter and Epstein[7] recommended that recording extubation time and monitoring the incidence of prolonged extubation are very important especially at facilities that have at least 8 h of cases and turnovers. Previous studies also implied that longer-than-average anesthesia times strongly influence the academic anesthesiology departments by increasing the staffing costs and decreasing hourly productivity.[8,9] The ACT between propofol-based total intravenous anesthesia (TIVA) and desflurane (DES) anesthesia in different surgeries was investigated; nevertheless, the results are controversial.[4,10-18]

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Stevanovic *et al*.[19] reported that sevoflurane anesthesia provided faster extubation time compared with propofol-based TIVA in LC. However, Grundmann *et al*.[20] showed no statistically significant difference in extubation time between propofol-based TIVA by syringe pump infusion and DES anesthesia in LC. Moreover, different propofol delivery techniques such as target-controlled infusion (TCI) and syringe pump infusion were used in these studies which may lead to different results. The present study aimed to determine whether the use of TIVA with TCI system is more effective than DES anesthesia in reducing ACT in patients undergoing elective LC.

METHODS

This retrospective study was reviewed and approved by the Ethics Committee of Tri-Service General Hospital (approval number: 100-05-168). All the electronic databases and medical records from January 2010 to December 2011 were retrieved from Tri-Service General Hospital. We enrolled 622 patients (American Society of Anesthesiologists [ASA] Class I–III) who received laparoscopic cholecystectomy (LC) or cholelithotomy under propofol-based TIVA or DES anesthesia. Patients with age <18 years, emergent surgeries, unplanned explorative laparotomy, combined inhalation anesthesia with propofol or other inhaled anesthetics besides DES, or incomplete data were excluded from the study. For the purposes of this study, the following times (minutes) were calculated: waiting for anesthesia time, arrival in the OR to anesthesia was introduced; surgical time, incision to surgical completion and application of dressings; anesthesia time, start of anesthesia to extubation; extubation time, from the end of skin closure until extubation; total OR stay time, arrival in the OR to departure from the OR; postanesthesia care unit (PACU) stay time, arrival in the PACU to discharge from the PACU to the general ward; and ACT, arrival in the OR to discharge from the OR. In addition, other parameters included demographic data and ASA physical status. All the times, determination was recorded by OR staff and anesthetic nurses using electronic database.

There was no premedication before the induction of anesthesia. Regular monitoring, such as noninvasive blood pressure, arterial line, electrocardiography (lead II), pulse oximetry, and end-tidal carbon dioxide ($EtCO_2$), was applied in each patient. Anesthesia was induced with fentanyl and propofol in all patients. The patients were then intubated and maintained with propofol or DES and the analgesic fentanyl. In our common practice, we take patients to the PACU after extubation and did not extubate in the PACU.

In the TIVA group, anesthesia was induced using IV fentanyl (2 μg/kg) and 2% lidocaine (1.5 mg/kg). Continuous infusion of propofol (Fresofol 1%) was delivered subsequently using Schneider's kinetic model of TCI (Fresenius Orchestra Primea; Fresenius Kabi AG, Bad Homburg, Germany) with the effect-site concentration (Ce) of 4.0 μg/mL. Rocuronium (0.6 mg/kg, IV) was administered when patients lost consciousness, followed by tracheal intubation. Anesthesia was maintained using TCI with propofol Ce 3–4 μg/mL and an oxygen flow of 0.3 L/min. Repetitive IV bolus injections of rocuronium (or cisatracurium) and fentanyl were prescribed as required throughout the procedure.[12-18,21-24]

In the DES group, the patients were induced with IV fentanyl (2 μg/kg), 2% lidocaine (1.5 mg/kg), and propofol (1.5–2 mg/kg). When patients lost consciousness, 0.6 mg/kg of rocuronium IV was administered, followed by endotracheal intubation. Anesthesia was maintained using 8%–12% DES (inhaled concentration) in an oxygen flow of 300 mL/min under a closed system without nitrous oxide. Repetitive IV bolus injections of rocuronium (or cisatracurium) and fentanyl were prescribed as required throughout the procedure.[12-18,21-23]

Maintenance of the Ce for the TCI with propofol and DES concentration was adjusted at the range of 0.2 μg/mL and 0.5%, respectively, according to the hemodynamics. If two increments or decrements were unsuccessful, the range of Ce for TCI propofol and DES was increased to 0.5 μg/mL and 2%, respectively. The $EtCO_2$ was maintained at 35–45 mmHg by adjusting the respiration rate and maximum airway pressure. Once neuromuscular function returns, rocuronium (5–10 mg, IV) or cisatracurium (2 mg, IV) was administered as required.[12-18,21-23]

Ce of propofol or DES concentration was tapered to 2.0 μg/mL or 5%, respectively, at the beginning of skin closure. At the last five stitches of suture, propofol or DES was discontinued, but the oxygen flow was kept at 300 mL/min. At the end of the skin closure, the lungs were ventilated with 100% oxygen at a fresh gas flow of 6 L/min. Reversal of neuromuscular function was achieved by administrating neostigmine (0.03–0.04 mg/kg, IV) with glycopyrrolate (0.006–0.008 mg/kg, IV) once spontaneous breathing returned to prevent residual paralysis. When the patient regained consciousness by name with spontaneous and smooth respiration, the endotracheal tube was extubated, and the patient was sent to the postanesthesia care unit (PACU) for further care.

Data were presented as the mean and standard deviation, number of patients, or percentage. Demographic and perioperative variables were compared using Student's *t*-tests. Categorical variables were compared using Chi-square test. Multivariable logistic regression analyses were performed to assess the association between variables contributed to

prolonged extubation. The level of statistical significance was determined as $P < 0.05$. Statistical analyses were done using SPSS software v. 21.0. (IBM SPSS Statistics, IBM Corporation, Chicago, IL, USA).

RESULTS

Of the 747 patients scheduling for LC enrolled to the retrospective study, 125 patients were excluded from the analysis. Of those excluded, 45 patients received combined inhalation anesthesia with propofol, 56 patients received sevoflurane anesthesia, and 24 patients had incomplete data [Figure 1].

Table 1 shows the patient characteristics, and there was no significant difference in patient demographics. Extubation time was significantly less in the TIVA group than in the DES group (7.8 ± 0.4 vs. 10.9 ± 0.4 min; $P < 0.001$). Exit from OR after extubation was significantly faster in the TIVA group than in the DES group (6.8 ± 0.5 vs. 9.3 ± 0.5 min, $P < 0.001$). The incidence of prolonged extubation was significantly lower in the TIVA group than in the DES group (4.5% vs. 10.1%; $P = 0.01$). There was no difference among waiting for anesthesia time, surgical time, anesthesia time, total OR stay time, and PACU stay time between the two groups [Table 2].

The result of multiple linear regressions comparing extubation time among several variants is shown in Table 3. Older age, female, DES anesthesia, and longer anesthesia time were factors that contribute to extubation time. The patients with shorter surgical time or TIVA had faster extubation time.

DISCUSSION

The major findings in this retrospective study show that propofol-based TIVA with TCI system significantly reduced the extubation time, exit from OR after extubation, and the incidence of prolonged extubation relative to the DES anesthesia in patients undergoing elective LC. In addition, we found that the factors of prolonged extubation were age, sex, anesthetic technique, and anesthesia time.

The results of previous studies comparing the extubation time of DES with propofol-based TIVA have been controversial.[4,10-18] Some studies comparing DES with TIVA found no significant difference in terms of extubation.[20,25,26] Our previous studies found that the use of TIVA with TCI system is more effective than DES anesthesia in reducing ACT[13-18,27] because the awakening time can be predicted by TCI system.[28] In another study, Dolk *et al*.[29] reported that there was shorter extubation time for DES anesthesia compared with propofol delivered by TCI in knee surgery. The difference would have been caused by using nitrous oxide as an adjuvant

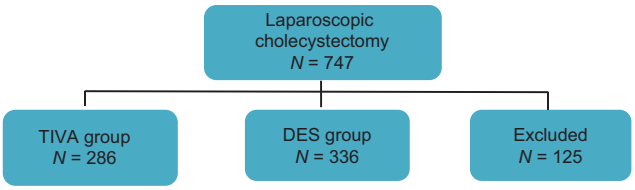

Figure 1: The flow diagram. TIVA: Total intravenous anesthesia, DESL: Desflurane anesthesia

Table 1: Patient characteristics

	Group DES (*n*=336)	Group TIVA (*n*=286)	*P*
ASA I/II/III	68/196/72	50/191/45	
Sex (male/female)	146/190	129/157	0.78
Age (years old)	57.1±15.5	56.5±16.5	0.63
Height (cm)	164.0±8.4	164.0±8.3	0.96
Weight (kg)	67.4±12.2	67.0±12.0	0.66

Data shown as mean±SD or *n*. ASA: American Society of Anesthesiologists, SD: Standard deviation

Table 2: Operating room time measurement between the desflurane and total intravenous anesthesia groups

	Group DES (*n*=336)	Group TIVA (*n*=286)	*P*
Waiting for anesthesia time (min)	9.6±0.5	10.0±0.5	0.22
Surgical time (min)	96.6±4.6	94.7±4.2	0.92
Anesthesia time (min)	127.4±5.4	124.1±4.4	0.98
Extubation time (min)	10.9±0.4	7.8±0.4	<0.001
Exit from OR after extubation (min)	9.3±0.5	6.8±0.5	<0.001
Total OR stay time (min)	146.7±5.4	140.6±4.4	0.27
PACU stay time (min)	44.4±1.6	43.6±1.4	0.92
Prolonged extubation (≥15 min), *n* (%)	34 (10.1)	13 (4.5)	0.01

Data shown as mean±SD or *n* (%). OR: Operating room;
PACU: Postanesthetic care unit, SD: Standard deviation, DES: Desflurane, TIVA: Total intravenous anesthesia

Table 3: Comparisons of extubation time among variants by multiple linear regression

	β	SE	*P*
Age	−0.0245	0.00944	0.010
Sex	0.617	0.303	0.042
Height	0.0127	0.0224	0.570
Weight	−0.0240	0.0155	0.121
Group	−3.113	0.299	<0.001
Surgical time	−0.0287	0.00931	0.002
Anesthesia time	0.0337	0.00824	<0.001
Waiting anesthesia time	−0.0489	0.0358	0.172

β: Difference between each variant using extubation time as dependent variable, Group: DES=0, TIVA=1. *P*<0.05 was considered statistically significant. SE: Standard error, DES: Desflurane, TIVA: Total intravenous anesthesia

to anesthetics, which reduce the requirement of DES during the maintenance period and facilitate early emergence. Moreover, the present result was consistent with our previous studies reporting that GA using propofol-based TIVA could achieve faster extubation than that of using DES anesthesia in different surgeries.[13-18,27]

In this study, we showed that the mean time to departure from OR to PACU was 6.8 in the TIVA group and 9.3 min in the DES group, which might be due to the more stable hemodynamics in TIVA group compared with DES anesthesia during emergence from anesthesia and paramedical factors.[16,30] We found that the total OR stay time was reduced to 6.1 min in the TIVA compared with DES anesthesia. McIntosh *et al*.[31] revealed that each 5-min reduction in intraoperative time should be treated as reducing costs, and the reduction is approximately 20% larger than the cost per 5 min of OR time. Thus, the reduction in ACT, as reported in our study, might be reasonably treated as having economic benefit.[32]

The overall incidence of prolonged extubation was 15% of all cases.[3,33] In this study, the incidence of prolonged extubation in the DES group was higher than that in the TIVA group (10.1% vs. 4.5%; $P < 0.001$), which might be due to the predicted awakening time by TCI system.[28] Previous researches showed the risk factors of prolonged extubation including prone position, prolonged surgical time, significant blood loss, and larger volume of crystalloid and colloid infusion.[34,35] Moreover, our previous studies reported that older age and lengthy anesthesia time contributed to prolonged extubation in upper and lower abdominal surgeries.[12,13] In the present study, according to previous reports, older age was a risk factor for prolonged extubation, which might be due to the decrease in renal and hepatic reserve and reduced anesthetics metabolism in elderly patients. Besides, the weight of the human brain decreases with age, and the brain's gray matter decreases more than the white matter, which may be more sensitive to anesthetics.[36] Elderly patients have increased body fat with a greater volume of distribution, which might prolong the clinical effect of anesthetics. In this study, we found that female gender was a risk factor for prolonged extubation, Consistently, Yu *et al*. and Tercan *et al*.[37,38] demonstrated that females awaken slower than males from GA. In contrast, a pharmacokinetic analysis demonstrated that women have a larger volume of redistribution and higher clearance in propofol.[39] Moreover, females consume more propofol and have faster emergence than males, which has been supported by clinical studies.[2,13,40,41] Moreover, we found no sex difference in prolonged extubation in our previous study.[12] The results are still controversial, which might be due to different surgeries, different anesthesia time, and age-related hormonal influences on the effect of hypnotic drugs. Hence, further investigation is necessary.

Consistently, we also found that lengthy anesthesia time contributed to prolonged extubation. During lengthy surgical procedures, higher-than-necessary propofol infusion dose may accumulate and be redistributed from the fatty tissue and muscle to the plasma, which leads to delayed recovery,[27,42] even under TCI.[12,13] Redistribution of DES in the fatty tissue and muscle in lengthy anesthesia may result in delayed emergence.[27] Therefore, keeping anesthetic depth within the recommended range may improve anesthetic delivery and postoperative recovery from relatively deep anesthesia.[43] Accordingly, Bispectral Index (BIS) use is strongly recommended in patients with older age or prolonged surgical time (>210 min).[12,13]

There were some limitations in this study. First, our study is a retrospective study. Considering the comparability and standardization of the study groups, a retrospective study may contribute to bias. Although the choice of anesthetic management was not randomly allocated but rather by the availability of the TCI devices, the results showed no difference in the characteristics of the patients between the two groups. This study, performed under clinical conditions, reflects more precisely the clinically relevant benefits. Second, we did not compare the effect of body temperature on extubation time because hypothermia may delay awakening.[44] However, in our cases, we used the patient warming system including fluid warming kit and convective air warming system to keep their core temperature ≥35°C perioperatively. Third, we did not use BIS in our common practice. Our incidence of prolonged extubation was 7.6%, which was lower than the overall 11.5% reported by a previous study in 1–2 h surgery.[7] However, use of BIS in older age has been still suggested in LC. Finally, in this study, the amounts of opioid and nondepolarizing muscle relaxants between the propofol-based TIVA and DES anesthesia were similar with our previous intraperitoneal procedures.[12,13] Thus, the detail statistical analysis was not performed in the presented study.

CONCLUSIONS

Our results showed that propofol-based TIVA by TCI reduced the extubation time, exit from OR after extubation, and the incidence of prolonged extubation compared with DES anesthesia in elective LC. In addition, older age, female, DES anesthesia, and lengthy anesthesia time were factors affecting prolonged extubation.

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Conflicts of interest

There are no conflicts of interest.

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