Sevoflurane is an effective adjuvant to propofol-based total intravenous anesthesia for attenuating cough reflex in nonintubated video-assisted thoracoscopic surgery

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Abstract

Background: Nonintubated video-assisted thoracic surgery (VATS) has been widely developed during the recent years. Cough reflex is an inevitably encountered problem while approaching lung lesions, and it may induce major bleeding. Sevoflurane anesthesia may attenuate cough reflex by inhibiting the pulmonary irritant receptors. However, the incidence of postoperative nausea and vomiting (PONV) in inhalational anesthesia is higher than in the propofol-based total intravenous anesthesia (TIVA). We investigated the effect of sevoflurane combination with propofol-based TIVA on cough reflex and PONV in nonintubated VATS.

Methods: Ninety patients undergoing nonintubated VATS with laryngeal mask airway (LMA) and spontaneous breathing were randomly assigned for TIVA or propofol/sevoflurane anesthesia. In the TIVA group (n = 45), anesthesia was induced and maintained with propofol and fentanyl; in the propofol/sevoflurane (P/S) group (n = 45), 1% sevoflurane anesthesia was added to propofol and fentanyl anesthesia. The primary outcome measurements were cough reflex. In addition, the incidence of PONV and extubation time were investigated.

Results: Patients with cough reflex were significantly fewer in the P/S group than in the TIVA group (10/45 vs 34/45; P < .001). The cough severity (35/5/5/0 vs 11/17/17/0; P < .001) and limb movement (40/5/0/0 vs 28/17/0/0; P < .001) were lower in the P/S group than in the TIVA group. Besides, incremental fentanyl bolus for cough reflex was 5 (0 [0–1]) in the P/S group and 17 (0 [0–3]) in the TIVA group (P < .05). There was no one conversion to general anesthesia, postoperative hemorrhage, aspiration pneumonia, or PONV in the 2 groups. Besides, there was no significant difference in extubation time (TIVA: 5.04 ± 2.88 vs P/S: 4.44 ± 2.98 minutes; P = .33).

Conclusion: Sevoflurane attenuated cough reflex under propofol-based TIVA and did not increase the incidence of PONV and extubation time in nonintubated VATS.

Abbreviations: ASA = American Society of Anesthesiology, BIS = bispectral index, BMI = body mass index, Ce = effect-site concentration, ETCO2 = end-tidal carbon dioxide, HR = heart rate, IRB = institutional review board, IV = intravenous, LAST = local anesthetic systemic toxicity, LMA = laryngeal mask airway, LOC = loss of consciousness, MABP = mean arterial blood pressure, NSAIDs = nonsteroidal anti-inflammatory drugs, OLV = one lung ventilation, P/S = propofol/sevoflurane, PONV = postoperative nausea and vomiting, RR = respiratory rate, SD = standard deviation, TCI = target controlled infusion, TEA = thoracic epidural anesthesia, TIVA = total intravenous anesthesia, VATS = video-assisted thoracic surgery.

Keywords: anesthesia, cough reflex, nonintubated video-assisted thoracic surgery, postoperative nausea and vomiting, propofol, sevoflurane

1. Introduction

The use of nonintubated video-assisted thoracic surgery (VATS) has increased as an important minimally invasive procedure recently, it is feasible and safe in a variety of thoracic procedures, including pulmonary resection, empyema, and excision of pleural and mediastinal tumors.[1] Cough reflex and unexpected lung movement can be encountered during pulmonary manipulation. Using intrathoracic vagal nerve blockade, the cough reflex and unexpected lung movement could be effectively abolished.[2] However, vagal nerve blockade may induce local anesthetic systemic toxicity (LAST), nerve injuries[3], or aspiration.[4,5] Sevoflurane anesthesia can inhibit the pulmonary irritant receptors and attenuate cough reflex.[6] Unfortunately, sevoflurane anesthesia was associated with a higher incidence of postoperative nausea and vomiting (PONV) compared with propofol-based total intravenous anesthesia (TIVA) in patients undergoing ambulatory surgery.[7] PONV can lead to postoperative complications especially in a patient that cannot tolerate elevated heart rate (HR) or blood pressure, or intrathoracic...
pressure. A previous study reported that TIVA should be well-controlled to balance smooth spontaneous respiration and anesthetic depth. Moreover, TIVA with local anesthesia or thoracic epidural anesthesia (TEA) is technically feasible and safe in spontaneous breathing VATS. Therefore, propofol-based TIVA is suit for nonintubated VATS with spontaneous breathing. In the literature, a rigorous comparison of the effects of propofol-based TIVA and propofol/sevoflurane anesthesia on cough reflex and PONV has not yet been performed in VATS. Therefore, in this study, we prospectively compared the effects of propofol-based TIVA and propofol/sevoflurane anesthesia on cough reflex and PONV in patients who underwent nonintubated VATS.

2. Methods

This study was approved by the Ethics Committee (TSGHIRB No: 2-105-05-010) of Tri-Service General Hospital, Taipei, Taiwan (Chairman, Professor Yu Mu Hsien) on March 14, 2016. All patients provided written informed consent before being enrolled. All methods were performed in accordance with the relevant guidelines and regulations by our IRB.

From April 2016 to November 2017, 90 patients in our medical center scheduled to undergo nonintubated VATS by one surgeon under spontaneous breathing anesthesia with laryngeal mask airway (LMA) were enrolled in this study. Patients were randomized 1:1 into the propofol-based TIVA (TIVA group) or propofol/sevoflurane anesthesia groups (P/S group) by using a table of random, computer-generated digits in sealed and numbered envelopes by an anesthesiologist. Participants and the surgeon were blinded after assignment to interventions. Exclusion criteria were as follows: age < 20 years or older than 80 years, American Society of Anesthesiologists (ASA) physical status of more than III, body mass index (BMI) > 30 kg/m², possible pregnancy, emergent surgeries, uremia, liver disease, and the presence of congenital or acquired oropharyngeal malformations.

All patients fasted overnight before surgery, and there was no premedication before induction of anesthesia. Regular monitoring, such as noninvasive arterial blood pressure, electrocardiography (lead II), pulse oximetry, end-tidal carbon dioxide pressure (EtCO₂) were applied in each patient. Intra-arterial blood pressure monitoring was used to patients undergoing lobectomy. Anesthesia was induced with fentanyl and propofol in all patients, then maintained with propofol or propofol/sevoflurane after LMA insertion. All procedures were performed with the patient in the lateral decubitus position. Besides, all patients were monitored under bispectral index (BIS).

Before surgery, all patients were given thoracic epidural catheters inserted into the T7-8 or T8-9 space with the test dose (2 mL) of 2% lidocaine only for postoperative patient-controlled epidural analgesia use. In the TIVA group, anesthesia was induced using intravenous (IV) fentanyl 100 μg (50 μg for thoracic epidural catheter insertion and 50 μg for LMA insertion). Continuous infusion of propofol was delivered subsequently using Schneider’s kinetic model of target-controlled infusion (TCI; Fresenius Kabi AG, Bad Homburg, Germany) with the effect-site concentration (Ce) of 4.0 mg/ml. Anesthesia was maintained using TCI with propofol infusion and spontaneous breathing with 1.0 L/min flow (100% oxygen). In the P/S group, the anesthesia induction were as the TIVA group patients, whereas anesthesia was maintained using propofol infusion and fixed 1% sevoflurane (inhaled concentration) with an oxygen flow of 1 L/min with 100% oxygen.

Maintenance of the Ce for the TIVA and P/S was adjusted to keep bispectral index value between 40 and 60, mean arterial blood pressure (MABP) and HR at baseline levels ± 20%. The SpO₂ was maintained ≥ 90%. Incremental intravenous injections of fentanyl (25 μg) were administrated as: the presence of moderate to severe cough with limb movement affecting the surgical procedure, to keep a respiratory rate (RR) of 12 to 20 breaths / min.

All patients received the intraoperative multilevel thoracic intercostal nerve blocks administered through the working port by infiltration of 0.5% bupivacaine (1.5 mL for each intercostal space) from the third to the 8th intercostal space under the parietal pleura, 2 cm lateral to the sympathetic chain by the surgeon. Keterolac 30 mg IV was administrated to the patients without nonsteroidal anti-inflammatory drugs (NSAIDs) allergy before skin closure.

At the end of the procedure, propofol and sevoflurane were discontinued and the lungs were ventilated with 100% oxygen at a fresh gas flow of 6 L/min. When the patient regained consciousness by name, the LMA was removed and the patient was sent to the postoperative anesthesia care unit for further care.

The primary outcome measurements were the incidence of cough reflex. Cough severity (1 = none, 2 = slight, 3 = moderate, 4 = severe) and limb movement (1 = none, 2 = slight, 3 = moderate, 4 = severe) were recorded during the surgery. In addition, the incidence of PONV within 24 hours after surgery, extubation time, loss of consciousness (LOC) Ce of propofol during induction, awakening Ce of propofol, maintenance Ce of propofol, maintenance end-tidal (Et) concentration of sevoflurane (%), awakening Et concentration of sevoflurane (%), and fentanyl bolus for cough reflex and limb movement, fentanyl and propofol consumption were recorded. We also recorded the pulmonary lesions as central or peripheral by chest x-ray.

Based on the same surgical population in our institution, a power analysis was performed by reducing cough reflex and limb movement as the primary variable. We calculated a sample size so that a reducing 50% of cough reflex and limb movement would permit a one-tailed type I error rate of α = 0.05 with a power of 80%. This analysis indicated that a sample size of at least 37 patients per group was necessary. To allow for potential dropouts, we enrolled a total of 45 patients in each group. Data are presented as the mean and standard deviation (SD) or number of patients. Demographic and perioperative variables were compared using Student’s t-tests or Mann–Whitney test while the data were not normally distributed. Categorical variables were compared using chi-square. Differences in the severity of symptoms between 2 groups were evaluated by Kruskal–Wallis tests. Furthermore, the Dunn’s procedure was applied to compare the difference between 2 groups. Statistical significance was accepted for 2-tailed P values of < 0.05. The statistics was performed by using SigmaStat 3.5 for Windows.

3. Results

Ninety patients undergoing elective nonintubated VATS with LMA and spontaneous breathing were performed successfully without excluded. Ultimately, 90 patients completed the study: 45 in the TIVA group and 45 in the P/S group (Fig. 1).

The 2 groups showed similar patients’ characteristics and surgical procedures (Table 1). Table 2 showed comparison of...
perioperative characteristics and outcomes for the 2 groups. There was no significant difference between the 2 groups in terms of (1) operation time (TIVA group: 69.2 ± 24.4 vs P/S group: 67.8 ± 25.1 minutes, \( P = .80 \)), (2) anesthesia time (TIVA group: 102.8 ± 29.8 vs P/S group: 102.4 ± 30.2 minutes, \( P = .95 \)), (3) extubation time (TIVA group: 5.04 ± 2.88 vs P/S group: 4.44 ± 2.98 minutes, \( P = .33 \)), and (4) the LOC propofol Ce (TIVA group: 3.46 ± 0.44 vs P/S group: 3.46 ± 0.51 mg/mL, \( P = .98 \)). The maintenance propofol Ce was 2.66 ± 0.46 in the TIVA group and 2.38 ± 0.48 mg/mL in the P/S group (\( P < .05 \)). Maintenance and awakening Et concentration of sevoflurane in the P/S group was 0.7 and 0.13 ± 0.06%, respectively. The awakening propofol Ce was 0.96 ± 0.15 mg/mL in the TIVA group and 0.73 ± 0.16 mg/mL in the P/S groups (\( P < .001 \)). Fentanyl consumption during the procedure was 145.0 ± 41.1 mg in the TIVA group and 128.3 ± 31.4 mg in the P/S group (\( P < .05 \)).

Table 2: Comparison of perioperative characteristics and outcomes for the 2 groups.

|                   | Group TIVA (n = 45) | Group P/S (n = 45) | \( P \) value |
|-------------------|--------------------|--------------------|--------------|
| Operation time, minutes | 69.2 ± 24.4 | 67.8 ± 25.1 | .80 |
| Anaesthesia time, minutes | 102.8 ± 29.8 | 102.4 ± 30.2 | .95 |
| Extubation time, minutes | 5.04 ± 2.88 | 4.44 ± 2.98 | .33 |
| LOC propofol Ce, \( \mu \)g/mL | 3.46 ± 0.44 | 3.46 ± 0.51 | .98 |
| Maintenance propofol Ce, \( \mu \)g/mL | 2.66 ± 0.46 | 2.38 ± 0.48 | < .05 |
| Maintenance Et SEVO (%) | 0 | 0.7 | .07 |
| Awakening propofol Ce, \( \mu \)g/mL | 0.96 ± 0.15 | 0.73 ± 0.16 | < .001 |
| Awakening Et SEVO (%) | 0 | 0.13 ± 0.06 | .05 |
| Fentanyl consumption, \( \mu \)g | 145.0 ± 41.1 | 128.3 ± 31.4 | < .05 |
| Fentanyl bolus for cough reflex (n; median [range]) | 17 (0 [0–3]) | 5 (0 [0–1]) | < .05 |
| Propofol consumption, mg | 570.0 ± 157.6 | 525.6 ± 164.8 | .12 |
| Patients with cough reflex (n; %) | 34 (75.6%) | 10 (22.2%) | < .001 |
| Cough severity (1/2/3/4) | 11/17/17/0 | 35/5/5/0 | < .001 |
| Limb movement (1/2/3/4) | 28/17/0/0 | 40/5/0/0 | < .001 |
| Cough reflex in central lung lesions | 6/6 (100.0%) | 4/7 (57.1%) | .07 |
| Cough reflex in peripheral lung lesions | 28/39 (71.8%) | 6/38 (15.8%) | < .001 |
| Patients with PONV (n) | 0 | 0 | .05 |

Data shown as mean ± SD or number, or median (range).

Ce = effect-site concentration, Et = end-tidal, LOC = loss of consciousness, P/S = propofol/sevoflurane, PONV = postoperative nausea and vomiting, SEVO = sevoflurane. TIVA = total intravenous anesthesia.
Table 3

|                        | Group TIVA (n=45) | Group P/S (n=45) | P value |
|------------------------|-------------------|------------------|---------|
| **Anesthetic, hemodynamic, and respiratory data before OLV and during surgery for the 2 groups.** |                   |                  |         |
| **BIS**                |                   |                  |         |
| Before OLV             | 48.2±2.4          | 48.0±2.4         | .73     |
| During surgery         | 49.3±1.7          | 49.2±1.4         | .79     |
| Ce of propofol, µg/mL  |                   |                  |         |
| Before OLV             | 2.64±0.45         | 2.37±0.46        | <.05    |
| During surgery         | 2.71±0.47         | 2.40±0.49        | <.05    |
| Et sevoflurane (%)     |                   |                  |         |
| Before OLV             | 0                 | 0.7              |         |
| During surgery         | 0                 | 0.7              |         |
| Heart rate, beats/min  |                   |                  |         |
| Before OLV             | 76.9±5.8          | 75.6±6.8         | .96     |
| During surgery         | 81.3±6.0          | 80.0±6.9         | .95     |
| MAPB                   |                   |                  |         |
| Before OLV             | 83.1±3.6          | 83.3±3.1         | .75     |
| During surgery         | 84.1±4.1          | 84.4±3.2         | .67     |
| Respiratory rate       |                   |                  |         |
| Before OLV             | 13.9±1.6          | 13.4±1.5         | .11     |
| During surgery         | 16.3±1.9          | 16.3±2.0         | .12     |

Data shown as mean±SD or number.

BIS = bispectral index, Ce = effect-site concentration, Et = end-tidal, MAPB = mean arterial blood pressure, OLV = one lung ventilation, P/S = propofol/sevoflurane, TIVA = total intravenous anesthesia.

4. Discussion

The major findings of this study revealed that combination with 1% sevoflurane anesthesia attenuated cough reflex under propofol-based TIVA in nonintubated VATS. In addition, we also found that propofol combination with 1% sevoflurane anesthesia did not increase the incidence of PONV and extubation time in nonintubated VATS under TIVA monitoring.

Coughing is initiated by activation of mechanically and chemically sensitive vagal afferent nerves innervating the airways. All afferent nerve subtypes innervating the airways can modulate the cough reflex. At present, vagal bronchopulmonary afferent nerves are typically considered to belong to one of 3 general categories, namely C-fibres, rapidly adapting receptors, and slowly adapting stretch receptors.[17] Vagal block ensures cough abolition during 12 hours so most anatomical resections can be safely performed. It is better to block the vagal transmission before initiating parenchyma or bronchial pulling maneuvers in order to avoid cough reflex triggering.[18] Some other techniques have been described for cough control, such as intravenous or aerosolized local anesthetic.[19] However, nerve blockades may induce LAST, nerve injuries.[3] or aspiration.[4,5] For these reasons, the routine use of vagal block is not recommended by our surgeon, and anesthetics that attenuate cough reflex are usually requested, especially for nonintubated VATS.

Chen et al.[20] routinely performed intraoperative thoracoscopic vagal block for cough reflex suppression. For the sake of decreasing cough suppression duration, incremental intravenous fentanyl is applied in place of vagal block,[11] because cough suppression is part of the pharmacodynamic profile of fentanyl.[21] Tagaito et al.[22] found that increasing doses of fentanyl in subjects under propofol anaesthesia modified upper airway reflexes, with the cough reflex being the most susceptible even at doses of 50 µg, and that after 4 doses (total 200 µg fentanyl) only slight adduction of the vocal folds for airway closure was observed endoscopically following instillation of distilled water into the larynx. However, most serious adverse effects of fentanyl are dose-dependent respiratory depression and aspiration pneumonia.[21] Therefore, higher dose of fentanyl use is not suit for nonintubated VATS with LMA and spontaneous breathing. The fentanyl consumption was less than 200 µg, and there was no aspiration pneumonia in this study. Though the cough reflex was suppressed by fentanyl in our study, the optimal and maximal doses of fentanyl for cough reflex suppression in nonintubated VATS were needed to investigate.

Here, we first found that sevoflurane can attenuate cough reflex without vagal block. Cough reflex is one of the first challenges while facing nonintubated VATS. It seems that dissecting vascular structures without cough control is not safe due to the risk of a major bleeding.[13] The lower airway contains specific cough-producing receptors/fibers such as slowly adapting stretch receptors, rapidly adapting receptors (irritant receptors) and pulmonary C-fibers.[23-25] Also, laryngeal irritant receptors and C-fibers presented in the upper airway participate in cough reflexes.[26] Among these, pulmonary and laryngeal irritant receptors are the main afferents most readily associated with the cough reflex.[26] Sevoflurane anesthesia can inhibit the pulmonary irritant receptors and attenuate cough reflex.[6] In contrast, cough reflex occurred significantly more frequently in propofol anesthesia compared with sevoflurane anesthesia in a stimulation technique.[27] Furthermore, subanesthetic concentration of sevoflurane might attenuate cough reflex via reducing agonist affinity at nicotinic acetylcholine receptors on vagal afferent nerves.
neurons in the brain site. Therefore, we think that the effect of cough reflex suppression in the P/S group was based on sevoflurane inhibiting the pulmonary irritant receptors compared with propofol. Taking together, we used fentanyl and sevoflurane for modifying depth of anesthesia to attenuate cough and the result was consistent with previous studies reporting that depth of anesthesia can modify cough reflex. However, there was no significant difference in BIS value between 2 groups before OLV and during surgery in this study.

In this study, the overall incidence of cough reflex in central lung lesions was 76.9% (10/13) with small sample size, and sevoflurane attenuated cough reflex in the central lesion without statistical significance (100% vs 57.1%; P = .07). Therefore, we suggested that vagal block was needed in central lung lesions for attenuating cough reflex. In addition, we showed that the cough reflex was significantly suppressed in the peripheral lesion by sevoflurane (71.8% vs 15.8%). Thus, we concluded that subanesthetic of sevoflurane might be applied in place of vagal block in nonintubated VATS under propofol-based TIVA and BIS monitoring for peripheral lung lesions. From another point of view, Dong et al reported that the incidence of cough reflex resulting from lobe traction without vagal block was 9.1% (2/22) in nonintubated VATS under remifentanil and propofol anesthesia combination with TEA. We did not use remifentanil in this study due to remifentanil available in our country since 2018, and further investigation was needed.

Sevoflurane and propofol had similar efficacy for anesthesia, nevertheless, propofol based TIVA may still be the preferred anesthetic because of its favorable anesthesia characteristics, such as high patient satisfaction and less frequent incidence of PONV. In this study, we found no patient with PONV in the 2 groups. This finding may be resulting from that the patients received propofol/sevoflurane anesthesia, the anesthetic technique was propofol predominant and adjuvant sevoflurane. As our best knowledge, however, the optimal concentration of sevoflurane for attenuating cough reflex and PONV in nonintubated VATS remains unclear and need to further investigate.

This study has some limitations. First, ninety patients received different surgical procedures (77 patients undergoing VATS with wedge resection, 11 patients undergoing VATS with segmentectomy, and 2 patients undergoing VATS with lobectomy). However, such a discrepancy between the TIVA and P/S groups was minimal due to 39/38 patients undergoing VATS with wedge resection, 5/6 patients undergoing VATS with segmentectomy, and 1/1 patients undergoing VATS with lobectomy. Second, we did not exclude smokers. Cough reflex sensitivity might be diminished in current-smokers compared with nonsmokers. One proposed mechanism, chronic cigarette smoke-induced desensitization of airway cough receptors, is supported by the demonstration that smoking cessation leads to prompt enhancement of cough reflex sensitivity, even after many years of smoking.

However, number of smokers was no significantly different between 2 groups. Third, our study was underpowered for PONV. We did not see any PONV in the 2 groups, and further investigation is needed. Finally, NSAIDs might attenuate cough reflex, however, we used NSAIDs just before skin incision.

In conclusion, we showed that combination with 1% sevoflurane anesthesia and propofol anesthesia attenuated cough reflex during nonintubated VATS. Besides, we found no significant difference in extubation time between 2 groups under BIS monitoring, no postoperative hemorrhage, and no PONV in the 2 groups. It might suggest the acceptable clinical effect on the propofol combination with 1% sevoflurane anesthesia in nonintubated VATS with LMA and spontaneous breathing.

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References
[1] Hung MH, Hsu HH, Cheng YJ, et al. Nonintubated thoracoscopic surgery: state of the art and future directions. J Thorac Dis 2014;6:2-9.
[2] Chen KC, Cheng YJ, Hung MH, et al. Nonintubated thoracoscopic surgery using regional anesthesia and vagal block and targeted sedation. J Thorac Dis 2014;6:31-6.
[3] McNlyk V, Brinon JW, Kentor ML, et al. Updated retrospective single-center comparative analysis of peripheral nerve block complications using landmark peripheral nerve stimulation versus ultrasound guidance as a primary means of nerve localization. J Ultrasound Med 2018; doi: 10.1002/jum.14603. [Epub ahead of print].
[4] Reynolds RP, Effer GW, Bendick MP. The upper esophageal sphincter in the cat: the role of central innervation assessed by transient vagal blockade. Can J Physiol Pharmacol 1987;65:96–9.
[5] Neville AL, Grookes P, Velmahos GC, et al. Esophageal dysfunction in cervical spinal cord injury: a potentially important mechanism of aspiration. J Trauma 2005;59:905–11.
[6] Nishino T, Kochi T, Ishii M. Differences in respiratory reflex responses from the larynx, trachea, and bronchi in anesthetized female subjects. Anesthesiology 1996;84:70–4.
[7] Kumar G, Stendall C, Mistry R, et al. A comparison of total intravenous anaesthesia using propofol with sevoflurane or desflurane in ambulatory surgery: systematic review and meta-analysis. Anaesthesia 2014;69:1138–50.
[8] Szemere DC, Grose BW. Postoperative nausea, StatPearls [Internet]. 2018;StatPearls Publishing, Treasure Island, FL.Szemere DC, Grose BW. Postoperative nausea. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-Apr 28.
[9] Yang ML, Hung MH, Chang YH, et al. Intravenous multiple intercostal nerve blocks exert anesthetic-sparing effect: a retrospective study on the effect-site concentration of propofol infusion in nonintubated thoracoscopic surgery. Acta Anaesthesiol Taiwan 2016;54:77–80.
[10] Guo Z, Yin W, Wang W, et al. Spontaneous ventilation anaesthesia: total intravenous anaesthesia with local anaesthesia or thoracic epidural anaesthesia for thoracoscopic bullectomy. Eur J Cardiothorac Surg 2016;50:927–32.
[11] Yang JT, Hung MH, Chen JS, et al. Anesthetic consideration for nonintubated VATS. J Thorac Dis 2014;6:10–3.
[12] Huang RC, Hung NK, Lu CH, et al. Removal of laryngeal mask airway in adults under target-controlled, propofol-fentanyl infusion anesthesia: awake or deep anesthesia? Medicine (Baltimore) 2016;95:e5441.
[13] Lai HC, Chang YH, Huang RC, et al. Efficacy of sevoflurane as an adjuvant to propofol-based total intravenous anesthesia for attenuating secretions in oculary surgery. Medicine (Baltimore) 2017;96:e6729.
[14] Tsai TM, Lin MW, Hsu HH, et al. Nonintubated uniporal thoracoscopic wedge resection for early lung cancer. J Vis Surg 2017;3:3155.
[15] Tsai CJ, Chu KS, Chen TL, et al. A comparison of the effectiveness of dexmedetomidine versus propofol target-controlled infusion for sedation during fiberoptic nasotracheal intubation. Anaesthesia 2010;65:254–9.
[16] Fauchois P, Milman N, Dirsken A, et al. Classification of pulmonary lesions into central and peripheral with a template applied on chest X-ray. Respir Med 1996;90:349–52.
[17] Canning BJ, Mori N, Mazzone SB. Vagal afferent nerves regulating the cough reflex. Respir Physiol Neurobiol 2006;152:223–42.
[18] Galvezes C, Navarro-Martinez J, Bolufer S, et al. Nonintubated uniporal VATS pulmonary anatomical resections. J Vis Surg 2017;3:120.
[19] Navarro-Martínez J, Gálvez C, Rivera-Cogollos MJ, et al. Intraoperative crisis resource management during a non-intubated video-assisted thoracoscopic surgery. Ann Transl Med 2015;3:111.
[20] Chen JS, Cheng YJ, Hung MH, et al. Nonintubated thoracoscopic lobectomy for lung cancer. Ann Surg 2011;254:1038–43.
[21] Kelly HE, Shaw GM, Brett CN, et al. The effect of titrated fentanyl on suppressed cough reflex in healthy adult volunteers. Anaesthesia 2016;71:529–34.
[22] Tagaito Y, Isono S, Nishino T. Upper airway reflexes during a combination of propofol and fentanyl anesthesia. Anesthesiology 1998;88:1459.
[23] Bolser DC. Mechanisms of action of central and peripheral antitussive drugs. Pulm Pharmacol 1996;9:357–64.
[24] Canning BJ. Interactions between vagal afferent nerve subtypes mediating cough. Pulm Pharmacol Ther 2002;15:187–92.
[25] Reynolds SM, Mackenzie AJ, Spina D, et al. The pharmacology of cough. Trends Pharmacol Sci 2004;25:569–76.
[26] Haji A, Kimura S, Ohi Y. A model of the central regulatory system for cough reflex. Biol Pharm Bull 2013;36:501–8.
[27] Oberer C, von Ungern-Sternberg BS, Frei FJ, et al. Respiratory reflex responses of the larynx differ between sevoflurane and propofol in pediatric patients. Anesthesiology 2003;103:1142–8.
[28] Rada EM, Tharakan EC, Flood P. Volatile anesthetics reduce agonist affinity at nicotinic acetylcholine receptors in the brain. Anesth Analg 2003;96:108–11.
[29] Cooper E. Nicotinic acetylcholine receptors on vagal afferent neurons. Ann N Y Acad Sci 2001;940:110–8.
[30] Ishikawa T, Isono S, Tanaka A, et al. Airway protective reflexes evoked by laryngeal instillation of distilled water under sevoflurane general anesthesia in children. Anesth Analg 2003;101:1615–8.
[31] Nishino T, Hiraga K, Mizuguchi T, et al. Respiratory reflex responses to stimulation of tracheal mucosa in enflurane-anesthetized humans. J Appl Physiol (1985) 1988;65:1069–74.
[32] Dwivedi MB, Puri A, Dwivedi S, et al. Role of opioids as conduction agent with propofol and their effect on apnea time, recovery time, and sedation score. Int J Crit Illn Inj Sci 2018;8:4–8.
[33] Dong Q, Liang L, Li Y, et al. Anesthesia with nontracheal intubation in thoracic surgery. J Thorac Dis 2012;4:126–30.
[34] Fredman B, Nathanson MH, Smith I, et al. Sevoflurane for outpatient anesthesia: a comparison with propofol. Anesth Analg 1995;81:823–8.
[35] Tang J, Chen L, White PF, et al. Recovery profile, costs, and patient satisfaction with propofol and sevoflurane for fast-track office based anesthesia. Anesthesiology 1999;91:253–61.
[36] Joo HS, Perks WJ. Sevoﬂurane versus propofol for anesthetic induction: a meta-analysis. Anesth Analg 2000;91:213–9.
[37] Dicpinigaitis PV. Cough reflex sensitivity in cigarette smokers. Chest 2003;123:685–8.
[38] Sitkauskiene B, Dicpinigaitis PV. Effect of smoking on cough reflex sensitivity in humans. Lung 2010;188(suppl 1):S29–32.
[39] Apfel CC, Roewer N, Korttila K. How to study postoperative nausea and vomiting. Acta Anaesthesiol Scand 2002;46:921–8.
[40] Foster G, Yeo WW, Ramsay LE. Effect of sulindac on the cough reflex of healthy subjects. Br J Clin Pharmacol 1991;31:207–8.
[41] Ishiura Y, Fujimura M, Yamamoto H, et al. COX-2 inhibition attenuates cough reflex sensitivity to inhaled capsaicin in patients with asthma. J Investig Allergol Clin Immunol 2009;19:370–4.
[42] Forget P, Machieli JP, Couble PG, et al. Neutrophil lymphocyte ratio and intraoperative use of ketorolac or diclofenac are prognostic factors in different cohorts of patients undergoing breast, lung, and kidney cancer surgery. Ann Surg Oncol 2013;20(suppl 3):S650–60.