

Patient quality of recovery on the day of surgery after propofol total intravenous anesthesia for vitrectomy

A randomized controlled trial

Se Hee Na^a, Kyu Hee Jeong^b, Dahae Eum^b, Jin Ha Park^{a,*}, Min-Soo Kim^{a,*}

Abstract

Background: Vitrectomy under general anesthesia is considered as a candidate for ambulatory surgery. An anesthetic method with high quality of postoperative recovery should be selected for successful ambulatory surgery. We thus compared quality of postoperative recovery on the day of vitrectomy using the Quality of Recovery (QoR)-40 questionnaire between propofol total intravenous anesthesia (propofol group) and desflurane inhalation anesthesia (desflurane group) as the 2 representative anesthetic methods.

Methods: Eighty-four patients (20–80 years old) undergoing elective vitrectomy under general anesthesia were randomized into 2 groups. The propofol group received propofol and remifentanyl using effect-site target-controlled infusion (TCI), and the desflurane group received desflurane inhalation and remifentanyl using effect-site TCI. We assessed quality of recovery at 6 hours after surgery through interviews using the QoR-40 questionnaire. We also collected data related to recovery and complications during emergence and recovery period.

Results: The median of QoR-40 score on the day of surgery was significantly higher in the propofol group than that in the desflurane group (181.0 vs 169.5, respectively; $P = .033$). In particular, propofol group had significantly higher scores for physical comfort and physical independence dimensions. The amount of remifentanyl administered was significantly higher, and the emergence time was significantly longer in propofol group. However, there were no significant differences in other complications between the 2 groups.

Conclusions: Propofol total intravenous anesthesia provided significantly better quality of recovery on the day of surgery than desflurane inhalation anesthesia.

Abbreviations: ASA = American Society of anesthesiologists, BIS = bispectral index, BMI = body mass index, EtCO₂ = end-tidal carbon dioxide, HR = heart rate, MAP = mean arterial pressure, NMDA = N-methyl-D-aspartate, NRS = numerical rating scale, PACU = postanesthesia care unit, POD = postoperative day, PONV = postoperative nausea and vomiting, QoR-40 = Quality of Recovery-40 questionnaire, TCI = target-controlled infusion, TIVA = total intravenous anesthesia.

Keywords: anesthesia, postoperative, quality measures, vitrectomy

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1. Introduction

Various surgical procedures under general anesthesia are currently performed in the form of ambulatory surgery for the purpose of fast discharge with reduced costs and rapid return of daily activities.^[1,2] For a successful ambulatory surgery, adequate recovery from anesthesia is important requirements of today's anesthetics.^[1]

As patients' quality of life has recently become the primary endpoint in clinical researches, satisfactory recovery is being redefined as an improvement of overall quality of recovery, which includes the enhancement of comfort and prompt resumption of normal activities.^[1,3–5] However, the patient quality of recovery may not be easily assessed with conventional recovery indices, that is, awakening time, duration of stay, or adverse events. Instead of these traditional approaches, the Quality of Recovery-40 (QoR-40) questionnaire has been widely used to assess the difference in quality of recovery depending on the type of anesthesia or the use of adjuvant agents.^[3–5]

Several ophthalmic surgeries are commonly performed in an outpatient setting, so retina surgery such as vitrectomy is also considered as a candidate for ambulatory surgery.^[6,7] However, vitrectomy may require general anesthesia because of long operation time and delicate manipulation.^[8,9] Hence, it is

important to choose an anesthetic method with high quality of recovery to successfully perform retinal surgery under the general anesthesia as ambulatory surgery.

Two representative general anesthetic techniques are propofol total intravenous anesthesia (TIVA) and inhalation anesthesia.^[4] Lee et al reported that quality of recovery measured by QoR-40 on postoperative day 1 and 2 after thyroid surgery was superior with propofol TIVA compared with desflurane inhalation anesthesia.^[4] However, this study did not provide data on quality of recovery on the day of surgery, which may be of interest in terms of ambulatory surgery. We thus compared patient quality of recovery after propofol TIVA and desflurane inhalation anesthesia using the QoR-40 on the day of vitrectomy.

2. Methods

Institutional Review Board at Gangnam Severance Hospital (Seoul, Republic of Korea) approved this study protocol (3-2014-0104). This study was registered at www.ClinicalTrials.gov (ref. number: NCT02212340) and was performed at a single medical centre (Gangnam Severance Hospital), and written informed consent was obtained from all participants. The principles of the Declaration of Helsinki were followed throughout.

In all, 84 patients, 20–80 years of age, American Society of Anesthesiologists (ASA) class I-III, and presenting for elective vitrectomy under general anesthesia were included. Exclusion criteria were allergy to the anesthetic agents, anticipated difficult airway, body mass index (BMI) greater than 30, chronic obstructive pulmonary disease, heart failure, or unstable angina. Each patient was allocated to the propofol or desflurane group by a random-number list created without dividing blocks from a website (<http://www.random.org>). The enrolled patients, surgical personnel, postoperative outcome data investigator, ward nurses, and data analysts were masked to the group assignment. Because of distinct differences between the 2 anesthetic methods, attending anesthesiologists were aware of the group allocation.

The electrocardiogram, pulse oxygen saturation, noninvasive blood pressure, end-tidal carbon dioxide (EtCO₂), and the bispectral index (BIS; A-2000 BIS Monitor, Aspect Medical Systems Inc., Newton, MA) were monitored at regular intervals. In the propofol group, propofol and remifentanyl were administered with a target-controlled infusion (TCI) system (Orchestra Base Primea, Fresenius Vial, Brezins, France) for anesthesia induction and maintenance. In the desflurane group, anesthetic induction was established with a bolus administration of propofol 1.5 to 2 mg/kg, and the anesthetized state was maintained with desflurane inhalation and remifentanyl infusion through the TCI system. The effect-site concentrations of propofol and remifentanyl infused through the TCI system were determined by Schnider and Minto pharmacokinetic models, respectively.^[10,11] Rocuronium 0.6 mg/kg was injected to facilitate orotracheal intubation during the induction period. After tracheal intubation, mechanical ventilation was initiated with a tidal volume of 8 mL/kg and respiratory rate was adjusted to maintain an EtCO₂ of 30 to 40 mm Hg with 50% oxygen/air mixture. The anesthetics administered in each group were adjusted to provide a BIS value of 40 to 60 and mean arterial pressure (MAP) within 20% of preinduction values. Hemodynamic instability during anesthesia was managed with intravenous phenylephrine or ephedrine depending on the judgement of the attending anesthesiologist.

Ramosetron 0.3 mg for prophylactic antiemesis and propacetamol 1 g for analgesia were intravenously administered 10 minutes before the end of the operation. Once the operation was

Table 1

Ricker sedation-agitation scale and 4-point cough scale scores during emergence.

Ricker sedation-agitation scale	Score
Minimal or no response to noxious stimuli	1
Arousal with physical stimuli but does not communicate	2
Difficult to arouse but awakens to verbal stimuli or gentle shaking	3
Calm and follows commands	4
Anxious or physically agitated and calms with verbal instructions	5
Requires restraint and frequent verbal reminders of limits	6
Pulling at tracheal tube, trying to remove catheters or striking at staff	7
4-point scale	Score
No cough	0
Single cough	1
Persistent cough lasting <5 s	2
Persistent cough lasting ≥5 s or bucking	3

completed, neostigmine 0.04 mg/kg and glycopyrrolate 0.005 mg/kg were given intravenously, and all the anesthetic agents were discontinued. When adequate response to verbal command and sufficient spontaneous respiration were observed, tracheal extubation was performed. Every patient was admitted to the postanesthesia care unit (PACU) after stable vital signs, and spontaneous breathing with airway patency were confirmed.

From the time of discontinuation of anesthetic agents, the durations to the first verbal command and extubation were recorded. The total amount of remifentanyl and vasopressors administered during anesthesia, BIS value, and respiratory rate at the time of extubation were also recorded. To compare the amount of vasopressors administered to both groups, the amount of ephedrine was converted to the equivalent amount of phenylephrine by applying a relative potency ratio of 80:1 for phenylephrine:ephedrine.^[12] Emergence was defined as the time period from the discontinuation of anesthetic agents to 2 minutes after tracheal extubation.^[13] During emergence, the grade of agitation and cough was assessed using the Ricker sedation-agitation scale and a 4-point scale, respectively (Table 1).^[14–16] A sedation-agitation scale score ≥5 was considered as the presence of emergence agitation. A sedation-agitation scale score of 7 was regarded as dangerous agitation.^[14,15] Vital signs including MAP and heart rate (HR) were recorded before anesthesia induction, at 10 and 30 minutes after initiation of the operation, at the end of the operation, and at 1 and 2 minutes after tracheal extubation. In addition, BIS score at tracheal extubation and adverse events such as desaturation (SpO₂ <90%), airway obstruction, and laryngospasm were also recorded during emergence.

In the PACU, the scores on the sedation-agitation scale at the time of arrival, an 11-point numerical rating scale (NRS) for postoperative pain (0 = no pain and 10 = worst pain imaginable), and a 4-point nausea and vomiting scale (0 = no nausea, 1 = mild nausea, 2 = severe nausea requiring antiemetics, and 3 = retching, vomiting, or both) were recorded. Residual sedation was defined as a sedation-agitation scale score ≤3 at the time of arrival. If NRS was 5 or greater, fentanyl 50 μg was administered intravenously. When the 4-point nausea and vomiting scale score was 2 or greater, metoclopramide 10 mg was administered intravenously. Discharge from the PACU was permitted when the Aldrete score was 9 or more.^[13]

The quality of functional recovery at 6 hours after surgery was assessed through interviews using the QoR-40 questionnaire, which includes 5 dimensions of recovery: emotional state (9 items), physical comfort (12 items), physical independence (5 items), psychological support (7 items), and pain (7 items). Each item

was assessed with a 5-point score. The total score on the QoR-40 questionnaire ranges from 40 (extremely poor) to 200 (excellent).^[3,4]

The primary endpoint of this study was the total QoR-40 score at 6 hours after surgery. The mean and standard deviation of the postoperative QoR-40 questionnaire from a previous study were respectively 167 and 23.^[3] A sample size of 37 patients in each group was calculated to detect the difference of 15 points in the total QoR-40 score, under α of 0.05 and a power of 80%. Finally, 84 patients were included to allow for a dropout rate of 10%. Continuous variables were analyzed with an independent *t* test or Wilcoxon rank-sum test after Shapiro-Wilk normality testing. The chi-square test or Fisher exact test was used to compare categorical variables. A linear mixed model with repeated measures was applied to compare repeatedly measured variables including MAP and HR. If overall differences were confirmed among values at each time point, post hoc analysis for multiple comparisons was performed with the Bonferroni correction. A *P* value of $<.05$ was considered statistically significant.

3. Results

In all, 84 patients were enrolled in this investigation, and 84 were randomized, of whom 1 in the propofol group was

withdrawn due to the refusal to respond to the QoR-40, leaving 83 patients for final analysis (Fig. 1). Patient characteristics were similar between the propofol and desflurane groups (Table 2). There were no significant differences in operative time, anesthesia time, or baseline vital signs between the 2 groups.

Table 3 presents QoR-40 scores for the propofol and desflurane groups on the day of surgery. Total score was significantly higher in the propofol group than in the desflurane groups (median value 181.0 vs 169.5, respectively; $P = .033$). The propofol group demonstrated significantly higher scores in physical comfort and physical independence ($P = .031$ and $P = .045$, respectively). Other dimensions did not show significant differences between the 2 groups.

Perioperative data are shown in Table 4. In the intraoperative period, the amount of remifentanyl administered was significantly higher in the propofol group ($P < .001$). In the emergence period, the response time to verbal commands and extubation time was significantly longer in the propofol group ($P < .001$). In the PACU, agitation score, pain score, nausea/vomiting events, and the use of analgesics and antiemetics showed no significant differences.

The MAP and HR were not significantly different between the groups before anesthesia induction, at 10 and 30 minutes after

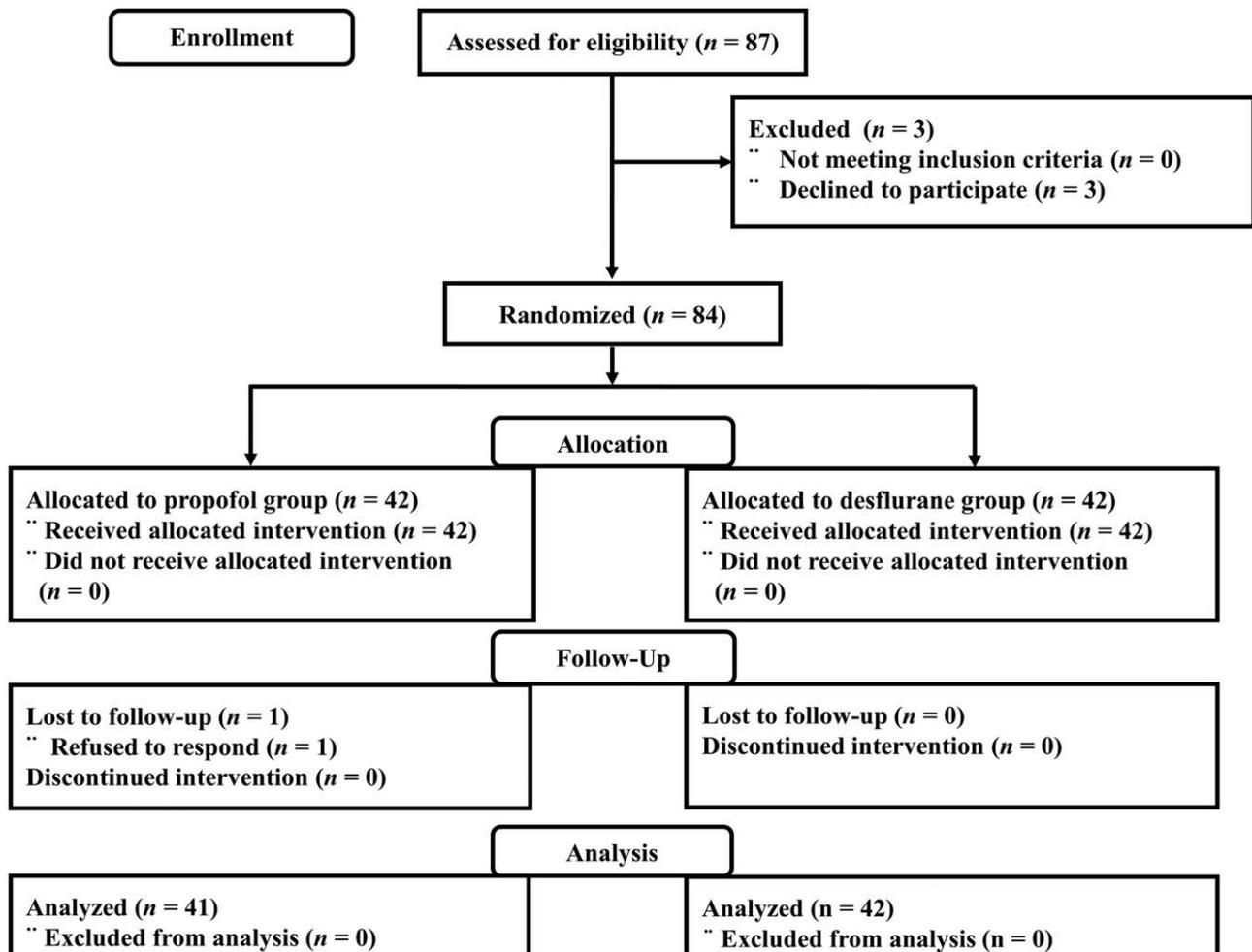


Figure 1. Patients flow diagram.

Table 2

Patient characteristics in the propofol and desflurane groups.

	Propofol group (n=41)	Desflurane group (n=42)	P
Age (y)	59.0 (51.0–64.0)	60.0 (50.0–70.0)	.458
Sex (M/F)	17 (41.5)/24 (58.5)	19 (45.2)/23 (54.8)	.900
Height (cm)	162.7 (8.7)	162.4 (10.0)	.908
Weight (kg)	64.1 (10.7)	63.9 (11.5)	.935
Diabetes mellitus	13 (31.7)	5 (11.9)	.055
Hypertension	12 (29.3)	15 (35.7)	.695
Coronary artery disease	1 (2.4)	1 (2.4)	1.000
ASA class (I/II/III)	14 (34.1)/19 (46.3)/8 (19.5)	15 (35.7)/18 (42.9)/9 (21.4)	.947
Operation time (min)	60.0 (44.0–79.0)	62.0 (48.0–91.0)	.289
Anesthesia time (min)	100.0 (95.0–125.0)	110.0 (100.0–135.0)	.160
Baseline vital signs			
Mean arterial pressure (mm Hg)	101.7 (18.0)	99.3 (14.9)	.509
Heart rate (beat/min)	71.0 (62.0–80.0)	72.0 (63.0–81.0)	.757

Data are presented as mean (SD), median (IQR), or n (%) as appropriate. ASA=American Society of Anesthesiologists, IQR=interquartile range, SD=standard deviation.

Table 3

QoR-40 scores for the propofol and desflurane groups on the day of surgery.

	Propofol group (n=41)	Desflurane group (n=42)	P
Physical comfort	54.0 (50.0–57.0)	49.5 (47.0–56.0)	.031
Emotional status	42.0 (40.0–44.0)	40.0 (35.0–43.0)	.072
Physical independence	23.0 (21.0–25.0)	21.0 (16.0–25.0)	.045
Psychological support	32.0 (27.0–35.0)	31.0 (27.0–34.0)	.395
Pain	31.0 (27.0–34.0)	29.5 (25.0–33.0)	.141
Total score	181.0 (163.0–191.0)	169.5 (155.0–184.0)	.033

Data are presented as median (IQR). IQR=interquartile range, QoR-40=40-item Quality of Recovery questionnaire.

initiation of the operation, and at the end of the operation. However, at 1 and 2 minutes after extubation, the desflurane group had a significantly higher HR than the propofol group (adjusted $P < .05$) (Fig. 2).

4. Discussion

Our study showed a significant improvement in the patient’s perception of overall quality of recovery in those with propofol TIVA compared with those with desflurane anesthesia. In detail, propofol TIVA led to significant higher scores in physical comfort and physical independence dimensions of the QoR-40 on the day of surgery compared with desflurane anesthesia.

Regional anesthesia techniques are currently preferred in ophthalmic surgery due to advantages including lower cost, early hospital discharge with rapid recovery, and avoidance of general anesthesia with tracheal intubation.^[17–19] Regional techniques may rarely be associated with serious adverse events, that is, globe perforation, bulbar hemorrhage, respiratory arrest, cardiovascular depression, and convulsion.^[20] In addition, there are still several problems such as pain, fear and anxiety of patients, and unexpected eye movement during intraocular

Table 4

Perioperative data of the propofol and desflurane groups.

	Propofol group (n=41)	Desflurane group (n=42)	P
Intraoperative data			
Remifentanyl dose (μg/kg/min)	0.066 (0.021)	0.049 (0.016)	<.001
Phenylephrine dose (μg/kg/min)	0.103 (0.133)	0.140 (0.129)	.201
Emergence data			
Time to verbal response (s)	799.0 (665.0–975.0)	497.5 (400.0–622.0)	<.001
Time to extubation (s)	867.0 (700.0–1072.0)	523.0 (440.0–635.0)	<.001
BIS score at extubation	77 (75–78)	82 (75–86)	.027
Agitation score during emergence (1/2/3/4/5/6/7)	0 (0)/4 (9.8)/5 (12.2)/28 (68.3)/4 (9.8)/0 (0)/0 (0)	0 (0)/0 (0)/4 (9.5)/27 (64.3)/10 (23.8)/1 (2.4)/0 (0)	.104
Incidence of emergence agitation	4 (9.8%)	11 (26.2%)	.097
Cough score during emergence (0/1/2/3)	18 (43.9)/13 (31.7)/7 (17.1)/3 (7.3)	15 (35.7)/13 (31.0)/11 (26.2)/3 (7.1)	.765
Desaturation events during emergence	0 (0)	1 (2.4)	>.999
Airway obstruction during emergence	0 (0)	1 (2.4)	>.999
PACU			
Agitation score on arrival (1/2/3/4/5/6/7)	0 (0)/0 (0)/2 (4.9)/39 (95.1)/0 (0)/0 (0)/0 (0)	0 (0)/0 (0)/1 (2.4)/39 (92.9)/2 (4.8)/0 (0)/0 (0)	.313
Maximum pain score	4.0 (2.0–4.0)	4.0 (3.0–4.0)	.943
Maximum nausea/vomiting score (0/1/2/3)	41 (100%)/0 (0)/0 (0)/0 (0)	41 (97.6%)/0 (0)/1 (2.4%)/0 (0)	>.999
Use of analgesic	2 (4.9%)	2 (4.8%)	>.999
Use of antiemetic	0 (0.0%)	1 (2.4%)	>.999
PACU time	40.0 (34.0–53.0)	39.5 (32.0–55.0)	.942

Data are presented as mean (SD), median (IQR), or n (%) as appropriate. BIS=bispectral index, IQR=interquartile range, PACU=postanesthesia care unit, SD=standard deviation.

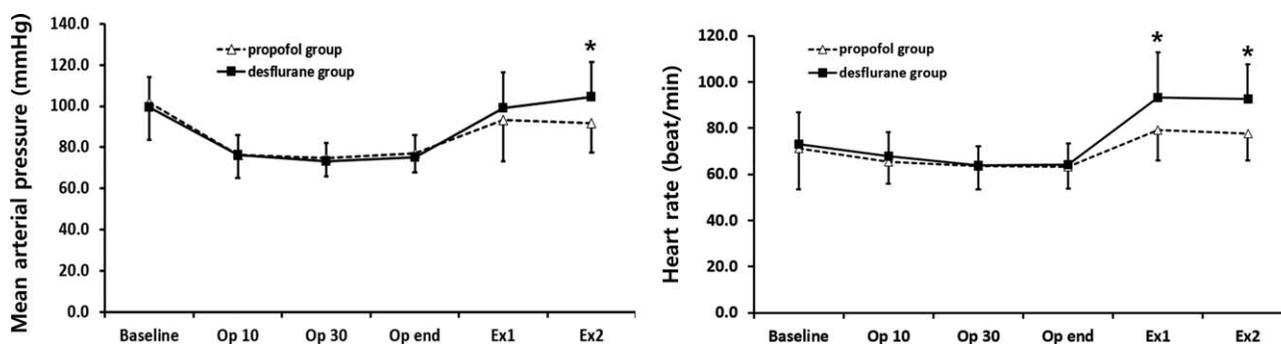


Figure 2. Changes of mean arterial pressure and heart rate during operation and emergence. Baseline, before anesthetic induction. Data are expressed as mean (SD). * $P < .05$ compared with propofol group (Bonferroni corrected). Ex 1 = 1 minute after extubation, Ex 2 = 2 minutes after extubation, Op 10 = 10 minutes after initiation of the operation, Op 30 = 30 minutes after initiation of the operation, Op end = end of operation.

procedures.^[9,19] Vitrectomy is usually accompanied by delicate peeling procedures, and its operation time is substantially longer than cataract operation. Thus, the relief of patients' suffering and the need to minimize movement are even more important during the procedure.^[9] For these reasons, sedative agents such as propofol and dexmedetomidine have been applied together with regional blocks during ophthalmic surgery.^[9,19] However, these drugs have several adverse effects including noncooperation, disorientation, and cardiovascular and respiratory depression related to oversedation during elaborate procedures.^[19]

The use of general anesthesia for retinal surgery allows the patients to be free from discomfort and keeps patients immobilized.^[8] Complications such as airway obstruction and apnea during sedation with regional blocks can be prevented through tracheal intubation during general anesthesia.^[19] However, maintenance of general anesthesia and additional airway procedures require the use of greater doses of anesthetics, which may result in increased costs and delayed recovery.^[7,8] In addition, patients undergoing vitreoretinal surgery may have greater comorbidities such as renal disease and coronary artery disease, which was associated with a significant increase of postoperative systemic adverse events after vitrectomy.^[21] Thus, an optimal anesthesia method for rapid and adequate recovery with minimal complications should be selected to perform vitrectomy with general anesthesia successfully, especially if performed under ambulatory setting.

Recently, the patients have been regarding a satisfactory recovery as overall improved quality of recovery, which includes the enhancement of comfort and prompt resumption of normal activities.^[3,4] However, conventional fragmentary indices regarding recovery and complications from general anesthesia have limitations in evaluating patient quality of recovery.^[22] Several previous studies have compared propofol TIVA and inhalation anesthesia using individual indices.^[4,23] As a result, we find difficulties with assessing and determining the fundamental and overall quality of recovery after general anesthesia based solely on the previous results.^[3,4] Recently, a 40-item Quality of Recovery (QoR-40) score was developed as a valid and reliable measure of quality of recovery after anesthesia and surgery.^[4] The 40 questions that make up the QoR-40 are classified into 5 dimensions, which include emotional state, physical comfort, psychological support, physical independence, and pain, and each question is scored from worst (1 point) to best (5 points).^[3]

Lee et al^[4] assessed the QoR-40 between propofol TIVA and desflurane anesthesia on postoperative days 1 and 2 (POD1 and POD2). From this previous study, QoR-40 on POD1 in TIVA

was significantly better than that in desflurane anesthesia (mean value 174 vs 161, respectively), and the scores of physical comfort and physical independence on POD1 and POD2 among the 5 dimensions were significantly higher in TIVA. These results confirm the superiority of propofol TIVA over the quality of recovery during overall postoperative recovery period, but it is difficult to confirm the quality of recovery immediately after surgery, which may be an important issue in ambulatory surgery. From our results, QoR-40 on the day of surgery was also improved in propofol TIVA compared with desflurane anesthesia. Therefore, the use of propofol TIVA is expected to contribute to the improvement of functional recovery after general anesthesia not only in surgery under admission but also in ambulatory surgery.

From our study, propofol TIVA showed significant higher scores in physical comfort and physical independence dimensions of the QoR-40 on the day of surgery compared with desflurane anesthesia. These results were consistent with the results from Lee et al's^[4] study. The physical comfort is composed of questions related to alleviation of short-term effects (eg, breathing, sleep, eating, resting, nausea, vomiting, dry retching, restlessness, and dizziness) after anesthesia and surgery. Hence, this domain may provide information regarding side effects and problems inherent in patients with ambulatory surgery.^[4,24] Previous studies have demonstrated that TIVA decreases postoperative nausea and vomiting (PONV) compared with inhalation anesthesia.^[25,26] Lee et al's study also showed lower incidence of PONV on POD1 in TIVA.^[4] Therefore, less PONV in patients with TIVA may have improved their physical comfort compared with using inhalation anesthesia. The physical independence mainly reflects the ability to conduct daily physical activities such as writing, working, speech, communication, and washing, which is related with rapid resumption of normal activities.^[3,4] Although the greater use of remifentanyl and delayed awakening time were observed in our study, TIVA provided better quality of recovery on the day of surgery. Based on these results, we could assume that rapid recovery of consciousness or respiration immediately after anesthesia does not necessarily guarantee good quality of recovery.

Studies have demonstrated that preoperative dexamethasone improves quality of recovery.^[27,28] These results suggest that quality of recovery may be related to the modulation of inflammatory and stress response, which were stimulated by surgical trauma and anesthesia.^[4,29] Propofol may inhibit pro-inflammatory cytokine including interleukin (IL)-6, IL- β , and tumor necrosis factor (TNF)- α , and enhance anti-inflammatory cytokine and free radical scavenging.^[30,31] In addition, the

increase of serum glucose level induced by perioperative stress was attenuated in TIVA, compared with inhalation anesthesia.^[32] Therefore, propofol TIVA might provide better quality of recovery by modulating the perioperative stress and inflammation responses adequately.

Some previous studies have shown that TIVA provided better postoperative analgesia compared to inhalation anesthesia.^[30,33,34] In vivo studies have found that propofol may modulate N-methyl-D-aspartate (NMDA) receptor,^[35,36] which plays an important role in pain signaling pathway.^[30,37] Aforementioned anti-inflammatory and NMDA receptor antagonistic properties of propofol may be suggested as the mechanisms of postoperative analgesic effect.^[30] However, the present study did not show significant differences in postoperative pain scores and pain dimension of QoR-40 between TIVA and desflurane anesthesia. Lee et al's^[4] study also reported no difference of pain dimension between the 2 anesthetic methods. Recent retrospective case-controlled study did not prove superiority of propofol in terms of postoperative pain.^[38] The effect of propofol on postoperative analgesia should be further elucidated through further studies.

There are some limitations or considerations to this study. First, the preoperative QoR-40 was not evaluated in this study. However, there was no difference in demographic data among patients. Additionally, some studies also obtained reliable results without preoperative QoR-40 scoring.^[13,39] Second, the Korean version of the questionnaire used in this study was not yet validated. However, the questionnaire used plain language that was not likely to change in meaning after translation. For this reason, the Korean version of the QoR-40 has been used in several studies.^[4,13] Thus, the effect of language differences on the results of the study may be insignificant. Third, since the sample size was calculated to detect the difference in total QoR-40 score between the 2 anesthetic methods, the sample size may not be sufficient to compare each dimension of QoR-40 and other postoperative outcomes, including nausea/vomiting and pain score between groups. Lastly, because we enrolled patients undergoing vitrectomy, our study results should be generalized with caution to those who receive other types of ambulatory surgery.^[4]

5. Conclusions

In conclusion, propofol TIVA showed the improved quality of recovery on the day of surgery than desflurane inhalation anesthesia. For vitrectomy under ambulatory setting, propofol TIVA should be preferentially considered as a general anesthetic method to facilitate patients' rapid resumption of normal activity. Given the limited external generalization of our results, further research is required to determine whether propofol improves the quality of recovery in other types of ambulatory surgery.

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