

SAFETY & QUALITY

Type of anaesthesia and patient quality of recovery: a randomized trial comparing propofol–remifentanyl total i.v. anaesthesia with desflurane anaesthesia

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Editor's key points

- Patient-centred outcome measures after surgery can include a quality of recovery score.
- Female patients typically have a poorer quality of recovery after surgery.
- Total i.v. anaesthesia can improve recovery characteristics in some settings.
- Individually titrated anaesthetic drug administration may improve the quality of recovery after surgery.

Background. Two common general anaesthetic methods are total i.v. anaesthesia (TIVA) and inhalation anaesthesia, but it is unclear whether this affects the patient's perception of their quality of recovery. The Quality of Recovery-40 questionnaire (QoR-40) is a valid and reliable method to evaluate the extent of functional recovery after surgery with general anaesthesia. This study therefore compared patient recovery using the QoR-40 in surgical patients who received TIVA with those who received desflurane anaesthesia.

Methods. Eighty females (20–65 years old) undergoing thyroid surgery were prospectively recruited and randomized to either the TIVA (effect-site target controlled infusion using propofol and remifentanyl) or DES (desflurane inhalation with manual infusion of remifentanyl) groups. The QoR-40 was administered by an investigator blind to group allocation before surgery, and postoperative days 1 and 2 (POD1 and POD2). Additional data including the incidence of nausea or vomiting, the consumption of antiemetic and analgesic agents in the post-anaesthesia care unit, and the duration of the hospital stay, were collected in all cases.

Results. The QoR-40 score on POD1 was significantly higher in the TIVA group compared with the DES group (174 vs 161, respectively; $P=0.004$), indicating a better quality of recovery in the TIVA group. Among the five dimensions of the QoR-40, physical comfort and physical independence were significantly better on POD1 and POD2 in the TIVA group.

Conclusion. This study demonstrates that the quality of recovery for female thyroid surgery patients is significantly better with TIVA compared with desflurane anaesthesia.

Clinical trial registration. www.clinicaltrials.org; ref.: NCT01760018.

Keywords: anaesthetics i.v., propofol; anaesthetics volatile, desflurane; recovery, postoperative

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Anaesthesia and surgery have certain inevitable negative impacts on the quality of life of patients, manifest as various discomforts after surgery even without specific complications. Moreover, prolonged recovery after surgery can lead to delayed hospital discharges and increased costs, which can impact resource utilization and mitigate patient satisfaction.^{1 2} As the clinical environment moves to perform more surgeries as ambulatory procedures with quicker discharge rates, anaesthesiologists must consider techniques that provide both fast and high quality recovery that minimizes both minor morbidities and the time to resume daily activities.³

The two most common general anaesthesia techniques are total i.v. anaesthesia (TIVA) and inhalation anaesthesia.⁴ Most

studies, however, have analysed primarily fragmentary measures such as recovery time, cardiorespiratory perturbations, pain, nausea and vomiting, duration of the hospital stay, or other various adverse sequelae.^{5 6} Such piecemeal factors do not sufficiently reflect patient recovery from general anaesthesia. A measurement that probes quality of life from the perspective of the patient is therefore an important factor in clinical studies that wish to investigate the effect of anaesthesia and surgery on patient recovery and satisfaction.⁵

The Quality of Recovery-40 questionnaire (QoR-40) probes a patient's recovery from general anaesthesia using five dimensions of health: physical comfort, physical independence, emotional state, psychological support, and pain. The validity,

reliability, ease of use, and responsiveness of the QoR-40 has been confirmed in previous studies,^{2,6} and has been used successfully to assess the degree of recovery after several different surgical and anaesthetic techniques. Few if any studies have used the QoR-40 to probe recovery outcomes after the administration of TIVA compared with volatile anaesthetics. We therefore compared recovery outcomes between patients who received effect-site target controlled infusion (TCI) of propofol and remifentanyl (i.e. TIVA) and patients who received desflurane anaesthesia supplemented with remifentanyl. The QoR-40 questionnaire was administered before surgery and 1 and 2 days post-surgery (POD1 and POD2, respectively) in female patients scheduled for thyroidectomy who were randomly assigned to receive either propofol and remifentanyl (TIVA group) or desflurane and remifentanyl (DES group).

Methods

This double-blind, randomized trial was approved by the Institutional Review Board at Severance Hospital (4-2012-0748) and registered with ClinicalTrials.gov (NCT01760018). Written informed consent was obtained from all participants.

We enrolled female patients aged 20–65 yr old with an ASA physical status I–II who were undergoing thyroid surgery for neoplasm. Patients who were taking any sedative, opioid, or sleep aid drugs, who had an allergic history of any study drug, who were obese as defined by a BMI of more than 30 kg m⁻², or who were pregnant or breastfeeding, were excluded from the study.

Each patient was randomly assigned to the TIVA or DES group. Patients in the TIVA group were administered anaesthesia using an effect-site TCI of propofol and remifentanyl, and patients in the DES group were administered anaesthesia using desflurane and a manually controlled infusion of remifentanyl. Randomization was done on the morning of surgery using a web-based random-number generator available at www.random.org. Because of significant differences between the two anaesthetic techniques, the attending anaesthesiologist could not be blinded to group identity. Both the patient and the investigators were however blinded to group identity.

Study patients did not take any medications before surgery. Routine monitoring, including SpO₂, electrocardiogram, non-invasive arterial pressure, nasopharyngeal temperature, and measurement of the bispectral index (BIS VISTA Monitoring System; Aspect Medical Systems, Inc., Norwood, MA, USA) were commenced upon arrival to the operating theatre. Each measure was recorded every 1–5 min. Patients randomized to the TIVA group received an effect-site TCI of propofol and remifentanyl using a commercial TCI pump (Orchestra[®] Base Primea, Fresenius Vial, Brezins, France). TCI pump operation was based on Schnider's pharmacokinetic model for propofol and Minto's model for remifentanyl.^{7,8} Induction and maintenance was achieved with TCI propofol, 2–6 µg ml⁻¹, and remifentanyl, 2–6 ng ml⁻¹. In contrast, anaesthetic induction was achieved in the DES group with a bolus administration of 1.5–2 mg kg⁻¹ of propofol and 1–2 µg kg⁻¹ of remifentanyl, and anaesthesia was maintained using 4–7% desflurane with

an adjuvant i.v. infusion of 0.05–0.2 µg kg⁻¹ min⁻¹ of remifentanyl. Rocuronium, 0.6 mg kg⁻¹, was injected to facilitate tracheal intubation in all patients. Tracheal intubation was performed in all patients using a 6.5 mm (internal diameter) tracheal tube. Cuff pressure was maintained at 20–25 cm H₂O throughout the procedure. Mechanical ventilation was maintained with a tidal volume of 8 ml kg⁻¹ and ventilatory frequency was adjusted to maintain an end-tidal carbon dioxide concentration of 4.6–5.3 kPa with an air/oxygen mixture (fraction of inspired oxygen 0.5). Body temperature was maintained at 36–37°C. In both groups, the anaesthetic depth was titrated to maintain a BIS range between 40 and 55, and mean arterial pressure within 20% of pre-induction values.

Ramosetron, 0.3 mg, was used for antiemetic prophylaxis and ketorolac, 0.5 mg kg⁻¹, was used for analgesia, i.v. administered 30 and 10 min before the end of the surgery, respectively. Upon completion of the surgery all anaesthetics were discontinued, and 0.07 mg kg⁻¹ of neostigmine with 0.05 mg kg⁻¹ of glycopyrrolate was administered i.v. to reverse possible residual neuromuscular blocking. The tracheal tube was removed after consciousness was regained and sufficient spontaneous respiration was confirmed. After stable vital signs and respiration were confirmed, the patients were transferred to the post-anaesthesia care unit (PACU).

Pain, and postoperative nausea and vomiting (PONV), were measured using an 11-point numeric rating score upon arrival in the PACU and every 5 min thereafter. Fentanyl, 50 µg, or metochlorpromide, 10 mg, were administered for pain or PONV, respectively, if the rating of each respective item exceeded 4. The patients were discharged to the post-recovery ward when the Aldrete score was 9 or more.⁹

The quality of postoperative functional recovery was assessed using the QoR-40 questionnaire, which assesses five dimensions of recovery: physical comfort (12 items), emotional state (9 items), physical independence (5 items), psychological support (7 items), and pain (7 items). Each item was rated on a five-point Likert scale: none of the time, some of the time, usually, most of the time, and all of the time. The total score on the QoR-40 ranges from 40 (poorest quality of recovery) to 200 (best quality of recovery). The QoR-40 was administered three times, the day before surgery, POD1, and POD2, between 6 and 8pm. The primary outcome of interest was the QoR-40 score on POD1. The following data were collected as additional outcomes of interest: intraoperative and immediate postoperative vital signs, the total amount of remifentanyl used during surgery, the duration of time between the discontinuation of anaesthetic agents and response to a verbal command (response time), the duration of time between the discontinuation of anaesthetic agents and extubation (extubation time), the duration of the PACU stay, and the incidence of nausea in the ward.

Statistical analyses

The primary outcome was the global QoR-40 score on POD1. Our sample size calculation was based on the assumption that a difference in QoR-40 score of 10 or more would be

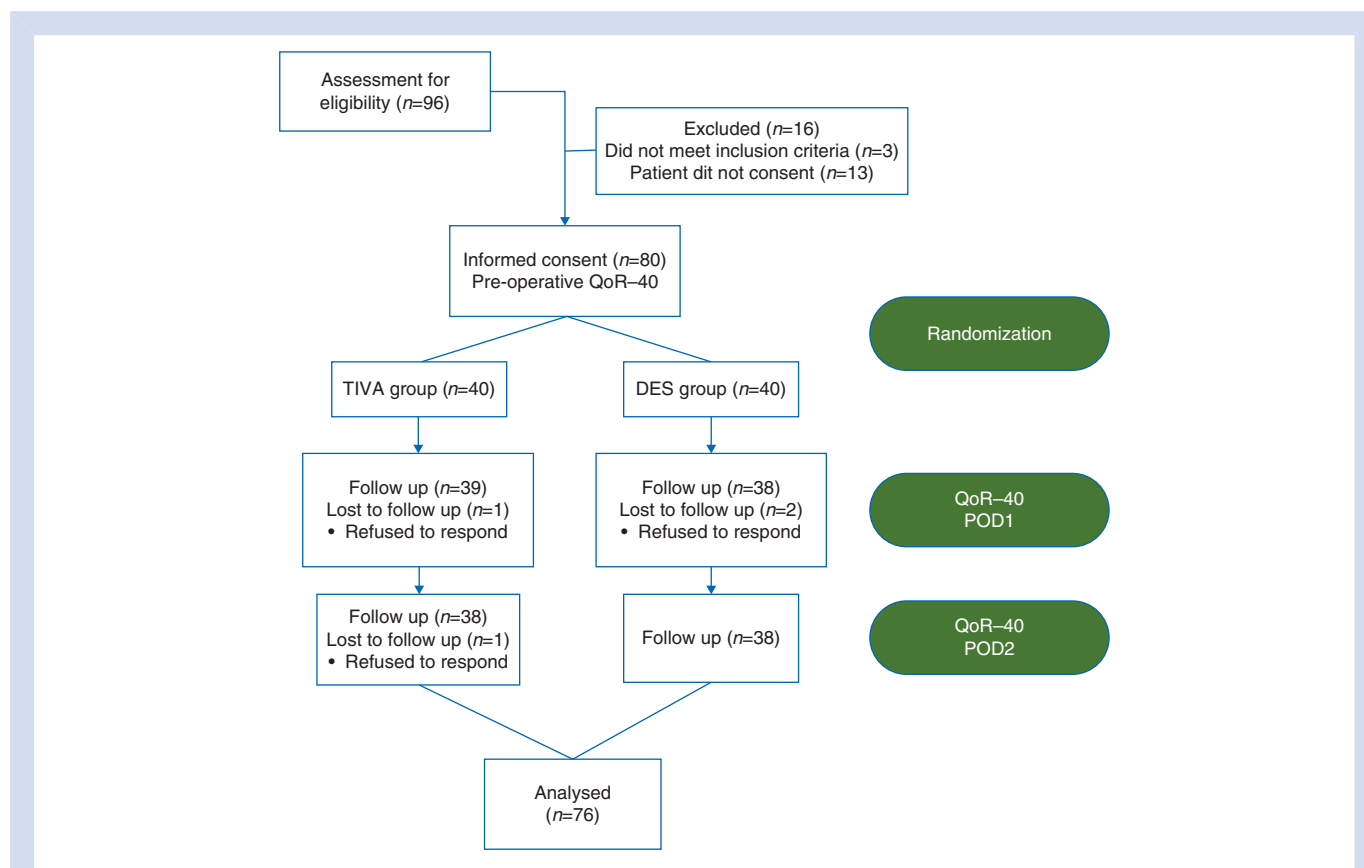


Fig 1 A flowchart that outlines patient selection, randomization, and analysis.

clinically significant because a 10-point difference represents a 15% improvement in the quality of recovery.¹⁰ Sample size calculations revealed that 34 subjects per group were required to achieve a power of 90% with a type 1 error of 0.05. In order to allow for a drop-out rate of up to 20%, we enrolled 80 subjects. Categorical data were compared using Fisher’s exact test. Ordinal data and non-Gaussian continuous data (presented as the median and range) were compared between groups using the Wilcoxon rank-sum test. Normally distributed data (presented as the mean and *sd*) were compared between groups using a two-sample independent *t*-test. A *P*-value of <0.05 was considered statistically significant.

Results

A total of 96 patients were assessed for eligibility and 80 patients were consented and randomly assigned into the study. Four of these 80 patients were withdrawn from the study. We therefore collected and analysed data from 76 patients. The flowchart in Figure 1 outlines the number of patients at each stage of the study and includes the reasons for exclusion at each stage. The patient characteristics of the patients who were included in the study are presented in Table 1. The duration of anaesthetic usage was comparable between both groups (Table 1).

The preoperative, POD1, and POD2 QoR-40 scores are presented in Table 2. The preoperative QoR-40 score was similar

Table 1 Patient characteristics of patients in the TIVA and DES groups. Data are presented as mean (range) for age, mean (*sd*), or number of patients (%) as appropriate. TIVA, total i.v. anaesthesia; DES, desflurane; MBP, mean blood pressure; PR, pulse rate

	TIVA group (n=38)	DES group (n=38)
Age (yr)	43.6 (23–60)	40.0 (25–61)
Height (cm)	160.1 (3.8)	160.1 (5.7)
Weight (kg)	59.2 (8.0)	56.6 (6.5)
BMI	23.1 (3.0)	22.1 (2.8)
ASA class I/II	19 (50)/19 (50)	24 (63)/14 (37)
Hospital stay duration (days)	5.13 (0.7)	5.16 (0.6)
Anaesthetic duration (min)	107.6 (44.5)	127.9 (55.9)
Robotic surgery/open surgery	11 (29)/27 (71)	17 (45)/21 (55)
Baseline vital signs		
MBP (mm Hg)	72 (14)	85 (20)
PR (beats min ⁻¹)	72 (9)	75 (12)

between the two groups (*P*=0.46). A significant difference (*P*=0.004) in QoR-40 scores was observed between the two groups on POD1 (174 vs 161 between the TIVA and DES groups, respectively). This difference seemed to persist, but

Table 2 QoR-40 scores between the TIVA and DES groups preoperatively, and on postoperative days 1 (POD1) and 2 (POD2). Data are presented as mean (SD). QoR-40, The 40-item Quality of Recovery 40 questionnaire; TIVA, total i.v. anaesthesia; DES, desflurane

	TIVA group	DES group	P-value
Preoperative			
Emotional status	39 (7.3)	41 (4.8)	–
Physical comfort	54 (8.6)	55 (5.4)	–
Psychological support	32 (3.9)	32 (3.6)	–
Physical independence	24 (2.6)	24 (2.7)	–
Pain	31 (5.4)	33 (2.8)	–
Total QoR-40	181 (24)	184 (14)	–
POD1			
Emotional status	40 (4.8)	38 (5.4)	0.11
Physical comfort	52 (5.9)	47 (8.6)	0.002
Psychological support	33 (2.8)	31 (3.8)	0.004
Physical independence	21 (3.4)	18 (4.7)	0.002
Pain	28 (4.3)	27 (4.5)	0.33
Total QoR-40	174 (17)	161 (22)	0.004
POD2			
Emotional status	42 (5.3)	40 (6.3)	0.14
Physical comfort	56 (5.0)	52 (7.5)	0.008
Psychological support	33 (3.5)	32 (3.6)	0.32
Physical independence	23 (2.5)	22 (3.4)	0.019
Pain	31 (4.7)	31 (4.0)	0.81
Total QoR-40	185 (18)	176 (21)	0.056

was not statistically significant ($P=0.056$), on POD2 (185 vs 176 between the TIVA and DES groups, respectively). Among the five dimensions of the QoR-40, physical comfort and physical independence scores were significantly higher in the TIVA group compared with the DES group on POD1 and POD2.

In the TIVA group, scores for the physical independence and pain dimensions were statistically reduced in POD1 compared with preoperative scores; however, they were restored to their preoperative scores on POD2. The other three dimensions did not change significantly after surgery in the TIVA group. In the DES group, the scores on all dimensions, except psychological support, were reduced significantly on POD1 compared with preoperative scores, and these reductions persisted on POD2.

The perioperative data are presented in Table 3. Heart rate and the BIS around the time of tracheal extubation were significantly higher in the DES group, and the amount of remifentanyl administered was higher in the TIVA group. The recovery response time and the tracheal extubation time were similar between the two groups. During the PACU stay, 7 patients in the DES group and 1 patient in the TIVA group complained of nausea, and 5 patients in the DES group took an additional antiemetic. On the ward, 26 patients in the DES group complained of nausea on POD1 compared with 17 patients in the TIVA group ($P=0.037$); this difference waned on POD2.

Table 3 Perioperative data comparisons between the TIVA and DES groups. Data are presented as mean (SD). TIVA, total i.v. anaesthesia; DES, desflurane; PR, pulse rate; BIS, bispectral index; Response time, time from cessation of main anaesthetics to patients' response to verbal command; tracheal extubation time, time from cessation of anaesthesia to tracheal extubation; remifentanyl usage, total amount of remifentanyl during intraoperative period; PACU, post-anaesthesia care unit; POD1, postoperative day 1; POD2, postoperative day 2

	TIVA group	DES group	P-value
Intraoperative period			
PR, 10 min after induction (beats min ⁻¹)	69.8 (9.4)	81.5 (15.7)	0.000*
PR, cessation of main anaesthetics (beats min ⁻¹)	62.3 (11.3)	69.6 (13.2)	0.012*
PR at tracheal extubation (beats min ⁻¹)	74.0 (12.0)	98.1 (21.3)	0.000*
BIS at tracheal extubation	80.7 (5.5)	85.5 (8.1)	0.004*
Response time (min)	5.5 (2.7)	5.0 (5.8)	0.32
Tracheal extubation time (min)	6.3 (2.9)	5.8 (1.7)	0.35
Remifentanyl usage (µg)	715.7 (322.8)	652.8 (260.7)	0.35
PACU			
PR, admission to PACU (beats min ⁻¹)	68.7 (12.7)	92.5 (19.3)	0.024
PR, discharge from PACU (beats min ⁻¹)	64.1 (8.9)	82.2 (15.0)	0.025
Duration in PACU (beats min ⁻¹)	42.2 (13.1)	38.0 (11.3)	0.14
Nausea	1	7	0.056
Use of antiemetic drug	0	5	0.069
Postoperative period			
Nausea on POD1	17	26	0.037
Nausea on POD2	7	11	0.28

Discussion

The present study demonstrated a significant improvement in the patient's perceived quality of recovery in those receiving TIVA compared with those receiving desflurane anaesthesia. TIVA resulted in significantly less reduction of the QoR-40 score on POD1 compared with the preoperative score, and was associated with a significantly higher score compared with desflurane anaesthesia. This difference seemed to persist to POD2, but the difference was no longer statistically significant.

Several comparisons between TIVA and volatile anaesthetics have been conducted previously. Traditionally, anaesthesiologists have regarded a desirable recovery as one in which consciousness is restored quickly with stable vital signs, and all perioperative physicians have regarded a desirable recovery to be free of serious complications with early hospital discharge. Patients, however, regard a good recovery to include improved comfort and impact on their quality of life in the early postoperative period.^{11 12} Conventional measures typically used by anaesthesiologists and surgeons often do not address patient quality of recovery, the time to restoration of normal daily

activities, and overall patient satisfaction. Few studies have compared the overall quality of recovery between TIVA and the volatile anaesthetic agent desflurane from the patient's perspective. Our results show that the anaesthetic method influences patient-perceived quality of recovery.

The most significant differences between the TIVA and DES groups were on the physical comfort and physical independence dimensions. The items on these dimensions include breathing, sleeping, eating, tiredness, nausea/vomiting, shivering, and the ability to perform daily physical activities such as working, writing, communicating, and washing. The physical comfort dimension is known to capture additional information about side-effects and may provide valuable insights into when these problems subside in patients undergoing outpatient surgery.¹³ For example, prior studies have shown that TIVA reduces PONV compared with volatile anaesthesia.^{14–17} Less nausea and vomiting was observed among patients who received TIVA in our study, which may have improved their perception of physical comfort compared with the DES group.

Alongside the impact on PONV, the other reason why physical comfort may have been rated higher in the TIVA group in our study is that each anaesthetic method could have differentially affected the modulation of the stress response.⁴ Anaesthesia and surgical trauma inevitably stimulate immunological and inflammatory responses. Studies have shown that the preoperative use of dexamethasone enhances patient satisfaction and quality of recovery,^{3 11} which suggests that the modulation of inflammatory and stress responses is associated with an improvement in the quality of recovery. Compared with volatile anaesthesia, i.v. anaesthesia with propofol may limit stress-related hormone and pro-inflammatory cytokines and to generate marked increases in anti-inflammatory cytokines.⁴ Additionally, serum glucose increase induced by surgical stress is also attenuated in TIVA.¹⁸ Together, these differences in the modulation of stress hormones and inflammatory responses between propofol and volatile anaesthetics suggest an effect on comprehensive recovery after general anaesthesia. In contrast however, some studies have found more positive outcomes with volatile anaesthesia.^{19 20} Attention is therefore required in the interpretation of these studies because different surgical types induce various types and degrees of stress and inflammation. In addition, another possible reason of our result is that anaesthesia with desflurane may lead to significantly impaired bronchociliary clearance compared with TIVA, which can lead to the retention of secretions, atelectasis, and lower respiratory tract infections and may therefore influence a patient's physical comfort.²¹

Some studies have also reported better neuroprotective and analgesic properties after TIVA compared with volatile anaesthetics.^{22–24} In the present study, the pain dimension of the QoR-40 was not different between the TIVA and DES groups. The questionnaire, however, includes items about extra-surgical pain such as headache, muscle pain, back pain, sore throat, and sore mouth. Pain comparisons across different anaesthetic techniques must therefore also account for the type of surgery that has been performed.

The QoR-40 was developed in 2000 by Myles and colleagues,⁵ and to date remains the only quality of recovery measurement instrument that fulfils the requirements for appropriateness, reliability, validity, responsiveness, precision, interpretability, acceptability, and feasibility.^{6 25} In a systematic review and meta-analysis the mean QoR-40 score in those without and with complications were 170 and 159, respectively, with a weighted mean difference of 11.⁶ The QoR-40 has been used in patients of both sexes and across all adult age groups, diverse cultural backgrounds, and different surgical types and anaesthetic techniques. The results of the QoR-40 can be generalized, therefore, to different situations.⁶ In the present study, the QoR-40 score in the TIVA group was 174 compared with a score of 160 in the DES group on POD1 with a difference of 14 points. Our results, therefore, seem to show a significant and large differential effect of TIVA and desflurane anaesthesia on functional recovery. The quality of recovery on the day after an anaesthetic procedure is known to be associated with recovery weeks and perhaps years afterwards. For example, a poor QoR-40 score on post-operative day 3 after cardiac surgery predicted poor quality of life 3 months after the surgery.²⁶ Although we did not conduct a long-term follow-up in the patients who participated in the present study, these results suggest value in a patient's later health status.

Poor quality of recovery negatively affects both the patient and the medical team. From the patient's perspective, a delayed return to normal activity lowers the patient's satisfaction for the medical services they received, and the patient also may suffer from significant postoperative discomfort. A prolonged stay in the recovery room or a delay of hospital discharge has a significant impact on resource utilization for the medical team. Every effort should be devoted, therefore, to improve patient satisfaction and resource utilization, especially in minor less-invasive surgeries.

There were several limitations to this study. First, we used the Korean written version of the QoR-40 questionnaire,²⁷ which has not been formally validated. However, a previous study has used the Korean version of the QoR-40 with reliable results.²⁸ In addition, the range of scores obtained in the present study is comparable with several prior studies. The mean total score in the DES group was 160.5, which is similar to the score of 161 observed in a control group who underwent minor surgery.³ The language difference, therefore, may not have skewed the results of the present study. A second limitation is that the sample size was calculated for the detection of differences in the total QoR-40 score between the TIVA and DES groups. This sample size may therefore be inadequate to compare each of the different dimensions between groups. Thirdly, the enrolled patients were relatively healthy, young and female undergoing relatively minor surgery. So our results may not be generalized to those with serious comorbidities or those undergoing more complex surgery.

In conclusion, we demonstrated that female patients undergoing thyroid surgery who were randomized to the TIVA group perceived a better quality of recovery on POD1 and POD2 compared with patients in the DES group. TIVA is less likely to

decrease a patient's physical function, which leads to better recovery. TIVA should be considered an anaesthetic technique of choice to facilitate a patient's rapid return to their normal activity.

Authors' contributions

W.-K.L.: this author helped to plan and conduct the study, analyse the data, and write the manuscript; M.-S.K.: this author helped to plan the study, analyse the data, and write the manuscript; S.-W.K.: this author helped to plan and conduct the study, and write the manuscript; S.K.: this author helped to plan and conduct the study, and write the manuscript; J.-R.L.: this author to helped plan and conduct the study, analyse the data, and write the manuscript.

Declaration of interest

None declared.

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