

# Ultrasound-guided Multilevel Paravertebral Blocks and Total Intravenous Anesthesia Improve the Quality of Recovery after Ambulatory Breast Tumor Resection

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## ABSTRACT

**Background:** Regional anesthesia improves postoperative analgesia and enhances quality of recovery (QoR) after ambulatory surgery. This randomized, double-blinded, parallel-group, placebo-controlled trial examines the effects of multilevel ultrasound-guided paravertebral blocks (PVBs) and total intravenous anesthesia on QoR after ambulatory breast tumor resection.

**Methods:** Sixty-six women were randomized to standardized general anesthesia (*control group*) or PVBs and propofol-based total intravenous anesthesia (*PVB group*). The *PVB group* received T1–T5 PVBs with 5 ml of 0.5% ropivacaine per level, whereas the *control group* received sham subcutaneous injections. Postoperative QoR was designated as the primary outcome. The 29-item ambulatory QoR tool was administered in the preadmission clinic, before discharge, and on postoperative days 2, 4, and 7. Secondary outcomes included block success, pain scores, intra- and postoperative morphine consumption, time to rescue analgesia, incidence of nausea and vomiting, and hospital discharge time.

**Results:** Data from sixty-four patients were analyzed. The *PVB group* had higher QoR scores than *control group* upon discharge (146 vs. 131;  $P < 0.0001$ ) and on postoperative day 2 (145 vs. 135;  $P = 0.013$ ); improvements beyond postoperative day 2 lacked statistical significance. None of the *PVB group* patients required conversion to inhalation gas-based general anesthesia or experienced block-related complications. *PVB group* patients had improved pain scores on postanesthesia care unit admission and discharge, hospital discharge, and postoperative day 2; their intraoperative morphine consumption, incidence of nausea and vomiting, and discharge time were also reduced.

**Conclusion:** Combining multilevel PVBs with total intravenous anesthesia provides reliable anesthesia, improves postoperative analgesia, enhances QoR, and expedites discharge compared with inhalational gas- and opioid-based general anesthesia for ambulatory breast tumor resection. (**ANESTHESIOLOGY 2014; 120:703-13**)

**P**ERIPHERAL nerve blocks provide several proven benefits when used as an alternative to general anesthesia (GA) in ambulatory surgery, including improved postoperative analgesia and shortened postanesthesia care unit (PACU) stay.<sup>1</sup> There is also evidence that the quality of recovery (QoR), a patient-based outcome measure evaluated by the QoR multidimensional assessment tool,<sup>2,3</sup> may be improved when regional anesthesia techniques replace GA for ambulatory surgery.<sup>4,5</sup> Furthermore, evidence suggesting that the choice of anesthetic technique influences the incidence rates

### What We Already Know about This Topic

- Regional anesthesia improves quality of recovery after surgery in many studies
- Previous studies with paravertebral blocks in this regard are limited due to high failure rate of landmark-guided techniques

### What This Article Tells Us That Is New

- By using ultrasound guidance, quality of recovery was improved in 64 women randomized to multilevel paravertebral blocks and total intravenous anesthesia for breast tumor resection compared with general anesthesia with sevoflurane and morphine

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of recurrence and metastasis after tumor resection underscores the importance of reliable GA alternatives.<sup>6–11</sup> In fact, several editorials have predicted that the future anesthetic of choice for tumor resection surgery will be one that minimizes the use of inhalational gases and opioids while capitalizing on the role of regional anesthesia techniques.<sup>12–15</sup>

The combination of thoracic paravertebral blocks (PVBs) and total intravenous anesthesia (TIVA) as an alternative to GA for breast tumor resection has been examined in several trials.<sup>16–19</sup> The identified advantages of the landmark-guided PVB technique include reduced postoperative pain, analgesic consumption, opioid-related side effects, and shorter PACU stay. However, the relatively high failure rates in achieving adequate surgical anesthesia associated with the use of landmark-guided PVB technique, reported to vary between 18.8<sup>16</sup> and 27.3%<sup>20</sup> for procedures more complex than simple lumpectomy, preclude its use as an alternative to conventional GA and may impede the full exploration of its benefits in breast tumor resection. Ultrasound guidance is believed to improve peripheral nerve block success rates.<sup>21,22</sup> An ultrasound-guided PVB technique was first described by Hara *et al.*<sup>23</sup> in 2009, with several alternative approaches subsequently described.<sup>24–28</sup> Whether the ultrasound-guided PVB technique combined with TIVA is capable of providing reliable surgical anesthesia for complex ambulatory breast tumor resection procedures, and the impact of this anesthetic technique on the postoperative QoR are areas that have not yet been explored.

This randomized, controlled trial is the first to examine the effects of an anesthetic that combines ultrasound-guided multilevel PVBs with TIVA (devoid of inhalational gas and opioids) on the QoR after ambulatory breast tumor resection. We hypothesized that such an anesthetic technique would enhance the patient-perceived QoR. Our secondary aims were to demonstrate the reliability of such an anesthetic technique and to evaluate its effect on analgesic outcomes (*e.g.*, pain, morphine consumption, incidence of nausea and vomiting, and hospital discharge time).

## Materials and Methods

All study procedures were completed at the Women's College Hospital (from July 2011 to February 2013), a University of Toronto–affiliated ambulatory center located in Toronto, Canada. This single-center study was approved by the Women's College Hospital Research Ethics Board and registered (NCT01654432) at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) after commencement of recruitment. After obtaining written informed patient consent, we enrolled women patients with American Society of Anesthesiologists physical status I to II who were scheduled for elective unilateral breast tumor resection in a prospective, randomized, double-blind, parallel-group, placebo-controlled clinical trial. The surgical procedures performed included partial mastectomy with sentinel lymph node biopsy; mastectomy; mastectomy with sentinel lymph node biopsy; modified radical mastectomy (mastectomy with axillary lymph node dissection); and mastectomy with implant insertion. Recruitment was

performed through the preadmission clinic; eligible patients were contacted during their visit before the scheduled procedure and were provided with a printed information package outlining the purpose of the study. Exclusion criteria included nonsuitability for regional anesthesia as deemed by the anesthesiologist assessing the patients in the preadmission clinic; contraindications to PVBs such as coagulopathy, infection, or history of allergy with local anesthetic agents; language barrier; body mass index greater than 35 kg/m<sup>2</sup>; age less than 18 or more than 85 yr; and history of gastroesophageal reflux disease. Consenting patients were randomized on a 1:1 ratio with no restrictions to receive either thoracic PVBs at the T1–T5 thoracic levels with TIVA consisting of propofol-based GA (*PVB group*) or sham subcutaneous local anesthetic injections with sevoflurane-based GA and opioid-based analgesia (*control group*). Randomization was performed by an investigator not involved in patient care using Random Allocation Software 2.0<sup>®</sup> (Isfahan University of Medical Sciences, Isfahan, Iran). A computer-generated sequence was used to allocate patients to the study groups; the allocation results were concealed in sealed opaque envelopes, which were not opened until the procedure day. Patients remained blind to the outcome of randomization until the conclusion of the study and the collection of all outcome data.

## Preoperative Procedure

Unless contraindicated, all patients received premedication with celecoxib 400 mg and acetaminophen 1,000 mg orally 1 h before surgery. After intravenous (IV) access was secured, standard monitoring including noninvasive blood pressure, pulse oximetry, and electrocardiogram was applied; oxygen was also delivered by face mask at a rate of 8 l/min. For anxiolysis and analgesia, all patients received IV midazolam 1–4 mg and/or fentanyl 25–50 µg as needed before block performance. All PVB and sham blocks were performed preoperatively in the prone position at the T1–T5 levels. In both groups, skin preparation with chlorhexidine 2% swabs of the upper back was performed, followed by scanning of the upper thoracic portion of the back, ipsilateral to the surgical side, using a 2–6 MHz curved array ultrasound transducer probe (model Z.one ultra; Zonare, Mountain View, CA) placed in a sterile sleeve. The probe was positioned in the vertical plane approximately 2–2.5 cm lateral to the spinous process to allow a parasagittal view of the transverse processes, parietal pleura, superior costotransverse ligaments, and to localize the desired paravertebral spaces ipsilateral to the surgical side for all patients. A skin wheal was created at the midpoint between two adjacent transverse processes using a 25-gauge needle to inject 1 ml of 1% lidocaine.

## Block Technique

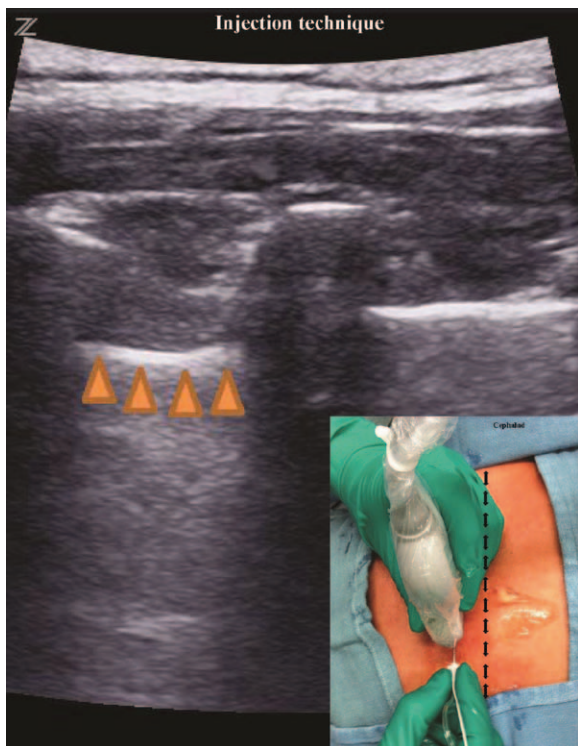
Starting with paravertebral space at the T1 level and proceeding caudally to T5, a 22 gauge, 50-mm, blunt insulated nerve block needle (B. Braun Medical Inc., Bethlehem, PA) was introduced in an in-plane approach relative to the ultrasound transducer toward the paravertebral space (*fig. 1*).<sup>28</sup> The needle was advanced under direct vision in a cephalad

orientation to puncture the superior costotransverse ligament at the desired level. We used the hydrolocation technique by injecting 0.5–1 ml saline to localize the needle tip and confirm proper placement in paravertebral space by observing anterior displacement of the parietal pleura upon injection (fig. 1). A volume of 5 ml ropivacaine 0.5% was then slowly injected after negative aspiration. Patients in the *PVB group* received a total volume of 25 ml of local anesthetics for the purpose of this study. For patients in the *control group*, ultrasound visualization of the thoracic paravertebral spaces was performed at each of the five levels, while applying pressure to the back, to simulate the procedure and duration of an actual PVB. The subcutaneous skin wheals produced by injecting 1 ml of lidocaine 1% at the designated five thoracic levels also served as sham blocks. All blocks were performed by two anesthesiologists (F.W.A. and P.J.M.).

### Intraoperative Procedure

The anesthesiologist providing intraoperative care was aware of group allocation. All patients received GA with a laryngeal mask airway device. GA was induced with IV propofol 2–4 mg/kg. Muscle relaxation was achieved with rocuronium 0.6 mg/kg when specifically requested by the surgeon. Patients in the *control group* also received fentanyl 1 µg/kg for induction. IV dexamethasone 4 mg was administered in all patients after induction of GA.

Anesthesia maintenance in the *PVB group* was achieved with propofol infusion at a rate of 25–50 µg kg<sup>-1</sup> min<sup>-1</sup>,



**Fig. 1.** Injection end point; orange arrows depict the anteriorly displaced pleura. Image in corner illustrates injection technique; dotted line depicts midline.

and patients were allowed to breathe spontaneously a 50:50 air:oxygen mixture. Hemodynamic responses (or patient movement) in response to surgical stimuli were treated by propofol boluses and increasing its infusion rate up to 100 µg kg<sup>-1</sup> min<sup>-1</sup>; if ineffective, opioid boluses of fentanyl to a total dose of 1 µg/kg and then morphine to a total dose of 15 mg were administered. If none of the interventions were successful, sevoflurane was administered.

Anesthesia maintenance in the *control group* was achieved with 1–2 minimum alveolar concentration of sevoflurane or as needed; patients were allowed to breathe spontaneously a 50:50 nitrous oxide:oxygen mixture. Hemodynamic responses or patient movement were treated by morphine boluses as needed to a maximum of 15 mg. Muscle relaxation was reversed with neostigmine 2.5 mg and glycopyrrolate 0.4 mg if muscle relaxants had been administered. Both patient groups received IV ondansetron 4 mg 30 min before the end of surgery, and a warming device (Bair Hugger; Augustine Medical Inc., Eden Prairie, MN) attached to a lower body blanket was used to maintain normothermia. Standard monitoring, including electrocardiogram, noninvasive blood pressure, pulse oximetry, and temperature, was used in all patients for the duration of surgery. All intraoperative medications were recorded including any possible opioid supplementation, other anesthetic agents, or conversion to GA.

### Postoperative Procedure

At the end of the procedure, all patients were transferred to the PACU I where they were monitored until they met the requirements of transfer to the same-day surgery unit (PACU II). PACU nursing staff, unaware of the patient allocation, monitored patients for pain and postoperative nausea and vomiting (PONV). Patients were discharged from PACU II, and eventually from the hospital, once they met the institutional discharge criteria.<sup>29,30</sup>

Patients having pain at rest, a Visual Analogue Scale score of 4/10, or patient request for rescue analgesia, were treated with IV morphine in 2–4 mg increments every 5 min as needed up to a total of 15 mg or with IV hydromorphone 0.2–0.4 mg increments every 5 min as needed up to a total dose of 2 mg. Patients having pain in PACU II was treated with subcutaneous morphine 2.5–5 mg or oral oxycodone 5–10 mg.

The first-line treatment of PONV consisted of IV ondansetron 1–2 mg twice as needed. If this proved ineffective, the second-line therapy consisted of IV dimenhydrinate 12.5–25 mg twice as needed. If this proved ineffective, the third-line therapy consisted of IV metoclopramide 10 mg as needed.

Discharged patients received a prescription for acetaminophen–codeine 300 mg/30 mg 1–2 tabs every 4 h as needed, or acetaminophen–oxycodone 325 mg/5 mg if intolerant to codeine.

### Outcomes

The primary outcome variable, the QoR, was measured by the ambulatory surgery QoR questionnaire.<sup>31</sup> As a validated comprehensive assessment tool,<sup>2,3</sup> the QoR questionnaire is

an increasingly popular tool for evaluating anesthetic interventions.<sup>32–34</sup> Although the original questionnaire was not designed for the ambulatory anesthesia and surgery setting,<sup>33</sup> an ambulatory variant of the questionnaire has been recently introduced and psychometrically tested by Idvall *et al.*<sup>31</sup> The ambulatory variant is a 29-item patient-based outcome measure that examines relevant postoperative quality of life dimensions such as emotional state (8 items), physical comfort (10 items), psychological support (4 items), and physical independence (5 items), in addition to pain (1 item) and general health (1 item). Each item uses a 5-point Likert scale (1 = none of the time and 5 = all of the time for positive items; the scoring is reversed for negative items).<sup>31</sup> The cumulative scores of the ambulatory QoR questionnaire can vary between 29 (extremely poor QoR) and 155 (excellent QoR). A 10-point score difference is considered clinically significant after anesthesia and surgery.<sup>3</sup> We used this tool to assess baseline differences between the two groups in the preadmission clinic preoperatively as well as to evaluate the QoR before discharge and on postoperative days (PODs) 2, 4, and 7 *via* telephonic follow-up.

The onset of sensory block was evaluated as a secondary outcome by the anesthesiologist performing the PVBs every 5 min after the completion of injection for 30 min. Block onset was tested with a 25-gauge needle along the anterior axillary line using a 3-point score: 2 = normal sensation, 1 = decreased sensation to pin prick, or 0 = loss of sensation compared with the normal contralateral chest. PVB success was defined as complete sensory block in all T1–T5 dermatomes within 30 min of injection; in addition, conversion to sevoflurane-based GA was considered block failure. It was decided, *a priori*, that any patients in the *PVB group* who did not achieve a complete sensory block in any of the T1–T5 dermatomes by 30 min would not receive supplemental injections and would be excluded from the study. We also recorded any block-related complications, specifically vascular puncture, hematoma formation, intravascular injection, systemic toxicity, paresthesiae, pleural puncture, pneumothorax, and epidural spread.

The analgesic effects of PVBs were sought as secondary outcomes. Postoperative rest pain Visual Analogue Scale scores upon admission to PACU I, discharge from PACU I, discharge from PACU II, as well as on PODs 2, 4, and 7 were recorded. The cumulative doses of intraoperative supplemental opioids and postoperative opioid analgesics were converted to IV and oral morphine equivalents, respectively.<sup>35</sup> The time to first request of rescue analgesia since PACU I admission, incidence of PONV, time to meet discharge criteria, and time to actual hospital discharge were also recorded. All outcome data were collected by an independent observer (research assistant) blinded to the group allocation. The success of maintained patient blinding was evaluated after completion of the QoR questionnaire on POD 7 by asking patients which block they thought they had received.

### Statistical Analysis

Our sample size estimation for the two-tailed testing of the PVB superiority hypothesis was based on the QoR questionnaire score. We considered a difference in the QoR score at hospital discharge equivalent to 10 as clinically significant<sup>3</sup> in the patients who received PVBs and TIVA (*PVB group*) compared with patients who received a sham block with sevoflurane-based GA and opioid-based analgesia (*control group*). An SD of the QoR score at discharge equivalent to 11.2 was estimated based on our institutional experience with patients undergoing ambulatory breast tumor resection under GA. A power analysis using a type I error estimate of 5% ( $\alpha = 0.05$ ) a power (1-Beta) of 90% indicated that a sample of 27 patients per group would be needed to perform such a comparison. Allowing for an approximate 20% incomplete follow-up or patient drop out, we aimed to enroll a total of 66 patients in this study.

We performed statistical analysis using SAS, version 9.2 (SAS Institute, Inc., Cary, NC). The Kolmogorov–Smirnov test was used to check for normality of distribution. Descriptive statistics were used to analyze the data; continuous data were described using the mean (SD) and ordinal data were described using median (95% CI), whereas categorical data were described using frequencies. For the primary outcome variable-related comparisons, we calculated the median difference and the 95% CI. Variables that were tested by the nonparametric Mann–Whitney U test were presented as median (interquartile range) under the assumption that the shapes of the parent populations from which these data derive do not vary substantially from normality. The nonparametric Mann–Whitney U test was applied when the assumptions of parametric testing with the Student paired *t* test were not met. The chi-square test was used for categorical data. The level of significance was considered at a *P* value of less than 0.05; and the Bonferroni–Holm adjustment<sup>36</sup> was used to obtain the corrected *P* value (*P*<sub>c</sub>) thresholds for outcomes where repeated measurements were performed.

### Results

We assessed 172 patients for eligibility to participate in the study (fig. 2). Of these, 48 patients did not meet the inclusion criteria, 58 declined enrollment, and the remaining 66 patients consented to the study. The allocation of the recruited patients included 34 to the *PVB group* and 32 for the *control group*. Two patients were later excluded, one from the *PVB group* because of protocol breaches and another from the *control group* because of an incomplete QoR questionnaire. A total of 64 patients randomized to treatment allocation completed the study, 33 from the *PVB group* and 31 from the *control group*, and their data were included in the analysis. Data for the primary outcome were complete, and there were minimal missing data for the secondary outcomes. Patient demographic characteristics were similar with no statistically significant differences ( $P > 0.05$ ) between groups (table 1).

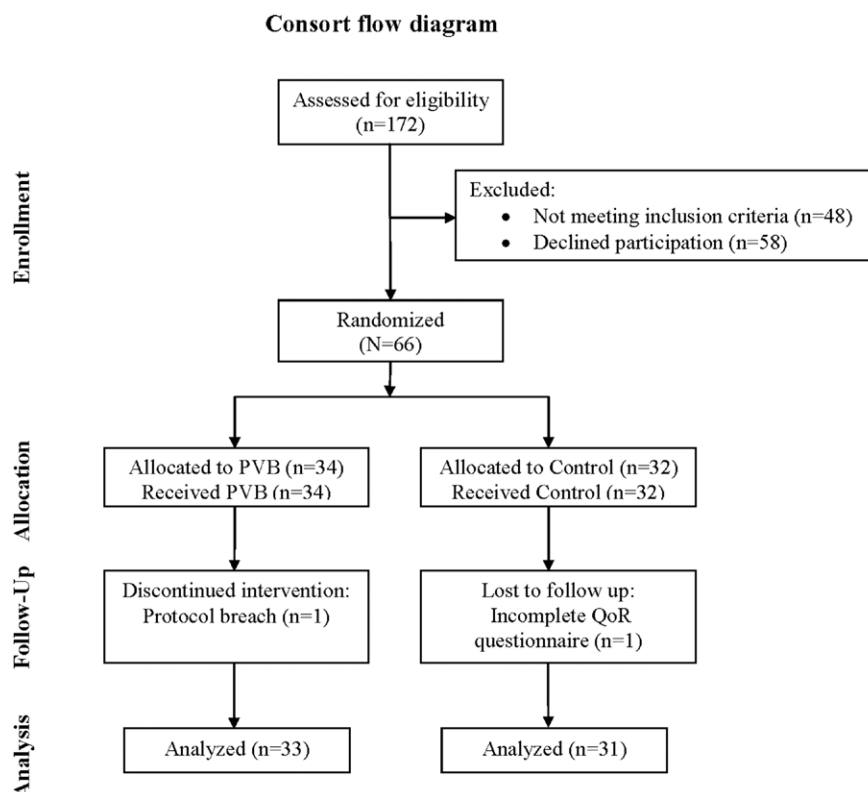
Patients in the *PVB group* had significantly higher QoR scores upon discharge from hospital and on POD 2 (24 h postsurgery), producing clinically relevant<sup>3</sup> improvements ( $\geq 10$  points) in their QoR (fig. 3). The impact of PVBs on the QoR appeared to extend to POD 4; but the difference did not reach statistical significance. The median (95% CI) of the QoR scores upon discharge, on POD 2, and on POD 4 were 146 (143–149), 145 (141–149), and 145 (143–148), respectively, for patients receiving PVB blocks compared with 131 (126–135);  $P < 0.0001$  with  $P_c = 0.0125$ , 135 (127–144);  $P = 0.013$  with  $P_c = 0.0167$ , and 143 (137–146);  $P = 0.06$  with  $P_c = 0.025$ , respectively, for patients in the *control group* (table 2). The improvement in QoR scores in the *PVB group* upon discharge, a median of 15 points, reflected improvements in the dimensions of emotional status (4 points), physical comfort (4 points), physical independence (4 points), postoperative pain (2 points), and perception of general health status at the time of discharge (1 point). Interestingly, all patients attained the same score on the psychological support dimension. The improvement in QoR on POD 2, a median of 10.75 points, reflected improvements in the dimensions of emotional status (1.5 point), physical comfort (1.5 point), physical independence (4.5 points), postoperative pain (2 points), and general health status (1 point). The difference in QoR scores between the two groups was not statistically significant when the questionnaire was conducted preoperatively in the preadmission

clinic, on POD 4, and POD 7 (table 2). It is noteworthy that patients who received the combination of PVBs and TIVA were able to maintain their baseline median QoR scores (score = 145) at hospital discharge (score = 146) and on POD 2 (score = 145) (table 2 and fig. 3).

Block success in the T1–T5 dermatomes was documented for all patients in the *PVB group*; and no patients were excluded because of block failure. None of the patients in this group required conversion to sevoflurane-based GA; and no patients required admission for hospital stay. Time to achieve complete sensory block in all dermatomes was 10 min (10.3–14.3; table 3). There were no complications attributable to the PVBs.

Postoperative Visual Analogue Scale pain scores at rest were reduced after PVB on admission to PACU I, admission to PACU II, discharge from PACU II, POD 2, POD 4, and POD 7 (fig. 4); but the reduction was not statistically significant on PODs 4 and 7. Expressed as median (95% CI), an improvement in the Visual Analogue Scale scores equivalent to 3 (1–5);  $P < 0.0001$  with  $P_c = 0.0083$ , 2 (1–3);  $P = 0.0011$  with  $P_c = 0.0167$ , 2 (1–3);  $P < 0.0001$  with  $P_c = 0.01$ , 1.5 (1–2);  $P = 0.001$  with  $P_c = 0.0125$ , 0.5 (0–1);  $P = 0.05$  with  $P_c = 0.05$ , and 0.5 (0–1);  $P = 0.04$  with  $P_c = 0.025$ , respectively, was observed at the above-mentioned points.

Compared with the *control group*, a smaller proportion of the *PVB group* patients required intraoperative supplemental opioids; the cumulative dose of opioids administered



**Fig. 2.** Consolidated Standards of Reporting Trials (CONSORT) flow diagram depicting subject progress through the phases of the study. PVB = paravertebral group; QoR = quality of recovery.

**Table 1.** Patient Demographic Characteristics

Parameter	PVB (n = 33)	Control (n = 31)
Age, (yr)	53.1 ± 12.3	56.5 ± 12.5
Height (cm)	164.9 ± 7.6	161.5 ± 6.1
Weight (kg)	68.0 ± 9.4	67.6 ± 12.3
BMI (kg/m <sup>2</sup> )	24.7 (22.2–28.2)	24.7 (21.0–31.7)
Surgical side (R/L)	14/19	12/19
ASA classification (I/II)	11/22	13/18
Surgical procedure		
Partial mastectomy + SNB	22 (66.7)	21 (67.7)
Mastectomy	2 (6.1)	2 (6.5)
Mastectomy + SNB	7 (21.2)	4 (12.9)
MRM (Mastectomy + AND)	1 (3.0)	2 (6.5)
Mastectomy + implant insertion	1 (3.0)	2 (6.5)

Data are presented as mean ± SD or median (interquartile range) or number (percentage).

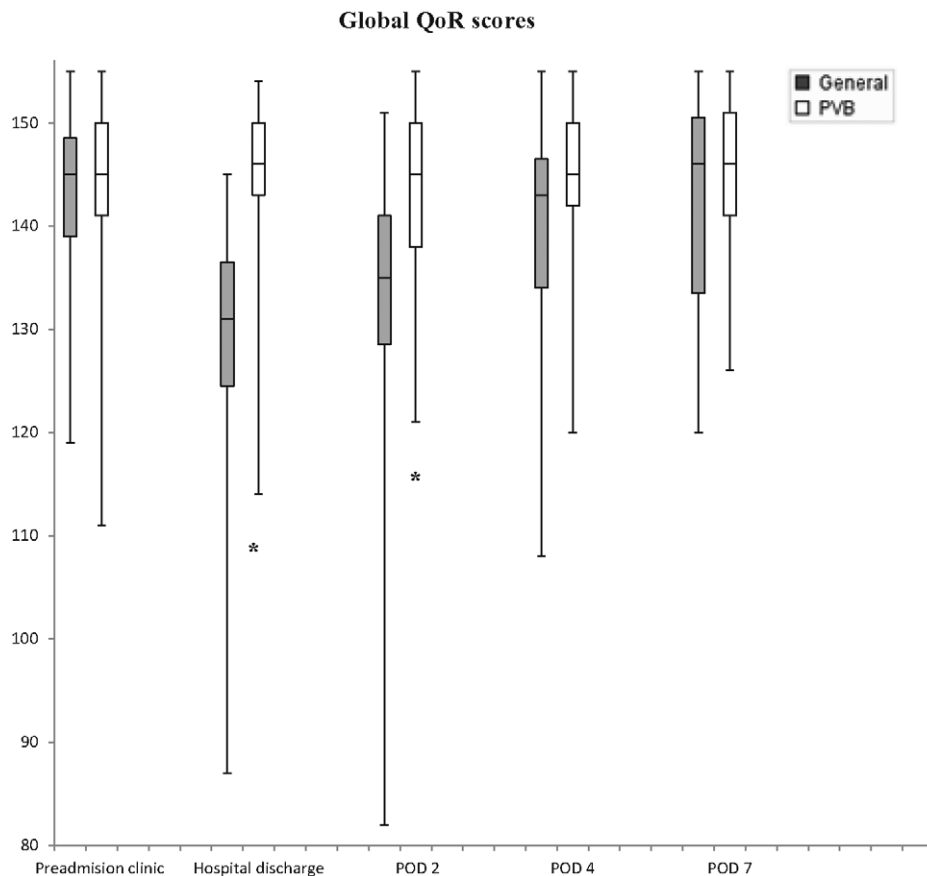
AND = axillary lymph node dissection; ASA = American Society of Anesthesiologists; BMI = body mass index; L = left; MRM = modified radical mastectomy; PVB = paravertebral group; R = right; SNB = sentinel lymph node biopsy.

(converted to IV morphine equivalents) was also significantly lower (table 4). In addition, a smaller proportion of *PVB group* patients required postoperative supplemental opioids in PACU I and II; but there was no difference in the cumulative dose of opioids administered (converted to oral morphine equivalents). The time to first request of rescue analgesia was not different between the two groups (table 4).

Patients in the *PVB group* experienced significantly reduced incidence of PONV, met PACU discharge criteria earlier (56.6 min or 25%), and had a shorter hospital discharge time (49.7 min or 20.7%; table 4). The proportion of patients who provided a correct answer to the question “Which block do you think you received?” was neither different between groups nor different from the proportion that provided a wrong answer within the same group.

## Discussion

This study demonstrates that the combination of ultrasound-guided PVBs and TIVA enhances the QoR and seems to allow the preservation of the quality of life compared with



**Fig. 3.** Box plot of the cumulative quality of recovery (QoR) questionnaire scores for the control and paravertebral blocks (PVBs) groups in the preadmission clinic, upon hospital discharge, and on postoperative days (PODs) 2, 4, and 7. Median values are shown as *solid line* within box of 25th and 75th percentile values. *Whiskers* represent 5th and 95th percentile values. Data were compared using the Mann–Whitney U test and the Bonferroni–Holm correction. \* Different from control.

**Table 2.** Cumulative Quality of Recovery Scores

Assessment Time	PVB Median (95% CI)	Control Median (95% CI)	Difference Median (95% CI)	P Value	P <sub>c</sub> Value*
Preadmission clinic	145 (142–148)	145 (139–148)	0 (–4 to 4)	0.97	0.05
Before discharge	146 (143–149)	131 (126–135)	–15 (–19 to –11)	<0.0001	0.0125
POD 2	145 (141–149)	135 (127–144)	–10.75 (–18 to –1.5)	0.013	0.017
POD 4	145 (143–148)	143 (137–146)	–4.5 (–9 to 0)	0.06	0.025
POD 7	146 (142–149)	146 (138–150)	–2 (–6 to 2)	0.51	0.05

\* Bonferroni–Holm corrected *P* value thresholds designating the limit of statistical significance for the repeated measurements. POD = postoperative day; PVB = paravertebral group.

inhalational gas- and opioid-based GA in patients undergoing ambulatory breast tumor resection. With the exception of psychological support, patients receiving PVBs had better scores in all dimensions of the QoR questionnaire completed at discharge time compared with patients in the *control group*. The improvement in the QoR cumulative score persisted into POD 2 and POD 4, but the difference was not statistically significant on POD 4. Our results also demonstrate the reliability of this anesthetic technique for ambulatory breast tumor resection. Additional benefits of this anesthetic technique include improved postoperative pain relief up to 48 h after surgery, reduced PONV, as well as expedited PACU and hospital discharge.

The effect of PVBs and TIVA on the QoR after breast tumor surgery has not been illustrated before. An earlier report<sup>37</sup> examined the effect of adding a catheter-based infusion to landmark-guided PVBs on the QoR in patients undergoing ambulatory breast tumor resection. Limited by their trial design that lacked a control group, Buckenmaier *et al.* could not assess the impact of PVB *per se* on the QoR. Their addition of a PVB infusion also did not show any further benefits over single-injection PVBs. In addition, the preceding work by Marhofer *et al.*<sup>26</sup> that examined the feasibility of an opioid-free anesthetic regimen in breast cancer surgery was observational in nature, limited by the lack of assessment of PVB success, and examined simpler surgical procedures. Moreover, all earlier clinical trials that examined the role of PVBs for the same surgical procedure did not use ultrasound guidance.<sup>16–19,37–44</sup> This is also the first trial to demonstrate that such an anesthetic technique allows shorter recovery room stay and faster hospital discharge after

ambulatory breast tumor resection, a benefit of PVB that has also only been reported in retrospective reviews.<sup>45</sup>

Advances in the surgical management of breast cancer have reduced mortality and morbidity after breast tumor resection.<sup>46–49</sup> Arguably, the patient's quality of life and ability to resume normal activity postsurgery follow as important endpoints.<sup>33,50,51</sup> To measure changes in the postoperative quality of life immediately after breast tumor resection, we used an ambulatory variant of the QoR tool, a shorter version that has been shown to be sensitive to up to 14 days after ambulatory procedures.<sup>31</sup> Our designation of the QoR as a primary outcome is also in keeping with the trend of adopting patient-related outcomes as measures of the quality of health care.<sup>52</sup> The recent increased interest in changes to ambulatory anesthetic interventions that can potentially improve the quality of care seems to reflect the gradual, yet progressive, endorsement and implementation of this trend in anesthetic practice.<sup>4,5,31,53,54</sup>

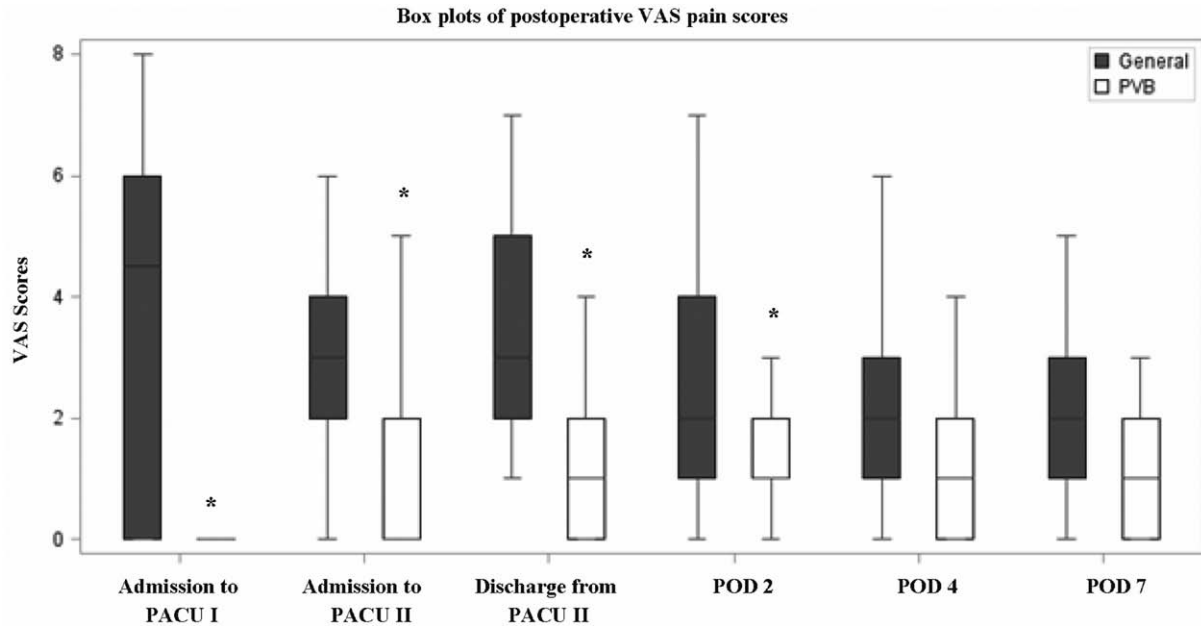
Relying on nerve blocks to provide surgical anesthesia for breast surgery is a challenging endeavor owing to the complexity of breast innervation that is derived from the anterior and lateral branches of the first to seventh intercostal nerves.<sup>55</sup> Furthermore, depending on the complexity of surgery, and whether or not concomitant axillary surgical interventions are performed, zones innervated by the superficial cervical plexus, the medial and lateral pectoral nerves,<sup>56</sup> as well as the long thoracic and thoracodorsal nerves<sup>57</sup> may also be involved. Hence, the block of the intercostobrachial nerve by a T2 PVB may not provide sufficient surgical anesthesia for procedures involving the axilla. This may plausibly explain the lack of difference in postoperative supplemental opioid consumption we observed. Indeed, the majority of patients in the *PVB group* requiring postoperative opioids localized the source of their discomfort to the axilla. This may also explain why single-<sup>16,58</sup> and even multilevel<sup>20,59,60</sup> landmark-guided PVBs, stand alone, have high failure rates (estimates vary between 14.7,<sup>60</sup> 20,<sup>59</sup> and 27.3%<sup>20</sup>) in providing adequate surgical anesthesia for more extensive tumor resection procedures. Consequently, the combination of multilevel ultrasound-guided PVBs and TIVA seems to bring into actuality the recommended anesthetic technique<sup>12–15</sup> that excludes inhalational gas and opioids.

Postoperative pain and PONV are among the most common causes of prolonged hospital stay after ambulatory

**Table 3.** Complete Sensory Block Onset Time (Sensory Score = 0)

Dermatome	Time to Achieve Complete Sensory Block (min)
T1	10 (10.3–13.1)
T2	5 (8.3–9.9)
T3	5 (6.8–8.0)
T4	5 (6.4–7.2)
T5	5 (6.5–8.2)
All T1–T5	10 (10.3–14.3)

Data are presented as Median (95% CI). T = thoracic dermatomal level.



**Fig. 4.** Box plots of postoperative Visual Analog Scale (VAS) pain scores at rest for the control and paravertebral blocks (PVBs) groups on admission and discharge from postanesthesia care unit (PACU) I, discharge from PACU II, postoperative day (POD) 2, and POD 7. Median values are shown as *solid line* within box of 25th and 75th percentile values. *Whiskers* represent 5th and 95th percentile values. Data were compared using the Mann–Whitney U test and the Bonferroni–Holm correction. \* Different from control.

surgery;<sup>61</sup> this may explain the expedited discharge noted with PVBs. Although improved analgesia and reduced opioid-related side effects are consistent with earlier findings,<sup>62,63</sup> prolonged analgesia lasting into POD 2 is uncommon as it exceeds the duration of long-acting local anesthetics used in single-shot blocks.<sup>64</sup> Nevertheless, extended analgesia lasting an average of 23 h (range, 9–38) after PVBs has been described in two earlier reports.<sup>60,65</sup> Although the mechanism for the extended duration of analgesia observed after thoracic PVBs block is unclear, the possible effect of local anesthetic induced sympathectomy<sup>66</sup> on postoperative pain has been postulated.<sup>67</sup>

The results of our study are subject to some limitations. First, the QoR questionnaire we used was tested in the Swedish population; cultural differences between

countries<sup>68,69</sup> may limit its generalizability. A more recent short-form QoR questionnaire, the QoR-15, may offer improved utility in the ambulatory setting<sup>70</sup> and may overcome the validity limitations of the psychological support dimension of Idvall's QoR tool<sup>31</sup> that were reflected in our results. Second, the awareness of the anesthesiologist providing intraoperative care of patient allocation as well as the propofol-related analgesic effects<sup>71,72</sup> may have influenced our results, particularly the intraoperative opioid consumption. Third, our assessment of sensory block onset risks compromising the blinding of the patients though our evaluation of data indicated adequacy of blinding. In addition, our study design did neither include an additional comparative group that receives both GA and PVBs nor use bispectral index monitoring, which would allow additional

**Table 4.** Analgesic Outcomes Results

Outcome	PVB (n = 33)	Control (n = 31)	P Value
Proportion requiring intraoperative supplemental opioids	8 (24.2)	29 (93.5)	<0.00001
Cumulative intraoperative IV morphine equivalent consumption (mg)	1.7 ± 3.0	15.9 ± 7.8	<0.0001
Proportion requiring postoperative supplemental opioids in PACU	7 (21.2)	15 (48.4)	0.03
Cumulative postoperative oral morphine equivalent consumption (mg)	10.6 ± 13.5	14.6 ± 14.7	0.27
Time to first request of rescue analgesia	58.2 ± 36.5	68.6 ± 81.0	0.59
Incidence of PONV	3 (9.1)	12 (38.7)	0.004
Time to meet PACU II discharge criteria	168.9 ± 38.3	225.5 ± 49.2	0.0037
Time to hospital discharge	190.2 ± 51.6	239.9 ± 78.4	0.005
Gave a correct answer to the question: "Which block do you think you received?"	20 (60.6)	13 (41.9)	0.14

Data are presented as mean ± SD or number (percentage).

IV = intravenous; PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting; PVB = paravertebral group.



appreciation of the effects of GA and PVBs on the QoR. Furthermore, the diversity in the types of surgical procedures studied and the stages of tumor resected may pose further limitations to our conclusions. Finally, our study does not evaluate oncological variables such as disease-free survival though PVBs have been reported to influence this important outcome.<sup>73</sup>

## Conclusion

We conclude that an opioid- and inhalational gas-free anesthetic technique utilizing a combination of multilevel ultrasound-guided PVBs and TIVA provides reliable anesthesia, better QoR, improved postoperative analgesia, as well as a shorter discharge time than conventional GA in patients undergoing ambulatory breast tumor resection. When no contraindications exist, PVBs seem to be a better anesthetic option that may allow the preservation of the quality of life, thus the improvement in postoperative QoR they produce compared with GA should be taken into consideration when designing the management plan for this surgical procedure. Future trials are required to examine the effects of PVBs in other breast surgeries.

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## Competing Interests

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