

Anything Other than Pain that Matters after Breast Cancer Surgery? A Randomized Controlled Study Comparing Three Anesthetic Modalities

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Abstract

Background: Paravertebral block (PVB) was shown to reduce postoperative pain and postoperative nausea and vomiting for breast surgery. However, there is no evidence showing that these benefits were solely provided by PVB and positively influence patient-perceived outcomes after breast cancer surgery.

Methods: One hundred breast cancer patients were randomized into three groups: general anesthesia (GA, n=34), GA with PVB (GA+ PVB, n=33), PVB with sedation (PVB, n=33). The quality of recovery (QoR) score was assessed preoperatively as baseline, 6 hours postoperatively, and on postoperative day (POD) 1. Analgesia effects, adverse events, and perioperative satisfactions were also assessed.

Results: The rate of QoR 6 hours reaching 18 in GA group (25.53%) seemed to be lower compared with GA+PVB (30.3%) or PVB (42.42%) but without statistical significance. Nevertheless, multivariate logistic regression analysis demonstrated that modality of PVB affected QoR 6 hours (p=0.04). Analgesic consumptions and pain scores were significantly higher and time to first request of analgesics shorter in GA group. The incidences of the GA-related undesired effects were significantly lower and satisfaction with emergence significantly better (P < 0.0001) in PVB group when compared with GA group. There was no difference between GA and GA+PVB in these outcomes.

Conclusions: Anesthesia modalities containing PVB provided better pain control. Anesthesia modalities avoiding GA, i.e. PVB alone, led to significantly lower incidences of GA-related adverse events, significantly better satisfaction with the process of emergence, and contribution to QoR 6hours reaching 18.

Keywords: Breast Cancer Surgery; Paravertebral block; General Anesthesia; Patient-Perceived Outcome

Abbreviation: PVB: Paravertebral Block; GA: General Anesthesia, QoR: Quality of Recovery

Introduction

Acute postoperative pain is a risk factor for the development of persistent chronic postoperative pain after breast surgery, [1,2] which further affects the quality of life in the long run [3,4]. General anesthesia (GA) is a popular anesthesia modality for breast cancer surgery. However, GA does not provide postoperative analgesia. In addition to postoperative pain, myriads of side effects including sore throat, postoperative nausea and vomiting (PONV) are common in the immediate postoperative period, [5,6] and may adversely affect patient-oriented outcomes. Paravertebral block (PVB) for breast surgery was shown to reduce pain and PONV compared with GA [7-11]. A recent study also showed that combining PVB with total intravenous anesthesia improved quality of recovery (QoR) compared with GA in ambulatory breast tumor resection [12].

Despite the emphasis on measuring patient-oriented outcomes in many fields of health care and acceptance of these outcomes as a valid endpoint in clinical trials, [13-15] few studies have examined the effect of anesthesia-related complications on patient-oriented outcomes in the immediate postoperative period.

We hypothesized that anesthetic modality containing PVB would positively while that containing GA would negatively affect patient-perceived outcomes for breast cancer surgery. We conducted a randomized controlled study to further discern the impacts of GA, PVB, and GA combined with PVB on QoR and satisfactions after breast cancer surgery.

Materials and Methods

This study was registered on ClinicalTrials.gov (NCT01499836) and approved by Institutional Review Board of Koo Foundation Sun Yat-Sen Cancer Center. This was a parallel, prospective, randomized controlled trial. All participants provided their written informed consent prior to surgery.

Patients were eligible for inclusion if they had histological proven unilateral breast cancer and were scheduled to have unilateral wide excision or mastectomy with sentinel lymph node biopsy or axillary dissection. American Society of Anesthesiologists(ASA) physical status class 3 or less, female, 18 to 70 years of age, being able to read a newspaper in Chinese, without contraindication of GA or PVB, and being able to provide informed consent were inclusion criteria. Exclusion criteria included a history of chronic pain or long term analgesics usage, allergy to local anesthetics or nonsteroidal anti-inflammatory drugs, being pregnant, or breast-feeding.

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The purposes of the study and the risks and benefits of each anesthetic technique were explained by physicians to eligible patients in the preoperative evaluation clinic. If eligible patients consented to join the study, they would be randomized into one of three groups, GA, GA+PVB and PVB groups. We used a computer generated randomization list produced by a statistician in the Office of Clinical Research. Sealed, opaque envelopes with allocation codes concealed inside and sequential number outside were put in a locked drawer. After reconfirmation of the eligible and consenting patients' willingness to join the study on the day of surgery, envelopes were retrieved sequentially just before surgery for each participant by an administering nurse anesthetist neither involved in the anesthetic intervention in the operating room nor in the data collection postoperatively.

Preoperative anxiety makes an independent contribution to predicting acute pain after breast surgery [16]. To have this variable controlled, all patients were evaluated preoperatively with a validated questionnaire, the Hospital Anxiety and Depression Scale [17].

Procedure of anesthesia

In GA and GA+PVB groups, propofol (2–3 mg/kg), cisatracurium (0.15 mg/kg) and fentanyl (100 µg) for endotracheal intubation and 5–8% desflurane titrated according to age, blood pressure, and vital signs for maintenance were given.

In PVB group, the patients received PVB after sedation with intravenous midazolam 3–5 mg and intravenous fentanyl 50–100 µg. Intraoperative sedation were provided with target controlled infusion (TCI) propofol driven by the Schnider model in effect site control titrated to reach moderate sedation defined as Observer Assessment of Alertness/Sedation score of 2 to 3. During operation, individualized emetic prophylaxis including one or a combination of the following medications: dexamethasone 4mg, granisetron 1 mg and droperidol 0.625 mg, was given according to each patient's Apfel Risk Score and consensus guidelines [18,19]. Granisetron 1 mg was used for PONV after surgery as the rescue antiemetic medication.

Procedure of ultrasound-guided paravertebral block

The block was performed using the in-plane technique described by Renes [20] and multi-level injection technique from T2 to 6 according to a previous study demonstrating that multilevel injections lead to optimal anesthesia [21]. After induction of general anesthesia or sedation, patients in the GA+PVB and PVB groups were placed in a lateral decubitus position with the side to be operated upward. After aseptic preparation, a high-frequency (HFL38X linear probe, 6–13 MHz, SonoSite, inc., WA, US) probe was placed lateral to the spinous process at the level of interest to locate the wedge-shaped paravertebral space. Then a 22-gauge, 3.5-inch spinal needle (Terumo) was inserted in a lateral-to-medial direction from the outer edge of the probe and advanced until the needle tip penetrated through the internal intercostal membrane. Depending on the patient's body mass, 3–5 ml of 0.5% bupivacaine with 1:400,000 epinephrine was injected after a negative aspiration of blood or air at each level. Direct visualization of the needle-tip position and the pleura being seen pressed ventrally during local anesthetic injection was considered the end point of a successful block.

Quality of Recovery (QoR) Score

We adopted the nine-item QoR [22] as it is a validated and easy-to-use instrument to assess general quality of recovery in the immediate postoperative period. A QoR summary score, ranging from 0 to 18, was obtained by asking the patient questions regarding degree of general well-being, support from others; general mental function, ability to perform personal hygiene, bowel/bladder function, ease of respiration, presence of headache-backache-myalgias, emesis, and pain. The

validated Chinese version nine-item QoR [23] questionnaire was used. A baseline QoR score was obtained preoperatively. QoR scores 6 hours and POD1 were collected.

Satisfaction

At the preoperative visit, the research assistant verified the telephone number, obtained best contact times, and informed patients that they would be called. She made four attempts to contact each patient within 24 hours after discharge to minimize recall bias with increasing time between treatment and survey completion.

Patients were queried about whether they were satisfied: 1. that they didn't recall during operation, 2. with the process of emergence, 3. with postoperative pain control. Responses to questions requiring patients to rate their experiences based on a five-point Likert scale of strongly agree, agree, undecided, disagree, and strongly disagree.

Postoperative pain and adverse events

NRS pain scores at rest and with movement were collected 1 hour, 6 hours postoperatively, and on POD 1. Patients were asked to move their arms ipsilateral to the surgical areas to an angle of 90° away from their bodies when assessing pain with movement. Postoperative analgesics including intravenous 0.1 mg/kg morphine and intravenous 30mg ketorolac were provided to achieve the numeric rating scale (NRS) pain score less than 4. The amounts of morphine and doses of ketorolac required and time to first request of rescue analgesics were recorded.

We recorded PVB-related (accidental vascular puncture, pneumothorax, nerve damage, local anesthetics toxicity, and so on) and other anesthesia-related adverse events.

Statistical methods

The primary endpoint was the rate of QoR 6 hours postoperatively reaching 18. Sample size was calculated based on a pilot study in which the rate of QoR 6 hours of 18 among control subjects in GA group was 0.36 and for experimental subjects in GA+PVB group was 0.73 [14]. We need to study 32 experimental subjects in GA+PVB group and 32 control subjects in GA group to be able to reject the null hypothesis that the rate of QoR=18 for experimental and control subjects are equal with probability of 0.8. Two pair-wise comparisons of the control arm (GA) to each experimental arm (GA+PVB, PVB) were made. We assumed the difference of the rates of QoR=18 between GA and PVB groups would be greater than or at least equal to that of GA and GA+PVB groups. The Type I error probability associated with this test of this null hypothesis is 0.025. We used Fisher's exact test to evaluate this null hypothesis. We inflated the sample size to 33/34 in each group to take into account loss to follow-up and withdrawal.

Normally distributed data were presented as mean (SD) (standard deviation). Non-Gaussian data were presented as median (25th percentile and 75th percentile). Nonparametric Wilcoxon two-sample test and Fisher's exact test were used to test differences between control arm and each experimental arm. A P-value of 0.025 was considered significant. The Kaplan Meir survival graph was used to analyze the post-operative time to first request of analgesics interval. Multivariate logistic regression analysis was used to adjust the confounding variables. All of the analyses were carried out using SAS 9.3 software (SAS Institute INC, Cary, NC).

Results

During Oct 2012 to Apr 2013, a total of 100 patients were included. Data from all 100 patients were subjected to the final analysis (Figure 1). Patient characteristics showed no difference between groups (Table 1).

Although a trend of higher rates of QoR 6 hours reaching 18 was

shown in the experimental arms (30.3% in GA+ PVB, and 42.42% in PVB group, vs. 25.53% in GA group), pair-wise comparisons showed no significant difference (Table 2). Nevertheless, in the multivariate analysis adjusted for breast procedure, axillary procedure, operation duration, baseline QoR, and anesthesia technique, only anesthesia technique of PVB influenced the rate of QoR 6 hours=18 with significance (p=0.04) (Table 3).

GA group had the highest pain scores and the largest cumulative

morphine and ketorolac consumptions compared to the other two groups. In the two groups with PVB, patients took longer to request analgesics compared with group GA on the log-rank test (p=0.0002) (Figure 2).

There was no difference between GA and GA+PVB in the incidences of PONV, sore throat, headache, and dizziness. The incidences of these adverse effects were significantly lower and injection site soreness significantly higher in PVB group when compared to GA group (Table 2).

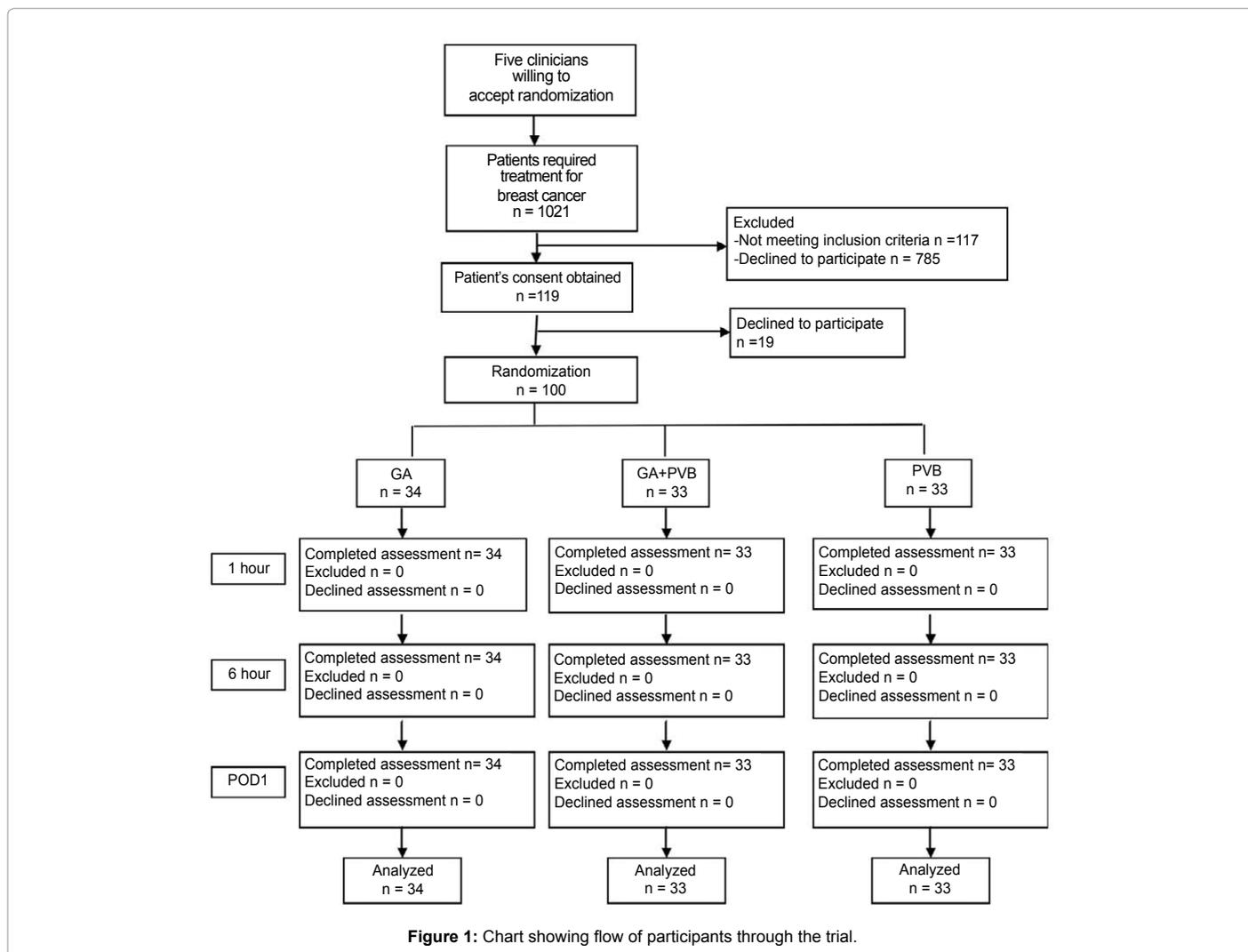


Table I: The main demographic and clinical characteristics of three groups are shown according to treatment arm.

	GA (n= 34)	GA+PVB (n= 33)	P ¹	PVB (n= 33)	P ²
Age(year) mean(SD)	47.41 (8.70)	48.45 (10.93)	0.67	47.39 (9.00)	0.99
BMI (kg m ⁻²) mean(SD)	22.68 (2.54)	23.33 (2.85)	0.32	22.36 (2.61)	0.62
ASA I/II/III(n)	9/24/1	14/19/0	0.25	9/22/2	0.92
Risk for PONV low/medium/high (n)	0/29/5	4/26/3	0.11	3/25/5	0.27
Preoperative anxiety scale mean(SD)	8.29 (3.66)	8.58 (3.56)	0.75	7.33 (4.21)	0.32
Preoperative depression scale mean(SD)	4.21 (2.96)	5.21 (4.43)	0.28	4.58 (4.00)	0.67
Preoperative QoR = 18 n (%)	19 (55.88)	19 (57.58)	1	21 (63.64)	0.62
Mastectomy n (%)	21(61.76)	16(48.48)	0.33	13(39.39)	0.09
ALND n (%)	14(41.18)	6(18.18)	0.06	14(42.42)	1
Operation duration (min) mean(SD)	103.71 (27.32)	105.39 (29.51)	0.81	121.21 (37.45)	0.03

Risk of PONV = low risk denoted Apfel Risk Score of 1; medium risk denoted Apfel Risk Score of 2-3; high risk denoted Apfel Risk Score of 4
 GA: General Anesthesia, PVB: Paravertebral Block, SD: Standard Deviation, BMI: Body Mass Index, ASA status: American Society of Anesthesiologists Physical Status Classification, PONV: Postoperative Nausea and Vomiting, QoR: Quality of Recovery, ALND: Axillary Lymph Node Dissection Values are expressed as the mean (SD), or the number of patients
 P¹, P²: = the p values of Group GA compared with Group GA+PVB and Group PVB, respectively

All patients were successfully contacted within 24 hours after discharge. In contrast to GA and GA+ PVB groups in which quite a few patients were not satisfied, PVB group had every patient satisfied in every dimension. However, the P-values were greater than 0.025 except that of the dimension comparing comfort at emergence. In this dimension, PVB group had significantly more satisfied patients than GA group did ($p < 0.0001$). No difference was shown between GA+PVB and GA groups (Table 2). None of the patients had pneumothorax, or other PVB-related complications.

Discussion

By comparing three anesthetic modalities, interesting findings of better pain control in modalities containing PVB, i.e. GA+PVB or PVB alone; while a trend of higher rate of QoR 6 hours reaching 18 without

statistical significance, significantly lower incidence of GA-related adverse events, and significantly better satisfaction with emergence in modality avoiding GA, were revealed.

In previous studies, length of hospital stay was shortened by PVB in major breast surgeries [7,8]. Since it is the institutional policy to discharge uneventful breast surgery patients 1 day after surgery, using economic end point such as length of stay was not feasible for our study. We used QoR score because it is a validated summary measure of outcome in perioperative clinical trials [22]. Our study failed to show the difference of the rate of QoR 6hours reaching 18 when comparing each experimental arm (GA+PVB, PVB) to GA group. However, we demonstrated that the modality of PVB without GA is the only factor affecting QoR 6 hours after adjusting possible confounding factors. Technique of PVB combined with GA would not improve the rate of

Table II: Two pair-wise comparisons of outcomes between the control arm (GA) and each experimental arm (GA+PVB, PVB).

	GA (n= 34)	GA+PVB (n= 33)	P ¹	PVB (n= 33)	P ²
QoR 6 hours n (%)	8 (25.53)	10 (30.3)	0.59	14 (42.42)	0.12
QoR POD1 n (%)	19 (55.88)	19 (57.58)	1	21 (63.64)	0.62
Dissatisfied/Undecided/Satisfied n/n/n					
1. I am very satisfied that neither did I recall nor was I aware during operation.	1/2/31	0/1/32	1	0/0/33	0.36
2. I am very satisfied with the process of emergence.	7/6/21	3/6/24	0.47	0/0/33	< 0.0001
3. I am very satisfied with the postoperative pain control.	2/3/29	0/5/28	0.48	0/0/33	0.05
Postop 1 hour					
Pain at rest	5.5 (3, 7)	2 (1, 4)	0.0003	0 (2, 3)	< 0.0001
Pain with movement	6 (3, 7)	3 (1, 5)	0.0009	0 (2, 3)	< 0.0001
Postop 6 hours					
Pain at rest	2 (1, 3)	1 (0, 2)	0.01	1 (0, 2)	0.03
Pain with movement	2.5 (1, 3)	1 (0, 2)	0.05	1 (0, 2)	0.08
POD1					
Pain at rest	1 (0, 2)	1 (0, 3)	0.43	0 (0, 2)	0.43
Pain with movement	1 (0, 2)	1 (0, 3)	0.99	1 (0, 2)	0.50
Morphine (mg) mean(SD)	6.24 (4.09)	3.73 (2.58)	0.003	4.03 (2.73)	0.008
Ketorolac (dose) mean(SD)	0.29 (0.52)	0.06 (0.24)	0.02	0	0.003
PONV n (%)	14(41.18)	12(36.36)	0.80	4(12.12)	0.01
Sore throat n (%)	18 (52.94)	18 (54.55)	1	0 (0)	< 0.0001
Headache n (%)	7 (20.59)	3 (9.09)	0.30	0 (0)	0.01
Dizziness n (%)	15 (44.12)	14 (42.42)	1	4 (12.12)	0.006
Soreness on back n (%)	0 (0)	2 (6.06)	0.24	5 (15.15)	0.02

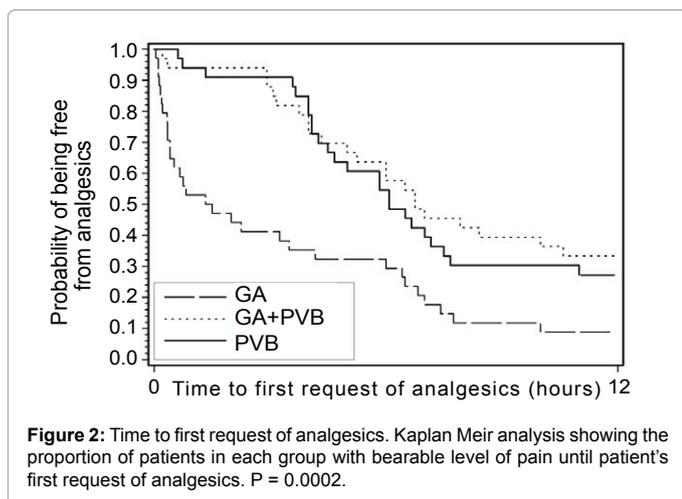
GA: General Anesthesia, PVB: Paravertebral Block, QoR: Quality of Recovery, POD 1: Postoperative Day 1, PONV: Postoperative Nausea and Vomiting
 QOR 6 hours: Patients with QoR of 18 at postoperative 6 hours, QoR POD1: Patients with QoR of 18 on postoperative day 1
 Values are expressed as the mean (SD), or the number of patients. The paired numbers in each parenthesis indicate 25th percentile and 75th percentile
 P¹, P², the p values of Group GA compared with Group GA+PVB and Group PVB, respectively

Table III: Multivariate logistic regression analysis of effects of surgery, operation duration, baseline QoR, and anesthesia technique on QoR 6 hours in women after breast surgeries.

	No (%) of patients		Unadjusted		Adjusted*	
	QoR = 18	QoR < 18	OR (95% CI)	P	OR (95% CI)	p
Breast procedure						
mastectomy	9	25	1.00 (0.43 - 2.32)	0.40	1.11 (0.45 - 2.72)	0.82
BCS	23	43	1		1 (reference)	
Axillary procedure						
ALND	16	34	0.67 (0.27 - 1.68)	1	0.69 (0.25 - 1.88)	0.47
SLND	16	34	1		1 (reference)	
Operation duration			1.00 (0.98 - 1.01)	0.48	0.99 (0.98 - 1.01)	0.37
Baseline QoR						
= 18	11	14	2.02 (0.79 - 5.16)	0.14	2.45 (0.91 - 6.64)	0.08
< 18	21	54	1		1 (reference)	
Anesthesia technique						
GA+PVB	10	23	1.41 (0.48 - 4.19)	0.53	1.37 (0.44 - 4.27)	0.59
PVB	14	19	2.40 (0.84 - 6.85)	0.10	3.34 (1.05 - 10.64)	0.04
GA	8	26	1		1 (reference)	

QoR: Quality of Recovery, BCS: Breast Conserving Surgery, ALND: Axillary Lymph Node Dissection, SLND: Sentinel Lymph Node Dissection, GA: General Anesthesia, PVB: Paravertebral Block.

*Adjusted for mastectomy/BCS, ALND/SLND, operation duration, baseline QoR, and anesthesia techniques among 100 patients



QoR 6hours=18, although GA+ PVB and PVB groups both showed significant better pain control.

Unsurprisingly, better analgesia was found in the two groups with PVB. These findings were compatible with those of previous studies [7-11]. However; the difference was not clearly evident in the rate of QoR6 hours reaching 18. Neither was the difference evident in the satisfaction with pain control. The minor nature of breast surgery with median worst-pain scores of NRS 4 or less on the first day of surgery [24] could be responsible for the insignificant impact of anesthesia modalities on patients' satisfaction with postoperative analgesia. Nine-item QoR was found to be highly related to satisfaction with anesthesia [25]. Patients who experienced any of several perioperative complications, not just postoperative pain, had lower nine-item QoR Scores [25]. Thus the significant difference in postoperative pain might not be considered the only factor relevant for clinical practice in breast surgery.

Patients in PVB group were significantly more satisfied with the process of emergence. There was no difference in satisfaction in this dimension between the two groups with inhalational gas and intubation, with or without PVB. This could be explained by the followings. The common undesirable effects of inhalational gas-based and intubated general anesthesia, such as sore throat, headache, and dizziness, were noted to be significantly lower in PVB group. These results were compatible with previous studies [5,6]. Among these discomforts, incidence of sore throat in the groups with GA was relatively high. Avoiding intubation by using supraglottic airways or by adopting regional anesthesia may decrease this airway discomfort. Besides, early recovery was more comfortable in PVB group probably due to a significantly infrequent PONV by virtue of using propofol infusion and avoidance of desflurane [26].

The analgesic effect of PVB in our study did not last that long as described in previous studies [7,9]. There could be multiple causes. Although there were no statistical differences among the three groups in surgical types or operation duration, PVB group had the largest proportion of patients with ALND, in which intercostal nerve injury is more likely than in SLND [16]. Secondly, longer operation duration in PVB group, although without statistical significance, implied inherently more extensive procedure albeit under randomization. These could have been sources of potential bias to the outcome of the study.

There are several limitations of the current study. Previous study showed a significant decrease of nine-item QoR scores at POD1, POD3 and POD5 compared with baseline in hepatectomy [27]. However, the difference of nine-item QoR scores=18 in the immediate postoperative period was not as evident in the current study. Minor nature of breast surgery, low postoperative pain level, and sensitivity of the nine-item

QoR may have contributed to it. The modified QoR-40 [28] for day surgery adopted in Abdallah et al.'s recent study [12] might be more sensitive for breast surgery as they have demonstrated the difference. However, since ours were inpatients due to the institutional policy, the recovery questionnaires for the ambulatory setting [28-30] were not considered for our study. QoR-40 [14] and nine-item QoR [22] was designed for both inpatient- and outpatient- surgeries. QoR-40 may be more sensitive 31 for breast surgery. We chose nine-item QoR for its superior feasibility, 32 being reliable for group measurement and comparison [22] and its validated version in Chinese [23]. More studies are needed to confirm the sensitivity of nine-item QoR as a tool in assessing recovery after breast surgery. To increase the sensitivity of the study and decrease type two error, increasing the sample size should also be considered in the future study. Besides, we didn't perform sham block in the GA group. Patients in the groups with PVB might be aware of the group assignment due to soreness on the back. This might have contributed to bias of the outcome.

In conclusion, PVB provided better analgesia, with or without GA. But only when adopting PVB and avoiding inhalational gas and intubation, could we observe that the QoR 6 hours postoperatively be affected, side effects of general anesthesia be reduced, and satisfaction with emergence process significantly improve.

Conflict of interest

The authors have no conflict of interest to report.

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References

1. Poleshuck EL, Katz J, Andrus CH, Hogan LA, Jung BF, et al. (2006) Risk factors for chronic pain following breast cancer surgery: a prospective study. *J Pain* 7: 626-634.
2. Gärtner R, Jensen MB, Nielsen J, Ewertz M, Kroman N, et al. (2009) Prevalence of and factors associated with persistent pain following breast cancer surgery. *JAMA* 302: 1985-1992.
3. Montazeri A (2008) Health-related quality of life in breast cancer patients: a bibliographic review of the literature from 1974 to 2007. *J Exp Clin Cancer Res* 27: 32.
4. Caffo O, Amichetti M, Ferro A, Lucenti A, Valduga F, et al. (2003) Pain and quality of life after surgery for breast cancer. *Breast Cancer Res Treat* 80: 39-48.
5. Wu CL, Berenholtz SM, Pronovost PJ, Fleisher LA (2002) Systematic review and analysis of postdischarge symptoms after outpatient surgery. *Anesthesiology* 96: 994-1003.
6. Swan BA, Maislin G, Traber KB (1998) Symptom distress and functional status changes during the first seven days after ambulatory surgery. *Anesth Analg* 86: 739-745.
7. Boughey JC, Goravanchi F, Parris RN, Kee SS, Frenzel JC, et al. (2009) Improved postoperative pain control using thoracic paravertebral block for breast operations. *Breast J* 15: 483-488.
8. Coopey SB, Specht MC, Warren L, Smith BL, Winograd JM, et al. (2013) Use of preoperative paravertebral block decreases length of stay in patients undergoing mastectomy plus immediate reconstruction. *Ann Surg Oncol* 20: 1282-1286.
9. Kairaluoma PM, Bachmann MS, Korpinen AK, Rosenberg PH, Pere PJ (2004) Single-injection paravertebral block before general anesthesia enhances analgesia after breast cancer surgery with and without associated lymph node biopsy. *Anesth Analg* 99: 1837-1843, table of contents.
10. Tahiri Y, Tran de QH, Bouteaud J, Xu L, Lalonde D, et al. (2011) General anaesthesia versus thoracic paravertebral block for breast surgery: a meta-analysis. *J Plast Reconstr Aesthet Surg* 64: 1261-1269.
11. Li NL, Yu BL, Tseng SC, Hsu CC, Lai WJ, et al. (2011) The effect on improvement of recovery and pain scores of paravertebral block immediately before breast surgery. *Acta Anaesthesiol Taiwan* 49: 91-95.
12. Abdallah FW, Morgan PJ, Cil T, McNaught A, Escallon JM, et al. (2013) Ultrasound-guided Multilevel Paravertebral Blocks and Total Intravenous

- Anesthesia Improve the Quality of Recovery after Ambulatory Breast Tumor Resection. *Anesthesiology* Sep 26. [Epub ahead of print].
13. Wu CL, Fleisher LA (2000) Outcomes research in regional anesthesia and analgesia. *Anesth Analg* 91: 1232-1242.
 14. Myles PS, Weitkamp B, Jones K, Melick J, Hensen S (2000) Validity and reliability of a postoperative quality of recovery score: the QoR-40. *Br J Anaesth* 84: 11-15.
 15. Macario A, Vasanawala A (2001) Improving quality of anesthesia care: opportunities for the new decade. *Can J Anaesth* 48: 6-11.
 16. Katz J, Poleshuck EL, Andrus CH, Hogan LA, Jung BF, et al. (2005) Risk factors for acute pain and its persistence following breast cancer surgery. *Pain* 119: 16-25.
 17. Herrmann C (1997) International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *J Psychosom Res* 42: 17-41.
 18. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N (1999) A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. *Anesthesiology* 91: 693-700.
 19. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, et al. (2003) Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg* 97: 62-71, table of contents.
 20. Renes SH1, Bruhn J, Gielen MJ, Scheffer GJ, van Geffen GJ (2010) In-plane ultrasound-guided thoracic paravertebral block: a preliminary report of 36 cases with radiologic confirmation of catheter position. *Reg Anesth Pain Med* 35: 212-216.
 21. Naja ZM, El-Rajab M, Al-Tannir MA, Ziade FM, Tayara K, et al. (2006) Thoracic paravertebral block: influence of the number of injections. *Reg Anesth Pain Med* 31: 196-201.
 22. Myles PS, Hunt JO, Nightingale CE, Fletcher H, Beh T, et al. (1999) Development and psychometric testing of a quality of recovery score after general anesthesia and surgery in adults. *Anesth Analg* 88: 83-90.
 23. Chan MT, Lo CC, Lok CK, Chan TW, Choi KC, et al. (2008) Psychometric testing of the Chinese quality of recovery score. *Anesth Analg* 107: 1189-1195.
 24. Gerbershagen HJ1, Aduckathil S, van Wijck AJ, Peelen LM, Kalkman CJ, et al. (2013) Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. *Anesthesiology* 118: 934-944.
 25. Myles PS, Reeves MD, Anderson H, Weeks AM (2000) Measurement of quality of recovery in 5672 patients after anaesthesia and surgery. *Anaesth Intensive Care* 28: 276-280.
 26. Voigt M, Fröhlich CW, Waschke KF, Lenz C, Göbel U, et al. (2011) Prophylaxis of postoperative nausea and vomiting in elective breast surgery. *J Clin Anesth* 23: 461-468.
 27. Arnberger M, Vogt A, Studer P, Inderbitzin D, Pulver C, et al. (2009) Evaluation of physical and mental recovery status after elective liver resection. *Eur J Anaesthesiol* 26: 559-565.
 28. Idvall E, Berg K, Unosson M, Brudin L, Nilsson U (2009) Assessment of recovery after day surgery using a modified version of quality of recovery-40. *Acta Anaesthesiol Scand* 53: 673-677.
 29. Oakes CL, Ellington KJ, Oakes KJ, Olson RL, Neill KM, et al. (2002) Assessment of postanesthesia short-term quality of life: a pilot study. *AANA J* 70: 267-273.
 30. Kleinbeck SV (2000) Self-reported at-home postoperative recovery. *Res Nurs Health* 23: 461-472.
 31. Gornall BF, Myles PS, Smith CL, Burke JA, Leslie K, et al. (2013) Measurement of quality of recovery using the QoR-40: a quantitative systematic review. *Br J Anaesth* 111: 161-169.
 32. Herrera FJ, Wong J, Chung F (2007) A systematic review of postoperative recovery outcomes measurements after ambulatory surgery. *Anesth Analg* 105: 63-69.