Can J Anesth/J Can Anesth (2022) 69:1288–1299
https://doi.org/10.1007/s12630-022-02295-0

REVIEW ARTICLE/BRIEF REVIEW

Association of peripheral nerve blocks with patient-reported quality of recovery in female patients receiving breast cancer surgery: a systematic review and meta-analysis of randomized controlled studies

L'association entre les blocs nerveux périphériques et la qualité de récupération telle que rapportée par les patientes bénéficiant d'une chirurgie du cancer du sein : revue systématique et méta-analyse d'études randomisées contrôlées

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Received: 27 November 2021 / Revised: 12 April 2022 / Accepted: 20 May 2022 / Published online: 26 July 2022

Abstract

Purpose *This systematic review and meta-analysis investigated the impact of peripheral nerve blocks (PNBs) on patient-reported quality of recovery (QoR) following breast cancer surgery.*

Source *Medline, EMBASE, Cochrane Library, and Google scholar databases were searched for randomized controlled trials (RCTs) comparing the QoR with or without PNBs in patients receiving breast cancer surgery from inception to September 2021. Using a random effects model, the primary outcome was total scores of postoperative QoR scales (i.e., QoR-15 and QoR-40).*

Principal findings *Eight RCTs (QoR-15, n = 4; QoR-40, n = 4) involving 653 patients published from 2018 to 2021 were included. For the QoR-40 scale, pooled results revealed a significantly higher total score (mean difference [MD], 12.8 [8.2%]; 95% confidence interval [CI], 10.6 to 14.9; I^2 = 59%; five RCTs; n = 251) and scores on all subscales, except psychological support, in the PNB group than in controls at 24 hr after surgery. For the QoR-15 scale, pooled results also showed favorable QoR (MD, 7.7 [5.2%]; 95% CI, 4.9 to 10.5; I^2 = 75%; four RCTs; n = 402) in the PNB group at 24 hr after surgery. Sensitivity analysis showed no effect on the QoR-40 score and the difference in total QoR-15 score was no longer significant when a single trial was omitted. The use of PNBs was associated with a significantly lower opioid consumption and risk of postoperative nausea and vomiting without*

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Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12630-022-02295-0.

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significant differences in the pain score between the two groups.

Conclusion *Our results verified the efficacy of PNBs for enhancing postoperative QoR using two validated patient-reported tools in female patients receiving breast cancer surgery under general anesthesia.*

Study registration *PROSPERO (CRD42021272575); first submitted 9 August 2021.*

Résumé

Objectif *Cette revue systématique et méta-analyse a étudié l'impact des blocs nerveux périphériques (BNP) sur la qualité de récupération (QoR) rapportée par les patientes après une chirurgie du cancer du sein.*

Sources *Les bases de données Medline, EMBASE, Cochrane Library et Google Scholar ont été analysées pour en tirer les études randomisées contrôlées (ERC) comparant la QoR avec ou sans BNP chez les patientes bénéficiant d'une chirurgie de cancer du sein, de leur création jusqu'en septembre 2021. À l'aide d'un modèle à effets aléatoires, le critère d'évaluation principal était les scores totaux sur les échelles de QoR postopératoire (c.-à-d. QoR-15 et QoR-40).*

Constatations principales *Huit ERC (QoR-15, n = 4; QoR-40, n = 4) impliquant 653 patientes publiées de 2018 à 2021 ont été incluses. Pour l'échelle QoR-40, les résultats regroupés ont révélé un score total (différence moyenne [DM], 12,8 [8,2 %]; intervalle de confiance [IC] à 95 %, 10,6 à 14,9; I2 = 59 %; cinq ECR; n = 251) et des scores sur toutes les sous-échelles significativement plus élevés, à l'exception du soutien psychologique, dans le groupe BNP que dans le groupe témoin 24 heures après la chirurgie. Pour l'échelle QoR-15, les résultats groupés ont également montré un QoR favorable (DM, 7,7 [5,2 %]; IC 95 %, 4,9 à 10,5; I2 = 75 %; quatre ECR; n = 402) dans le groupe BNP 24 heures après la chirurgie. L'analyse de sensibilité n'a montré aucun effet sur le score de QoR-40 et la différence dans le score total de QoR-15 n'était plus significative lorsqu'une seule étude était omise. L'utilisation de BNP a été associée à une consommation d'opioïdes significativement plus faible et à un risque de nausées et vomissements postopératoires sans différences significatives dans le score de douleur entre les deux groupes.*

Conclusion *Nos résultats ont confirmé l'efficacité des BNP pour améliorer la QoR postopératoire à l'aide de deux outils validés rapportés par les patientes recevant une chirurgie du cancer du sein sous anesthésie générale.*

Enregistrement de l'étude *PROSPERO (CRD42021272575); soumis pour la première fois le 9 août 2021.*

Keywords breast surgery · peripheral nerve block · QoR-40 · QoR-15 · quality of recovery

Although most breast cancer surgeries are categorized as low-morbidity procedures,[1] they may still significantly impact the quality of patient recovery, which is defined as a return to full health encompassing a resumption of optimal functional capacity as well as emotional wellbeing.[2–5] A previous investigation has revealed significant negative impacts of surgery and anesthesia on the patient-reported quality of recovery (QoR) in physical independence, physical, and emotional aspects as well as pain.[6] Indeed, a study on 46 individuals after breast surgery reported a reduction in the total scores of QoR-40 scale from a median of 188 points at baseline to 174 points at 24 hr after surgery,[7] indicating a notable impairment ($\geq$ 8) of postoperative patient-perceived QoR.[8] The increasing popularity of ambulatory breast surgery further highlights the importance of reinforcing the recovery quality of outpatients to optimize their satisfaction and wellbeing.[9,10]

A number of clinical studies have revealed a significant association between perioperative opioid use and an impaired postoperative quality of recovery.[11,12] Peripheral nerve blocks (PNBs) with local anesthetics are common means of achieving intraoperative and postoperative analgesia for a variety of surgeries.[13,14] Although several studies have shown an enhancement of patient-reported QoR through perioperative use of PNBs in female patients undergoing breast surgery,[15–17] such positive results were not reproduced by other authors.[18,19] Nevertheless, no published systematic review or meta-analysis has addressed this issue.

Quality of recovery-40 and QoR-15 scales (Electronic Supplementary Material [ESM] eFig. 1) are the validated tools most commonly used to quantify the experience of patients after anesthesia and surgery.[4,20,21] A study comparing the QoR-40 and the QoR-15 reported the latter to be more efficient for evaluating QoR after anesthesia and surgery (i.e., taking on average 2.5 min to complete) despite comparable effectiveness of the two assessment tools.[21] To avoid heterogeneity of results by

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including widely different assessment items and the introduction of bias to our outcome measurement, this meta-analysis investigated the impact of PNBs focusing on QoR-40 and QoR-15 scales after surgery and anesthesia. Previous studies investigating the effects of PNBs on the QoR showed significant improvements at 24 hr after surgery[15–17] and showed no notable impact on postoperative days seven[18] or 30.[22] We hypothesized that PNBs could improve the patient-perceived QoR in female patients receiving breast surgery. The primary outcome was the patient-reported QoR scores at 24 hr after surgery, while the secondary outcomes were the individual dimensions of the QoR scales, postoperative opioid consumption, postoperative pain score, and the risk of postoperative nausea/vomiting (PONV).

Methods

This systematic review and meta-analysis was reported based on the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement.[23] The protocol was preregistered in the international prospective register of systematic reviews (PROSPERO: CRD42021272575; date of first submission, 9 August 2021; date of registration, 10 September 2021).

Data sources and literature search

A systematic literature search was executed using MEDLINE, Cochrane CENTRAL register of controlled trials, Embase, and Google Scholar databases from their inception dates till 28 September 2021. The following keywords and medical subject headings (i.e., MeSH terms in Medline) were used: ("Breast surgery" or "Breast conserving surgery" or "breast cancer surgery" or "Breast reconstruction" or "Mastectom*" or "Breast" or "Lumpectom*" or "Segmentectom*" or "Breast quadrantectom*") AND ("Nerve block*" or "Regional anesthesia" or "Pectoral nerves block*" or "serratus plane block*" or "Paravertebral block*" or "intercostal block*" or "Thoracic interfascial nerve block*" or "Pecs block*" or "erector spinae plane block*") AND ("quality of recovery score" or "QoR-40" or "Quality of recovery–40" or "Quality of recovery–15" or "QoR-15" or "Quality of recovery scale" or "Quality of recovery" or "Recovery"). Reference lists of the retrieved studies and related reviews were examined to minimize potential omissions. The search strategy for one of these databases is shown in ESM eTable 1. Eligibility criteria screening was conducted on 29 September 2021, and data extraction started on 1 October 2021.

Eligibility criteria

Studies that investigated the patient-reported QoR in patients receiving PNBs for breast cancer surgery were considered eligible. Studies were included if they fit into the following predefined population, interventions, comparison, and outcome (PICO) framework: 1) patient population: adult female patients undergoing breast cancer surgeries under general anesthesia, 2) intervention: use of ultrasound-guided PNBs, 3) comparison: the use of placebo (e.g., normal saline or local infiltration of anesthetics) or conventional analgesics as a control group, 4) outcomes: measurement of postoperative recovery using two patient-reported QoR scales (QoR-40 and QoR-15). No restrictions were applied to language, sample size, and publication date.

Exclusion criteria

Exclusion criteria were 1) non-randomized controlled trials (RCTs); 2) studies that involved the use of perioperative continuous intravenous lidocaine as a control group; 3) those not published in peer-reviewed journals or published only as letters or abstracts; 4) those in which information regarding primary outcome (i.e., postoperative QoR scores) was unavailable; 5) those that did not use QoR-40 or QoR-15 for outcome assessment; and 6) those in which PNBs were conducted intraoperatively under direct vision.

Screening process

The titles and abstracts of the retrieved articles were assessed by two authors independently. For RCTs that met the inclusion criteria, the full text was independently assessed by the two authors to determine whether they should be included in the final analysis. Any disagreements were resolved through discussion or involvement of a third reviewer.

Primary and secondary outcome

The primary outcome of this systematic review and meta-analysis was total score of patient-reported QoR scales at 24 hr after surgery. Secondary outcomes were the individual dimensions of patient-reported QoR scales, postoperative opioid consumption, postoperative pain score, and PONV. For the current study, we initially analyzed the total scores of the QoR-40 or QoR-15 scales, then pooled the results of both QoR scales to assess the overall effects of PNBs on the QoR. Morphine equivalent doses were computed from opioid doses of the included studies.

The QoR-40 scale is a 40-item questionnaire comprising five different dimensions: psychological support (seven items), physical comfort (12 items), emotional state (nine items), physical independence (five items), and pain (seven items) (ESM eFig. 1).[20] The total score and the subscales of the five dimensions are computed based on a five-point Likert scale ranging from 1 (i.e., never) to 5 (i.e., all of the time) for positive items with the scoring reversed for negative items. The total score, which is the sum of the scores of the five dimensions, ranges from 40 to 200. The QoR-15 scale is composed of 15 questions focusing on five domains of patient health-related quality of recovery (i.e., pain, comfort, physical independence, psychological support, and emotional state) (ESM eFig. 1). The answer to each question is assessed with an 11-point rating scale, on which the minimum score is 0 (i.e., very poor recovery) and the maximum score is 150 (i.e., excellent recovery).[21] For both QoR scales, a higher score reflects a better quality of postsurgical recovery. The minimal clinically important difference (MCID), which is the estimated threshold of change clinically relevant to a patient, is 8 points for QoR-15 and 6.3 points for QoR-40.[8]

Data extraction

The following data were collected: publication year, author names, patient characteristics (e.g., age), sample size, type of nerve block, the choice of QoR scale, type of local anesthetic, total scores of QoR scales, scores of individual dimensions of the QoR scales, postoperative opioid consumption, pain score, and incidence of PONV. The accuracy of data extraction using a standardized form by one author was confirmed by a second reviewer. Discrepancies were resolved by discussion. Authors who did not report complete outcomes (e.g., presentation of outcomes as median and interquartile range) were contacted twice through electronic messages for further information. If the authors could not be reached, data presented as median and interquartile range were converted into means and standard deviations using an approach previously described.[24]

Risk of bias assessment

For each study, we used the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions for assessing the risk of bias,[25] which was graded as "low," "unclear," or "high" in the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. We regarded the risk of "incomplete outcome data" bias of the included trials as "unclear" if the proportion of missing data were over 5%. We considered the risk of "selective outcome reporting" bias to be "unclear" for unpublished protocols or the absence of previous registration. Moreover, the sources of funding were assessed for the potential of other biases. Disagreements were settled by discussion. We analyzed the overall risk of bias of all the included studies as well as that of individual trials.

Statistical analysis

Assuming a heterogeneity across the included studies, our meta-analyses for the primary and secondary outcomes were performed using random effects models regardless of statistical heterogeneity. Effect sizes were expressed as mean differences (MD) or standardized MD (SMD) for continuous variables, while they were presented as risk ratios (RRs) including 95% confidence intervals (CIs) for dichotomized outcomes. Heterogeneity was statistically evaluated by the I^2 statistic with substantial heterogeneity being predefined as $I^2 > 50\%$.[26] Sensitivity analysis was performed to assess the potential impact of the result of a single trial on the overall outcome of meta-analysis using a leave-one-out approach. Percentage improvements in the QoR assessed by the QoR-40 and QoR-15 were calculated based on the equation: percentage change = MD/pooled QoR score from the control group $\times$ 100%. For all analyses, the level of significance was set at a probability value of less than 0.05.

Results

Study selection

Of the 373 records initially identified through title and abstract screening, 354 were removed for failing to meet the inclusion criteria (Fig. 1). Full-text review of the remaining 19 articles led to the exclusion of 11 studies, two of which were deemed ineligible because they used other QoR scales to assess postoperative outcomes.[27,28] Finally, a total of eight RCTs published from 2018 to 2021, involving 653 female patients undergoing breast cancer surgery were included in the current meta-analysis.[15–19,22,29,30]

Characteristics of studies

The characteristics of the included trials are shown in Table 1. The mean or median age of the participants ranged from 47 to 60 yr. Seven RCTs reported mean body mass index (range: 22–28 $kg{\cdot}m^{-2}$, four trials) or body weight (range: 56–62 kg, three trials), while one study[19] did not

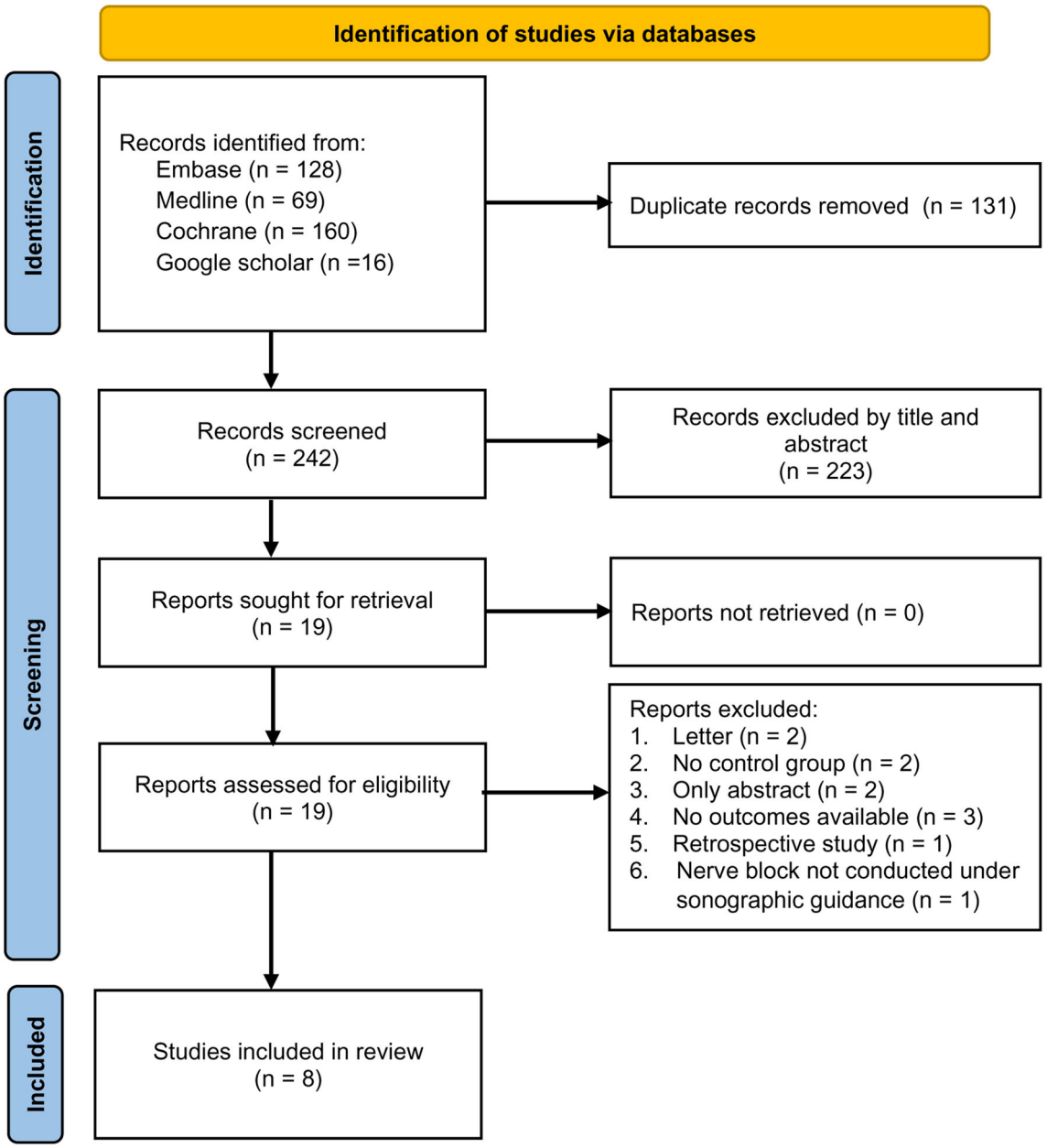

Fig. 1 PRISMA flow diagram of study selection for the current meta-analysis

specify this information. The sample sizes of individual RCTs varied between 40 and 179. Ultrasound-guided nerve block was performed in all RCTs.[15–19,22,29,30] The adopted techniques included serratus plane block,[15,17,18] erector spinae plane block,[30] thoracic paravertebral block,[16] pectoral nerve blocks combined with intercostal nerves blocks,[19,22] and rhomboid intercostal block.[29] Nerve blocks were performed before anesthetic induction in six trials that involved a sham procedure for blinding the participants in the control group,[15–19,30] while nerve blocks were conducted after anesthetic induction in the other two RCTs.[22,29] Regarding the local anesthetics used, ropivacaine was applied in six trials,[15–19,30] bupivacaine in one trial,[29] and levobupivacaine in one trial.[22] The QoR-40 scale was applied in four RCTs,[16,17,22,29] while the QoR-15 scale was adopted in the other four RCTs.[15,18,19,30] All studies provided total scores of the two QoR scales at 24 hr postoperatively. Multimodal analgesia was adopted in all studies to provide postoperative pain control (ESM eTable 2).

Risk of bias assessment

The risks of bias of individual studies and the overall risk of bias are shown in Fig. 2 and ESM eFig. 2, respectively. Although the risks of selection, performance, detection,

Table 1 Characteristics of included studies (n = 8)

	Mean age (yr)	Mean BMI (kg/m^2)	Number	ASA class	Surgery	Nerve block	Anesthetic technique	QoR scales	Country
Abdallah 2021	58 *vs* 57	26 *vs* 25	40	I-III	Mastectomy	SPB	Desflurane	QoR-15	Canada
Altiparmak 2020	52 *vs* 54	27 *vs* 28	56	I-II	MRM	RIB	Desflurane	QoR-40	Turkey
Barrington 2020	60 *vs* 59	NA	104	I-III	Breast cancer surgery	PECS II block	Sevoflurane	QoR-15	Australia
Kamiya 2018	55 *vs* 53	23 *vs* 22	59	I-II	Breast cancer surgery	PECS II block	TIVA	QoR-40	Japan
Qian 2021	52 *vs* 51	23 *vs* 23	179	I-II	MRM	SPB	Sevoflurane	QoR-15	China
Rao 2021	54 *vs* 53	60 *vs* 62[a]	68	I-II	MRM	TPVB	Sevoflurane	QoR-40	China
Yao 2019a	51 *vs* 53	60 *vs* 59[a]	79	I-II	MRM	ESPB	Sevoflurane	QoR-15	China
Yao 2019b	47 *vs* 48	57 *vs* 56[a]	68	I-II	Breast cancer surgery	SPB	Sevoflurane	QoR-40	China

ASA class = American Society of Anesthesiologists Physical Status classification; BMI = body mass index; [a]total body weight; MRM = Modified radical mastectomy; SPB = Serratus plane block; ESPB = Erector spinae plane block; TPVB = thoracic paravertebral block; PECS II blocks = pectoral and intercostal nerves blocks; RIB = Rhomboid intercostal block; TIVA = total intravenous anesthesia; NA = not available; QoR = quality of recovery

reporting, and other biases were deemed low in all studies, the attrition bias was unclear in three trials[15,17,29] as the proportion of excluded patients was more than 5% (range: 5.6–9.6%). The risks of bias of individual trials are detailed in ESM eTable 3.

Outcomes

PRIMARY outcome: impact of nerve blocks on total scores of QoR scales

Based on a forest plot (Fig. 3), two studies showed no significant improvement in recovery quality through the use of PNBs,[18,19] while the other six RCTs showed positive effects.[15–17,22,29,30] Four RCTs investigated the effect of nerve block on QoR-40 scale at 24 hr after surgery.[16,17,22,29] Our findings revealed a significantly higher total QoR-40 score in the PNB group than in the control group (MD, 12.8; 95% CI, 10.6 to 14.9; $P < 0.001$; $I^2 = 59\%$; $n = 251$) with a percentage improvement of 8.2% (Fig. 3A). Sensitivity analysis showed no significant impact on the total QoR-40 score by excluding certain trials. In addition, the heterogeneity was reduced to zero when one study[17] was excluded.

Four RCTs assessed the influence of PNBs on the QoR-15 scale at 24 hr after surgery.[15,18,19,30] Our results showed a significantly higher total QoR-15 score in the PNB group than in the control group (MD, 7.7; 95% CI, 4.9 to 10.5; $P < 0.001$; $I^2 = 75\%$; $n = 402$) with a percentage improvement of 5.2% (Fig. 3B). Nevertheless, sensitivity analysis showed a loss of significant difference in total QoR-15 score between the two groups when two trials were removed one at a time.[15,30] The heterogeneity remained significant (i.e., $I^2 > 50$) during sensitivity analysis. These findings provided weak evidence to support the beneficial effects of nerve block on total QoR-15 scores.

The overall effect of PNBs on patient-reported QoR is shown in ESM eFig. 3. Our analysis showed a favorable combined QoR score in the PNB group (SMD, 1.8; 95% CI, 0.92 to 2.60; $P < 0.001$; $I^2 = 95\%$; $n = 653$), suggesting a significant overall positive impact (i.e., SMD > 0.8)[31] of PNBs on the QoR among patients after breast cancer surgeries when the outcomes of the two QoD scales were merged. Subgroup analysis of the two assessment scales (i.e., QoR-40 *vs* QoR-15 scales) showed no significant difference in the effect sizes of their total scores when the PNB group was compared with the control group (P = 0.16).

Secondary outcome: impact of nerve blocks on individual dimensions of QoR scale

While we evaluated the effects of PNBs on individual dimension scores of the QoR-40 scale provided in three trials,[17,22,29] the impact on individual dimensions of the QoR-15 scale was not assessed because the scores were only available in one study.[19] Of the three studies[17,22,29] giving information for secondary outcome analysis based on QoR-40, their forest plots showed beneficial impacts of PNBs on recovery quality. Our analysis revealed a

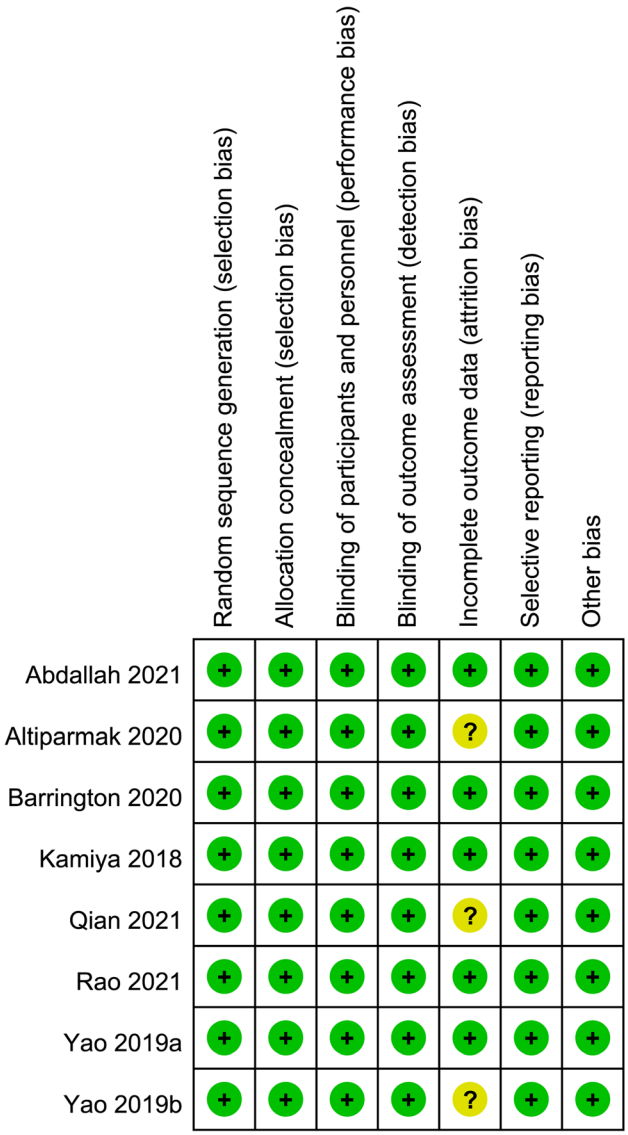

Fig. 2 Risks of bias of the included studies

significant association of PNBs with improvements in the emotional (MD, 2.5; 95% CI, 1.7 to 3.3; $P < 0.001$; I^2 = 0%; n = 183) (Fig. 4A), physical comfort (MD, 4.5; 95% CI, 2.5 to 6.4; $P < 0.001$; I^2 = 82%; n = 183) (Fig. 4B), physical independence (MD, 0.5; 95% CI, 0.19 to 0.88; P = 0.003; I^2 = 0%; n = 183) (Fig. 4C), and pain (MD, 3.6; 95% CI, 1.9 to 5.3; $P < 0.001$; I^2 = 84%; n = 183) (Fig. 4E) domains of the QoR-40 scale. There was no significant difference in the psychological support domain between the two groups (MD, 0.94; 95% CI, -0.55 to 2.42; P = 0.22; I^2 = 77%; n = 183) (Fig. 4D). Sensitivity analysis showed that the positive effects of PNBs on physical independence and pain domains became inconsistent by omitting certain trials, suggesting weak evidence in support of the beneficial effect of nerve block on the two domains.

Secondary outcome: impact of nerve blocks on postoperative morphine consumption and pain score

Our results showed that the use of nerve blocks was associated with a lower cumulative morphine consumption compared with that in the control group (MD, -14.5 mg; 95% CI, -21.5 to -7.5; $P < 0.001$; I^2 = 94%; four trials; n = 391) (Fig. 5A). Sensitivity analysis showed a loss of this association when two trials[15,16] were removed one at a time. Moreover, heterogeneity remained significant (i.e., I^2 > 50%) on sensitivity analysis, implying weak evidence endorsing the beneficial impact of nerve blocks on the reduction of postoperative cumulative morphine consumption.

Our findings showed comparable postoperative pain scores between patients with nerve blocks and those without (MD, -0.28; 95% CI, -0.7 to 0.14; P = 0.19; I^2 = 93%; six trials; n = 481) (Fig. 5B). Nevertheless, sensitivity analysis showed an association between nerve blocks and a reduction in pain score when one trial[30] was removed. Furthermore, heterogeneity was reduced to 37% when that study was excluded.[30] The findings suggested a weak link between nerve blocks and postoperative pain score.

Secondary outcome: impact of nerve blocks on postoperative nausea and vomiting

The incidences of PONV were 8.5% in the PNB group and 22.3% in the control group. Our results showed a significant correlation between the use of nerve blocks and a reduced risk of PONV (RR, 0.42; 95% CI, 0.27 to 0.66; $P < 0.001$; I^2 = 0%; six trials; n = 493) (ESM eFig. 4).[15–18,22,30] Omitting certain trials had no significant effect on this outcome in the sensitivity analysis.

Discussion

The current systematic review and meta-analysis showed an overall positive impact on the impacts of PNBs on patient-reported QoR, . Higher total QoR-40 scores were noted in all four included studies,[16,17,22,29] while better QoR-15 scores were shown in two[15,30] out of the four included trials.[15,18,19,30] Besides, the scores on all subscales of QoR-40 from three available studies,[17,22,29] except psychological support, were higher in the PNB group than in the control group. Despite similar pain scores between the two groups, the present study revealed additional benefits of PNBs including reduction in postoperative morphine consumption and risk of PONV.

Pain control after breast surgery is an important issue because up to 60% of patients experience significant acute pain and 8.2% experience chronic pain six to 12 months

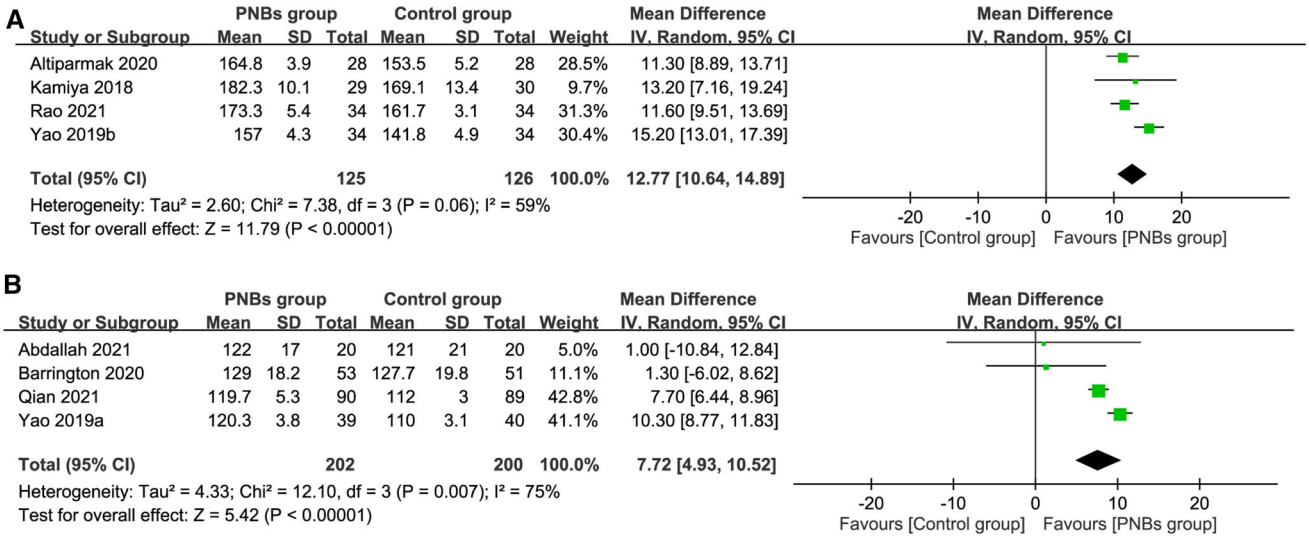

Fig. 3 Forest plot comparing the postoperative (A) quality of recovery (QoR)-40 score, and (B) QoR-15 score between peripheral nerve block (PNB) and control groups. CI = confidence interval; IV = inverse variance; SD = standard deviation

after the procedures.[32] Moreover, inadequate postoperative pain control has been found to delay patient recovery[33] and increase the likelihood of persistent pain.[34] Although a number of PNB techniques including pectoralis, erector spinae, serratus plane, and paravertebral blocks have been reported to provide superior analgesia in the early postoperative period and a higher reduction in opioid consumption compared with conventional analgesia techniques for breast surgery,[35–37] the current meta-analysis identified only weak associations between PNBs and the two secondary outcomes (i.e., pain score and morphine consumption). These weak associations may be attributed to a dilution of treatment effect from the variety of PNBs (i.e., up to five techniques) adopted in our included trials. Indeed, a previous study has reported variations in analgesic efficacy among different PNB approaches.[38] In addition, the application of multimodal analgesia for postoperative pain control in most of our included studies (ESM eTable 2) may mask some benefits of PNBs. Regarding the impact of PNBs on recovery quality, some studies suggested that the improvement in QoR related to PNBs may be attributed to their opioid-sparing effects.[29,39] In contrast, our results showed a better QoR despite the lack of a strong association of PNBs with morphine consumption. Although the reason remains unclear, a previous study reported that opioid-free anesthesia was only associated with an improvement in the physical comfort, physical independence, and pain-related dimensions of the QoR-40 scale.[11] On the other hand, the current meta-analysis showed that all subscales of the QoR-40, except psychological support, were enhanced with the use of PNBs, suggesting a possible multifactorial mechanism underlying the PNB-related improvement in patient-perceived QoR. Another possible explanation may be the ability of PNBs to reduce surgery-induced stress and inflammation response,[40,41] which was suggested by some authors who proposed a probable association of the QoR with a modulation of inflammation and stress response induced by surgical trauma and anesthesia.[42]

A previous study involving 204 patients reported a MCID (i.e., the smallest change in score signifying a meaningful change in health status)[43] of 8.0 for the QoR-15 scale and 6.3 for the QoR-40 scale.[8] The current meta-analysis showed that patients receiving PNBs had a higher total QoR-15 score (i.e., MD, 7.7 points) and QoR-40 score (i.e., MD, 12.8 points) than those without block intervention. Although the MCID for the QoR-15 scale was not significant, the MCID for the QoR-40 scale supported an improvement in early postoperative health status in patients receiving perioperative PNBs for their breast surgery. In addition, the weak evidence from sensitivity analysis in support of the beneficial effects of nerve block on our study outcomes using QoR-15 included two studies[18,19] that failed to show any beneficial effects of PNBs on pain score, opioid consumption, and QoR. Of the two studies, one focused on serratus plane block[18] and the other investigated pectoral and intercostal nerve (PEC II) blocks[19] in the setting of breast surgery. Considering that two large-scale recent meta-analyses have already provided evidence endorsing the association of serratus plane block or PEC II block with a lower postoperative opioid consumption and pain score at 24 hr after breast surgery,[44,45] selective inclusion of the two studies[18,19] since they adopted QoR-15 for patient assessment may have biased our results.

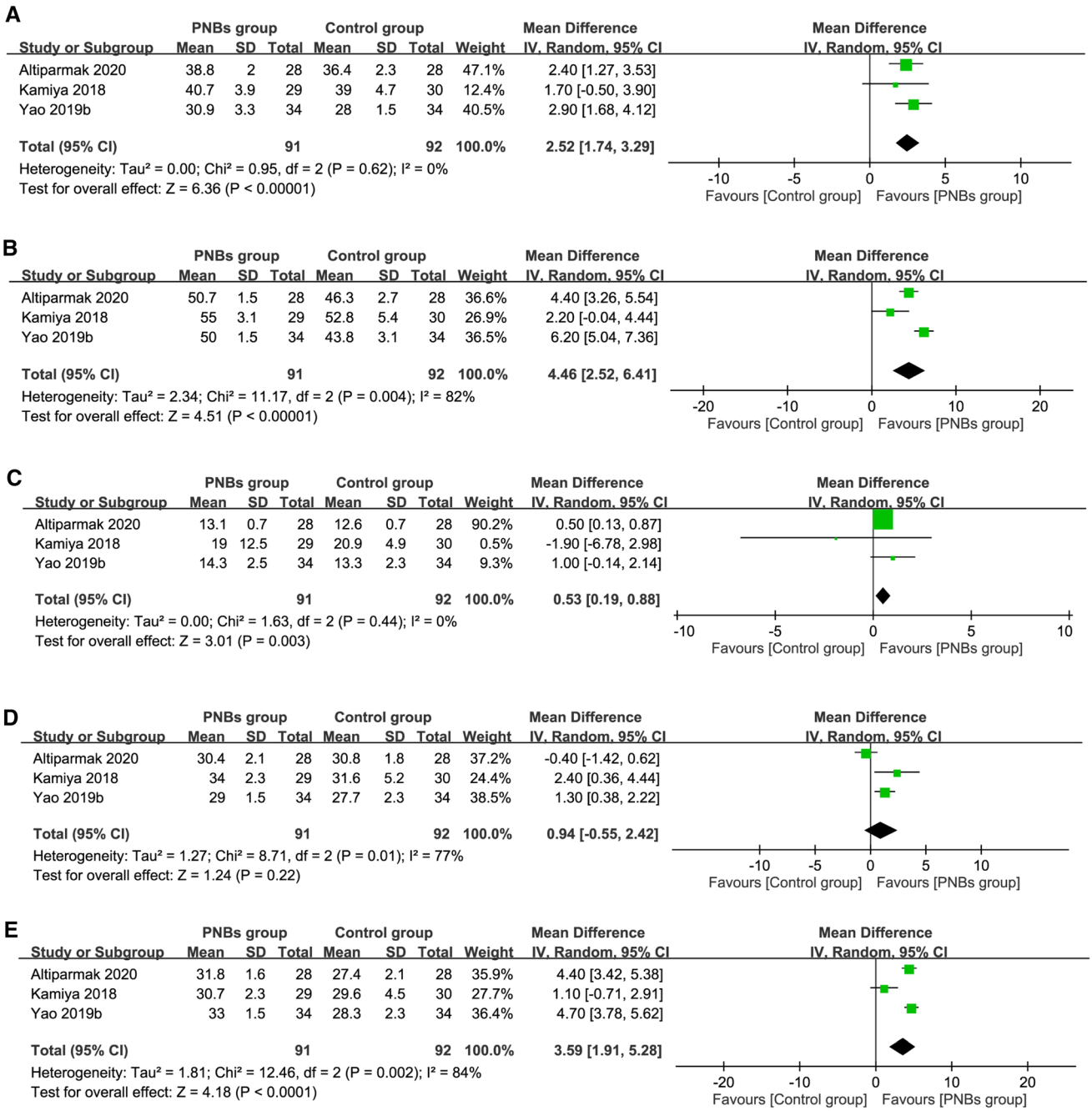

Fig. 4 Forest plot comparing postoperative scores on individual dimensions of the quality of recovery (QoR)-40 scale, including the (A) emotional, (B) physical comfort, (C) physical independence, (D) psychological support, and (E) pain domains between PNB and control groups. CI = confidence interval; IV = inverse variance; PNB = peripheral nerve block; SD = standard deviation

Although the relatively high heterogeneity (i.e., 75%) across the studies using QoR-15 remains unclear, a previous study using QoR-15 for postoperative patient evaluation reported an association between a poor quality of recovery and the frequency of comorbidities (e.g., diabetes mellitus and hypertension).[46] Therefore, the inclusion of two trials[18,19] that recruited patients with moderately severe comorbidities (i.e., American Society of Anesthesiologists [ASA] Physical Status classification III) out of the four studies with QoR-15 assessment[15,18,19,30] may have contributed to the heterogeneity. In contrast, the other four RCTs that focused on QoR-40 and only enrolled relatively healthy patients (e.g., ASA III)[16,17,22,29] showed a comparatively low heterogeneity of 59%.

There are several limitations in the current systematic review and meta-analysis. First, most studies only

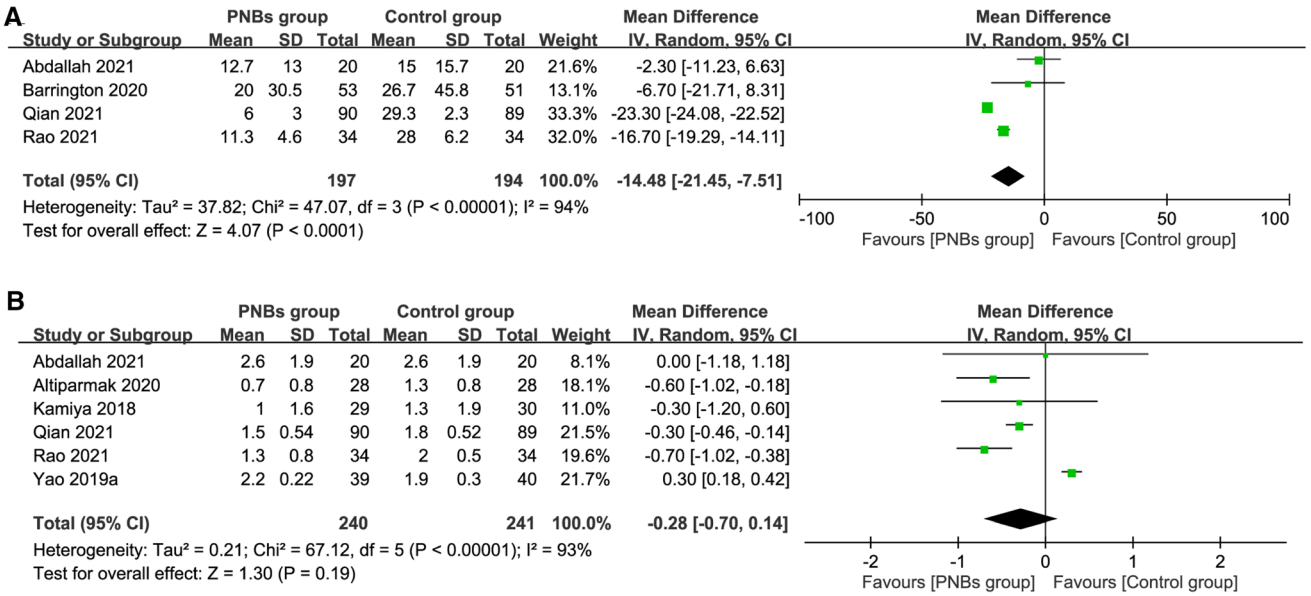

Fig. 5 Forest plot comparing postoperative (A) cumulative morphine consumption, and (B) pain score between PNB and control groups. CI = confidence interval; IV = inverse variance; PNB = peripheral nerve block; SD = standard deviation

investigated patient-reported QoR at 24 hr after surgery; therefore, the impact of PNBs on the late postoperative period remains unclear. Second, although a recent meta-analysis showed limited variations in postoperative analgesia for breast surgery among different regional anesthesia techniques,[37] the complexity of breast innervations (i.e., anterior and lateral branches of the first to seventh intercostal nerves)[47] may still introduce variations in analgesic effects from different PNB approaches, thereby contributing to heterogeneity in the current meta-analysis. The wide range of PNB techniques adopted in our included studies (i.e., five different approaches) precluded a meaningful comparison of patient safety in the current study. Variability of multimodal analgesia could be another potential source of heterogeneity. Third, while assessment of sensory block onset in six of the included studies before anesthesia induction may compromise blinding of the patients, PNBs after anesthetic induction in the other two trials would render the verification of nerve block efficacy impossible. Fourth, we only included studies that adopted the QoR-15 and QoR-40 scales, which are the most commonly used tools for QoR assessment, and excluded two studies that used other tools.[27,28] Fifth, because three studies using the QoR-40 provided detail on individual dimension scores but only one trial adopting the QoR-15 provided the information, we analyzed our secondary outcomes based on the former. Therefore, our findings on secondary outcomes need to be interpreted with caution. Finally, the limited number of included studies (eight) may impair the robustness of our conclusion.

Conclusion

The current study found a better patient-reported QoR in individuals undergoing breast cancer surgery with ultrasound-guided PNBs compared with those in the control group but without a positive impact on pain score at 24 hr after surgery. This approach was also associated with a lower postoperative opioid consumption and risk of PONV. Despite these promising results, future large-scale trials investigating each block separately are warranted to support our findings.

Author contributions *Ku-Chuan Hung* and *Ching-Chung Ko* contributed to conceptualization and literature search. *Chih-Wei Hsu* contributed to the methodology. *Chih-Wei Hsu* and *Yu-Li Pang* contributed to trial selection. *Jen-Yin Chen* contributed to data analysis. *Ku-Chuan Hung* and *Jen-Yin Chen* contributed to data extraction. *Ku-Chuan Hung*, *Jen-Yin Chen*, and *Cheuk-Kwan Sun* contributed to original draft preparation. *Ku-Chuan Hung* and *Cheuk-Kwan Sun* contributed to reviewing and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of interest The authors declare no conflict of interest.

Funding This research received no external funding.

Editorial responsibility This submission was handled by Dr. Stephan K. W. Schwarz, Editor-in-Chief, *Canadian Journal of Anesthesia/Journal canadien d'anesthésie.*

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