Single-Shot Interscalene Block: Light and Shadows

Alain Borgeat, MD

The boom of peripheral nerve blocks during the last years was supported by the hope that patients' outcomes would be greatly improved, and has led to the introduction of a number of new approaches. However, for many of these blocks, robust data demonstrating real patient benefits are still inconsistent.

Until now, single-shot regional anesthesia has been shown not to have medium-term or long-term benefits.[1–3] In a systematic review and meta-analysis in this issue of *Anesthesia & Analgesia*, Abdallah et al.[4] challenged the question of whether single-shot interscalene block improved short-term outcomes. Despite the methodologic limitations of a systematic review and meta-analysis, this work has sufficient evidence to conclude that a single-shot interscalene block provided better pain control only up to 6 hours with motion and 8 hours at rest after various shoulder surgeries. Minor outcomes such as an opioid-sparing effect, reduced opioid side effects, and patient satisfaction were present but limited to the first 24 postoperative hours. These results raised the question whether it is still worthwhile to perform single-shot interscalene block in this context, knowing that interscalene block may be associated, although rarely, with serious complications.[5,6] For minor shoulder procedures to avoid general anesthesia in specific indications, single-shot interscalene block is still undoubtedly a good option. The real question is what to do with major shoulder procedures, such as rotator cuff repair or shoulder arthroplasty, which are very painful and require the possibility to perform early passive mobilization in the modern orthopedic world. In this setting, a single-shot interscalene block will neither significantly reduce opioid consumption nor allow early mobilization and therefore its use considering the risk/benefit ratio is questionable. To make this issue more complicated, blockade of delta fibers, necessary to allow early mobilization, is poorly achieved with opioids.[7]

This investigation also highlighted the occurrence of a new problem, that of rebound pain.[8] Rebound pain increasingly is recognized by anesthesiologists involved in the practice of peripheral nerve blocks. For the patient, it is very painful when the block wears off. Large amounts of opioids are necessary to provide adequate pain control, blunting one of the primary goals of regional anesthesia, which is avoidance or reduction of opioids. How should we cope with this issue? The most useful and logical technique is the use of a perineural interscalene catheter, which allows a soft transition from high to low local anesthetic concentration. A gradual decrease has been shown to be beneficial. This decrease is supported by an investigation after rotator cuff repair in which the authors demonstrated that the administration of ropivacaine 0.3% for the first 24 hours and then 0.2% for the following 24 hours was shown to provide the most benefits to the patient.[9]

The work of Abdallah et al.[4] highlights some important messages. The hope that perineural blocks greatly improved patients' medium-term and long-term outcomes is still unclear. Unfortunately, data showing definitive and undisputable long-term benefits are not available. The enthusiasm for single-shot perineural block should be tempered, and the current need to assess the risk/benefit of each block seems reasonable. Perineural block has reached adulthood and for anesthesiologists performing regional techniques the time to think "when to block, when not to block, and how to block" has come. ■

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Will the Real Benefits of Single-Shot Interscalene Block Please Stand Up? A Systematic Review and Meta-Analysis

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BACKGROUND: Interscalene block (ISB) can provide pain relief after shoulder surgery, but a reliable quantification of its analgesic benefits is lacking. This meta-analysis examines the effect of single-shot ISB on analgesic outcomes during the first 48 hours after shoulder surgery.
METHODS: We retrieved randomized and quasirandomized controlled trials examining the analgesic benefits of ISB compared with none in shoulder surgery. Severity of postoperative pain measured on a visual analog scale (10 cm scale, 0 = no pain, 10 = worst pain) at rest at 24 hours was the designated primary outcome. Secondary outcomes included pain severity at rest and with motion at 2, 4, 6, 8, 12, 16, 32, 36, 40, and 48 hours postoperatively. Opioid consumption, postoperative nausea and vomiting, patient satisfaction with pain relief, and postanesthesia care unit and hospital discharge time were also assessed.
RESULTS: A total of 23 randomized controlled trials, including 1090 patients, were analyzed. Patients in the ISB group had more severe postoperative pain at rest by a weighed mean difference (95% confidence interval) of 0.96 cm (0.08–1.83; $P = 0.03$) at 24 hours compared with no ISB, but there was no difference in pain severity beyond that point. The duration of pain relief at rest and with motion after ISB were 8 and 6 hours, respectively, with a corresponding weighed mean difference in visual analog scale pain scores (99% confidence interval) of −1.59 cm (−2.60 to −0.58) and −2.20 cm (−4.34 to −0.06), respectively, with no additional pain relief benefits beyond these points. ISB reduced postoperative opioid consumption up to 12 hours, decreased postoperative nausea and vomiting at 24 hours, and expedited postanesthesia care unit and hospital discharge. The type, dose, and volume of local anesthetic used did not affect the results.
CONCLUSIONS: ISB can provide effective analgesia up to 6 hours with motion and 8 hours at rest after shoulder surgery, with no demonstrable benefits thereafter. Patients who receive an ISB can suffer rebound pain at 24 hours but later experience similar pain severity compared with those who do not receive an ISB. ISB can also provide an opioid-sparing effect and reduce opioid-related side effects in the first 12 and 24 hours postoperatively, respectively. These findings are useful to inform preoperative risk-benefit discussions regarding ISB for shoulder surgery. (Anesth Analg 2015;120:1114–29)

Interscalene block (ISB) of the brachial plexus can provide analgesic benefits to patients undergoing shoulder surgery, including a reduction in pain scores, opioid consumption, and postoperative nausea and vomiting (PONV).[1,2] Although continuous ISB may extend these benefits, compared with single-shot ISB, the routine use of catheters for less invasive shoulder surgeries has been described as impractical and unrealistic[3] and is not welcomed by most shoulder surgeons.[4] Additionally, despite emerging evidence supporting the analgesic effectiveness of perineural adjuvants to prolong the duration of single-shot ISB,[5,6] there are insufficient safety data supporting their routine use. Real concerns regarding the intrinsic neurotoxicity of adjuvants, worsening of local anesthetic-induced neurotoxicity,[7] and adjuvant-mediated early-onset hyperalgesia and rebound pain[8] persist. Consequently, single-shot ISB is widely considered to be the gold standard for pain relief after shoulder surgery and is central to both multimodal postoperative and preventive analgesic strategies.[9–11]

A reliable estimate of the duration and magnitude of these analgesic benefits of ISB is lacking.[1,2] Although some authors claim that ISB can provide clinically important pain relief and opioid-sparing effects lasting for 12[12,13] and even 24 hours[14,15] postoperatively, others report a significantly shorter duration of pain relief not exceeding 6 to 8 hours[16] at best and even describe a rebound pain phenomenon occurring at 24

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hours in patients who receive ISB for shoulder surgery.[17] Furthermore, the risks of ISB may be significant. ISB has long been associated with respiratory compromise[18–20] and likely carries a higher risk of transient and long-term neurologic complications compared with other peripheral nerve blocks.[21–27] Recent evidence suggests that ISB may cause permanent phrenic nerve damage.[28,29] Therefore, the decision to perform ISB must be based on valid and reliable understanding of the duration and extent of analgesic benefits in the setting of shoulder surgery. As the primary objective of this meta-analysis, we aimed to investigate pain severity at 24 hours after shoulder surgery with a single-shot ISB; we also examined the effect of ISB on clinically important analgesic outcomes during the first 48 hours as a secondary objective. We hypothesized that single-shot ISB provides effective pain relief up to and including 24 hours.

METHODS

The authors followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines[30] in the preparation of this meta-analysis. Randomized and quasirandomized controlled trials (RCTs) that examined the duration of analgesia after single-shot ISB were reviewed and evaluated using a predesigned protocol.

Literature Search

Two of the authors (FWA and RB) independently searched the U.S. National Library of Medicine database (MEDLINE), the Medline In-Process and Other Non-Indexed Citations databases, the ExcerptaMedica database (EMBASE), Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials database. The databases were searched using medical subject headings, text words, and controlled vocabulary terms relating to the main components of the research question; these included (1) interscalene block, (2) shoulder or shoulder surgery, (3) postoperative pain, and (4) analgesia, which were used individually and in various combinations (Supplemental Digital Content, Appendix 1, http://links.lww.com/AA/B87). The bibliographies of included articles were also handsearched for additional RCTs meeting the inclusion criteria. Studies in human subjects ≥18 years of age published between January 1970[31] and April 2014 were considered. The authors also sought and retrieved relevant abstracts of the following international meetings: American Society of Anesthesiologists (2000–2013), American Society of Regional Anesthesia (2005–2014), and European Society of Regional Anaesthesia (2007–2013). Additionally, the published trials registry website at www.clinicaltrials.gov was examined.

Eligibility Criteria

We retrieved full reports and abstracts of RCTs examining the effects of ISB (ISB group) compared with placebo, systemic analgesia, or general anesthesia (control group) on analgesic outcomes in patients undergoing arthroscopic or open shoulder surgery. Blocks administered for surgical anesthesia and/or postoperative analgesia were considered. We excluded studies if analgesic outcomes (pain scores or analgesic consumption) were not reported; if catheter-based continuous ISB were used; if the analgesic effect of ISB could not be assessed in isolation from other concurrent analgesic interventions, such as local anesthetic wound infiltration or intraarticular injection; if surgeries involved anatomical areas other than the shoulder joint, such as the proximal humerus or axilla; if shoulder procedures did not involve surgery, such as closed reduction; or if adjuvants other than epinephrine were added to local anesthetics. Additionally, dose-ranging trials or involving nonadult patients were also excluded. No language restrictions were imposed on inclusion in this meta-analysis. We used a combination of on-line electronic translation confirmed by human translation for RCTs published in languages other than English.

Selection of Included Studies

Two authors (FWA and RB) independently evaluated the results of the literature search. The decision on including qualifying studies in the review was taken by consensus between 2 of the authors; papers that failed to meet the inclusion criteria were excluded at this phase. If an agreement could not be reached, the opinion of a third evaluator (KA) was sought.

Methodological Quality Scoring

The quality of the reviewed RCTs was independently assessed using the modified Jadad scale[32] by 2 of the authors (FWA and RB). The scale evaluates RCTs for randomization, adequacy of randomization method, evaluation of double blinding, allocation concealment, and completeness of data at follow-up. A Jadad score was assigned to each RCT by consensus; if an agreement could not be reached, the opinion of a third evaluator (KA) was sought. Trials were not excluded based on the quality scores; however, but RCTs were excluded if they had <10 subjects per group to reduce the probability of publication bias.

Data Extraction

A standardized data collection form developed for this review was used by the authors, independently, to extract data. The authors resolved any discrepancies by re-examining the source data; if consensus could not be reached, the opinion of a third evaluator (KA) was sought. Extracted data included the primary author; year of publication; surgical procedure performed; nature of surgical anesthetic provided; sample size; comparative groups; number of patients in each group; nature of primary outcome studied; pain severity scores at rest and with motion at 2, 4, 6, 8, 12, 16, 24, 32, 36, 40, and 48 hours; interval opioid consumption at 12, 24, 36, and 48 hours postoperatively; cumulative opioid consumption at 24 and 48 hours; time to first analgesic request (minutes); frequency of opioid-related side effects (PONV, pruritus, and excessive sedation); frequency of block-related complications; patient satisfaction with pain relief; and postanesthesia care unit (PACU) and hospital discharge times. We also extracted details of the ISB technique (localization technique and type and dose of local anesthetics) as well as analgesic regimen used. The postoperative pain scores were assessed at frequent time points to capture the best estimate of the duration of analgesic efficacy of singe-shot ISB.

For the purpose of this review, pain numerical rating scale scores or verbal rating scale scores were converted[33] to a 0 to 10 visual analog scale (VAS) scores, where 0 = no pain and 10 = worst pain imaginable. All opioid medications

consumed during the first 48 hours postoperatively were converted into equianalgesic doses of IV morphine.[34] The extent of patient satisfaction with postoperative pain relief at 24 hours was expressed as VAS score (0 = least satisfied and 10 = most satisfied).

Definition of Relevant Outcome Data

The severity of pain (VAS) at rest at 24 hours postoperatively after shoulder surgery was designated as the primary outcome. This time point was selected to capture the maximal reported duration of local anesthetic action for ISB[14,15] as well as the effects, if any, of ISB on both preventive analgesia[35,36] and rebound pain.[17] We performed an exploratory evaluation of several analgesic secondary outcomes. These included pain severity at rest and with motion at 2, 4, 6, 8, 12, 16, 32, 36, 40, and 48 hours postoperatively. We also assessed the interval opioid consumption at 12, 24, 36, and 48 hours postoperatively as well as the cumulative opioid consumption at 24 and 48 hours. Additionally, we examined the frequency of opioid-related side effects, patient satisfaction with pain relief, and PACU and hospital discharge times.

A Priori Hypothesis for Sources of Heterogeneity

To investigate the potential sources of heterogeneity in our data, we identified, a priori, the characteristics of individual studies that may lead to variations in the results and subsequently examined their contribution to heterogeneity using subgroup analysis. Based on evidence suggesting an impact on postoperative pain severity and duration of analgesia after shoulder surgery, the following factors were selected: (1) low-volume (<15 mL) versus high-volume ISB[37–39]; (2) intermediate-acting (lidocaine and mepivacaine) versus long-acting (bupivacaine, levobupivacaine, and ropivacaine) local anesthetics[40]; (3) addition of epinephrine as an adjuvant versus no epinephrine[41]; (4) surgical versus analgesic ISB[42]; (5) preincisional versus postincisional ISB[43,44]; (6) nerve stimulator versus ultrasound (US)-guided ISB[45]; (7) multimodal postoperative analgesia (combined use of opioid analgesics and analgesic adjuncts such as acetaminophen and nonsteroidal anti-inflammatory drugs) versus unimodal postoperative analgesia (use of opioid analgesics only)[46,47]; and (8) open versus arthroscopic shoulder surgery.[48] The primary outcome results, 24 hours pain scores at rest, were examined using alternative subgroup analysis to inspect the extent of variation across studies that was due to heterogeneity introduced by the aforementioned factors rather than chance alone.

Statistical Analysis

Results presented in published tables were considered as the primary source of data for extraction. For data not presented in tables, we attempted contacting authors of the respective manuscripts. In the event that authors did not respond or provide the requested data, we abstracted from published figures as a secondary data source. Authors of abstracts included in the review were also contacted for additional information regarding methodology, missing details, and outcome data.

Dichotomous data describing patient satisfaction data reported as odds ratios (ORs) were converted to continuous effect size to facilitate quantitative analysis.[49] Dichotomous data reporting opioid-related side effects were converted to incidence (n/N) during a given time interval; and the single highest incidence was used to capture patients who experienced a particular side effect at least once. Continuous data were recorded as mean and SD, and the median was used to estimate the mean if its value was not provided.[50] When the value of the SD was not stated or graphically represented, it was estimated as range/4[50] or interquartile range/1.35.[51] Whenever necessary, the 95% confidence interval (CI) was used to estimate the range, and the SD of a variable was estimated as the most extreme values. If the value of a particular outcome was reported more than once during a prespecified time interval, the most conservative value was used herein.

Meta-Analysis

The outcome data were entered into the statistical program (Revman 5.1; Cochrane Library, Oxford, England) and cross-checked by 2 of the authors (FWA and RB). The authors made an arbitrary pre hoc decision to include data only when available from ≥100 subjects or results from 3 RCTs could be combined. We used meta-analytic techniques to combine and analyze both continuous and dichotomous data. As a variety of shoulder surgeries were examined, the DerSimonian random effect modeling[52] was selected. When >1 intervention group received ISB, these groups were combined into a single group using techniques outlined in the Cochrane Handbook.[53]

For the primary outcome (severity of pain at rest at 24 hours postoperatively), we calculated the weighed mean difference and 95% CI. A statistically significant difference from control was considered when P value <0.05 and the 95% CI did not include 0. For the secondary outcomes, a conservative approach was selected to account for the exploratory nature of the analysis, the smaller number of studies pooled, and the risk of multiple testing bias associated with repeated comparisons during several time intervals.[54,55] We calculated the weighed mean difference and 99% CI for continuous outcomes, the OR and 99% CI for dichotomous outcomes, and the ratio of means and 99% CI for time-to-event outcomes.[56,57] Additionally, a statistically significant difference from control was considered when P value <0.01, and the 99% CI did not include 0 for continuous outcomes or 1 for dichotomous outcomes.

The I^2 statistic was used to examine the extent of heterogeneity among the trials reviewed.[58] For significant heterogeneity (I^2 > 50%), we planned to investigate the sources of heterogeneity of the primary outcome data (i.e., pain scores at rest at 24 hours) using a series of subgroup analysis according to the preidentified potential heterogeneity sources.[59] We also planned sensitivity analysis to examine the impact of eliminating 1 RCT with largest treatment effect on the pooled outcome analysis.

Finally, we evaluated the risk of publication bias by checking for asymmetry of the funnel plots, as described in the Egger regression test.[60] We also sought trials in www.clinicaltrials.gov to determine whether or not additional unpublished data were available.

RESULTS

Our search retrieved 70 studies, 23 of which were published between 1994 and 2013 and met the inclusion

criteria.[13–17,42,61–77] Appendix 2 (Supplemental Digital Content, http://links.lww.com/AA/B88) summarizes the reasons for excluding 47 studies, and Figure 1 represents the study selection process. The sources RCTs included 22 full manuscripts[13–17,42,61–69,71–77] and 1 published dissertation.[70] The decision to include these RCTs was reached by consensus in 22 of 23 cases. Of these, 6 studies required full-text electronic translation that was confirmed by human translation: 1 Chinese,[73] 1 German,[70] 1 Japanese,[69] and 3 Korean.[66,68,71] Additional methodological details needed to decide on inclusion were available from the authors of 6 studies,[16,64,65,68,74,77] whereas unpublished data relating to the outcomes assessed were available from the authors of 8 studies.[13,42,62,63,65,72,76,77] Unpublished relevant trials registered on www.clinicaltrials.gov were still in progress, whereas all completed relevant trials had already been published.

Data relating to a total of 1090 patients were available for analysis: 577 patients in the ISB group and 513 in the control group. Table 1 summarizes the trial characteristics and the outcomes of interest that were assessed in each trial. All 23 trials reported pain scores and analgesic consumption, whereas only 10[17,42,64,65,69–71,74,76,77] reported pain scores both at rest and with motion. The ISB techniques used in the reviewed trials differed with respect to the volume and nature of local anesthetics used, the intent (surgical versus analgesic) and timing of ISB, its means of localization, the accompanying analgesic regimens, and the surgical approach used. Table 2 summarizes the analgesic interventions used in each trial. Low-volume ISB was examined in 4 trials,[62,66,69,75] whereas high-volume ISB was studied in 19 trials.[13–17,42,61,63–65,67,68,70–74,76,77] Intermediate-acting local anesthetics were used for ISB in 3 trials,[66,72,73] whereas long-acting local anesthetics were used in 20.[13–17,42,61–65,67–71,74–77] ISB was used to provide surgical anesthesia in 6 trials[42,67,68,71,76,77] and postoperative analgesia in 17.[13–17,61–66,69,70,72–75] The timing of ISB was preincisional in 21 trials,[13–17,42,62–71,73–77] and postincisional in 2.[61,72] Brachial plexus localization for ISB depended on paresthesia in 2 trials,[61,63] nerve stimulation in 14,[13–17,42,62,64–66,70,72,74,75] US in 4,[67,69,73,77] and nerve stimulation combined with US in 3.[68,71,76] Multimodal analgesic regimens supplemented ISB in 16 trials,[13,15–17,42,61–63,65,67–69,71,74,76,77] whereas unimodal regimens were used in 7.[14,64,66,70,72,73,75] Surgical approach was open in 4 trials[42,61,64,72] and arthroscopic in 19.[13–17,62,63,65–71,73–77] One trial[77] included 2 patient groups that received ISB: an analgesic ISB and a surgical ISB; only the analgesic ISB was included in the review. Another trial had 2 comparisons involving 4 groups,[65] 2 of which were excluded as they included analgesic cointerventions (infiltration).

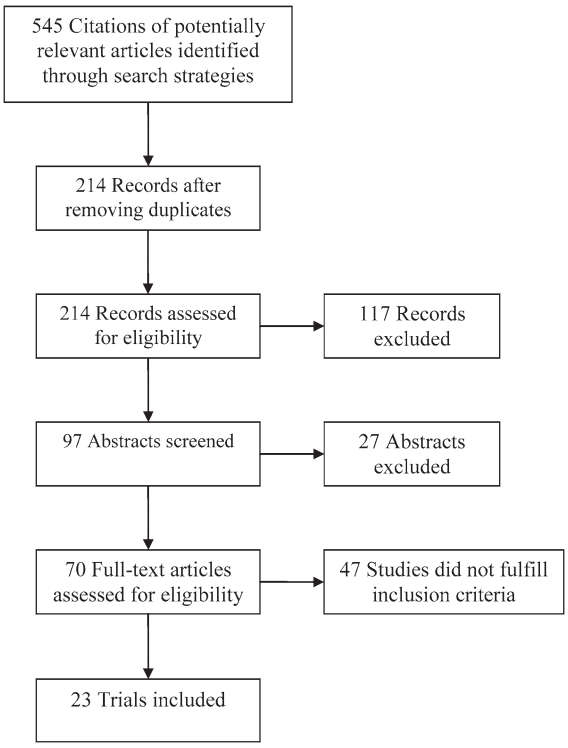

Figure 1. Flowchart summarizing the study selection process and depicting retrieved, included, and excluded randomized controlled trials.

The methodological quality score[32] median (range) for the 23 RCTs included was 4 (2–5). Eighteen of trials included were randomized, 5 were quasirandomized, and all reported complete patient follow-up. Seventeen of the trials were double blinded, 11 described adequate blinding techniques, and 15 described adequate randomization techniques. Eight of the 23 trials achieved a quality score of 5 of 5, that is, were double blinded, randomized, described adequate blinding and randomization techniques, and reported complete patient follow-up.

Pain at Rest

Data regarding postoperative pain at rest at 24 hours were available from 18 trials[13–17,42,62–65,68–72,74,76,77] inclusive of 891 patients, with 468 patients in the ISB group and 423 in the control group. Compared with no ISB, a single-shot ISB increased pain severity at rest by 0.96 cm (0.08–1.83; $P = 0.03$) at 24 hours postoperatively (Fig. 2).

The primary outcome, pain at rest at 24 hours, results were characterized by high heterogeneity (I^2 = 98%; $P < 0.00001$). The limited number of trials (<3) in the low-volume local anesthetic (LA),[62,69] intermediate-acting LA,[72] and postincisional ISB[72] subgroups precluded a meaningful subgroup analysis for the respective hypothesized heterogeneity sources. As for the other sources of heterogeneity, respective subgroup analysis confirmed that both ISB patient subgroups experienced worse pain scores at rest at 24 hours compared with control, regardless of the potential heterogeneity sources. Specifically, subgroup analysis comparing both subgroups to control suggests that the VAS pain scores at rest were significantly higher in the ISB group for patients who received local anesthetics without epinephrine 1.1 (0.25–1.9; $P < 0.00001$), an analgesic block 1.0 (0.17–1.9; $P < 0.00001$), nerve stimulation–guided block 1.0 (0.04–2.0; $P < 0.00001$), unimodal postoperative analgesia 2.4 (0.7–4.1; $P < 0.00001$), or had an open surgery 2.8 (0.26–5.3; $P < 0.00001$) compared with patients who received local anesthetics with epinephrine 0.94 (0.51–1.4), a surgical block 0.78 (0.13–1.4), US-guided block 0.89 (0.23–1.6), multimodal postoperative analgesia 0.88 (0.05–1.7), or had arthroscopic shoulder surgery 0.90 (0.11–1.7), respectively. Nevertheless, these comparisons remain limited by their indirect nature and should only be considered as hypothesis generating. Furthermore, the statistical weight of the treatment effect of the trials varied between 4.6% and 5.9%, with trials having

Table 1. Outcomes of Interest Assessed in the Reviewed Trials

Author	Jadad score	Surgery	N	Groups (*n*)	Anesthesia	Primary outcome
Kinnard[61]	5	Open acromioplasty, rotator cuff repair	30	1. ISB + GA (15) 2. Control + GA (15)	GA	N/D
Al-Kaisy[62]	5	Arthroscopic surgery	30	1. ISB + GA (15) 2. Sham block + GA (15)	GA	N/D
Bain[63]	3	Arthroscopic acromioplasty	40	1. ISB + GA (20) 2. Control + GA (20)	GA	N/D
Gohl[64]	2	Open shoulder surgery	52	1. ISB + GA (28) 2. Control + GA (15)	GA	N/D
Singelyn[15]	5	Arthroscopic acromioplasty	120	1. ISB + GA (30) 2. Control + GA (30) 3. Suprascapular block + GA (30)[a] 4. Intraarticular inj + GA (30)[a]	GA	Postoperative pain (time not specified)
Hadzic[42]	4	Open rotator cuff repair	50	1.ISB (25) 2. GA (25)	ISB versus GA	Time to discharge readiness
Oh[65]	4	Arthroscopic surgery	84	1. ISB + GA (20) 2. Control + GA (21) 3. Infilt + GA (20) 4. ISB + Infilt + GA (21)	GA	N/D
Nisar[13]	3	Arthroscopic acromioplasty	60	1. ISB + GA (19) 2. Control + GA (15) 3. Subacromial inj + GA (19)	GA	Cumulative 24 hours opioid consumption
Cho[66]	4	Arthroscopic surgery	40	1. ISB + GA (20) 2. Sham block + GA (20)	GA	Cumulative 2 hours opioid consumption
Fontana[14]	5	Arthroscopic surgery	120	1. ISB + GA (20) 2. Control + GA (20) 3. Intraarticular inj + GA (19) 4. Subacromial inj + GA (21) 5. Intraarticular + subacromial inj + GA (23)[a]	GA	Cumulative 24 hours opioid consumption
Gonano[67]	3	Arthroscopic surgery	40	1. ISB (20) 2. GA (20)	ISB versus GA	Anesthesia costs
Shin[68]	4	Arthroscopic surgery	60	1. ISB (20) 2. Control + GA (20) 3. Suprascapular block + GA (20)[a]	ISB versus GA	N/D
DeMarco[17]	5	Arthroscopic surgery	61	1. ISB + GA (28) 2. Sham block + GA (25)	GA	Postoperative pain (time not specified) + Cumulative 80 hours opioid consumption
Taninishi[69]	4	Arthroscopic rotator cuff repair	84	1. ISB + GA (49) 2. Control + GA (35)	GA	Postoperative pain (time not specified)
Rose[70]	5	Arthroscopic surgery	90	1. ISB + GA (30) 2. Control + GA (30) 3. Intraarticular inj + GA (30)	GA	Quality of recovery
Kim[71]	3	Arthroscopic surgery	40	1. ISB (20) 2. Control + GA (20)	ISB versus GA	Postoperative pain (time not specified)
Mahmoodpoor[72]	4	Open shoulder surgery	50	1. ISB + GA (25) 2. Control + GA (25)	GA	N/D
Bin[73]	3	Arthroscopic surgery	60	1. ISB + GA (29) 2. Control + GA (30)	GA	N/D
Cho[74]	2	Arthroscopic rotator cuff repair	60	1. ISB + GA (30) 2. Control + GA (30)	GA	Postoperative pain at 24 hours
Lee[75]	3	Arthroscopic rotator cuff repair	50	1. ISB+ GA (25) 2. Sham block + GA (25)	GA	N/D
Lee[16]	2	Arthroscopic rotator cuff repair	61	1. ISB + GA (26) 2. Control + GA (17) 3. Suprascapular block + axillary block + GA (18)	GA	N/D
Salviz[76]	5	Arthroscopic rotator cuff repair	71	1. ISB (23) 2. GA (20)	ISB versus GA	Postoperative pain at 1 week
Lehmann[77]	5	Arthroscopic surgery	120	1. ISB (40) 2. Control + GA (40) 3. ISB + GA (40)	ISB versus GA	N/D

Table 1. *Continued*

Rest pain scores		Dynamic pain scores		Opioid consumption		Time to first analgesic request	Opioid-related adverse effects	Block-related complications	Patient satisfaction	PACU discharge time	Hospital discharge time	Functional outcomes
0–24 hours	24–48 hours	0–24 hours	24–48 hours	0–24 hours	24–48 hours							
●				●	●			●				
●				●		●	●	●	●		●	
●				●			●	●				●
●	●						●		●			
●		●		●			●		●			
●	●						●	●	●		●	
●	●						●				●	
●				●		●	●			●	●	
●				●			●	●				
●				●			●		●			
●							●	●		●		
●							●	●			●	
●	●			●	●			●				
●	●			●	●	●	●	●				
●	●	●	●	●	●	●	●		●			
●	●							●				
		●							●			
●								●	●			
●	●			●	●		●	●				●
		●		●								
●				●			●		●			
●	●			●	●	●	●	●		●	●	
●	●			●	●				●			

(●) = outcome assessed; GA = general anesthesia; infilt = infiltration; inj = injection; ISB = interscalene block; *N* = number recruited; *n* = number analyzed; N/D = not defined; PACU = postanesthesia care unit.

[a]Comparative group not included in the analysis.

similar contribution to the weighed mean difference; sensitivity analysis could not uncover 1 single study or a small group of studies that would alter the pain scores at rest at 24 hours pooled results if eliminated from the analysis. Finally, the construction of Begg funnel plot and assessment of the degree of symmetry using the Egger test do not suggest significant publication bias ($P = 0.16$) (Fig. 3).

Pain at Rest for Other Time Points

Compared with control, ISB reduced pain at rest at 2, 4, 6, and 8 hours postoperatively by 3.66 cm (−4.83 to −2.49; $P < 0.00001$), 3.33 cm (−4.70 to −1.96; $P < 0.00001$), 3.05 cm (−5.25 to −0.84; $P = 0.0004$), and 1.59 cm (−2.60 to −0.58; $P < 0.0001$), respectively (Table 3). The 8 hours evaluation of pain at rest was the last time point at which a significant reduction in pain attributed to ISB could be observed (Figs. 4 and 5) At 16 hours postoperatively, ISB increased pain at rest by 1.16 cm (0.02–2.30; $P = 0.009$) compared with the control (Table 3 and Fig. 2). There were no differences in pain at rest between the 2 groups beyond 24 hours (Table 3). Figure 6 plots the changes in the pain at rest (VAS scores, weighed mean difference) between the 2 groups over time.

Pain with Motion

Compared with control, ISB reduced pain with motion at 2, 4, and 6 hours after shoulder surgery by 4.76 cm (−7.65 to −1.88; $P < 0.0001$), 2.98 cm (−5.95 to −0.01; $P = 0.01$), and 2.20 cm (−4.34 to −0.06; $P = 0.008$), respectively (Table 3). No further pain with motion benefits attributable to ISB were observed beyond 6 hours (Table 3). Figure 7 plots the changes in the pain with motion (VAS scores, weighed mean difference) between the 2 groups over time.

Time to First Analgesic Request

The time to first postoperative analgesic request after shoulder surgery was prolonged in patients who received an ISB compared with those who did not. The prolongation, expressed as lower CI limit (point estimate), was at least 7.77-fold (point estimate 8.04-fold) (Fig. 8).

Opioid Consumption

ISB reduced postoperative opioid (IV morphine equivalent) consumption for the 0 to 12 hours interval by 12.1 mg (−21.75 to −2.45; $P = 0.001$), or a 48.3% relative reduction, compared with control (Fig. 9A and Table 3). However, the ISB and control groups had similar postoperative opioid consumption during the 12 to 24 hours interval (Fig. 9B) as well as during the 0 to 24 hours interval as a whole (Table 3).

No significant differences in postoperative opioid consumption between the ISB and control group were observed between 24 and 48 hours postoperatively (Table 3). Furthermore, the opioid consumption during the 24 to 36 hours and 36 to 48 hours intervals was not statistically different between the 2 groups.

Opioid-Related Side Effects

The incidence of PONV during the first 24 hours after shoulder surgery was reduced in the ISB group by an OR (99% CI) of 0.41 (0.18–0.92; $P = 0.004$), or a 59% decrease in the odds, compared with control (Table 3 and Fig. 10). Inconsistency of reporting precluded quantitative and qualitative evaluation of the effect of ISB on postoperative pruritus and sedation.

Patient Satisfaction with Pain Relief

Patient satisfaction with pain relief measured on a VAS scale was higher for the ISB group by 0.55 (0.15–0.95; $P = 0.0004$), or a 6.0% relative increase, compared with control (Table 3 and Fig. 11).

Discharge Time

ISB reduced the duration of PACU stay after shoulder surgery[13,64,67,76] compared with control; the reduction, expressed as lower CI limit (point estimate), was ≥4% (point estimate: 15%) (Table 3). The duration of hospital stay after ambulatory shoulder surgery[42,62,76] was also reduced by ≥43% (point estimate: 63%) in the ISB group compared with control (Table 3 and Fig. 12).

Other Outcomes

We performed a qualitative assessment on 2 outcomes: block-related complications and postoperative functional outcomes. None of the trials reviewed herein reported any block-related complications. Heterogeneous functional recovery assessment protocols in the 2 trials[63,74] that examined this outcome prevented any conclusions beyond absence of the effect of ISB on this particular outcome.

DISCUSSION

This quantitative systematic review underscores the early clinical benefits of ISB in the setting of shoulder surgery; single-shot ISB offers effective pain control up to 8 hours, an opioid-sparing effect up to 12 hours, reduction in PONV up to 24 hours, and expedited PACU and hospital discharge. However, our results suggest that the duration of analgesia associated with ISB in the setting of shoulder surgery is limited to 6 and 8 hours with motion and at rest, respectively, which is not as prolonged as traditionally described.[12–15] Importantly, patients receiving an ISB can experience more pain between 16 and 24 hours postoperatively than those without ISB, and their analgesic outcomes are not different from their control counterparts at any time beyond that point. Such findings should be presented to patients in risk-benefit and informed consent discussions regarding the duration of ISB analgesia.

Previous qualitative systematic reviews[1,2] have reported that single-shot ISB is associated with significant reduction of pain scores up to 24 hours after shoulder surgery, a finding deduced from only a relatively small number of trials that compared single-shot ISB to control. In contrast, the present meta-analysis is the first to report the actual treatment effect of single-shot ISB by statistically pooling the results across 23 trials; in so doing, we could not demonstrate analgesic benefits of single-shot ISB beyond 8 hours. Our work is also the first to provide evidence of rebound pain at 16 and 24 hours after shoulder surgery in patients who receive a single-shot ISB. Although the magnitude of the rebound pain that we observed may seem modest, it is noteworthy that the absolute value of the minimal clinically important difference in pain severity continues to be debatable, but

values varying between 0.9 and 1.1 cm on a 10 cm VAS scale have been reported to be clinically significant.[78,79]

Our findings challenge the role[80] of ISB in the provision of preventive analgesia.[81,82] Not only did ISB fail to reduce pain at 24 hours but also was associated with worsened pain between 16 and 24 hours postoperatively among patients who received the ISB block compared with those who did not. Rebound pain after nerve blocks is a real concern for patients and practitioners alike; practitioners often prompt patients receiving blocks to start taking oral analgesics well before the nerve block effect wears off.[83,84] Rebound pain has been reported in several RCTs after popliteal block for ankle surgery[85] and femoral block for knee replacement.[86] In a recent retrospective study of 84 patients, Williams et al.[87] also reported a 20% increase in pain severity after nerve block resolution in patients who received a single-shot femoral block for anterior cruciate ligament repair compared with those who did not. Although the physiologic mechanisms underlying such rebound pain remain speculative,[88–91] the type of local anesthetic used appears not to matter.[7]

The role of ISB for shoulder surgery has recently been brought to the fore. Clinical studies,[25] retrospective data,[92] and cadaveric data[93,94] suggest that the nerve roots of the interscalene brachial plexus may be particularly susceptible to nerve injury from ISB; indeed, ISB is associated with higher risks of transient[26,95] and long-term[27] neurologic complications compared with other peripheral nerve blocks. Although ISB has traditionally been associated with transient diaphragmatic paresis and the risk of pneumothorax, more recent data[28,29] implicate ISB in delayed-onset phrenic nerve damage[96] and permanent unilateral diaphragmatic paralysis.[29,97,98] Taken together, it is not surprising that some experts have questioned the opportunity cost of ISB in favor of alternative local anesthetic–based analgesic strategies for shoulder surgery.[1,28,99–102] Evidence suggests that supraclavicular brachial plexus,[103] suprascapular nerve,[16,99,100] and axillary nerve blocks,[16,100] as well as subacromial bursa[104] and intraarticular[105] local anesthetic instillation, may offer analgesic benefits for patients undergoing shoulder surgery. However, none of these techniques has been shown to be superior or as effective as ISB.

Limitations

Our review has several limitations. First, the source data were drawn from diverse settings in which anesthetic and analgesic management varied, leading to considerable heterogeneity affecting primary and secondary outcome results. We also did not stratify our results according to the specific type of shoulder surgery. The duration and severity of postoperative pain may vary depending on the type of shoulder surgery (i.e., rotator cuff repair, Bankart repair, superior labrum anterior posterior repair, shoulder open reduction and internal fixation, and shoulder arthroplasty). Most of the RCTs reviewed herein involved a small number of subjects, with a maximal group size of 40 patients. Such small trials tend to increase the possibility of reporting results by random chance and increase the risk of estimation of treatment by publication bias. Third, although our secondary outcome analysis of the repeated comparisons of pain severity scores and opioid consumption used a conservative 99% CI as well as a $P = 0.01$ threshold of statistical significance, this analysis may still be subject to multiple testing bias. Fourth, individual patient data were not available for analysis, which precludes the use of a composite outcome inclusive of both opioid consumption and pain scores.[106] Fifth, analgesic techniques other than ISB, such as subacromial or intraarticular[104,105] local anesthetic infiltration as well as suprascapular and axillary nerve blocks,[99,100] have been shown to provide pain relief after shoulder surgery, whether in conjunction or as alternatives to ISB. The effect of these techniques on the duration of ISB analgesia is beyond the scope of our review. Additionally, we excluded local anesthetic adjuvants and continuous ISB analgesic options capable of prolonging pain relief associated with ISB. Finally, none of the trials reviewed herein reported the presence and/or severity of preoperative pain, which prevented any correlation between this predictor of postoperative pain[107] and the duration of ISB analgesia.

In contrast, our results also have several points of strength. Our literature search was exhaustive, included all relevant databases, and the inclusion criteria we used limited the evidence reviewed to RCTs. All foreign-language articles meeting the inclusion criteria were translated and included. Finally, despite the heterogeneity characterizing the primary outcome results, these results remained robust despite our attempts to explore heterogeneity according to its identified potential sources. These factors underscore the validity of our results.

CONCLUSIONS

In conclusion, ISB can provide effective analgesia up to 6 hours with motion and 8 hours at rest after shoulder surgery, with no demonstrable benefits thereafter. Patients who receive an ISB can suffer rebound pain at 24 hours but experience similar pain severity later compared with those who do not receive an ISB. ISB can also provide an opioid-sparing effect and reduce opioid-related side effects in the first 12 and 24 hours postoperatively, respectively. These findings are useful to inform preoperative risk-benefit discussions regarding ISB for shoulder surgery.

Table 2. Analgesic Regimens

Author	Preincisional analgesia	Surgical analgesia	Supplemental postoperative analgesia	ISB block			
				Block timing	Localization	Assessment of block success	ISB bolus
Kinnard[61]	N/A	N/D	IV hydromorphone, then oral acetaminophen with codeine	Postoperative	Anatomical, paresthesias	N	20 mL 0.5% bupivacaine
Al-Kaisy[62]	N/A	IV fentanyl	IV morphine, then oral acetaminophen with codeine, oral ketorolac	Preoperative	N-Stim	Y	10 mL 0.125% bupivacaine + Epi
Bain[63]	N/A	IV fentanyl	IV pethidine, then IV PCA pethidine and oral acetaminophen with codeine	Preoperative	Anatomical, paresthesias	N	30 mL 0.5% bupivacaine
Gohl[64]	N/A	IV fentanyl	IV morphine, then IV pethidine	Preoperative	N-Stim	N	3 mg/kg 0.5% bupivacaine + Epi
Singelyn[15]	N/A	IV sufentanil	IV acetaminophen, subcutaneous morphine	Preoperative	N-Stim	Y	20 mL 0.25% bupivacaine + Epi
Hadzic[42]	Alfentanil in ISB group	ISB versus IV fentanyl	Wound infiltration in GA group, IV morphine, then oral acetaminophen with codeine	Preoperative	N-Stim	Y	35–40 mL 0.75% ropivacaine
Oh[65]	N/A	IV fentanyl, IV ketorolac	IV PCA fentanyl, IV ketorolac, IV meperidine	Preoperative	N-Stim	Y	20 mL 0.25% ropivacaine
Nisar[13]	N/A	IV fentanyl, IV morphine, IV parecoxib	IV PCA morphine, oral acetaminophen, oral codeine, oral diclofenac	Preoperative	N-Stim	N	10 mL 0.5% bupivacaine + 20 mL 1% prilocaine
Cho[66]	N/A	IV remifentanil	IV fentanyl	Preoperative	N-Stim	Y	10 mL 1% mepivacaine + Epi
Fontana[14]	N/A	IV fentanyl, IV ketorolac	IV PCA fentanyl	Preoperative	N-Stim	Y	30 mL 0.5% levobupivacaine + Epi
Gonano[67]	N/A	ISB versus IV fentanyl	IV acetaminophen, IV piritramide	Preoperative	Ultrasound	Y	20 mL 0.75% ropivacaine
Shin[68]	N/A	ISB versus IV remifentanil	IV PCA alfentanil with ketorolac	Preoperative	Ultrasound + N-Stim	N	15 mL 1.5% lidocaine + 15 mL 0.5% levobupivacaine
DeMarco[17]	N/A	N/D	Oral acetaminophen with oxycodone, subacromial local anesthetic infusion	Preoperative	N-Stim	Y	30 mL 0.5% ropivacaine
Taninishi[69]		IV remifentanil	Oral or rectal diclofenac, IV PCA morphine	Preoperative	Ultrasound	N	7–10 mL 0.375% ropivacaine
Rose[70]	N/A	IV fentanyl, IV remifentanil	IV morphine, then IV PCA morphine	Preoperative	N-Stim	N	30 mL 0.5% ropivacaine
Kim[71]	N/A	ISB versus IV fentanyl	IV ketorolac, then IV PCA	Preoperative	Ultrasound + N-Stim	N	15 mL 2% lidocaine + 15 mL 2% levobupivacaine
Mahmoodpoor[72]	N/A	IV fentanyl	IV morphine	Postoperative	N-Stim	Y	20 mL 1.5% lidocaine
Bin[73]	Phencyclidine	IV fentanyl, IV remifentanil	IV PCA sufentanil	Preoperative	Ultrasound	Y	15 mL 1.5% lidocaine
Cho[74]	Local anesthetic infiltrations, both groups	N/D	Oral oxycodone, oral acetaminophen, oral NSAID, then oral tramadol with acetaminophen, oral NSAID, IM diclofenac	Preoperative	N-Stim	Y	20 mL 0.25% ropivacaine
Lee[75]	N/A	N/D	Oral tramadol	Preoperative	N-Stim	N	10 mL 0.5% ropivacaine
Lee[16]	N/A	N/D	IV PCA fentanyl with ketorolac	Preoperative	N-Stim	Y	5 mL 2% mepivacaine + 10 mL 0.75% ropivacaine
Salviz[76]	IV fentanyl preoperatively	ISB versus IV fentanyl	IV acetaminophen, wound infiltration, then oral acetaminophen and oral hydrocodone	Preoperative	Ultrasound + N-Stim	Y	20 mL 0.5% ropivacaine
Lehmann[77]	N/A	ISB versus IV sufentanil	Oral diclofenac, oral acetaminophen, then IV acetaminophen, oral metamizole, oral piritramide	Preoperative	Ultrasound	Y	10 mL 1% mepivacaine + 20 mL 0.375% ropivacaine

Epi = epinephrine; N = no; N/A = not applicable; N/D = not defined; N-Stim = nerve stimulator; NSAID = nonsteroidal anti-inflammatory; PCA = patient-controlled analgesia; Y = yes; ISB = interscalene block; GA = general anesthesia.

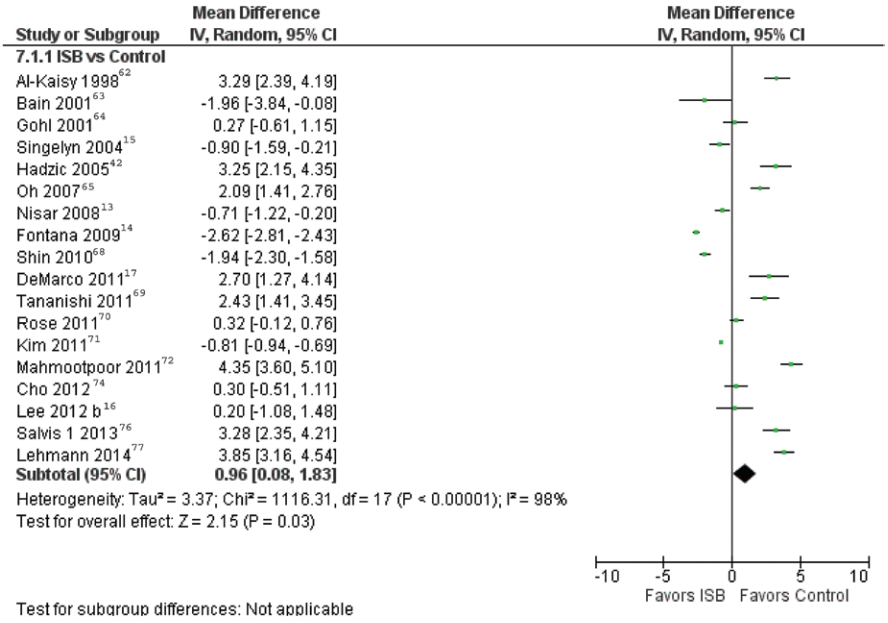

Figure 2. Forest plots of rest pain visual analog scale scores at 24 hours. The pooled estimates of the mean difference are shown. The 95% confidence intervals (CIs) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

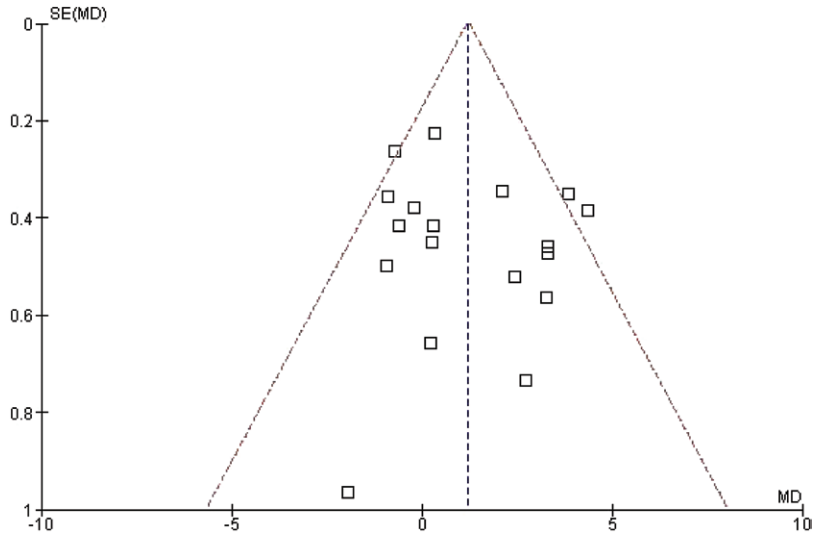

Figure 3. Pain at rest at 24 hours funnel plot assessing publication bias. Plotted is the standard error (SE) versus standard difference in mean (MD). Vertical line represents the combined effect for pain; and the diagonal lines designate the expected 95% confidence intervals from the combined effect. Studies outside the funnel indicate heterogeneity.

DISCLOSURES

Name: Faraj W. Abdallah, MD.
Contribution: This author helped in designing and conducting the study, collecting and analyzing the data, and preparing the final manuscript, and he is the archival author.
Attestation: Faraj W. Abdallah attests to the integrity of the original data and the analysis reported in this manuscript and has approved the final manuscript.
Name: Stephen H. Halpern, MD, FRCPC.
Contribution: This author helped in analyzing the data and preparing the final manuscript.
Attestation: Stephen H. Halpern has approved the final manuscript.
Name: Kazuyoshi Aoyama, MD.
Contribution: This author helped in conducting the study, collecting the data, and preparing the final manuscript.
Attestation: Kazuyoshi Aoyama has approved the final manuscript.
Name: Richard Brull, MD, FRCPC.
Contribution: This author helped in designing and conducting the study, collecting and analyzing the data, and preparing the final manuscript.
Attestation: Richard Brull attests to the integrity of the original data and the analysis reported in this manuscript and has approved the final manuscript.
This manuscript was handled by: Spencer S. Liu, MD.

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Table 3. Secondary End Point Results

Outcome	Studies included	Interscalene block, mean or *n/N*	Control, mean or *n/N*	Odds ratio, weighed mean, or ratio of means (99% confidence interval)	*P* Value for statistical significance	*P* Value for heterogeneity	I^2 test for heterogeneity
Rest pain at 2 hours (cm)	13–16,62,64,66,67,70,74	1.42	5.17	−3.66 (−4.83 to −2.49)	<0.00001	<0.00001	93%
Rest pain at 4 hours (cm)	13–15,68,70,71	1.27	4.46	−3.33 (−4.70 to −1.96)	<0.00001	<0.00001	99%
Rest pain at 6 hours (cm)	14,17,61,63	3.15	5.72	−3.05 (−5.25 to −0.84)	0.0004	0.0004	83%
Rest pain at 8 hours (cm)	13,16,65,68,71	3.64	4.96	−1.59 (−2.60 to −0.58)	0.0001	<0.00001	93%
Rest pain at 12 hours (cm)	13,14,17,63,64,68,69,71,72,77	3.95	4.57	−1.08 (−2.67 to 0.52)	0.08	<0.00001	99%
Rest pain at 16 hours (cm)	16,65	5.58	4.62	1.16 (0.02 to 2.30)	0.009	0.5	0%
Rest pain at 24 hours (cm)	13–17,42,62–65,68–72,74,76,77	4.36	3.08	0.96 (0.08 to 1.83)[a]	0.03	<0.00001	98%
Rest pain at 32 hours (cm)	17,65	5.08	4.99	0.14 (−1.25 to 1.52)	0.8	0.39	0%
Rest pain at 36 hours (cm)	63,69	5.04	4.89	−0.41 (−4.27 to 3.45)	0.78	0.002	90%
Rest pain at 40 hours (cm)	17,65	4.27	4.09	0.16 (−1.15 to 1.48)	0.75	0.7	0%
Rest pain at 48 hours (cm)	42,63–65,69–71,74,76	3.45	3.31	−0.13 (−0.79 to 0.54)	0.63	<0.00001	83%
Dynamic pain at 2 hours (cm)	15,70,75	1.7	6.63	−4.76 (−7.65 to −1.88)	<0.0001	<0.00001	96%
Dynamic pain at 4 hours (cm)	15,75	2.63	5.78	−2.98 (−5.95 to −0.01)	0.01	0.0002	93%
Dynamic pain at 6 hours (cm)	70,75	1.89	4.73	−2.20 (−4.34 to −0.06)	0.008	0.0008	91%
Dynamic pain at 12 h (cm)	72,75	4.69	5.01	−0.44 (−1.74 to 0.86)	0.38	0.1	62%
Dynamic pain at 24 hours (cm)	15,70,72,75	4.42	4.55	−0.04 (−1.93 to 1.85)	0.96	<0.00001	90%
Dynamic pain at 48 hours (cm)	70	3.97	3.97	0.00 (−1.25 to 1.25)	1.0	N/A	N/A
Time to first analgesic request (min)	13,62,69,70,76	225.5	26.16	8.04 (7.77 to 8.31)	<0.00001	<0.00001	99%
Morphine consumption for 0–12 hours (mg)	13,17,61,77	11.34	21.95	−12.10 (−21.75 to −2.45)	0.001	<0.00001	97%
Morphine consumption for 12–24 hours (mg)	13,17,61,77	11.41	12.63	−1.48 (−6.59 to 3.63)	0.45	0.0005	83%
Cumulative morphine consumption for 0–24 hours (mg)	13–16,42,62,63,70	19.67	30.35	−13.98 (−30.93 to 2.96)	0.03	<0.00001	98%
Morphine consumption for 24–36 hours (mg)	17	12.01	9.77	2.24 (−3.42 to 7.90)	0.31	N/A	N/A
Morphine consumption for 36–48 hours (mg)	17	19.14	15.05	4.09 (−2.53 to 10.71)	0.11	N/A	N/A
Cumulative morphine consumption for 24–48 hours (mg)	42,61,70	10.79	12.36	−1.17 (−4.92 to 2.57)	0.42	0.99	0%
Incidence of PONV at 24 hours (*n/N*)	15,42,62,64–67,69,70,74,76	36/290	64/261	0.41 (0.18 to 0.92)	0.004	0.14	32%
Incidence of pruritus at 24 hours (*n/N*)	74	0/30	0/30	N/A	1.0	N/A	N/A
Incidence of sedation at 24 hours (*n/N*)	74	1/30	2/30	0.48 (0.02 to 12.18)	0.56	N/A	N/A
Patient satisfaction at 24 hours (cm)	15,16,42,62,70	8.34	7.88	0.55 (0.15 to 0.95)	0.0004	0.78	0%
PACU discharge time (min)	13,64,67,76	63.20	104.00	0.96 (0.85 to 1.07)	<0.00001	0.0003	84%
Hospital discharge time (min)	42,62,76	119.92	263.78	0.57 (0.37 to 0.76)	<0.00001	0.12	53%

N/A = not applicable; PONV = postoperative nausea and vomiting; PACU = postanesthesia care unit.
[a]95% confidence interval.

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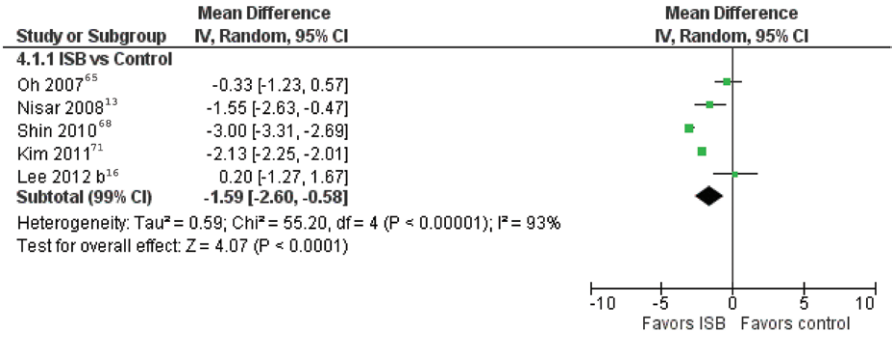

Figure 4. Forest plots of rest pain visual analog scale scores at 8 hours. The pooled estimates of the mean difference are shown. The 99% confidence intervals (CIs) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

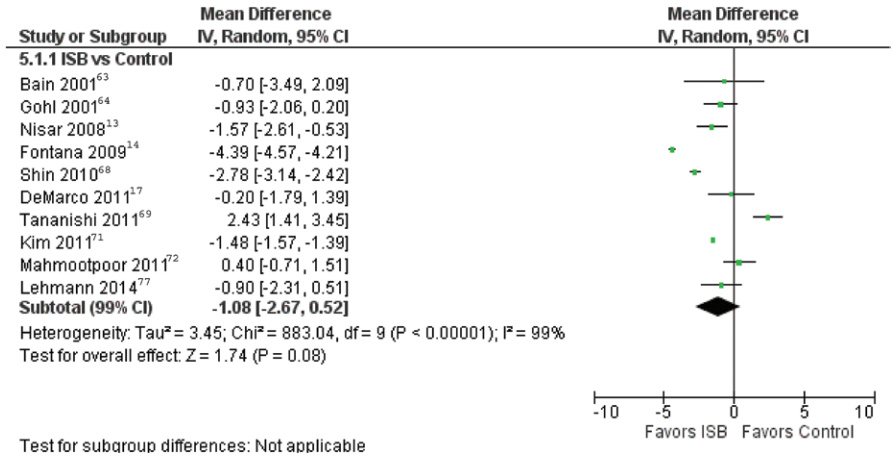

Figure 5. Forest plots of rest pain visual analog scale scores at 12 hours. The pooled estimates of the mean difference are shown. The 99% confidence intervals (CI) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

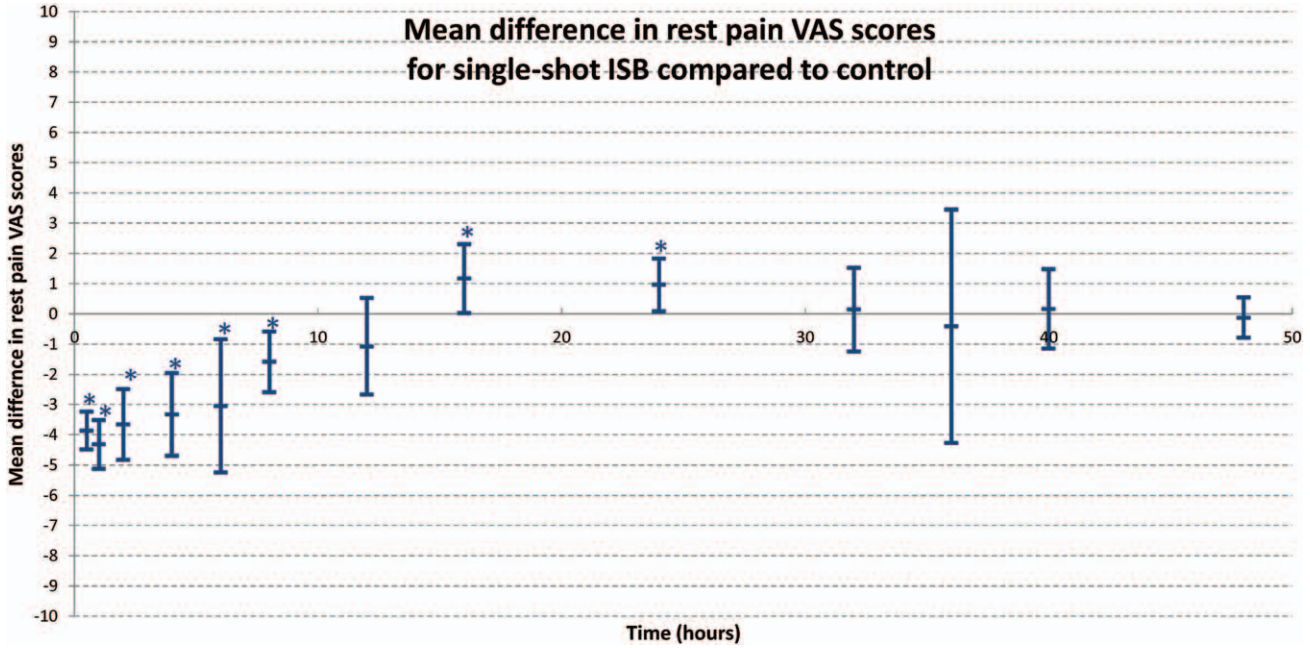

Figure 6. Plot of the changes in the rest pain visual analog scale (VAS) scores weighed mean difference between the 2 groups over time. ISB = interscalene block.

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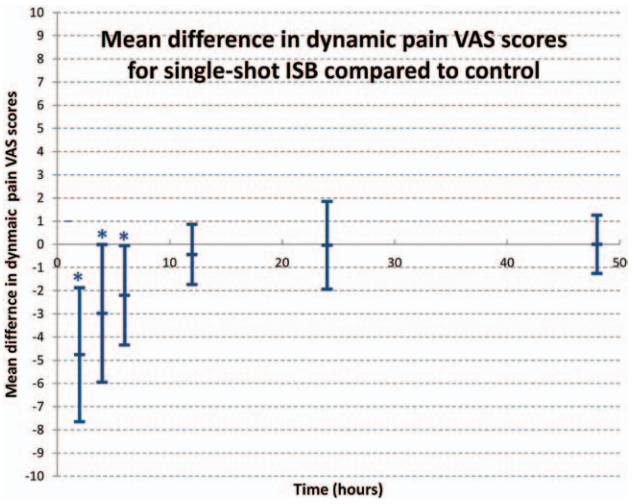

Figure 7. Plot of the changes in the dynamic pain visual analog scale (VAS) scores weighed mean difference between the 2 groups over time. ISB = interscalene block.

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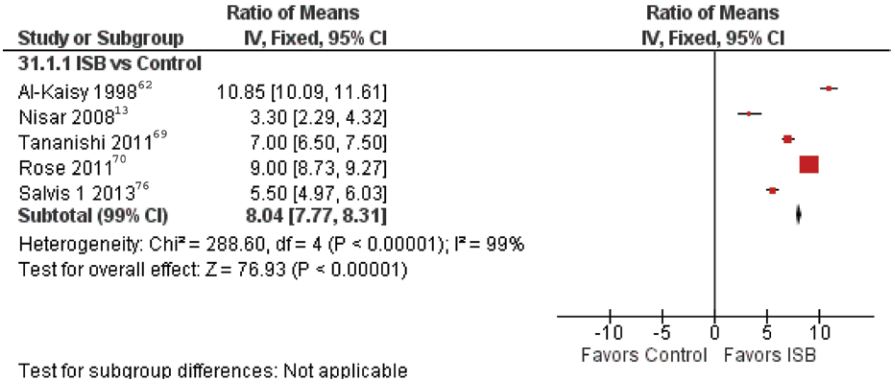

Figure 8. Forest plots of the time to first analgesic request. The pooled estimates of the ratio of means are shown. The 99% confidence intervals (CIs) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

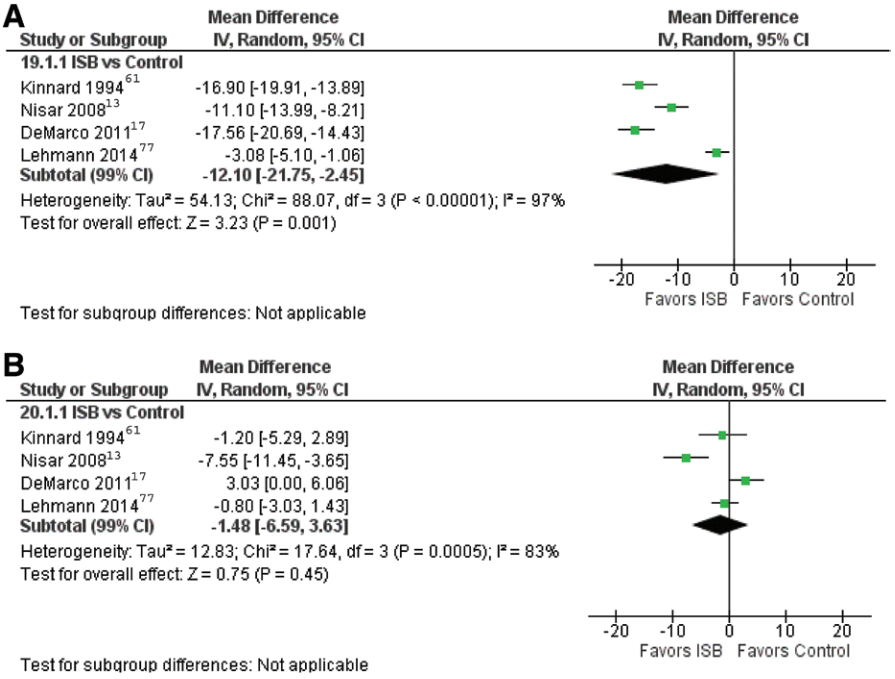

Figure 9. Forest plot of cumulative (A) 0–12 hours and (B) 12–24 hours intravenous morphine equivalent consumption. The pooled estimates of the mean difference are shown. The 99% confidence intervals (CIs) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

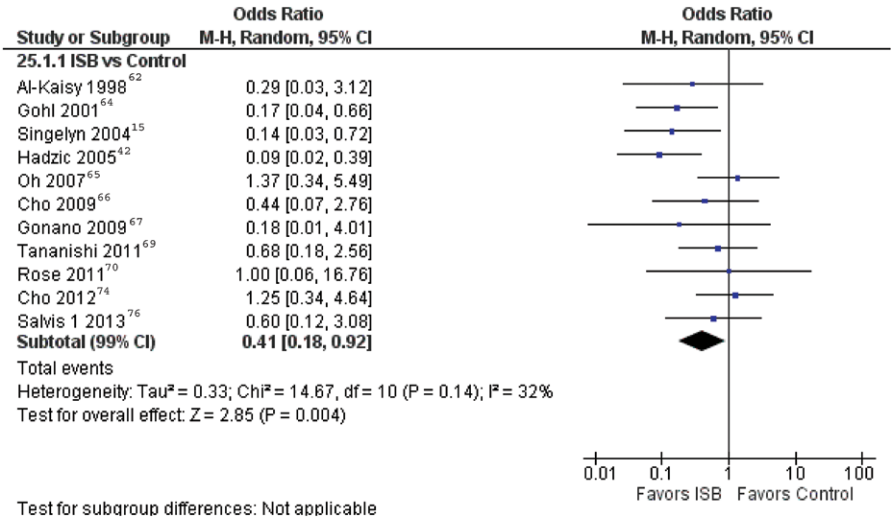

Figure 10. Forest plot of the incidence of postoperative nausea and vomiting in the first 24 hours. The pooled estimates of the odds ratio are shown. The 99% confidence intervals (CIs) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

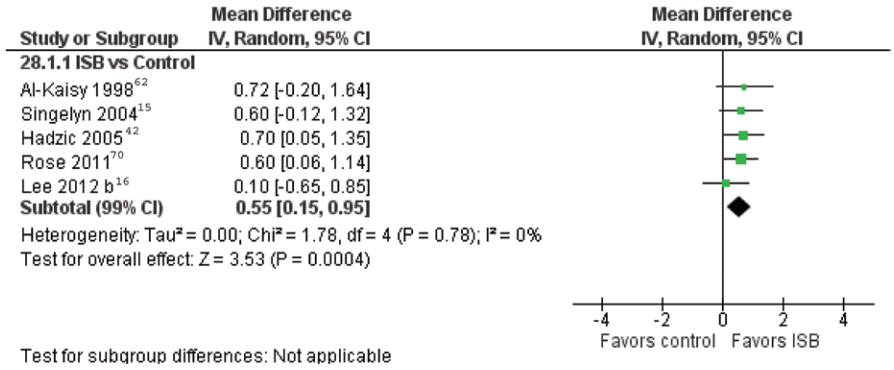

Figure 11. Forest plot of patient satisfaction with pain relief at 24 hours. The pooled estimates of the mean difference are shown. The 99% confidence intervals (CIs) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

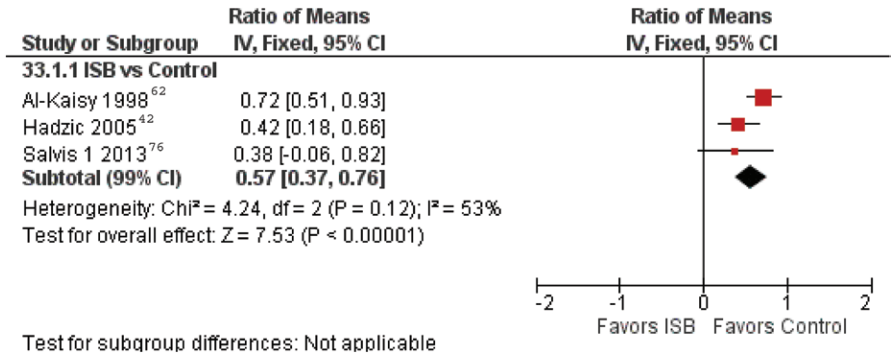

Figure 12. Forest plot of time to hospital discharge after ambulatory shoulder surgery. The pooled estimates of the ratio of means are shown. The 99% confidence intervals (CIs) are shown as lines for individual studies and as diamonds for pooled estimates. ISB = interscalene block.

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