

The effect and safety of dexmedetomidine added to ropivacaine in brachial plexus block

A meta-analysis of randomized controlled trials

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Abstract

Background: Dexmedetomidine has been used as an adjuvant added to local anesthetics to prolong analgesia following peripheral nerve blockade. The aim of this meta-analysis was to investigate the effect and safety of dexmedetomidine added to ropivacaine in brachial plexus block (BPB).

Methods: A search strategy was created to identify eligible randomized clinical trial (RCT) in PubMed, Embase, and The Cochrane Library (updated May, 2018). The methodologic quality for each included study was evaluated using the Cochrane Tool for Risk of Bias by 2 independent researchers.

Results: Twelve RCTs were included in the meta-analysis (n=671). As an adjuvant to ropivacaine, dexmedetomidine significantly reduced the onset time of sensory (mean difference [MD], -3.86 minutes, 95% CI -5.45 to -2.27 minutes; $I^2=85%$) and motor (MD, -5.21 minutes; 95% CI -7.48 to -2.94 minutes; $I^2=94%$). In addition, it increased the blockade duration of sensory (MD, 228.70 minutes; 95% CI 187.87–269.52 minutes; $I^2=93%$) and motor (MD, 191.70 minutes; 95% CI 152.48–230.91 minutes; $I^2=92%$). Moreover, the combination prolonged the duration of analgesia (MD, 303.04 minutes; 95% CI 228.84–377.24 minutes; $I^2=86%$). There was no difference of the incidence of bradycardia (risk difference [RD], 0.01, 95% CI -0.02 to 0.05, $I^2=45%$; $P=.45$) and hypotension (RD, 0.01, 95% CI -0.01 to 0.03, $I^2=0%$; $P=.57$) between 2 groups.

Conclusion: Dexmedetomidine added to ropivacaine in BPB has a better analgesia effect (shorter onset time and longer duration) compared to ropivacaine alone. At the same time, there was no difference in the incidence of bradycardia and hypotension.

Abbreviations: BPB = brachial plexus block, CIs = confidence intervals, MDs = mean differences, RCTs = randomized controlled trials, RD = risk difference, RR = relative risk, SD = standard deviation, SMD = standardized mean difference.

Keywords: brachial plexus block, dexmedetomidine, meta-analysis, ropivacaine

1. Introduction

With the development of ultrasound-guided techniques, the use of local anesthetic peripheral nerve blocks for surgical anesthesia and postoperative pain management has increased significantly. The brachial plexus block (BPB) has been widely applied for surgery of the upper extremity as an alternative to general anesthesia. Compared with general anesthesia, BPB can effectively block the transmission of nerve signals. BPB not only acts as a method for effectively intraoperative anesthesia, but also prolongs postoperative analgesic time, improves the effect of

postoperative pain relief, reduces the postoperative consumption of opioids, and avoids the general anesthesia-related adverse events, which make the choice of anesthesia procedure more flexible and can improve patient satisfaction.^[1] As one of auxiliary means to BPB, the technique of ultrasound-guided positioning has markedly improved success rate and safety of anesthesia.^[2]

Commercially available local anesthetics have a limited duration of analgesia that frequently leaves patients complaining of pain for the first time during their first postoperative night when they are likely most vulnerable. As a long-acting amide local anesthetic, ropivacaine is one of the main drugs used for BPB anesthesia. Compared with bupivacaine and levobupivacaine, the lower lipid solubility of ropivacaine provides greater sensory and motor blockade and prompt motor functions recover faster.^[3–6] It has been considered effective in local anesthetic and beneficial for postoperative analgesia when ropivacaine is used alone. But the duration of sensory block is still not sufficient to provide long time analgesia and avoid the postoperative use of opioids. Catheter-based techniques allow for sustained pain management during the perioperative period, but they can present challenges related to patient management, displacement of the catheter postoperatively, and the potential for increased infection risk.^[7] While a growing number of randomized controlled trials (RCTs) have shown that adjuvants, such as dexmedetomidine, opioids, clonidine, and neostigmine added into ropivacaine in BPB can prolong the analgesic duration and reduce the consumption of analgesic after surgery, thus it makes the anesthetic effect better than ropivacaine alone.^[6–10] However,

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several side-effects have been reported including bradycardia, hypotension, and respiratory depression. In contrast, dexmedetomidine has been considered more effective than other above adjuvants.^[11] The current meta-analysis only generalized the effect of dexmedetomidine combined with local anesthetics on BPB. It has not been summarized systematically for the effect and the safety of dexmedetomidine combining with ropivacaine for BPB. Therefore, the purpose of this study was to clarify the role of dexmedetomidine in combination with ropivacaine in BPB.

2. Materials and methods

2.1. Search strategy

We searched the electronic database including PubMed, Embase, and Cochrane Library from the establishment of the database to May, 2018. The procedure of searching was systematically performed by 2 researchers independently without language restrictions. The search keywords were as follows: “ropivacaine,” “dexmedetomidine,” “brachial plexus block,” “ropivacaine hydrochloride,” “precedex,” “dexmedetomidine hydrochloride,” “brachial plexus anesthesia,” and “blockade, brachial plexus.” We obtained additional articles by reviewing the reference lists to check for the other relevant published and ongoing studies. The purpose of this meta-analysis was to establish the direct link between 2 anesthetic regimens, thus only RCTs that directly compare the 2 regimens could be included.

2.2. Study selection

Those studies were considered eligible: RCT only, patients over 18 years old and belongs to ASA I–III, patients accepted BPB only for regional anesthesia without general anesthesia, patients treated with ropivacaine plus dexmedetomidine as a comparison to those with ropivacaine treated only. By scanning titles and abstracts, we excluded irrelevant trials, reviews, duplicate reports, case reports, conference abstracts, and the letters. Further, we read the full articles to exclude studies that did not meet our inclusion criteria.

2.3. Data extraction

We extracted the information from the inclusions as followed: the last name of the first author, publication date, amounts of participants in experimental and control groups, the details of interventions, outcomes, and the adverse events. Two independent reviewers conducted the procedure of extracting the associated data from the studies included. Only one trial provided data in seconds, and we converted it into minutes for data consolidation.^[12] In a 3-arm randomized controlled study, we chose one of the experimental groups for data analysis.^[13]

2.4. Quality assessment

The risk of bias of the articles included was assessed by using the Cochrane Collaboration Tool for the RCTs. The risk of bias assessment was expressed in 3 types: low risk (+), unclear risk (?), or high risk (–) of bias for each study. All the procedures were conducted by 2 independent reviewers. When the judgment differed from each other, it was necessary to make the final decision by a third reviewer.

2.5. Statistical analysis

For continuous variables, the mean difference (MD) or standardized mean difference (SMD) was the alternative effector. The 95% confidence intervals (CIs) of all results were calculated or extracted. Due to the different unit of outcomes from Koraki et al,^[12] we finally chose MD as the effect indicator. The adverse events as a second endpoint belong to dichotomous, so the relative risk (RR) was applied. Q test and I^2 statistics were used to qualify the statistical heterogeneity among trials in the procedure of meta-analysis. It was considered statistically significant with P -values $<.05$ in the treatment effect of heterogeneity in Q test. I^2 statistic was identified with low, moderate, and high levels of heterogeneity corresponding to the I^2 of $<25\%$, 25% to 50% , and $>50\%$. Sensitivity analysis should be performed if obvious heterogeneity existed. The fixed-effects was applied when $I^2 \leq 50\%$, and the random-effects model was applied when $I^2 \geq 50\%$. All the data calculations were performed by Review Manager 5.3.

3. Result

3.1. Literature search

Initially, a total of 93 articles were searched from all databases, and 42 duplicate articles exclude. Then, 24 articles were excluded after screened titles and abstracts. And 15 articles were excluded after full-text reading for the following reasons: reviews or system reviews, without required outcomes, the general anesthesia after local anesthesia. Finally, 12 RCTs remained eligible to meet the inclusion criteria for the current meta-analysis. And the flow diagram of study selection is shown in Figure 1.

3.2. Study characteristics and quality assessments

The main characteristics of the 12 RCTs are listed in Table 1. Figure 2 shows a low level of overall risk of bias for included trials. According to the puncture position, 3 types of brachial plexus anesthesia were reported in these trials, including supraclavicular block, axillary block, and intermuscular block.

3.3. Time to sensory block onset

The time to onset of sensory block was reported in 12 studies^[12–23] and 671 patients were included. Dexmedetomidine combined with ropivacaine reduced the onset time to sensory block significantly (MD, -3.86 minutes, 95% CI -5.45 to -2.27 minutes, $I^2 = 85\%$; $P < .00001$) (Fig. 3). With the obvious heterogeneity the subgroup analysis was conducted according to the type of BPB and the dosage of dexmedetomidine. Compared with ropivacaine alone, dexmedetomidine added to ropivacaine showed significant decrease of the time to sensory block onset in supraclavicular (MD, -2.95 minutes, 95% CI -5.88 to -0.02 minutes, $I^2 = 90\%$; $P = .05$), intermuscular (MD, -5.44 minutes, 95% CI -8.45 to -2.43 minutes, $I^2 = 87\%$; $P < .00001$), and axillary anesthesia (MD, -4.41 minutes, 95% CI -5.86 to -2.96 minutes, $I^2 = 0\%$; $P < .00001$) (Fig. 3). And adding dexmedetomidine to ropivacaine obviously decreased the time to sensory block onset both in groups with dosage greater^[12,14,16–21,23] (MD, -2.97 minutes, 95% CI -4.94 to -1.01 minutes, $I^2 = 86\%$; $P = .003$) and less^[13,15,22] (MD, -6.96 minutes, 95% CI -11.85 to -2.06 minutes, $I^2 = 86\%$; $P = .005$) than $50 \mu\text{g}$ (Table 2).

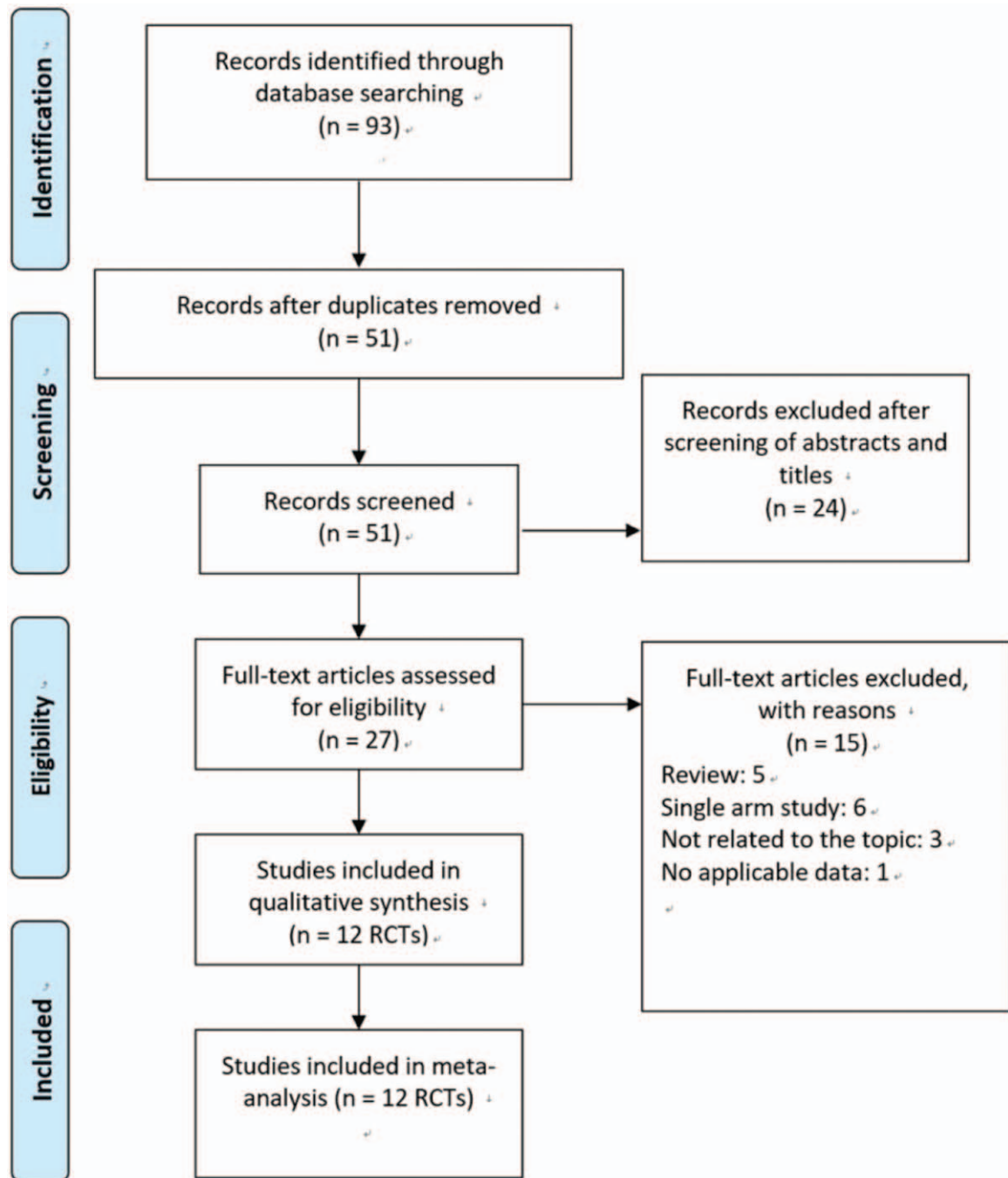


Figure 1. Flow diagram of study selection.

3.4. Duration of sensory block

A total of 637 patients from 11 studies provided the duration of sensory blockade.^[12–17,19–23] The addition of dexmedetomidine increased the duration of sensory block significantly of 228.70 minutes in average compared with the group with ropivacaine treated alone (MD, 228.70 minutes; 95% CI 187.87–269.52 minutes, $I^2=93%$; $P<.0001$) (Fig. 4). Subgroup analyses indicated a significant increase of the duration of sensory blocked in supraclavicular (MD, 255.98 minutes; 95% CI 187.82–324.14 minutes, $I^2=90%$; $P<.0001$), axillary (MD, 337.97 minutes; 95% CI 133.56–542.37 minutes, $I^2=85%$;

$P=.0001$), and intermuscular BPB (MD, 136.29 minutes; 95% CI 24.16–248.42 minutes, $I^2=99%$; $P=.02$) (Fig. 4). In subgroups of dexmedetomidine dosage greater (MD, 228.61 minutes; 95% CI 193.30–263.91 minutes, $I^2=82%$; $P<.0001$) and less (MD, 280.44 minutes; 95% CI 45.17–515.72 minutes, $I^2=94%$; $P=.02$) than 50 μg , dexmedetomidine prolonged the duration of sensory blocked (Table 2).

3.5. Time to motor block onset

The data of time to motor block onset were reported in 11 studies including 637 patients in all.^[12–17,19–23] The addition of

Table 1**Characters of included randomized controlled trials.**

Study	Location	Simple size (RD/R)	Interventions	Location	Primary endpoint	Other results
Das, 2014	India	RD/R 40/40	RD 30 mL 0.5% R+1 mL (100 µg) D R 30 mL 0.5% R+1 mL NS	SBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Total analgesic need, VAS, hemodynamics, and side-effects
Zhang, 2014	China	RD1/RD2/R 15/15/15	RD1 (40 mL 0.33%+1 mL 50 µg D) RD2 (40 mL 0.33%+1 mL 100 µg D) R (40 mL 0.33%+1 mL NS)	ABPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Hypertension, bradycardia, hypotension
Das, 2016	India	RD/R 40/40	RD (30 mL 0.5% R+1 µg/kg D) R (30 mL 0.5% R+placebo)	SBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Duration of analgesia Side effect
Kathuri, 2015	India	RD/R 20/20	RD (30 mL 0.5% R+50 µg D+50 mL NS) R (30 mL 0.5% R+50 mL NS)	SBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	The side effect of hemodynamics
Kwon, 2015	Korea	RD/R 30/30	RD (40 mL 0.5% R+1 µg/kg D) R (40 mL 0.5% R + 0.01 mL/kg NS)	SBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Bradycardia and changes in hemodynamics
Bangera, 2016	India	RD/R 40/40	RD 39 mL 0.375% R + 1 µg/kg D (1 mL NS) R (39 mL 0.375% R+1 mL NS)	ABPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Changes in hemodynamics
Lee, 2016	Korea	RD/R 17/17	RD 20 mL 0.5% R+2 mL (100 µg)D R 20 mL 0.5% R+2 mL NS	ABPB	1. Onset of sensory block 2. Duration of sensory block	Hypotension, bradycardia/hypoxemia nausea, and vomiting
Chinnappa, 2017	India	RD/R 30/30	RD 30 mL 0.5% R+1 µg/kg D R 30 mL 0.5% R+1 mL NS	SBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	The side effect of (hypotension, bradycardia, nausea, and vomiting, Horner syndrome)
Farooq, 2017	India	RD/R 35/35	RD 3mg/kg 0.75% R+1 µg/kg D R 3mg/kg 0.75% R+ NS Total (35mL)	IBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Changes in hemodynamics and pain score
Koraki, 2018	Greece	RD/R 19/18	RD 15 mL 0.5% R+100 µg (1 mL)D R 15 mL 0.5% R+1 mL NS	ABPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Hypotension, bradycardia
Rashmi, 2017	India	RD/R 30/30	RD30 mL 0.75% R+50 µg (0.5 mL)D R 30 mL 0.75% R+0.5 mL NS	IBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Hemodynamic parameters
Mathew, 2018	India	RD/R 20/20	RD30 mL 0.5% R+1 µg/kg D R 30 mL 0.5% R+1 mL NS	SBPB	1. Onset of sensory and motor block 2. Duration of sensory and motor block 3. Duration of analgesia	Sedation score and requirement of intercostobrachial nerve block

ABPB = axillary brachial plexus block, D = dexmedetomidine, IBPB = interscalene brachial plexus block, NS = normal saline, R = ropivacaine, SBPB = supraclavicular brachial plexus block, VAS = visual analog scale.

dexmedetomidine reduced the time to motor block significantly (MD, -5.21 minutes; 95% CI -7.48 to -2.94 minutes, $I^2 = 94\%$; $P < .0001$) (Fig. 5). Subgroup analysis was conducted grouped by the location of BPB and the dose of dexmedetomidine for the high heterogeneity. Three blocked positions, supra-

clavicular (MD, -5.04 ; 95% CI -8.83 to -1.24 minutes, $I^2 = 95\%$; $P = .009$), axillary (MD, -6.14 minutes; 95% CI -9.42 to -2.85 minutes, $I^2 = 41\%$; $P = .0003$), and intermuscular BPB (MD, -4.71 minutes; 95% CI -5.67 to -3.75 minutes, $I^2 = 0\%$; $P < .0001$) all indicated that the addition of dexmedetomidine

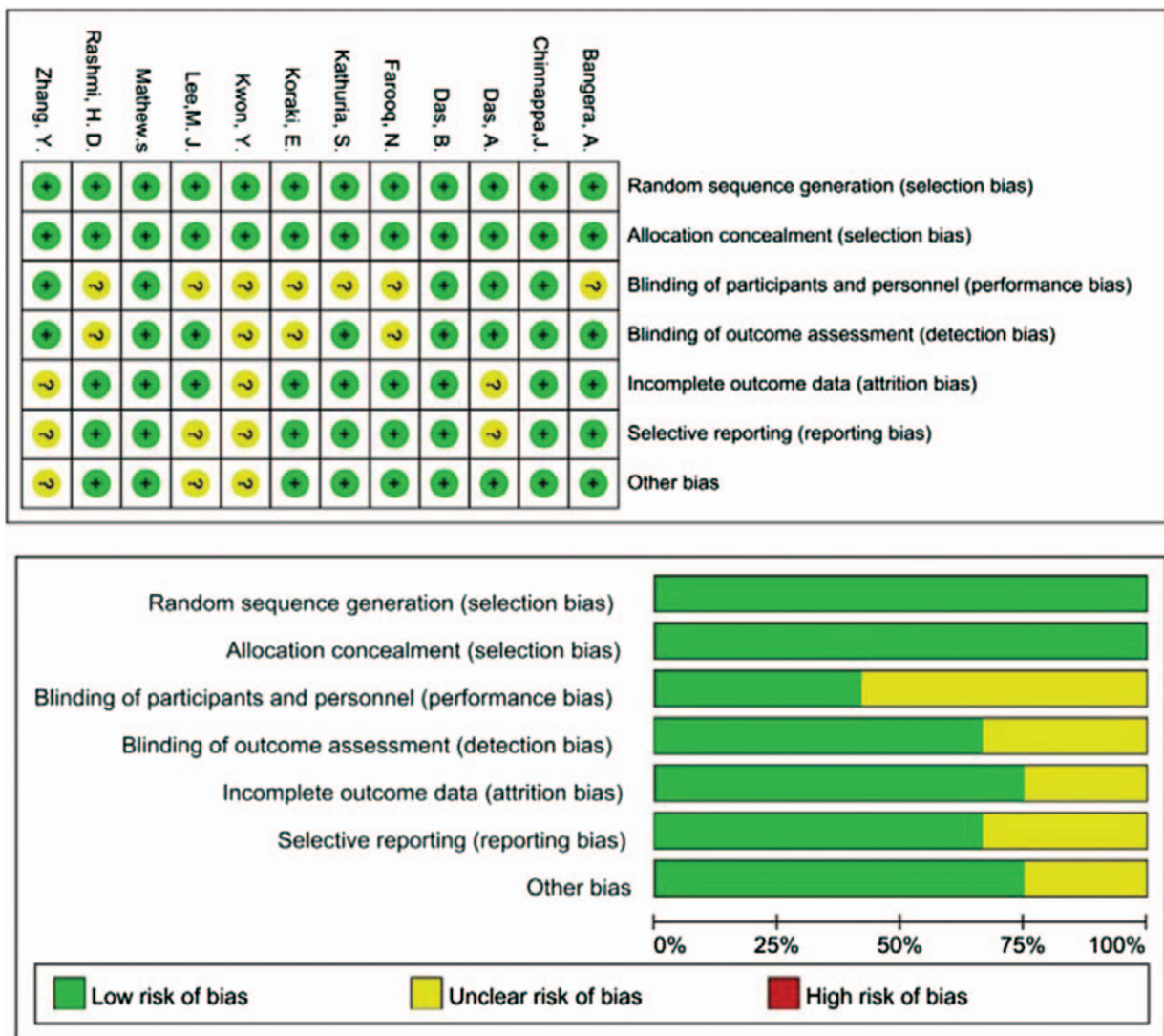


Figure 2. The risk of bias summary. Green circle=low bias risk, red circle=high bias risk, yellow circle=unclear bias risk.

decrease the time to motor blocked onset (Fig. 5). The addition of dexmedetomidine increased the time to motor block onset in comparison to control irrespective of the dosage (>50 µg, or ≤50 µg) (Table 2).

3.6. Motor block duration

Eleven studies evaluated the duration of motor block and 637 patients were included.^[12-17,19-23] The addition of dexmedetomidine increase the duration of motor block significantly compared with the group treated with ropivacaine alone (MD, 191.70 minutes; 95% CI 152.48–230.91 minutes, $I^2=92%$; $P<.0001$) (Fig. 6). In addition, there was a significant increase of the duration of motor blocked with supraclavicular BPB (MD, 217.05 minutes; 95% CI 144.33–289.76 minutes, $I^2=86%$; $P<.00001$); however, it was not found in axillary (MD, 345.49 minutes; 95% CI 17.35–673.64 minutes, $I^2=94%$; $P=.04$) and intermuscular BPB (MD, 102.55 minutes; 95% CI 0.17–204.93 minutes, $I^2=98%$; $P=.05$) (Fig. 6). Moreover, there was a trend of increasing the duration of motor blocked without significant difference compared to the group with ropivacaine treated alone. The combination of ropivacaine and dexmedetomidine increased

the duration of motor blocked in subgroups of dosage greater (MD, 165.52 minutes; 95% CI 114.04–217.01 minutes, $I^2=89%$; $P<.0001$) and less (MD, 337.27 minutes; 95% CI 121.48–553.06 minutes, $I^2=95%$; $P=.02$) than 50 µg (Table 2).

3.7. Duration of analgesia

Only 6 studies reported the duration of analgesia and had complete data to pooling.^[12,14,17,19,20,22] The result indicated that dexmedetomidine as an adjuvant prolonged the duration of analgesia significantly by an average of 303.04 minutes compared with the control group (MD, 303.04 minutes; 95% CI 228.84–377.24 minutes, $I^2=86%$; $P<.00001$) (Fig. 7). The subgroup analysis was not conducted because of the not enough data in other subgroups.

3.8. Adverse events

The major postoperative adverse events were bradycardia and hypotension, while postoperative drowsiness, dyspnea and Horner syndrome were also reported. As the main adverse events, statistic difference was not observed in the subgroup

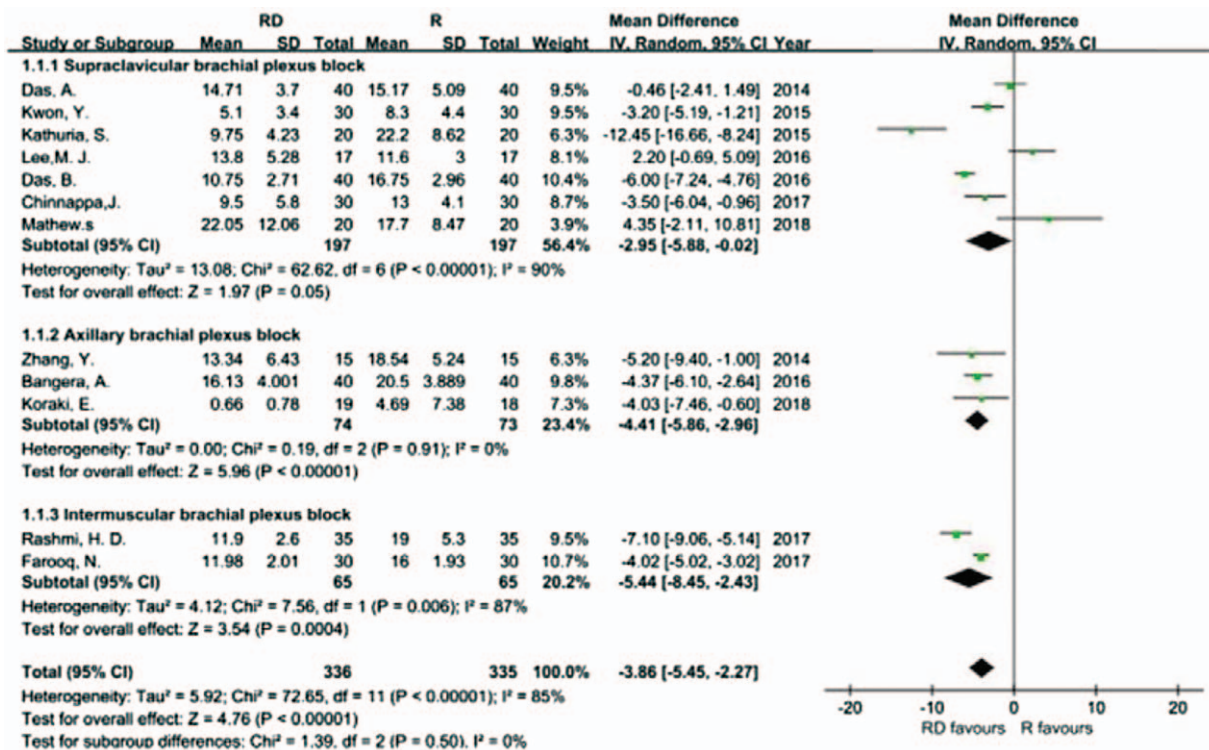


Figure 3. The time to sensory block onset of BPB. Dexmedetomidine combined with ropivacaine reduced the onset time to sensory block significantly (MD, -3.86 minutes, 95% CI -5.45 to -2.27 minutes; P < .00001). BPB=brachial plexus block, CI=confidence interval, MD=mean differences, R=ropivacaine, RD=ropivacaine + dexmedetomidine.

analysis of bradycardia (risk difference [RD], 0.05, 95% CI 0.00–0.10, I²=77%; P=.05) and hypotension (RD, 0.01, 95% CI -0.01 to -0.02, I²=0%; P=.59) (Figs. 8 and 9). There was no significant difference for the bradycardia in supraclavicular (RD, 0.05; 95% CI -0.01 to -0.11, I²=61%; P=.08), axillary (RD, 0.26; 95% CI -0.62 to -1.14, I²=98%; P=.56), and intermuscular BPB (RD, 0.00; 95% CI -0.04 to 0.04, I²=0%; P=1). In dosage subgroup, it indicated no difference both in greater (RD, 0.04; 95% CI -0.01 to 0.08, I²=64%; P=.11) or less (RD, 0.14; 95% CI -0.10 to 0.39, I²=94%; P=.26) than 50 µg (Table 2). As for hypotension, it indicated no difference in patients treated with dexmedetomidine plus ropivacaine compared with the control group no matter the supraclavicular (RD, 0.01; 95% CI -0.02 to 0.03, I²=0%; P=.59), axillary (RD, 0.05; 95% CI -0.13 to 0.22, I²=69%; P=.59), or intermuscular

BPB (RD, 0.00; 95% CI -0.04 to 0.04, I²=0%; P=1). In subgroup analysis, both in groups of greater (RD, 0.01, 95% CI -0.01 to 0.04, I²=0%; P=.25) or less (RD, 0.06, 95% CI -0.02 to 0.12, I²=29%; P=.20) than 50 µg showed a trend of higher risk to obtain hypotension with dexmedetomidine plus ropivacaine treated but without significant difference (Table 2).

4. Discussion

More and more studies on the application of dexmedetomidine as an adjuvant to enhance the effect of peripheral nerve block. There were 2 meta-analysis studies focused on the effect of dexmedetomidine as an adjuvant to local anesthesia in BPB. However, not only ropivacaine but also levobupivacaine, bupivacaine, lidocaine were included in the studies. To our knowledge, this is the

Table 2

The pooled-outcome of subgroup analysis.

Subgroup	Dose of dexmedetomidine				Location of block					
	≤50 µg		>50 µg		Supraclavicular		Axillary		Interscalene	
	MD	95%CI	MD	95%CI	MD	95%CI	MD	95%CI	MD	95%CI
Sensory block onset time	-6.96	-11.85, -2.06	-2.97	-4.94 to -1.01	-2.95	-5.88 to -0.02	-4.41	-5.86 to -2.96	-5.44	-8.45 to -2.43
Sensory block duration	280.44	45.17, 515.72	228.61	193.30–263.91	255.98	187.82–324.14	337.97	133.56–542.37	136.29	24.16–248.42
Motor block onset	-9.32	-15.94, -2.71	-4.15	-6.78 to -1.53	-5.04	-8.83 to -1.24	-6.14	-9.42 to -2.85	-4.71	-5.67 to -3.75
Motor block duration	337.27	121.48, 553.06	165.52	114.04–217.01	217.05	144.33–289.76	345.49	17.35–673.64	102.55	0.17–204.93
	RD	95%CI	RD	95%CI	RD	95%CI	RD	95%CI	RD	95%CI
Adverse event: bradycardia	0.14	-0.10, 0.39	0.04	-0.01 to 0.08	0.05	-0.01 to 0.11	0.26	-0.62 to 1.14	0.00	-0.04 to 0.04
Adverse event: hypotension	0.05	-0.02, 0.12	0.01	-0.01 to 0.04	0.01	-0.02 to 0.03	0.05	-0.13 to 0.22	0.00	-0.04 to 0.04

CIs=confidence intervals, MD=mean difference, RD=risk difference.

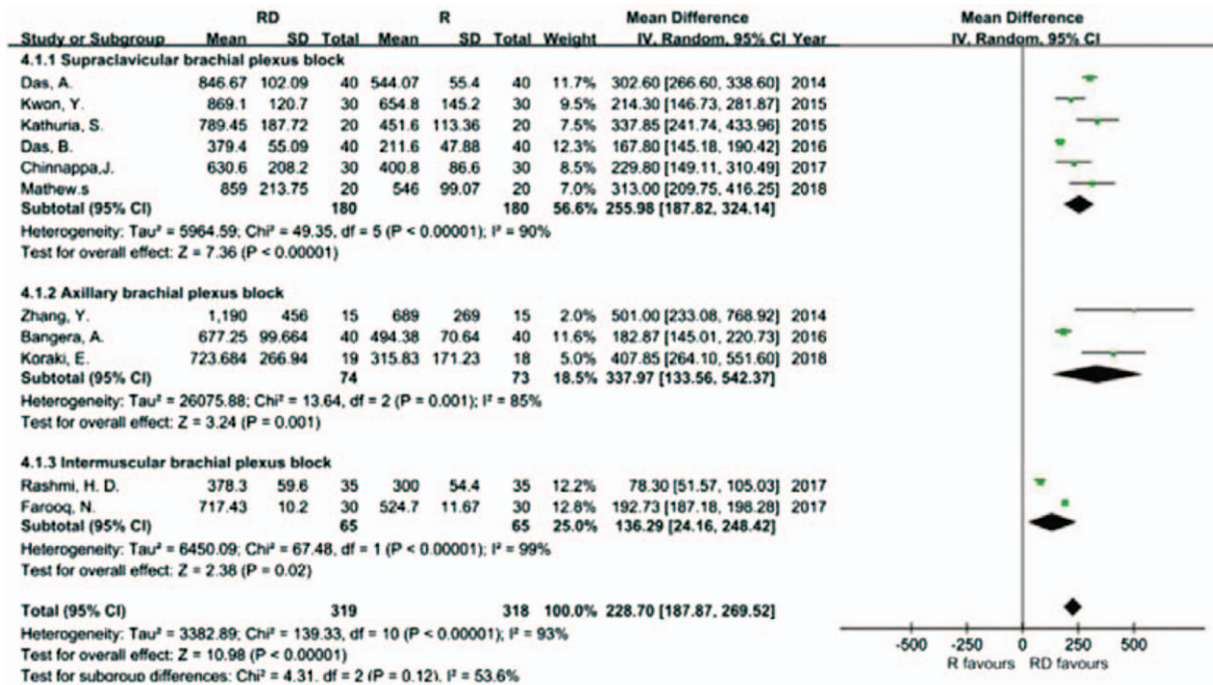


Figure 4. The duration for sensory block of BPB. Pooled analysis showed significantly prolonged duration of sensory block in the RD group compared with those without dexmedetomidine (MD, 228.70 minutes; 95% CI 187.87–269.52 minutes; P < .0001). BPB=brachial plexus block, CI=confidence interval, MD=mean differences, R=ropivacaine, RD=ropivacaine + dexmedetomidine.

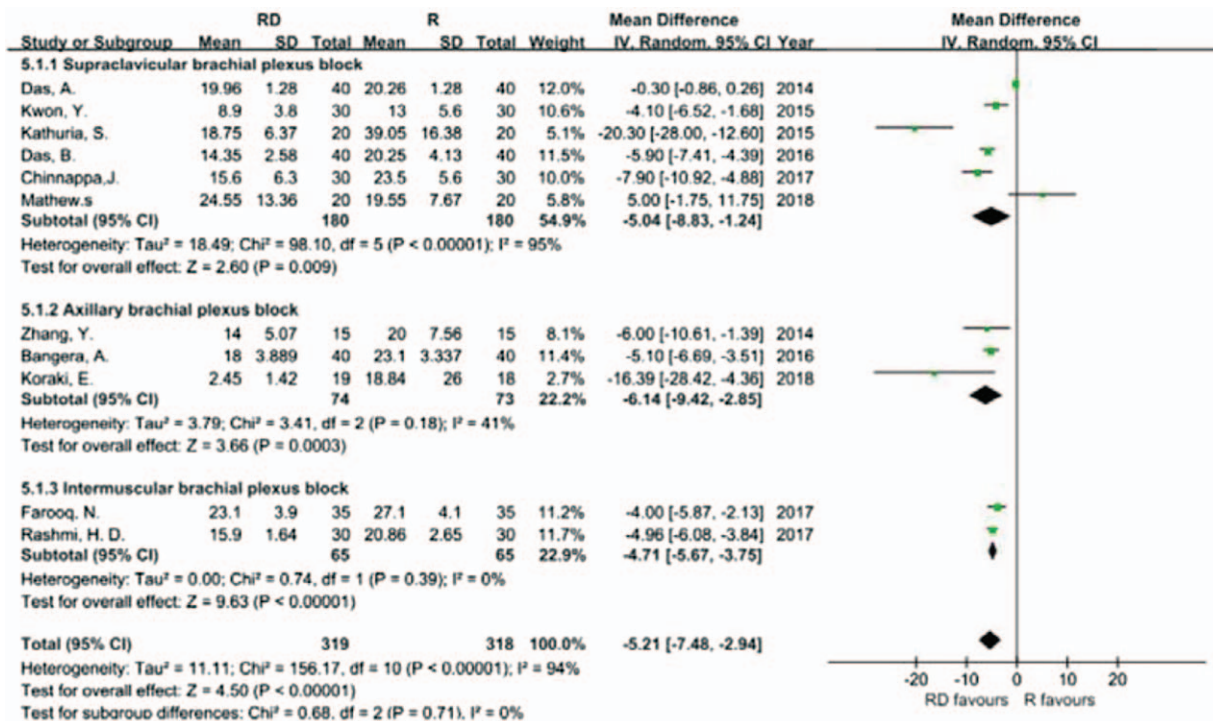


Figure 5. The time to motor block onset of BPB. Dexmedetomidine combined with ropivacaine reduced the onset time to motor block significantly (MD, -5.21 minutes; 95% CI -7.48 to -2.94 minutes; P < .0001). BPB=brachial plexus block, CI=confidence interval, MD=mean differences, R=ropivacaine, RD=ropivacaine + dexmedetomidine.

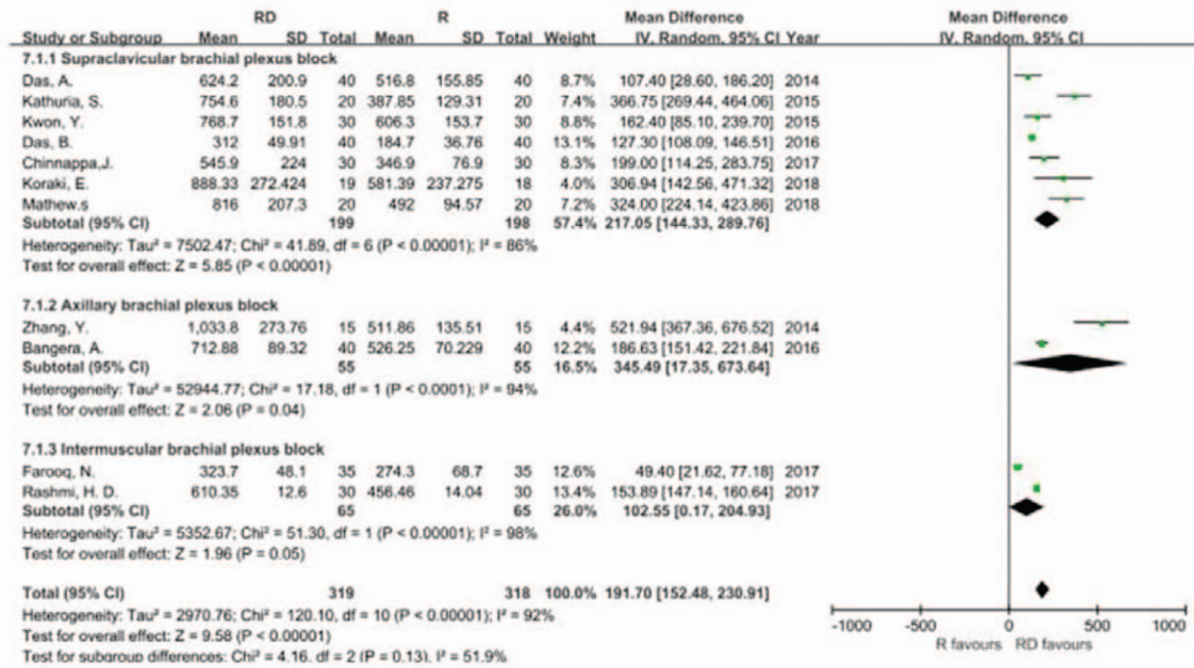


Figure 6. The duration of the motor block of BPB. Pooled analysis showed significantly prolonged duration of motor block in the RD group compared with those without dexmedetomidine (MD, 191.70 minutes; 95% CI 152.48–230.91 minutes; $P < .0001$). BPB=brachial plexus block, CI=confidence interval, MD=mean differences, R=ropivacaine, RD=ropivacaine + dexmedetomidine.

first meta-analysis to investigate the effect and the safety of only ropivacaine combined with dexmedetomidine for BPB.

As a result of the meta-analysis, the addition of dexmedetomidine did prolong the duration both in sensory and in motor block, at the same time reduce the sensory and motor block onset time significantly, and the effect was not associated with the dose of dexmedetomidine. When subgroups performed in the condition of different dose of dexmedetomidine and location for the BPB, there was no significant difference. A previous meta-analysis showed that $>50 \mu\text{g}$ of dexmedetomidine combined with local anesthetic drugs can more significantly produce motor and sensory block in BPB.^[24] However, in our subgroup analysis, high doses ($>50 \mu\text{g}$) and low doses ($<50 \mu\text{g}$) of

dexmedetomidine all improved BPB. This suggests that the effect of ropivacaine for BPB may not be related to the dose of dexmedetomidine.

The optimal dosage of dexmedetomidine has not been confirmed as an adjuvant to BPB. The result in Jung et al^[25] research showed that $2 \mu\text{g}/\text{kg}$ was the most optimal dosage for BPB after compared with 1 and $1.5 \mu\text{g}/\text{kg}$. However, general anesthesia was induced after BPB in this study. Whether the general anesthesia process makes a difference to the effect of dexmedetomidine was unclear when comparing to the local nerve block anesthesia alone. More trials should be designed to investigate the effect of dose dependent for dexmedetomidine in peripheral nerve block.

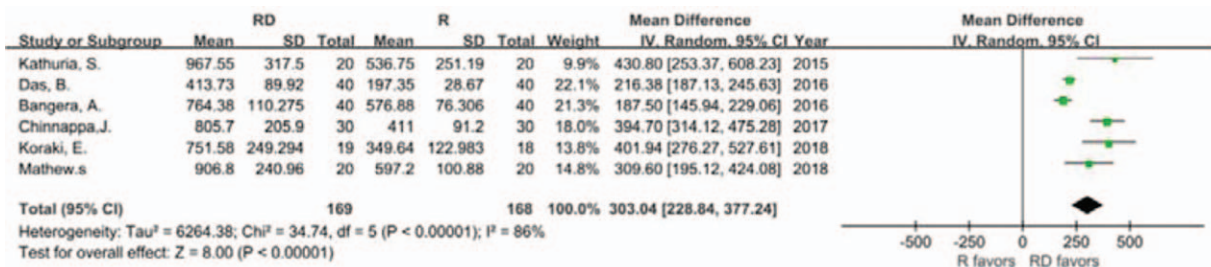


Figure 7. The duration of analgesia. Pooled analysis showed dexmedetomidine as adjuvant could prolong the duration of analgesia (MD, 303.04 minutes; 95% CI 228.84–377.24 minutes; $P < .00001$). BPB=brachial plexus block, CI=confidence interval, MD=mean differences, R=ropivacaine, RD=ropivacaine + dexmedetomidine.

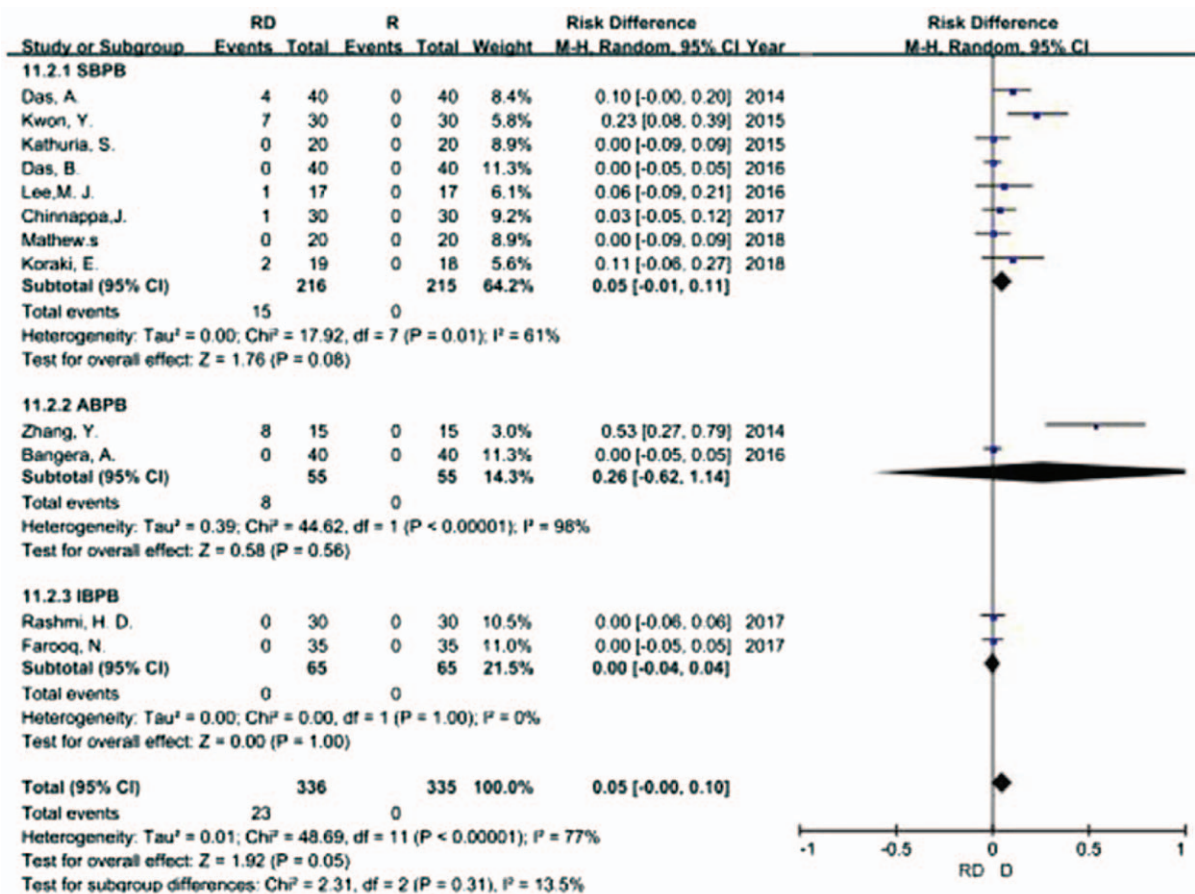


Figure 8. Mean risk difference of the bradycardia in BPB. Pooled analysis showed no significant difference in RD group compared with those without dexmedetomidine on bradycardia (RD, 0.05, 95% CI 0.00–0.10, $P = .05$). BPB=brachial plexus block, CI=confidence interval, R=ropivacaine, RD=risk difference, RD=ropivacaine + dexmedetomidine.

Furthermore, when the combination of dexmedetomidine with ropivacaine was used in BPB, the axillary approach seemingly appeared to be earlier of onset time and lasted longer than the supraclavicular and interscalene approach. More clinical trials need to be performed in the future to make the effect of the nerve block location clearly.

Dexmedetomidine was first approved as a sedative agent for use in the intensive care unit and currently was used as an analgesic in peripheral nerve blocks. Current perineural applications for dexmedetomidine has relied on off-label uses of the drug, therefore we must pay attention to medication safety. The perioperative adverse events have been the most focused point when dexmedetomidine as an adjuvant was applied for the BPB, because they were the most important evidence to judge the safety. And the most commonly reported adverse events were bradycardia and hypotension. Previous meta-analysis indicated that the dosage of dexmedetomidine > 50 μg caused higher risk to obtain bradycardia.^[24] While in this study, there was no difference of bradycardia and hypotension in the subgroups of different dexmedetomidine dosage and the location of BPB. The different criteria for inclusion and heterogeneity among the studies may be the reasons for the different results from previous studies.

It is noteworthy that intraoperative hemodynamics changed obviously on the heart rate and mean blood pressure, while

mostly did not need any special intervention. What is more, the consumption for the postoperative analgesic and postoperative pain score were also reflected for the effect when dexmedetomidine added into ropivacaine. No enough data and the different scales for pain score lead to a difficult process to make a comparison. However, parts of studies showed that it can reduce the use of postoperative opioids and postoperative pain score.

Limitation of this meta-analysis should be acknowledged. High heterogeneity was found across the result. Firstly, the small sample size was considered the main sources of heterogeneity. Secondly, the different characteristic among patients might be an important reason. Finally, the different scales and criteria for the judgment might cause heterogeneity. However, high-level evidence and superiority were provided to prove that adding dexmedetomidine to ropivacaine strengthened the effect of BPB.

In conclusion, this meta-analysis showed a better effect in prolonging the duration of sensory block, motor block, and analgesia when dexmedetomidine as an adjuvant adding into ropivacaine in BPB. In addition, the combination of dexmedetomidine and ropivacaine does not increase the incidence of bradycardia and hypotension. Further research should be conducted to find more effective and safer doses of dexmedetomidine.

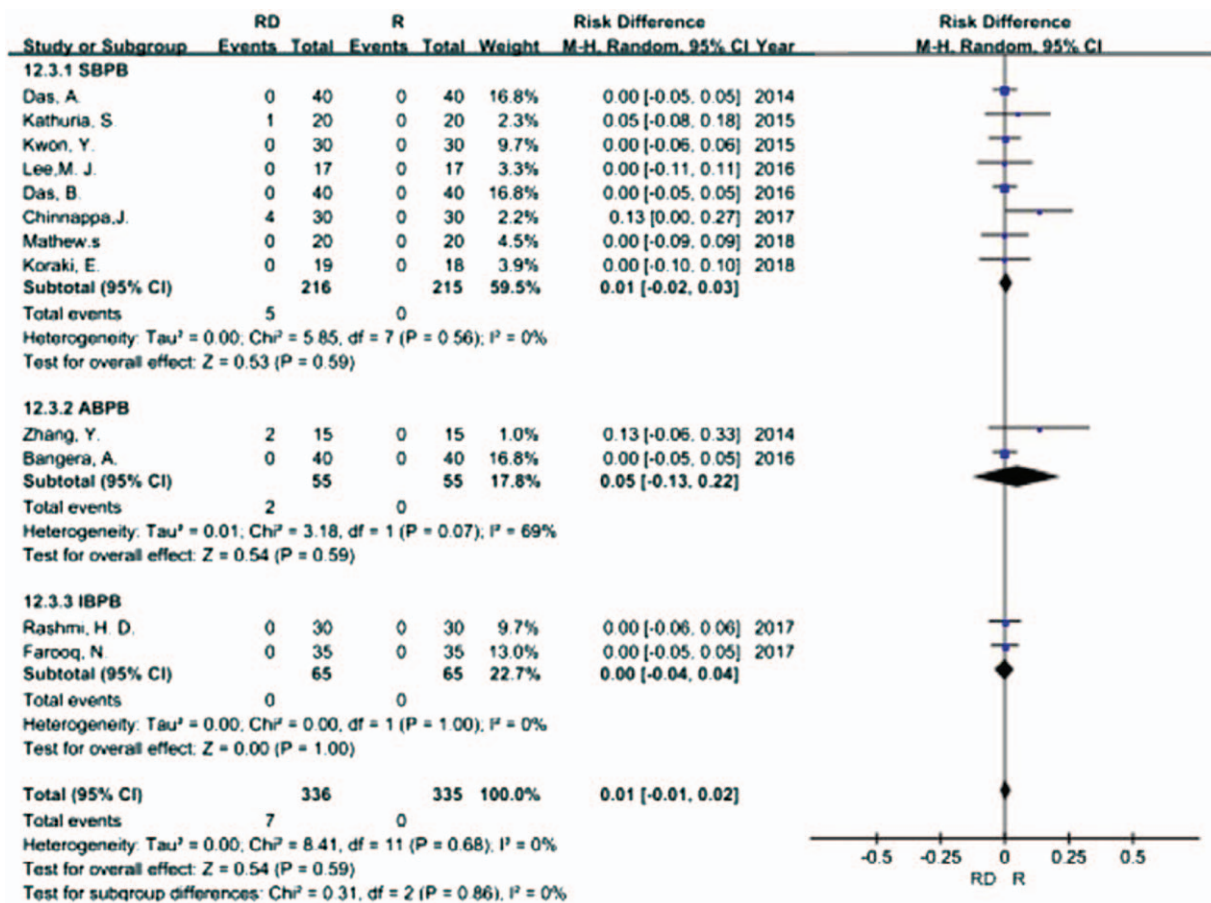


Figure 9. Mean risk difference of the hypotension in BPB. Pooled analysis showed no significant difference in RD group compared with those without dexmedetomidine on hypotension (RD, 0.01, 95% CI -0.01 to 0.02 , $P = .59$). BPB=brachial plexus block, CI=confidence interval, R=ropivacaine, RD=risk difference, RD=ropivacaine + dexmedetomidine.

Author contributions

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