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Ultrasound-Guided Cervical Medial Branch Blocks: A Systematic Review and Meta-Analysis

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Abstract

Objective: Cervical medial branch blocks (CMBBs) are useful in differentiating facetogenic pain from other sources of cervicogenic headaches and neck pain. The purpose of this systematic review and meta-analysis is to determine the efficacy, performance time, pain reduction, and adverse events associated with ultrasound (US) guided CMBB compared with other commonly used guidance methods such as fluoroscopy and computed tomography (CT).

Methods: Searches of MEDLINE, EMBASE, Cochrane Library, and Ovid were completed to identify studies addressing CMBBs utilizing ultrasound compared to other imaging techniques. Three reviewers independently screened the titles, abstracts, and full texts, extracting data from eligible studies. Outcomes of interest including success rate, efficacy, performance time and complication profile were analyzed in meta-analysis. All other reported measures and complication profiles were analyzed descriptively.

Results: A total of 9 studies were included. Four randomized controlled trials (RCTs) and 5 cohort studies satisfied inclusion criteria. US-guided CMBBs demonstrated similar success rates (OR = 1.05, 95% CI = 0.15 to 7.52, z = 0.05, P = 0.96) and similar pain efficacy (SMD = -0.54, 95% CI = -1.91 to 0.83, z = -0.77, *P* = 0.44) compared to traditional guidance techniques. However, US-guided CMBBs demonstrated reduced performance time (SMD = -1.77, 95% CI = -2.65 to -0.89, z = -3.94, *P* <0.01) and rate of vascular injury/injection (OR = 0.09, 95% CI = 0.01 to 0.75, z = -2.23, *P* = 0.03) compared to fluoroscopy guided CMBBs.

Conclusion: This review and meta-analysis demonstrated that US-guided cervical medial branch blocks are a reliable alternative to fluoroscopy- and CT-guided CMBBs, with similar efficacy but a potentially improved safety and performance time.

Introduction

Chronic neck pain is the fourth most common cause of years lived with disability worldwide [1]. Nearly 116 million American adults live with neck pain, a higher number than the total affected by cancer, diabetes and heart disease combined [2, 3, 4]. Episodes of neck pain commonly subside with or without treatment, although 50% of people continue to suffer from chronic neck pain [5]. Lack of timely anatomical diagnosis leads to poor long-term outcomes with conservative treatment of neck pain. Patients with persistent neck pains frequently progress to a trial of a diagnostic block of nerves that supply cervical zygapophyseal joints owing to a lack of valid clinical or radiologic signs for affected joints.

Cervical medial branch blocks (CMBBs) involve anesthetizing the neural supply to the cervical facet joints, typically at several levels [2, 6, 7]. These blocks provide essential diagnostic information regarding the anatomic pain generators and predict the response to subsequent radiofrequency ablation that can result in sustained pain relief for up to 12-18-months [2, 6, 7]. As such, these procedures necessitate the need for reliability, safety and time efficiency [8, 9, 10].

Traditionally, CMBBs have been performed utilizing either fluoroscopy or computed tomography (CT) to confirm correct needle placement [11]. Real-time fluoroscopy with contrast injection is necessary to confirm needle placement and lack of vascular penetration [12, 13, 14]. Limited availability of specialized equipment, qualified personnel and associated cost are barriers to widespread use of CT in cervical facet interventions. Ultrasound (US) guidance is an emerging imaging modality in the field of spine interventions that may offer several advantages [7, 15]. For instance US guided CMBB: 1) afford for easily accessible machine and or device use, 2) a potential to decrease block performance time, 3) significant reduction in radiation dose and 3) potential reduction in adverse effects due to unintentional intravascular injections [7, 16, 17, 18, 19, 20].

The objective of this systematic review and meta-analysis is to examine the clinical efficacy, performance time, pain reduction, and complication profile of US-guided CMBBs compared to traditional guidance methods of CT or fluoroscopy. We hypothesize that US-guided CMBBs have similar efficacy with improved performance time and reduced adverse events thus serving as a reasonable and safe alternative for the guidance of CMBBs.

Methods

Protocol and registration

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [21]. The review protocol was registered on PROSPERO via study number CRD42020153433 [22].

Eligibility Criteria

Studies were included if they were comparison studies reporting the results of CMBB completed under US-guidance (intervention) versus CMBB completed under fluoroscopy or CT-guidance (controls) in adults, >18 years of age, with chronic neck pain. Included studies consisted of randomized control trials (RCTs) and cohort studies reporting: (1) success rate of the block, (2) measure of pain level change after intervention, (3) performance time of CMBB, or (4) adverse effects such as aberrant

spread or vascular puncture. Cohort studies and RCTs were chosen to provide the best clinical evidence. Studies classified as: reviews, editorials or technique papers, case reports, animal models or cadaveric studies, and/or studies published in a language other than English were excluded. In addition, studies examining nerve blocks performed at levels other than the cervical spine, studies involving pediatric populations, or studies employing guidance other than US, CT, or fluoroscopy were excluded.

Information sources and searches

MEDLINE, EMBASE, Cochrane Library and OVID were searched from database inception to September 1st, 2019. Initial search was completed on January 1st, 2017 and repeated on September 1st, 2019. Search terms "cervical medial branch block," "neck pain," "ultrasound-guided," and "nerve block" were used.

Study selection

The titles, abstracts, and full texts were reviewed independently and in duplicate by two investigators to determine the relevance of studies (SP, DA). Any discordant articles were reviewed by a third reviewer (DS) to determine the individual article's eligibility. In addition, the references of included studies were reviewed to identify any additional articles for inclusion.

Data Abstraction

Data abstraction was performed by two reviewers (SP, DA) and reviewed and verified by a third reviewer (DS). Authors of selected articles were contacted via email to collect additional numerical data not available in published manuscripts. If communication with authors was not successful, data were collected through graphics and converted from the available data through standardized formulas presented in the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [23].

Quality Assessment

The quality of the included RCTs was assessed using the updated guidelines by the Cochrane Neck and Back Group [24]. No scoring system was adopted. Quality assessments were used for descriptive purposes. The risk of bias assessment was performed in the following domains: selection bias (criteria 1, 2, 9), performance bias (criteria 3, 4, 10, 11), attrition bias (criteria 6, 7), detection/measurement bias (criteria 5, 12), reporting bias (criterion 8) and other bias (criterion 13). These domains include all the criterion reported in Cochrane risk of bias tool with additional clarity.

The risk of bias of the individual cohort studies was assessed using the guidelines for methodologic quality assessment of nonrandomized studies of interventional techniques and ROBINS-I [25, 26]. This quality assessment was performed by one of the authors (DA) and checked by additional authors (NM and DS). The ROBINS-I assessment tool is designed primarily for cohort studies with interventional and control groups that investigate clinical outcomes. It utilizes the technique of imagining a "target study" to help conceptualize a study's possible deficiencies compared to an ideal RCT of the same topic. Bias is assessed in seven domains with signaling questions following a standardized format leading to a "triangulation" between similar studies to refine the analysis [26]. This is a thorough method which ensures full consideration of the domains in question, but we found that single arm and/or feasibility studies with more technical outcomes were less valid targets of the ROBIN-I. To address this concern, we supplemented the evaluation with the IPM-QRBNR tool, designed specifically for the assessment of bias of pain medicine interventions [25].

Statistical analysis

Statistical analysis was performed using Comprehensive Meta-Analysis® (CMA®) version 2.2.046 (Biostat®, Englewood, NJ). Binary outcomes were compared via estimation of the odds ratios (OR) with 95% confidence interval (CI). Continuous outcomes were compared by calculation of the standardized mean differences (SMDs) and their 95% CI. Estimates from included studies were pooled using the DerSimonian and Laird Random-Effects Method (REM) or the Mantel-Haenszel Fixed-Effects Method (FEM), depending on the presence or absence of significant heterogeneity, respectively.

Sub-group analysis was performed, whenever applicable, by pooling of studies sub-grouped according to the study design (RCT or retrospective) or according to the comparator modality (fluoroscopy or CT) examined versus the US. Point

estimates were calculated by pooling of all included studies. Studies included in the meta-analysis were tested for heterogeneity using the Cochran Q Chi-squared test and by calculation of the I-squared (I2) index.

Publication bias was assessed by examination of funnel plots of the estimated effect size on the horizontal axis versus a measure of study size (standard error for the effect size) on the vertical axis. In addition, the Duval and Tweedie Trim and Fill method was used to impute missing studies, if any, and to re-compute an adjusted combined effect.

Results

Search Results and Study Characteristics

A combined search of MEDLINE, EMBASE, Cochrane Library and OVID yielded 152 results after duplications were removed. Following the title screen, 18 were included in the abstract screening, of which nine progressed to full text review. Nine studies were excluded at the abstract screening stage because they didn't meet the inclusion criteria, specifically, they did not address cervical medial branch injections. Of the nine studies included, five studies were cohort studies [7, 15, 27, 28, 29] and four studies were RCTs [10, 30, 31, 32] **(Figure 1)**. All studies included in the full text review met eligibility criteria. Five of the 9 studies were included in the meta-analysis. One cohort study [28] was included in the meta-analysis because this study evaluated two comparable groups. Other cohort studies included only one group of patients. No additional articles were retrieved through manual reference search of the included articles. **Table 1** summarizes study characteristics, primary outcomes, and principal findings of the studies.

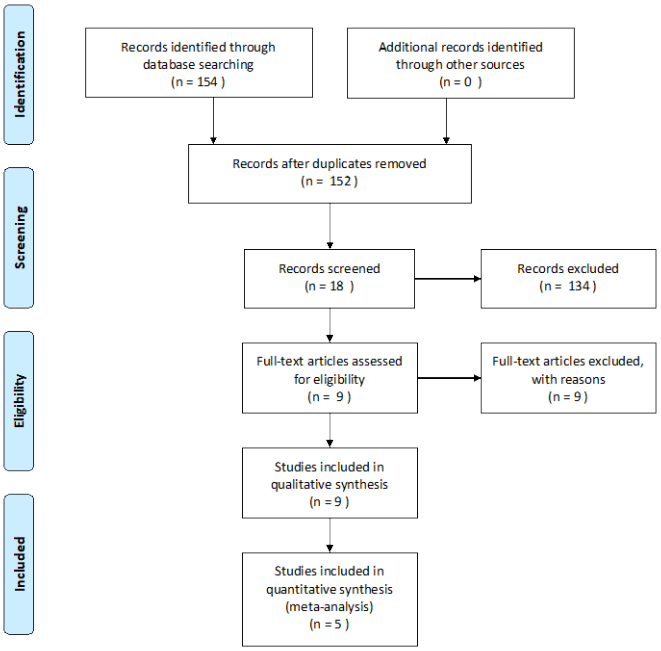

Figure 1. PRISMA Flow Diagram

Risk of Bias Assessment

The risk of bias summary for RCTs is presented in **Table 2**. All RCTs scored a low risk of bias for all the domains except performance bias as three out of four studies did not blind patients or assessors. Data were adequate to examine publication bias for performance time and percentage of pain relief for RCTs. There was no evidence of publication bias regarding either outcome.

Included cohort studies demonstrated appropriate study design, setting, image guidance, statistical methods, outcome assessment and funding. However, there was generally a privation of cohort studies with regards to assessment and reporting of potential patient factors, including baseline potential prognostic factors or confounders. Two different bias assessment tools for the cohort studies aided to provide a comprehensive view of these studies. The results of cohort studies assessment using ROBINS-I tool [26] presented in **Table 3**. The results of the assessment with the IPM-QRBNR tool [25] presented in **Table 4**. The overall risk of bias was found to be low, corresponding to the current trend in pain medicine [33]. The specific comments on the individual studies are presented in comments to **Table 3**.

Procedural Success of CMBB under US-guidance

Two RCTs compared CMBB performed with US or fluoroscopy guidance, assessing the correct needle placement for CMBB under each guidance technique [30, 31]. A successful block of the third occipital nerve (TONB) was determined as a block that resulted in hypoesthesia of the suboccipital area [30]. Alternatively, a successful block of the C7 medial branch, was determined as a block that resulted in the presence of contrast agent continuous with the contour of the C7 superior articular process and covering the entire length and

proximal half of the transverse process in an anterior-posterior view [31].

In both studies, the success rates were similar for the standard technique using fluoroscopy guidance and investigative technique utilizing US guidance with no statistically significant difference between groups. Pooling of included studies using FEM demonstrated no statistically significant difference between US- or fluoroscopy-guidance, with an OR for successful block of 1.05, 95% CI = 0.15 to 7.52, z = 0.05, P = 0.96. These results **(Figure 2)** indicate no difference in success rates comparing the US- and fluoroscopy - guidance.

Percentage of pain relief

Three RCT's reported pain scores before and after CMBB, one utilized a Visual Analogue Scale (VAS) while two others utilized a Numerical Rate Scale (NRS) [30, 31, 32]. Individual studies did not demonstrate a statistical difference in pain relief between standard guidance methods and US-guidance. Pooling of included studies using REM demonstrated no statistically significant difference no statistically significant difference between US and all (US vs CT vs Fluoro) standard guidance techniques (SMD = -0.54, 95% CI = -1.91 to 0.83, z = - 0.77, P = 0.44). Sub-group analysis comparing US and fluoroscopy demonstrated no statistically significant difference between the modalities as well (SMD = 0.13, 95% CI = -0.28 to 0.55, z = 0.62, P = 0.53) **(Figure 3)**.

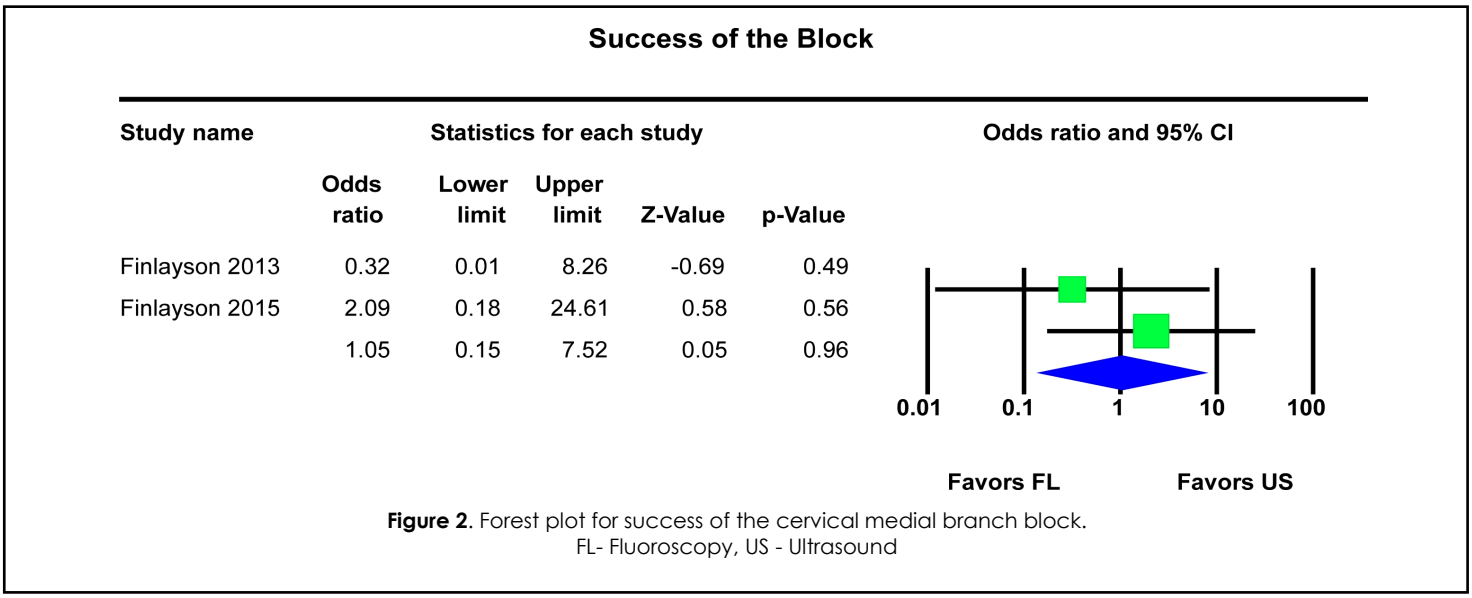

Figure 2. Forest plot for success of the cervical medial branch block.
FL- Fluoroscopy, US - Ultrasound

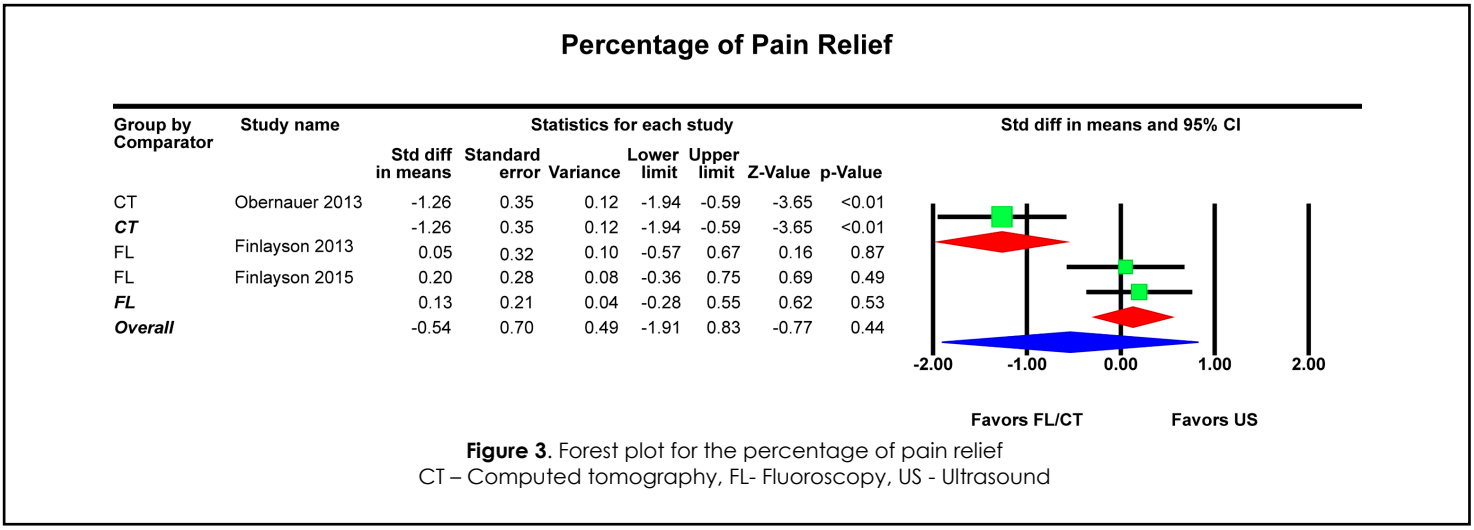

Figure 3. Forest plot for the percentage of pain relief
CT – Computed tomography, FL- Fluoroscopy, US - Ultrasound

Table 1. Trials Pertaining to Ultrasound-guided Cervical Facet/Medial Branch Blocks and Radiofrequency Ablation Published up to September 1st, 2019.

Authors (Year)	Study Type	Number of Patients/ Groups	Description	IP vs OOP approach	Fluoroscopy or CT utilized	Primary Outcome	Principal Findings
Eichenberger et al (2006)	RCT	11/ crossover trial	Volunteers underwent USG TONB with LA on one side and saline on the other	OOP approach	After USG TONB	Presence of cutaneous hypoesthesia in the distribution of the TON; needle position relative to fluoroscopic target point	Needle was correctly placed over the C2/C3 joint in all but one case. Cutaneous hypoesthesia was seen in seen in all but one of the LA blocks.
Siegenthaler et al, 2011	CH	15/1	Examined the effect of a shortened fluoroscopic radiofrequency neurotomy procedure (fewer lesions), using ultrasound assistance to guide cannula placement	N/A	For the RFA after the CMB was localized with USG	Reduction in pre-procedural pain intensity	A pain reduction of at least 80% was observed in 14 of the subjects at 15 days. Median duration of 50% pain relief was 44 weeks.
Siegenthaler et al 2012	CH	60/1	Volunteers underwent USG needle placements with contrast injection simulating CMBB and TONB	OOP approach	After USG CMBB	Needle tip position and contrast distribution relative to conventional fluoroscopic target points	Overall accuracy was 77% for needle placement and 84% for contrast distribution. Results varied by spinal level and were lowest at C7.
Finlayson et al 2012	CH	53/1	Two-phase study examining the accuracy of USG TONB and CMBB (C3-C6) in patients with neck pain	IP approach	After USG TONB and CMBB	Needle tip position and contrast distribution as assessed by post-procedural radiographs	Phase 1: 80.9% of needles placed correctly. Phase 2: contrast covered appropriate area in 94.5% of injections.
Finlayson et al 2013	RCT	40/2	Patients with suspected cervicogenic headaches underwent TONB using either fluoroscopy or USG	IP approach	In control group only	Performance time was the primary outcome; secondary outcomes included success rates and sensory distribution of the blocks	USG was associated with a significantly shorter performance time (212.8 vs 396.5 seconds; P = 0.000) and fewer needle passes (2 vs 6; P = 0.000). Both imaging modalities resulted in similar success rates (95% vs 100%).
Obernauer et al 2013	RCT	40/2	Patients undergoing cervical intraarticular facet blocks were assigned to CT guidance or USG	IP approach	In control group only	Primary outcomes were performance time and accuracy (as assessed by CT control); secondary outcomes included pain reduction at 30 minutes and 1 month	USG was associated with 100% accuracy and significant reduction in performance times (04:46 vs 11:12 minutes P <0.05) as well as radiation dose. Pain relief was similar in both groups.
Finlayson et al 2014	CH	40/1	Patients with cervical pain underwent USG CMBB at the C5 and C6 levels	bi-planar (IP) technique	After USG CMBB	Contrast distribution, as assessed by a blinded observer on anteroposterior and lateral radiographic views	Appropriate contrast distribution was seen in 100% and 97.5% of C5 and C6 levels, respectively.
Finlayson et al 2015	RCT	50/2	Patients undergoing a C7 CMBB were randomized to either USG or fluoroscopic guidance	bi-planar (IP) technique	In control group only	Performance time was the primary outcome and secondary outcomes included success rates, number of needle passes, and pain relief	Ultrasound guidance was associated with a shorter performance time (233.6 vs 390.6 seconds; P <0.001) and fewer needle passes. Both pain relief and success rates (92%-96%) were similar between groups.
Park et al 2017	CH	68 (USG) 58 (Fluoro)	Retrospective chart review of patients with neck pain who had undergone CMBB with either fluoroscopic or USG	IP approach	In fluoroscopy group only	Neck Disability Index and pain scores at 1, 3, and 6 months after injection. Secondary measures included performance time, number of needle passes, and complications.	USG was associated with a shorter performance time and fewer needle passes. Pain relief and functional improvement were similar for both groups. No major complications were noted.

Table 2. Bias assessment of randomized controlled trials in CMBB utilizing Cochrane review criteria [24]
Abbreviations: Y=Yes; N=No; U=Unsure; TON=Third occipital nerve

	Source of Possible Bias	Eichenberger (2006)	Finlayson (2013)	Obernauer (2013)	Finlayson (2015)
1	Randomization adequate	Y	Y	Y	Y
2	Concealed treatment allocation	Y	Y	N	U
3	Patients blinded	Y	N	N	N
4	Care provider blinded	Y	N	N	N
5	Outcome assessor blinded to intervention (*=primary outcome)	Y-Visualization of TON* Y-Hypoesthesia* Y- Needle position	N-Performance time* Y-Success rate Y-Pain levels Y-Area of hypoesthesia Y-Quality of block Y-Complications N-# of needle passes	U-Accuracy* N- Performance time* U-Radiation dose U- Pain relief	N- Performance time* Y-Success rate Y- Pain relief Y -Aberrant spread N- # of needle passes Y-Complications
6	Drop-out rate described and acceptable	Y	Y	Y	Y
7	Randomized participants analyzed in their group	Y	Y	Y	Y
8	Avoidance of selective outcomes reporting	Y	Y	Y	Y
9	Baseline group similarity	Y	Y	Y	Y
10	Co-interventions avoided or similar	Y	Y	Y	Y
11	Compliance acceptable in all groups	Y	Y	Y	Y
12	Similar timing of outcome assessments	Y	Y	Y	Y
13	Other sources of potential bias unlikely	Y	Y	Y	Y

Table 3. Bias assessment of observational studies in CMBB utilizing ROBINS-I assessment tool [26]
Additional Comments on Studies included in the assessment using ROBINS-I tool. [26]

	Risk of bias domains							
Study	**D1**	**D2**	**D3**	**D4**	**D5**	**D6**	**D7**	**Overall**
Siegenthaler (2011)	=	+	=	+	=	+	+	+
Siegenthaler (2012)	=	+	+	+	+	+	+	+
Finlayson (2012)	=	+	+	+	+	=	!	=
Finlayson (2014)	+	+	=	+	+	+	+	+
Park (2017)	+	=	+	!	+	+	+	=

Domains of bias
D1: Due to confounding
D2: In selection of participants into the study
D3: In classification of interventions
D4: Due to deviations from intended interventions
D5: Due to missing data
D6: In measurement of outcomes
D7: Bias in selection of the reported result

Risk of bias judgement
+ Low
= Moderate
! Serious
X Critical
NI No information

Table 3. continued

Siegenthaler (2011) [27]
D1: Low average BMI. Very small sample size.
D3: Comparator was 4 similar studies done previously which presumably had different population characteristics, procedure techniques, injectate, nerve targets, etc. Deficiencies noted but not significant: 3 patients sedated. Possible variance in operators (no discussion of who performed procedures). Most assessed at day 15 and others at 30. 1 treated with gabapentin for allodynia. Patients whose response fell below 50% of preoperative pain level were no longer followed, which resulted in loss of many data points which would have created a clearer picture of overall clinical outcomes. However, these did not affect the primary outcomes.

Siegenthaler (2012) [29]
Very well designed with many of the essential features of the "target study." The blinding of the observer, intentional misplacement of needles and agreement statistics ensure low risk of bias.
D1: All subjects young, with very low average BMI and no degenerative changes.

Finlayson (2012) [7]
Generally well-designed and low risk of bias in most domains.
D1: Subjects with previous surgeries (3) and severe DDD (2) could have been excluded. If included in both phases of the study, these could have included a maximum of 25 of the blocks included for analysis. This may have skewed analysis toward the comparator.
D7: The authors conclude that "US guidance offers a reliable alternative to fluoroscopy for TON and C3-6 CMBB." This is presumably true but seems too broad a statement when there were no clinical outcomes assessed.
The use of intentional misplacement would have resulted in even less risk of bias in the "measurement of outcomes" domain in phase I, but would not likely have changed results very much.

Finlayson (2014) [15]
No blinding of provider possible, which may have been relevant in the "target study." This may have influenced performance time and needle placement –leading to different clinical outcomes. Relatively low BMI in "convenience" sample.
D3: No discussion on inter-operator variability.

Park (2017) [28]
Decently designed for a retrospective study but limited by this design and population size.
D1: The second injection or reevaluation was not considered if there was an aggravation of pain, no relief of pain, or the patient satisfaction score equal to or below 'fair' grade.
D2: Group sizes may have been different enough to confound and were relatively small. Baseline p values may not have been as good as RCT, but probably not confounding.
D4: One provider doing procedure in both groups (unblinded), but probably not an influence on outcomes (procedure time) in a retrospective study. However, this may have influenced needle placement and, therefore, clinical outcomes. Relatively more non-responders in the FL group. Co-interventions could not be limited due to retrospective design.

Performance time

Three included studies described procedure performance time utilizing the US versus standard imaging techniques [30, 31, 32]. The time was recorded for US from initial skin contact following the application of sterile US gel until the procedure was "successfully complete," as determined by the sonographer detecting placement of the needle tip directly at the inter-articular space or facet joint and completion of the injection. For CT, the elapsed time was measured from the first CT scan until confirmation of the correct needle position on the final confirmation scan. For fluoroscopy, performance time was measured as the interval between the first radiograph and the end of injection.

Compared to both fluoroscopic imaging and CT, the US-guided procedure was associated with significantly shorter performance times in each individual study. Pooling of all guidance techniques versus US-guidance using REM demonstrated no statistically significant difference in performance time (SMD = 0.30, 95% CI = -3.82 to 4.42, z = -0.14, P = 0.89) **(Figure 4)**. However, sub-group analysis showed shortened CMBB performance time with US-guidance when compared to CMBB with fluoroscopic-guidance (SMD = -1.77, 95% CI = -2.65 to -0.89, z = -3.94, P <0.01).

Incidence of vascular puncture

Two included studies reported the incidence of vascular injection [28, 30]. The vascular puncture was defined as the aspiration of blood prior to the injection of local anesthetic during either US or standard techniques. Of the two included studies, both reported a benefit with US-guidance, with a fewer cases of vascular puncture due to early identification of vessels under ultrasound guidance and, therefore, prevention of puncture **(Figure 5)**. Meta-analysis of the included studies demonstrated

a significantly reduced rate of vascular injections with US-guidance compared to fluoroscopy-guidance (OR = 0.09, 95% CI =0.01 to 0.75, z = -2.23, P = 0.03).

Additional outcomes

Additional outcomes of the incidence of intra-articular injection, intra-foraminal injection, or other aberrant spread were analyzed. Two included studies reported the incidence of unintentional intra-articular injection [30, 31]. Meta-analysis of studies reporting TON blocks and CMBBs demonstrated no statistically significant difference between US-guidance and fluoroscopy guidance (OR = 0.19, 95% CI = 0.02 to 1.75, z = -1.46, P = 0.14 **(Figure 6)** [30, 31]. Only one study reported data on intra-foraminal or other aberrant spread. Odds Ratio was completed comparing US-guidance and fluoroscopy guidance, which showed no statistically significant difference between US and fluoroscopy [31].

Table 4. Quality assessment of cohort studies for CMBB utilizing IPM-QRBNR criteria [25]
Abbreviations: NA = Not applicable (scored as 0)

			Siegenthaler (2011)	Siegenthaler (2012)	Finlayson (2012)	Finlayson (2014)	Park (2017)
I.	**STROBE OR TREND Guidance**						
1.	Study Design Guidance and Reporting	/4	4	4	4	4	4
II.	**DESIGN FACTORS**						
2.	Study design & type	/4	2	2	2	2	1
3.	Setting/physician	/2	2	2	2	2	2
4.	Imaging guidance	/3	3	3	3	3	3
5.	Sample size	/4	2	3	3	2	3
6.	Statistical methodology	/2	2	2	2	2	2
III.	**PATIENT FACTORS**						
7b.	Inclusiveness of population	/4	4	NA	NA	2	4
8.	Duration of pain	/2	2	NA	NA	2	2
9.	Previous treatments	/2	2	NA	NA	1	2
10.	Duration of follow-up with appropriate interventions	/4	3	NA	NA	1	2
IV.	**OUTCOMES**						
11.	Outcomes assessment for significant improvement	/4	4	NA	NA	3	3
12.	Description of dropout rate	/2	2	2	2	2	NA
13.	Baseline group similarity: prognostic indicators	/2	0	0	0	0	2
14.	Role of co-interventions	/2	NA	NA	NA	2	2
V.	**ASSIGNMENT**						
15.	Method of assignment of participants	/4	NA	NA	NA	NA	3
VI.	**CONFLICTS OF INTEREST**						
16.	Funding & sponsorship	/3	2	2	2	2	2
TOTAL /48 – NA ratings			34 /42	20 /26	20 /26	30 /44	37 /46

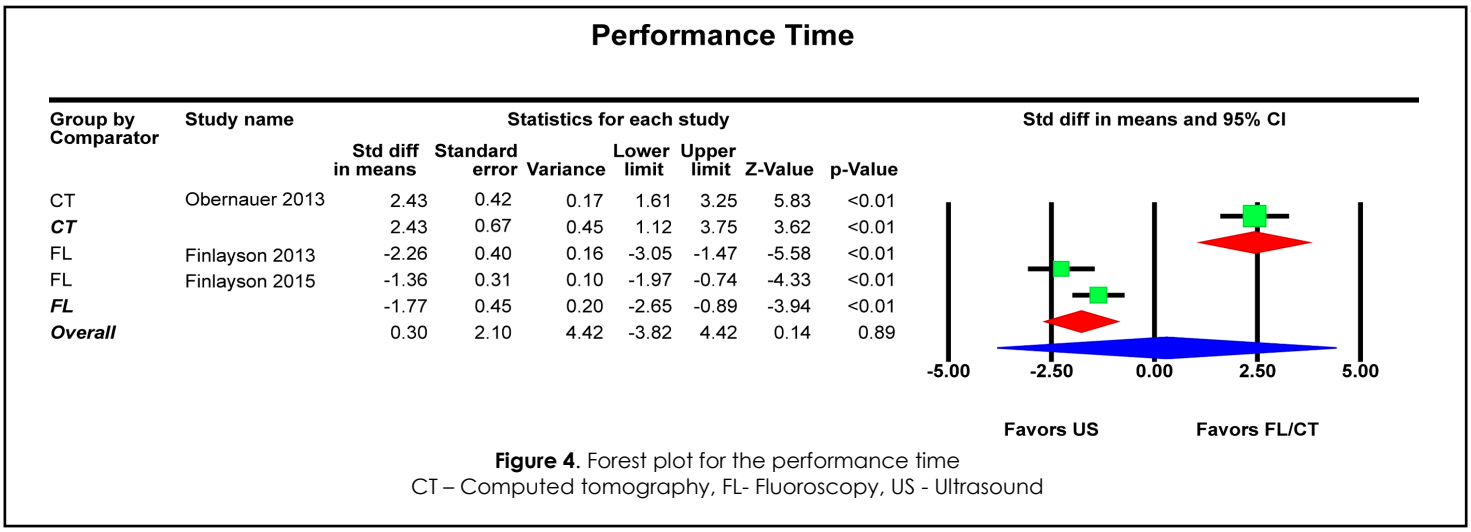

Figure 4. Forest plot for the performance time
CT – Computed tomography, FL- Fluoroscopy, US - Ultrasound

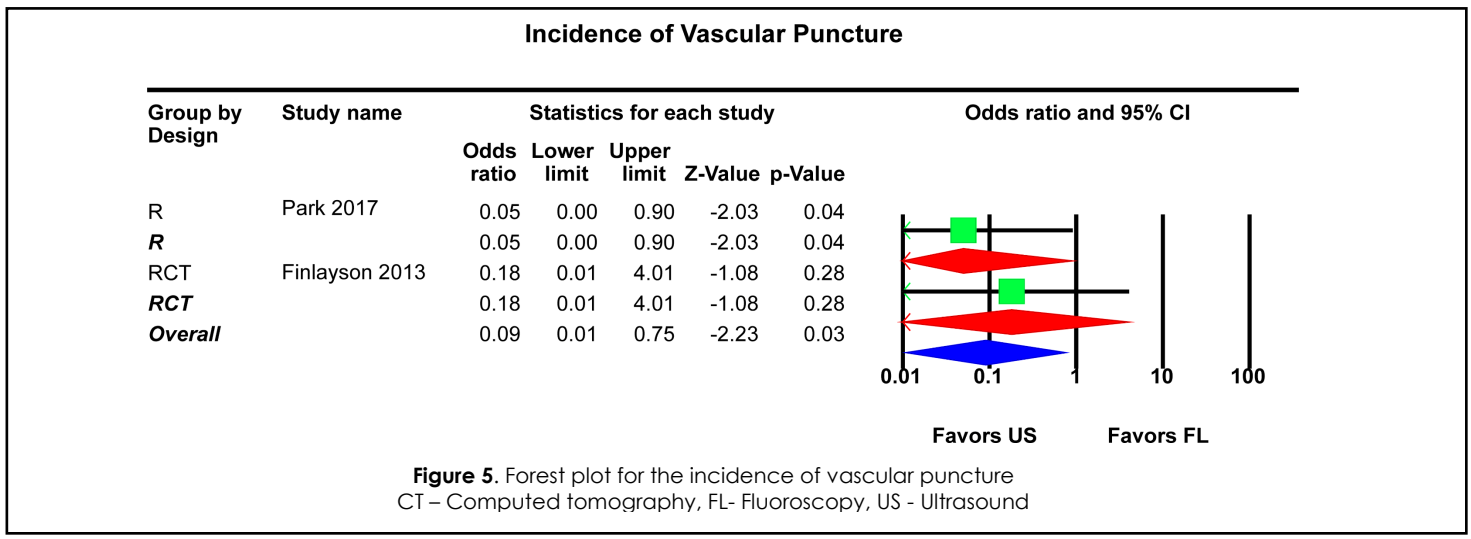

Figure 5. Forest plot for the incidence of vascular puncture
CT – Computed tomography, FL- Fluoroscopy, US - Ultrasound

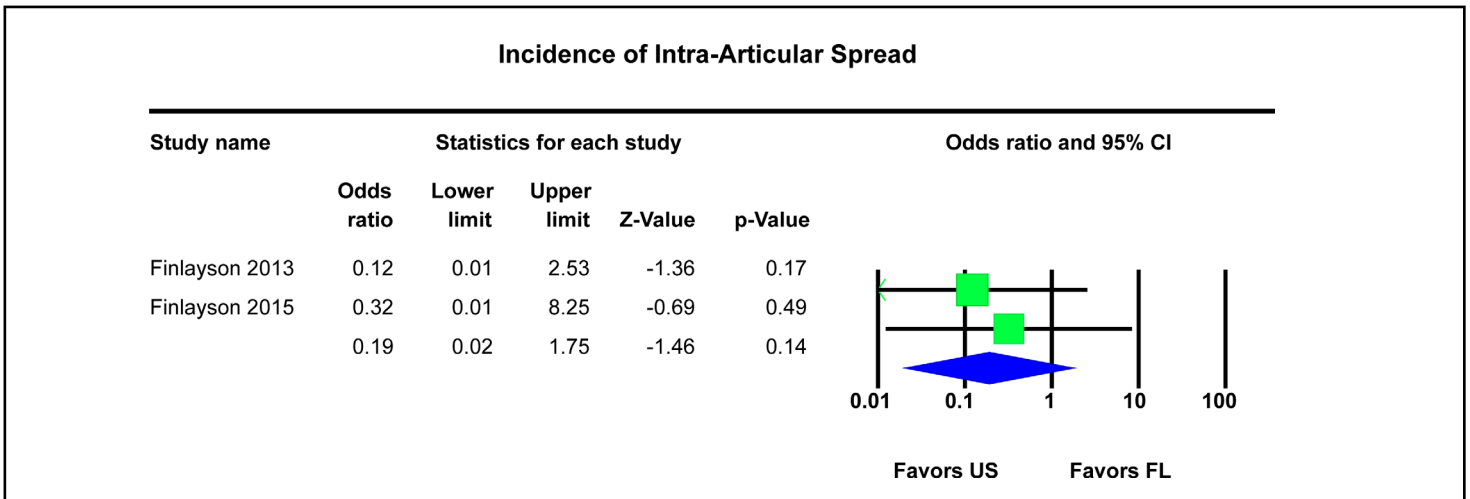

Figure 6. Forest plot for the incidence of intra-articular (IA) spread
CT – Computed tomography, FL- Fluoroscopy, US - Ultrasound

Discussion

This systematic review and meta-analysis demonstrate that US-guided CMBB is a reliable alternative to fluoroscopy and CT guidance with similar procedure success rates and pain relief level. US-guided CMBB also shown a significant potential to with significant potential to improve performance time and decrease risk of vascular injury. Moreover, there was no increase in aberrant spread of local anesthetic with the use of US-guided CMBB compared to other guidance techniques.

The wide-spread applicability of US including ease of accessibility and convenience as well as increase in the patient safety secondary to a reduction of radiation exposure, and the ability to visualize soft tissues and vascular structures, make US a promising tool for guiding nerve [8, 9, 10, 34, 35]. The findings of this systematic review and meta-analysis, are in line with previously published work demonstrating reliability of US-guided CMBB compared with fluoroscopy and CT guidance techniques. Finlayson and colleagues [15] concluded that US-guided CMBB is efficacious, efficient and safe. Ultrasonographic guidance was associated with an effective block at a frequency of 100% and 97.5% for C5 and C6 levels, respectively. Park et al [28] retrospectively compared the outcomes of CMBB performed with either US or fluoroscopy guidance in 126 patients with 6-months follow up. Pain scores and functional status improved similarly in both groups during the study period, and no complications were noted. It was also suggested that US offers dynamic real-time imaging of the cervical spine facets and surrounding tissue, therefore avoiding the need to continuously adjust the C-arm to obtain a true lateral view of the cervical spine necessary to correct parallax effects [36].

The ability to identify and avoid vessels in the trajectory of the needle is an important advantage of US-guided cervical spine interventions [30, 36, 37, 38]. Cohen et al reported a 7% incidence of unintentional intravascular injections during fluoroscopically guided CMBBs [39]. Ultrasonography is a valuable tool for detecting and, hence, preventing vascular injury during CMBBs, whereas contrast fluoroscopy can only demonstrate that the tip of the needle is intravascular, after the penetration of the vessel [37]. Cervical vessel penetration and/or injection can cause intravascular thrombosis [40] and other potentially life-threatening complications, including stroke [41, 42, 43]. It was hypothesized [37] that fluoroscopy may not detect that the needle has already traversed a vessel on its way to the target, whereas ultrasonography may help avoid this complication. Our systematic review and meta-analysis demonstrated that the rate of accidental puncture of paraspinal vessels was reduced. In addition, 10% of fluoroscopically guided cases were associated with vascular breach compared with no cases in the US-guided group [30].

While the success rate of TON and CMBBs, which were determined by the presence or absence of hypoesthesia in the suboccipital area, were similar between fluoroscopy and US-guidance (95%-100%), the performance times were significantly shorter with US guidance [30].

Another advantage of US-guided cervical facet and medial branch injections, in addition to shorter procedure time compared to fluoroscopy, is an option to insert only one needle [44]. Since the cervical medial branches and the TON have variable anatomy, it was suggested to place more than one needle to accommodate the anatomic variability and ensure targeting the selected nerve, when the procedure is performed under fluoroscopic guidance [45]. The location of both the TON and the lower cervical medial branches showed significant craniocaudal location variability from their proposed bony landmarks, which are the C2/3 joint cleft for the TON and the deepest point of the articular pillar for the C3–C6 medial branches [44, 46]. An upper limit craniocaudal range of 2.2 mm has been documented at the C4 level [46]. Real-time ultrasonography allows visualization of the TON and cervical medial branches in most cases and allows for the use of a single needle, which is of benefit to both patient and physician [44]. Even if the TON is not well visualized, the C2/3 articulation is typically obvious. Eichenberger et al [10] examined accuracy of needle position over the C2/C3. The investigators performed TON blocks in 10 volunteers using a transverse (short-axis view) and needle out-of-plane approach. They reported accurate needle position over the C2/C3 joint in 82% of blocks (as verified by fluoroscopy) and a success rate of 90%, as determined by the presence of hypoesthesia in the suboccipital area [10].

As in C2/C3 level procedures, our findings were that C7 CMBB completed under fluoroscopic imaging was associated with significantly longer performance times, more needle passes, and a higher incidence of vascular breach compared to US imaging [31, 44]. While fluoroscopically guided CMBBs at C7 level pose unique challenges, the ultrasound-guided technique at this particular level is no exception [44]. C7 medial branches were visualized on sonography in only one-third of cases [46]. Not surprisingly, a case of iatrogenic spinal cord injury from an US-guided C7 CMBB was reported [47]. This was the first, and, to the best of our knowledge, the only serious injury from the US-guided CMBBs. The authors confirmed previous concerns that extreme caution should be emphasized with the performance of certain cervical procedures, including CMBB at the C7 level, independently of the imaging modality used [29, 31, 40, 44, 46]. Some experts suggest to use US scanning before the planned procedure [37, 44] to help with the diagnosis of identifying underlying conditions, including facet joint effusions or vascular malformations. The pre-injection scanning can be performed in the short-axis view to identify blood vessels in the vicinity of the target structure, and then, during the procedure, the needle can be placed in the same view to avoid such blood vessels [44].

Although US-guidance is well established for CMBB, there has been only a single clinical study that has examined the use of US guidance for radiofrequency ablation (RFA) [27]. The feasibility of US-guided cervical medical branch RFA was initially proposed by Lee an co-authors [48]. Siegenthaler et al examined the effect of US assistance to refine cannula positioning and reduce the number of lesions performed during fluoroscopy-guided RFA. In a cohort of 15 patients, they demonstrated that accurate detection of the nerve under US guidance could decrease the number of lesions and performance time [27]. Kim et al reported two successful cases of pulsed RFA performed at C2/3 levels [49].

All studies comparing US-guided cervical interventions with fluoroscopy and CT-guided procedures emphasize the absence of radiation exposure with US guidance [37, 44, 45, 49, 50, 51, 52]. Radiation-free imaging is particularly important with cervical interventions because of increased scattered radiation from the C-arm [44, 53]. Only one group of authors chose to dismiss the risks of radiation exposure during cervical interventional procedures, suggesting that the level of radiation, with appropriate protection, is low [54]. It is necessary to emphasize that while the radiation exposure during the cervical interventions is considered to be below the conventional yearly limits, it can lead to appalling sequelae years later, including cell damage and genetic mutations, and, therefore, should be avoided if possible [55, 56].

The similarity in efficacy demonstrated in this review compared to traditional guidance techniques in combination with the intrinsic benefits of US, may increase the availability of CMBB in those with chronic neck pain and decrease the time to intervention that may translate to improved overall quality of life in patients with chronic neck pain [7, 8, 16, 30, 37, 57]. Finally, US-guided CMBB reduced risk for vascular injection/injury. US-guided CMBB, therefore, provides a safe option for chronic pain patients and physicians [7, 16, 18, 19, 20, 58]. A recent narrative review [54] suggested, without adequate evidence, that ultrasound-guided cervical injections "confers a unique risk profile" including spinal cord injury. In contrast, this rare, but devastating complication is not unique for ultrasound-guided injections [12, 13, 14]. Our systematic review and meta-analysis support the efficacy and safety of US-guided CMBBs.

One of the limitations of US-guided CMBB, similarly to any interventions, including fluoroscopy- or CT-guided procedures, is that any of these procedures require proper training. While basic training in US-guided injections may help learn how to visualize the tip of the needle, specialized training is necessary for verifying the levels of the cervical spine. This particular skill is essential for safe and effective US-guided CMBB.

Even though the rigorous methodology of this review (comprehensive literature search, screening process, and thorough assessment of bias) strengthens the conclusions outlined above [21, 23, 24, 26], there are limitations inherent in such an analysis. Limitations are the heterogeneity of the included studies, limited inclusion criteria, and variability of the outcomes reported. In addition, this paper is limited by the small number of studies published and the need for mixed study inclusion, including both RCTs and cohort

studies. Despite the high quality of few RCTs included, the addition of cohort studies may introduce additional bias and necessitates the need for further RCTs. Although several RCTs were included, the methodologies, including comparison guidance technique and outcomes reported, were variable and resulted in reduced numbers of papers included in each meta-analysis. This study demonstrates the usefulness and safety of US as a guidance technique for CMBBs. Additional high-quality RCTs are needed to further assess the subgroups of patients, including obese individuals, the elderly, and patients with advanced degenerative changes.

Conclusions

Current evidence suggests that US-guided cervical medial branch blocks may serve as feasible alternative to fluoroscopy-guided and/or CT-guided procedures. US-guided CMBB nerve blocks demonstrated similar efficacy, as well as potentially improved performance time safety compared to fluoroscopy-guided and/or CT-guided procedures. There was no increase in aberrant spread of local anesthetic with the use of US-guided CMBB compared to other guidance techniques. US-guided CMBBs demonstrated significantly decreased the risk of vascular injury. These findings, in addition to the inherent benefits of US compared to traditional imaging guidance techniques, can influence the growth of sonography as a promising imaging guidance modality for nerve blocks and denervation procedures. Additional high-quality clinical trials are needed to further assess the subgroups of patients, including obese individuals, the elderly, and patients with advanced degenerative changes. Although US has the potential to increase the safety of CMBB, specialized training is necessary to obtain expected outcomes, as success, similar to fluoroscopy- and CT-guided interventions, is operator dependent [15, 37, 44].

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Disclosures

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