Regional Nerve Blocks For Hip and Femoral Neck Fractures in the Emergency Department: A Systematic Review

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ABSTRACT

Objectives: Hip and femoral neck fractures are common in elderly patients, who are at an increased risk of complications if their pain is suboptimally managed. This systematic review seeks to determine if regional nerve blocks reduce pain, reduce the need for parenteral opiates, and reduce complications, compared to standard pain management with opiates, acetaminophen, or NSAIDs.

Data sources: Systematic review of MEDLINE, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials found 401 articles, of which nine were selected for inclusion.

Study selection: Randomized controlled trials including adult patients with a hip or femoral neck fracture (Population) who had a 3-in-1 femoral nerve block, traditional femoral nerve block, or fascia iliaca compartment block performed preoperatively (Intervention). Comparison must have been made with standard pain management with opiates, acetaminophen, or NSAIDs (Comparison) and outcomes must have included pain score reduction (Outcome).

Data synthesis: Eight out of nine studies concluded pain scores were improved with the regional nerve block compared to standard pain management. A significant reduction in parenteral opiate use was seen in five out of six studies. No patients suffered life-threatening complications related to the nerve block; however, more minor complications were underreported. Most of the studies were at a moderate to high risk of bias.

Conclusions: Regional nerve blocks for hip and femoral neck fractures have a benefit in reducing pain and the need for IV opiates. The use of these blocks can be recommended for these patients. Further high-quality randomized controlled trials are required.

RÉSUMÉ

Objectifs: Les fractures de la hanche et du col du fémur sont fréquentes chez les personnes âgées, qui connaissent un risque accru de complications si le soulagement de la douleur n'est pas suffisant. La revue systématique présentée ici visait à déterminer si l'analgésie régionale par blocage nerveux permettait d'atténuer la douleur, de réduire la nécessité d'administrer des opiacés par voie parentérale et de diminuer le risque de complications comparativement au traitement habituel de la douleur par les opiacés, l'acétaminophène ou les anti-inflammatoires non stéroïdiens (AINS).

Sources de données: Une revue systématique effectuée dans les bases de données MEDLINE, EMBASE, CINAHL et Cochrane Central Register of Controlled Trials a permis de relever 401 articles, dont 9 ont été retenus pour l'étude.

Sélection des études: Il s'agissait d'essais comparatifs à répartition aléatoire, menés chez des adultes qui avaient subi une fracture de la hanche ou du col du fémur (population) et qui avaient été traités par un bloc fémoral « 3 en 1 », un bloc fémoral classique ou un bloc de la loge du fascia iliaque en phase préopératoire (intervention). Les comparaisons devaient avoir été établies avec le traitement habituel de la douleur par les opiacés, l'acétaminophène ou les AINS (comparaison) et les résultats devaient faire état d'une réduction du score de la douleur (résultats [outcome]).

Synthèse des données: Dans huit études sur neuf, on a noté une réduction des scores de la douleur, liée à l'analgésie régionale par blocage nerveux comparativement au traitement habituel de la douleur. Une diminution importante de l'utilisation des opiacés par voie parentérale a été constatée dans cinq études sur six. Aucune complication potentiellement mortelle n'a été observée en lien avec l'analgésie régionale; toutefois, des complications bénignes ont été sous-déclarées. La plupart des études comportaient un risque moyen ou élevé de biais.

Conclusions: L'analgésie régionale par blocage nerveux pour les fractures de la hanche ou du col du fémur soulage efficacement la douleur tout en diminuant la nécessité d'administrer des opiacés par voie intraveineuse. Le recours à ce type d'analgésie est donc recommandable chez ces patients. Il faudrait toutefois mener d'autres essais comparatifs, à répartition aléatoire, de qualité.

Keywords: Hip Fracture, Regional analgesia, Analgesia, Nerve Blocks, Pain Management, Femoral Nerve, Emergency Medicine, Anesthesia, Orthopedics

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INTRODUCTION

Hip and femur fractures are common in patients presenting to the emergency department (ED). Pain management is often a challenge due to the advanced age, comorbidities, and increased sensitivity to side effects from systemic analgesics in this population. These patients are at a significant risk of delirium due to under-treatment of their pain,[1] but are also susceptible to becoming delirious from the use of opiate analgesics, and nonsteroidal antiinflammatory drugs (NSAIDs) are often contraindicated due to drug-drug interactions and risk of side effects. Therefore, regional nerve blocks performed in the ED are increasingly recommended for pain control in hip fracture patients to reduce the need for systemic analgesics, prevent delirium, and improve pain control prior to definitive treatment.

There are three described methods of providing regional nerve blocks for hip and femur fractures: the traditional femoral nerve block (FNB), the 3-in-1 femoral nerve block (3-in-1 FNB), and the fascia iliaca compartment block (FICB). The traditional FNB involves injecting local anesthetic directly surrounding the femoral nerve within the neurovascular bundle of the groin. This can be converted to a 3-in-1 FNB by placing pressure distal to the needle at the time of injection, which allows the anesthetic to track superiorly and also anesthetize the obturator and lateral femoral cutaneous nerves.[2] The FICB indirectly anesthetizes the same three nerves as the 3-in-1 FNB by inserting a needle lateral to the neurovascular bundle and filling the fascia iliaca compartment with a large volume of dilute local anesthetic, which theoretically tracks superiorly towards the lumbar plexus.[3]

The adoption of regional nerve blocks for hip and femoral neck fractures in the ED has been slow in North America, where the use of these techniques has largely been limited to a small number of providers with advanced training. A 2012 survey of three Toronto, Ontario–area hospitals found that only 33% of attending emergency physicians ever performed regional nerve blocks for hip fractures, and only 6% performed them "often" or "almost always."[4] In contrast, in the United Kingdom, regional nerve blocks are used quite commonly in the ED, with a 2009 survey finding that 55% of EDs regularly use regional anesthesia techniques for hip and femur fractures.[5] In order to find out whether regional nerve blocks should be more widely used in the ED, this systematic review intends to determine whether regional nerve blocks (FNB, 3-in-1 FNB, and FICB) effectively reduce pain, reduce the need for IV opiates, and reduce the risk of complications compared to standard pain management for adult ED patients with an acute hip or femoral neck fracture.

METHODS

We conducted a systematic review of the literature with a search on January 17, 2014, using MEDLINE (1946–2014), EMBASE (1947–2014), CINAHL (1960–2014), and the Cochrane Central Register of Controlled Trials (Issue 12 of 12, December 2013). The complete search strategy is provided in the Appendix. Additional articles were screened by searching the references of all articles selected for full-text review. There were no language restrictions.

Inclusion criteria were randomized controlled trials involving adult patients (16 years or older) with an acute hip or femoral neck fracture who had a single injection FNB, 3-in-1 FNB, or FICB. The injection must have been performed preoperatively and a pain score reduction recorded. Comparison must have been made to any method of "standard pain management," which was defined as opiates, acetaminophen, or NSAIDs. Articles were excluded if they were not a randomized controlled trial, if the nerve block was performed immediately prior to surgery, if the patient also received an epidural or spinal anesthetic in conjunction with the regional nerve block, if a continuous nerve block catheter was placed, or if the study only enrolled patients with mid-shaft femoral fractures.

After the initial literature search, the titles and abstracts were screened independently by two authors (BR and PP) for inclusion in the full-text review. Kappa values were calculated for inter-observer reliability. After selecting articles for full-text review, both authors independently extracted data from each article onto a data extraction form. This form included reasons for inclusion/exclusion, key study characteristics, demographics, risk of bias, and results. Key study characteristics recorded included the specialty and level of training of the physician performing the block, the needle guidance technique used, and any co-analgesics administered. Risk of bias was assessed for each study using the Cochrane Collaborations tool for assessing risk of bias in randomized trials.[6]

After the completion of data extraction, kappa values were calculated for inter-observer reliability for final

article selection. Any differences in article selection, data extraction, or risk of bias assessment between the two authors (BR and PP) were resolved by consensus. If consensus could not be reached, a third author (MW) was designated to mediate a final decision. In cases where information was unclear or not reported, attempts were made to contact the primary authors of the studies for clarification.

The primary outcome was a reduction in visual analog scale pain score with the FNB, 3-in-1 FNB, or FICB, compared to standard pain management. Secondary outcomes included a reduction in parenteral opioid use and complication rates. Pre-specified complications of interest were nausea/vomiting, respiratory depression, delirium, nerve injury, intravascular injection, and local anesthetic toxicity, although all reported complications were recorded.

The intent was to perform a meta-analysis of the primary and secondary outcomes if possible, assuming the results were reported in similar ways and the studies were clinically homogenous enough that a meta-analysis was considered valid. There was also an a priori subgroup analysis planned to see whether there were any differences between the primary and secondary outcomes, in studies that used ultrasound guidance versus other methods of needle guidance. The PRISMA guidelines were used in structuring the reporting of this systematic review.[7]

RESULTS

Our initial literature search identified 401 studies, after duplicates were removed. After screening the titles and abstracts of these 401 studies, 19 were selected for full-text review and potential inclusion. Inter-observer reliability for the initial screening phase was moderate with a kappa of 0.61 (95% CI, 0.39–0.82). After full-text review, nine were selected for inclusion in the systematic review with a kappa score of 0.79 (95% CI, 0.51–1.00). A study flow diagram, including the reasons studies were excluded, is illustrated in Figure 1. There were no additional studies identified from the references of included studies.

Of the included studies, two utilized the traditional FNB,[8,9] four used the 3-in-1 FNB,[10-13] and three used the FICB[14-16]. Baseline demographics were similar between studies, with a weighted mean age of 80.6, 79.5, and 76.4 years in the FNB, 3-in-1 FNB, and FICB studies respectively. The gender ratio of patients across studies was also similar, with 75.7%, 72.0%, and 67.3% of patients being female in the FNB, 3-in-1 FNB, and FICB studies respectively.

The only study at an overall low risk of bias was the article by Beaudoin et al.,[10] whereas every other article was at a moderate to high risk of bias, as described in Figure 2. The risk of bias came largely from a lack of double blinding in six out of nine studies;[8,9,11-13,15] however, the studies by Beaudoin et al.,[10] Foss et al.,[14] and Monzón et al.[16] attempted to blind patients and clinicians by performing sham nerve blocks. Five studies also suffered from inadequate blinding of outcome assessment,[9,12-15] and four studies included patients who were later unaccounted for in the final results.[8,11,12,16]

All of the included randomized controlled trials were small, ranging in size from 33 patients to 154 patients (Table 1). Two-thirds of the studies (66.7%) enrolled 50 or fewer patients. The most commonly used local anesthetic for performing the FNB and 3-in-1 FNB was bupivacaine 0.5%, which ranged in dose from 20–30 mL. The FICB studies all used different local anesthetics, which made direct comparison of these studies difficult. Only one study[10] used ultrasound guidance, whereas the remainder used either landmark technique[8,11,14-16] or nerve stimulator guidance[9,12,13]. An emergency physician or resident performed the nerve block in five out of nine studies[9-12,16]. In only one study[10] did the authors report any prior experience performing the block. In the studies that reported how physicians were trained to perform the nerve blocks, the procedure was learned quickly and easily.

Due to variable methods of reporting final outcome results, missing statistics, and clinical heterogeneity between studies, a meta-analysis could not be performed. Authors of various studies were contacted when necessary, but missing data were either unavailable[11,12] or we were unable to locate the authors[8,13]. Therefore, data are presented as a qualitative synthesis to summarize individual studies.

For the primary outcome of visual analog score pain reduction with a regional nerve block, eight out of nine studies[8-11,13-16] concluded there was an equal or superior benefit with a nerve block compared to standard pain management (Figure 3).

A summary of the conclusions of each article follows:

Femoral Nerve Block: Haddad et al.[8] found the nerve block arm experienced less pain at 15 minutes and two hours, but not at eight hours. Murgue et al.[9] found

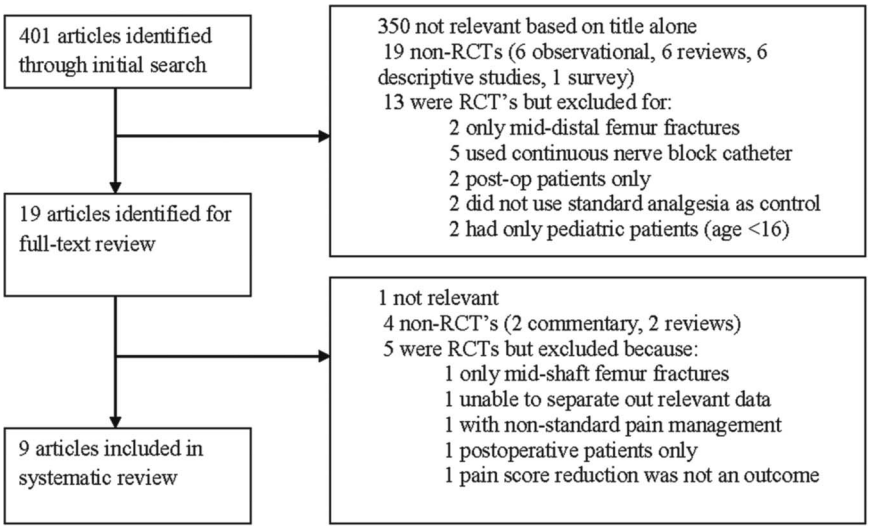

Figure 1. Study Flow Diagram, including reasons for exclusion at each stage.

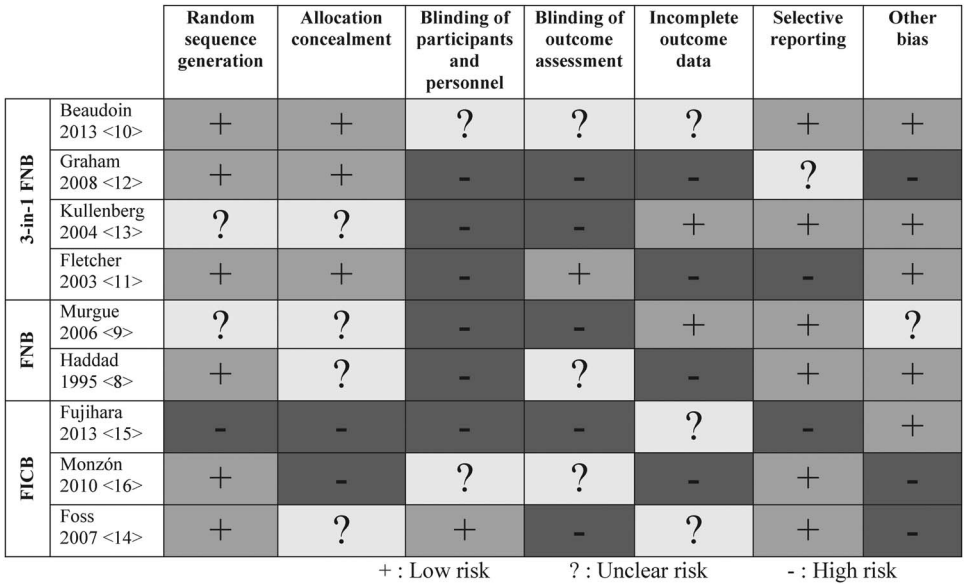

Figure 2. Risk of bias chart detailing the risk of each domain of bias in each individual study.

a decrease in pain with the FNB that was superior to either IV morphine or IV acetaminophen/NSAID combination.

3-in-1 Femoral Nerve Block: Beaudoin et al.[10] concluded the sum of the differences in pain scores between the 3-in-1 FNB and placebo was lower in the nerve block group after four hours ($p = 0.001$). Fletcher et al.[11] found lower aggregate mean pain scores with the 3-in-1 FNB up to 16 hours. Kullenberg et al.[13] found lower pain scores with nerve blocks "after treatment," but did not specify the time at which pain scores were collected. Graham et al.[12] was the only study that found no benefit to the nerve block.

Fascia Iliaca Compartment Block: Foss et al.[14] found that although the absolute pain scores were not different between the FICB and the intramuscular (IM) morphine groups, the relative change in pain score was superior at all time points for the FICB group, because the patients in the FICB group had significantly more baseline pain. Monzón et al.[16] found the FICB offered

Table 1. Summary of key study characteristics

Nerve Block	Primary author/year	Total (n)	Local anesthetic	Needle guidance	Operator
Femoral Nerve Block					
	Murgue 2006[9]	45	20 mL mepivacaine	Nerve stimulator	Emergency attending
	Haddad 1995[8]	45	0.3 mL/kg bupivacaine 0.25%	Landmark	Orthopedic resident
3-in-1 Femoral Nerve Block					
	Beaudoin 2012[10]	36	25 mL bupivacaine 0.5%	Ultrasound	Emergency attending
	Graham 2008[12]	33	30 mL bupivacaine 0.5%	Nerve stimulator	Emergency attending/resident
	Kullenberg 2004[13]	80	30 mL ropivacaine 0.75%	Nerve stimulator	Orthopedic attending
	Fletcher 2003[11]	50	20 mL bupivacaine 0.5%	Landmark	Emergency attending/resident
Fascia Iliaca Compartment Block					
	Fujihara 2013[15]	56	10 mL ropivacaine 0.75% and 10 mL mepivacaine 2%	Landmark	Orthopedic resident
	Monzón 2010[16]	154	0.3 mL/kg bupivacaine 0.25%	Landmark	Emergency attending
	Foss 2007[14]	48	40 mL mepivacaine 1% with 1:200,000 epinephrine	Landmark	Anesthesia resident

n = total number of patients in treatment and standard analgesia group

better pain relief than intravenous (IV) NSAIDs at 15 minutes ($p < 0.001$), but the opposite was true after eight hours. Fujihara et al.[15] found improved pain with the FICB at all times compared to rectally administered NSAIDs, but this study was at particularly high risk of bias.

For the secondary outcome of a reduction in IV opiate use, five out of six studies[8-11,14] using parenteral opiates for standard pain management demonstrated a statistically significant reduction in consumption of opiates with a regional block (Table 2). The study by Kullenberg et al.[13] also used opiates for analgesia, but was not included in the secondary outcome analysis, because it was not possible to quantify how much opiates the patients in each group received. Only the study by Graham et al.[12] failed to demonstrate a significant difference in opiate usage between the 3-in-1 FNB and IV morphine group. In a post-hoc sensitivity analysis where only the double blinded studies were considered, the patients in the nerve block arm required no breakthrough morphine in the study by Foss et al.,[14] and required significantly less breakthrough morphine in the study by Beaudoin et al.[10]

The reporting of complications was highly variable in the different studies, making it difficult to draw any firm conclusions regarding this outcome. Two studies[9,15] did not attempt to collect complications at all, and five studies[8,12-14,16] reported complications, but had significant problems in their methodology, including insufficient length of follow-up, a lack of predefined complications of interest, or absent description of how complications were monitored for and recorded. Only two studies[10,11] had adequate methodology and description of how complications were recorded. Therefore, we felt any aggregate data on the incidence of nausea/vomiting, respiratory depression, delirium, or nerve injury were likely invalid due to the risk of under-reporting of complications. However, it is worthwhile to note that no study reported any immediate life-threatening complications due to the nerve block, including cardiovascular collapse or local anesthetic toxicity.

The a priori planned subgroup analysis was not performed because only one study used ultrasound guidance.[10]

DISCUSSION

This systematic review found that regional nerve blocks are likely at least as effective and possibly superior at

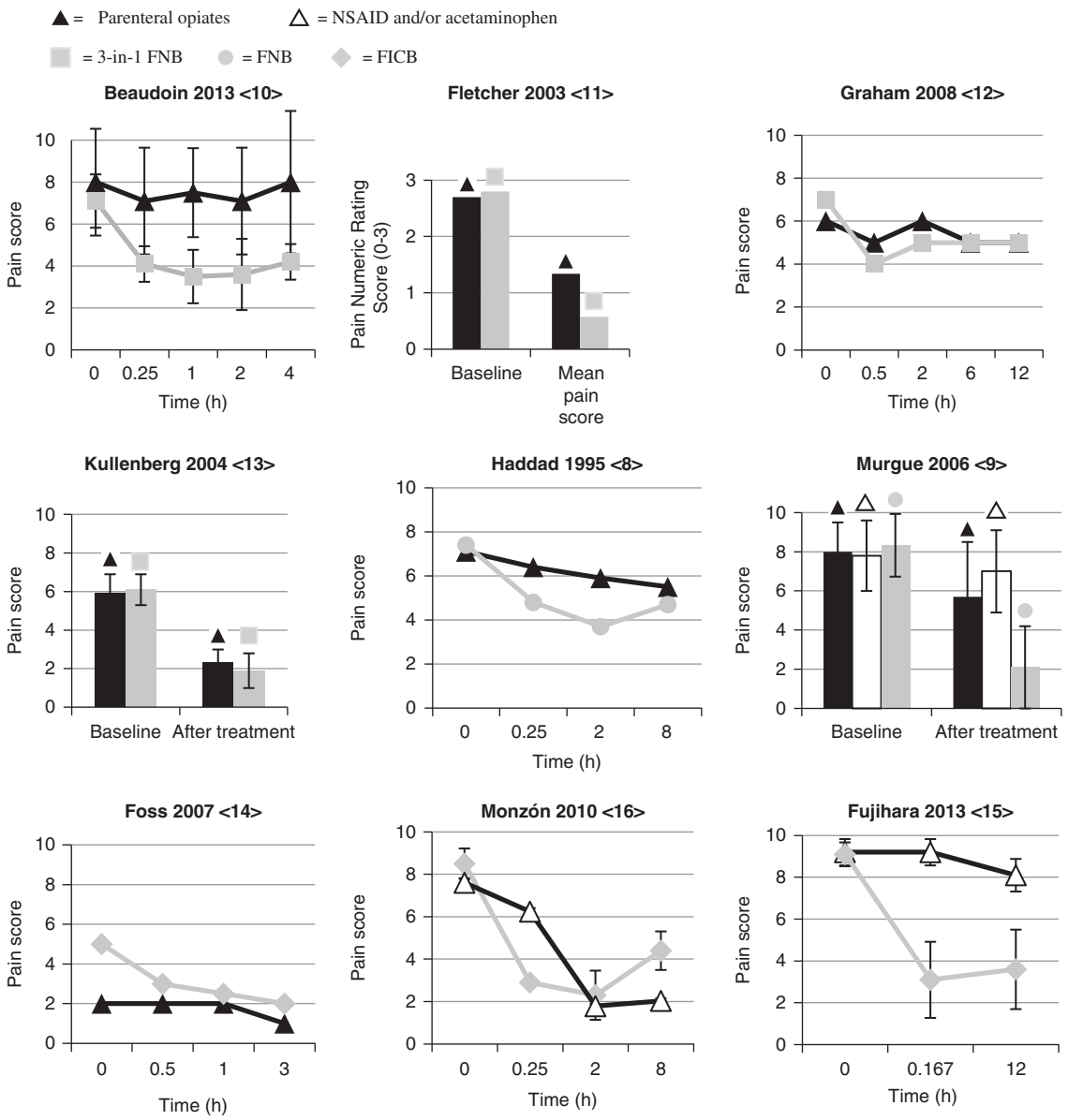

Figure 3. Pain score reduction over time in all studies. Error bars represent standard deviations where information was available.

reducing pain after a hip or femoral neck fracture compared to standard pain management. Many of the studies found the regional nerve block was significantly more effective at different time points, but there was little consistency between studies. This review found convincing evidence that regional nerve blocks decrease the reliance on opiate medications for pain control after hip or femoral neck fractures, by showing a significant decrease in opiate usage in five out of six studies that used opiates as a control.[8-11,14] This effect was maintained even in the only two studies which were double blinded,[10,14] which adds strength to the level of evidence that regional blocks reduce the reliance on IV opiates.

We were unable to draw conclusions regarding whether the reduction in the use of IV opiates led to a reduction in complications, due to under-reporting of complications in the majority of studies. None of the studies reported any immediate life-threatening complications of nerve blocks, and it is unlikely that a significant intravascular injection or local anesthetic toxicity would be missed, due to the rapid cardiovascular

Table 2. Summary of opiate consumption between regional block and standard pain management groups between studies

Nerve Block	Primary Author/Year	Parenteral Opiate Used	Opiate Consumption		Advantage
			Nerve Block	Control	
Femoral Nerve Block					
	Murgue 2006[9]	IV morphine	0 ± 0 mg	4 ± 1.7 mg	FNB
	Haddad 1995[8]*	IM meperidine	12 requests	35 requests	FNB ($p < 0.05$)
3-in-1 Femoral Nerve Block					
	Beaudoin 2012[10]	IV morphine	0 mg (range 0–6 mg)	5 mg (range 0–21 mg)	3-in-1 FNB ($p = 0.028$)
	Graham 2008[12]**	IV morphine	1.7 doses**	1.5 doses	No significant difference ($p = 0.58$)
	Fletcher 2003[11]	IV morphine	0.4 mg/h	1.2 mg/h	3-in-1 FNB ($p < 0.05$)
Fascia Iliaca Compartment Block					
	Foss 2007[14]	IM morphine	0 mg (IQR 0–0 mg)	6 mg (IQR 5–7 mg)	FICB ($p < 0.01$)

Opiate consumption given as a mean where applicable, except in the case of the study by Beaudoin et al., which reported results as a median.
*In Haddad et al.[8] there were also four patients in each group given oral doses of dihydrocodeine.
**In Graham et al.,[12] a "dose" was 0.1 mg/kg of IV morphine.

collapse, hypotension, arrhythmias, and seizures associated with these complications. However, the total number of patients in this review was small (40 received FNB, 97 received 3-in-1 FNB, 147 received FICB), and therefore the incidence of these rare, but serious complications should not be estimated from this review.

This is the largest systematic review of regional nerve blocks for hip and femoral neck fractures targeted to emergency medicine providers. There have been two prior systematic reviews by Parker et al.[17] and Abou-Setta et al.[18], which more broadly looked at regional anesthesia for hip and femoral neck fractures in a variety of settings. These prior reviews were not specifically focused on the use of regional nerve blocks in a way that is applicable to emergency medicine providers, because they included the use of continuous femoral nerve block infusion catheters and post-operative patients. Our review also includes a number of studies that were not included in these prior reviews.[10,12,13,15,16] However, both of these reviews reached similar conclusions to our own systematic review, finding that regional nerve blocks led to a significant reduction in pain levels with a reduction in systemic analgesia requirements. The main finding our study adds is that this benefit is directly applicable to patients in the ED, as soon as they arrive in hospital.

Delirium is a well known predictor of impaired functional recovery, quality of life, and increased length of hospital stay after a hip fracture.[19] We had hoped to show a reduction in delirium with the early administration of regional nerve blocks; however, we found the evidence to be lacking in the studies included in our review. The systematic review by Abou-Setta et al.[18] performed a meta-analysis on the incidence of delirium with regional nerve blocks versus standard pain management and found moderate-quality evidence that regional nerve blocks led to a statistically significant reduction in delirium (OR 0.33, 95% CI, 0.16-0.66). This is further supported by a controlled trial by Mouzopoulos et al.,[20] that found a 13.0% absolute risk reduction for delirium when patients received a daily FICB instead of IM opiates. These studies suggest there may be a benefit towards a reduction of delirium from using regional nerve blocks for patients with hip and femoral neck fractures, but larger studies are needed from the ED setting to show improved patient-oriented outcomes of better recovery and reduced length of stay.

We had initially hoped to perform an a priori subgroup analysis to show whether the use of ultrasound improved the efficacy of regional blocks. We found only one study[10] using ultrasound guidance for the regional nerve block, and so this subgroup analysis was not performed. However, there are several randomized trials suggesting that ultrasound guidance is superior to landmark or nerve stimulator guidance for the FNB and the FICB. Marhofer et al. performed two randomized controlled trials comparing ultrasound and nerve stimulator guidance for the 3-in-1 FNB and found that ultrasound significantly reduced the onset time, improved the quality of the sensory block, reduced the risk of vascular puncture, and reduced the volume of local anesthetic required

to perform the 3-in-1 FNB.[21,22] Dolan et al. performed an unblinded randomized controlled trial comparing the efficacy of the FICB with landmark versus ultrasound guidance and found sensory blockade of the anterior, lateral, and medial thigh increased from 47% to 82% with the use of ultrasound guidance.[23] We believe that with the increasing availability of portable ultrasound units in EDs, and evidence suggesting the superiority of ultrasound over landmark and nerve stimulator needle guidance, that ultrasound guidance should be used for needle localization in future studies.

LIMITATIONS

Limitations of this systematic review include the risk of publication bias due to the likelihood that smaller, negative studies may have gone unpublished. This review is also limited by the quality of the evidence, which was mostly at a moderate to high risk of bias. The studies also suffered from clinical heterogeneity by using different local anesthetics, opiates, acetaminophen, or even NSAIDs as standard pain control, which also needs to be considered when comparing the studies directly.

CONCLUSIONS

In conclusion, this systematic review suggests that regional nerve blocks may be superior to traditional analgesia for patients with hip and femoral neck fractures, and lead to a reduction in IV opiate usage. The performance of regional nerve blocks for hip and femoral neck fractures in the ED can be recommended despite the absence of a large, high-quality randomized controlled trial. There is still a need for further randomized controlled trials to determine the length and magnitude of treatment effect, cost and time effectiveness, and risk of complications. Ideally, future randomized controlled trials will be larger, use standardized reporting methods, will be double blinded or have blinded outcome assessment, and will have a structured system to assess the incidence of complications.

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APPENDICES

APPENDIX A: Search strategy for MEDLINE database from 1946 to January 17th, 2014

1 Analgesia/ or exp Analgesics/ (430402)
2 Anesthesia/ or Anesthesia, conduction/ or exp Nerve Block/ or nerve block$.tw. (64211)
3 ((an?esthet$ or an?esthesia) adj4 (regional$ or local$)).tw. (39541)
4 (femoral adj2 block$).tw. (624)
5 ("3-in-1" or "three-in-one").tw. (602)
6 (fascia iliaca adj2 block$).tw. (88)
7 (fnb or ficb).tw. (304)
8 or/1-7 (516098)
9 Femoral Fractures/ or exp Hip Fractures/ (28423)
10 ((hip$ or femur$ or femoral$ or trochant$ or pertrochant$ or intertrochant$ or subtrochant$ or intracapsular$ or extracapsular$) adj4 fracture$).tw. (2671)
11 9 or 10 (36360)
12 randomized controlled trial.pt. (359557)
13 controlled clinical trial.pt. (86972)
14 randomi?ed.ab. (333750)
15 placebo.ab. (148422)
16 clinical trials as topic.sh. (166454)
17 randomly.ab. (203605)
18 trial.ti. (119255)
19 or/12-18 (888382)
20 8 and 11 and 19 (160)
21 exp animals/ not humans.sh. (3863204)
22 **20 not 21 (149)**

APPENDIX B: Search strategy for EMBASE database from 1947 to January 17th, 2014

1 analgesia/ or exp *analgesic agent/ (376727)
2 anesthesia/ (110148)
3 exp nerve block/ (28098)
4 nerve block$.tw. (10580)
5 ((an?esthet$ or an?esthesia) adj4 (regional$ or local$)).tw. (59989)
6 (femoral adj2 block$).tw. (1018)
7 ("3-in-1" or "three-in-one").tw. (916)
8 (fascia iliaca adj2 block$).tw. (141)
9 (fnb or ficb).tw. (508)
10 or/1-9 (542023)
11 exp hip fracture/ or exp femur fracture/ (46955)
12 ((hip$ or femur$ or femoral$ or trochant$ or pertrochant$ or intertrochant$ or subtrochant$ or intracapsular$ or extracapsular$) adj4 fracture$).tw. (38042)
13 11 or 12 (54767)
14 10 and 13 (1425)
15 Clinical trial/ (900277)
16 Randomized controlled trial/ (367232)
17 Randomization/ (64876)
18 Single blind procedure/ (18855)
19 Double blind procedure/ (124397)
20 Crossover procedure/ (39822)
21 Placebo/ (249571)

22 Randomi?ed controlled trial$.tw. (99324)
23 Rct.tw. (13604)
24 Random allocation.tw. (1402)
25 Randomly allocated.tw. (20617)
26 Allocated randomly.tw. (1987)
27 (allocated adj2 random).tw. (898)
28 Single blind$.tw. (14686)
29 Double blind$.tw. (153405)
30 ((treble or triple) adj blind$).tw. (393)
31 Placebo$.tw. (210057)
32 Prospective study/ (262206)
33 or/15-32 (1438861)
34 Case study/ (32765)
35 Case report.tw. (285990)
36 Abstract report/ or letter/ (918902)
37 or/34-36 (1232009)
38 33 not 37 (1400557)
39 **14 and 38 (278)**

APPENDIX C: Search Strategy for Cochrane Central Register of Controlled Trials

ID	Search (Hits)
#1	MeSH descriptor: [Femoral Fractures] explode all trees 1216
#2	MeSH descriptor: [Hip Fractures] explode all trees 1048
#3	((hip* or femur* or femoral* or trochant* or pertrochant* or subtrochant* or intracapsular* or extracapsular*) near/4 fracture*):ti,ab,kw 2503
#4	**#1 or #2 or #3 2503**
#5	MeSH descriptor: [Anesthesia] explode all trees 15035
#6	MeSH descriptor: [Analgesia] explode all trees 5909
#7	MeSH descriptor: [Analgesics] explode all trees 15083
#8	MeSH descriptor: [Nerve Block] explode all trees 2538
#9	nerve block*:ti,ab,kw 4268
#10	((an?esthet* or an?esthesia) near/4 (regional* or local*)):ti,ab,kw 2531
#11	(femoral near/2 block*):ti,ab,kw 259
#12	(fascia iliaca near/2 block*):ti,ab,kw 32
#13	(fnb or ficb):ti,ab,kw 49
#14	("3-in-1" or "three-in-one"):ti,ab,kw 121
#15	**#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 33300**
#16	**#4 and #15 137**

APPENDIX D: Search strategy for CINAHL database

#	Query	Results	Action
S29	**S16 AND S28**	**65**	
S28	S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27	707,581	
S27	TX allocat* random*	121	
S26	(MH "Quantitative Studies")	9,351	
S25	(MH "Placebos")	6,868	
S24	TX placebo*	25,071	
S23	TX random* allocat*	2,441	
S22	(MH "Random Assignment")	30,277	
S21	TX randomi* control* trial*	41,877	

S20	TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))	588,236
S19	TX clinic* n1 trial*	115,795
S18	PT Clinical trial	51,015
S17	(MH "Clinical Trials+")	118,717
S16	S4 AND S15	238
S15	S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	42,802
S14	TI (((an?esthet* or an?esthesia) N4 local*)) OR AB (((an?esthet* or an?esthesia) N4 local*))	6,201
S13	TI (((an?esthet* or an?esthesia) N4 regional*)) OR AB (((an?esthet* or an?esthesia) N4 regional*))	2,415
S12	TI ((fnb or ficb)) OR AB ((fnb or ficb))	19
S11	TI (fascia iliaca N2 block*). OR AB (fascia iliaca N2 block*)	31
S10	TI (("3-in-1" or "three-in-one").) OR AB (("3-in-1" or "three-in-one").)	73
S9	TI (femoral N2 block*). OR AB (femoral N2 block*).	164
S8	TI nerve block* OR AB nerve block*	1,132
S7	(MH "Analgesics+")	19,721
S6	(MH "Analgesia")	2,396
S5	(MH "Anesthesia, Local") OR (MH "Nerve Block") OR (MH "Anesthesia+")	16,541
S4	S1 OR S2 OR S3	6,716
S3	((hip* or femur* or femoral* or trochant* or pertrochant* or subtrochant* or intracapsular* or extracapsular*) N4 fracture*)	6,716
S2	(MH "Femoral Fractures+")	5,233
S1	(MH "Hip Fractures+")	3,919