Critical Review Form Meta-Analysis

Riddell M, Ospina M, Holroyd-Leduc JM. Use of Femoral Nerve Blocks to Manage Hip Fracture Pain among Older Adults in the Emergency Department: A Systematic Review. CJEM. 2016 Jul;18(4):245-52.

<u>Objective:</u> "To examine the increasing body of research found around femoral nerve blocks used to address acute hip fracture pain in the ED." (p. 246)

Methods: This was a systematic review from Dec 2010 thru May 2014 intended to update a prior systematic review on the same topic that included the period January 1990 to December 2010. Because the older systematic review included a technical panel of experts from multiple medical fields and followed protocols described in the "Agency for Healthcare Research and Quality Methods Guide for Effectiveness and Comparative Effectiveness Reviews", the authors did not believe a re-analysis of the 1990-2010 results were necessary.

Inclusion criteria included randomized controlled trials (RCTs) instituting femoral nerve blocks in emergency department (ED) settings to treat acute hip fracture pain in patients 65 years of age or older when clinically important outcomes like pain or analgesic consumption were reported (p. 247). Other types of regional anesthesia such as <u>fascia iliaca compartment block</u> were excluded because the prior systematic review demonstrated "statistically significant results in favor of the femoral nerve block, but not the fascia iliaca block" (p 247). Titles and abstracts were screened by two independent reviewers to identify potentially relevant articles with disagreements resolved by discussion or (when necessary) a third reviewer. Two reviewers then independently extracted data using a standardized data abstraction form. Risk of bias was assessed using the <u>Cochrane Collaboration's Risk of Bias Tool</u>. A meta-analysis was not conducted due to the clinical heterogeneity across studies, including the types of femoral nerve block procedures used (catheter placement versus single nerve block) and the pain assessment method employed. Therefore, this systematic review presents a narrative synthesis of effectiveness outcomes across studies.

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Critical Review Form: Meta-Analysis

Guide	Comments
Are the results valid?	
Did the review explicitly address a sensible question?	Yes, the PICO question was "Does the use of femoral nerve blocks in the ED (preoperative) reduce acute pain, use of additional pain medications, and rates of delirium, and improve the functional status postoperatively of older adults (older than 65 years of age) with acute hip fracture as compared to placebo or standard care?" (p. 246)
Was the search for relevant studies detailed and exhaustive?	No. The authors report searches of Medline, EMBASE, and the Cochrane Central Registry of Controlled Trials and appear to include abstracts (Henderson 2008), but they neglect to report how they searched for research abstracts presented at annual meetings such as the American College of Emergency Physicians' Research Forum, Canadian Association of Emergency Physicians, or Society of Academic Emergency Medicine. Furthermore, they report their search strategy included combinations of relevant subject headings including hip fracture, femoral neck fracture, intertrochanteric fracture, pain therapy, anesthesia, analgesia, frail elderly, older patients, delirium, acute confusion, cognitive impairment, confusion, femoral block, and peripheral nerve block with "further details of the search available from the authors upon request". Ideally, authors provide exact terms and combinations for each electronic search engine as an appendix so that future authors can cut-and-paste into the same search engines to replicate the search. As reported here, if the authors did not respond or were unreachable, future authors would need to guess at which combinations were used for which search engines. They also do not report if any language restrictions were applied.
Were the primary studies of high methodological quality?	No – as noted in Table 2, except for Henderson 2008, all of the studies were at high or unclear risk of bias in most domains including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias. With the exception of Henderson 2008 which was overall low risk of bias, all 6 included RCTs were high overall risk of bias.
Were the assessments of the included studies reproducible?	Uncertain because the authors do not report any kappa values between the two individuals performing the Cochrane Risk of Bias assessments.
What are the results?	
What are the overall results of the study?	89 citations were reduced to 13 potentially relevant studies and then 7 that ultimately met inclusion criteria, including 4 employing a single femoral nerve block and 3 using a continuous catheter femoral nerve block. The results are synthesized as a narrative.
	Single Femoral Nerve Block Fletcher 2003 – UK study assessing numerical pain scale of 0-3 with femoral nerve block reducing pain on average 0.78 points (95% CI 0.54-1.02) with average reduction in morphine by 0.68 mg/hour (95% CI 0.12-1.23). (p. 247-248) Haddad 1995 – another UK study, this time assessing pain on 0-10 visual analogue scale with significantly lower pain scores after 15-minutes (1.6 points lower, no confidence intervals provided) and after 2-hours (2.2 points), as well as significant decrease in intermuscular opiates. The femoral nerve block group also had significantly fewer post-operative respiratory depression. (p. 248) Henderson 2008 – a 14 patient RCT published in ACEP Research Forum abstract form only in the US with 11-point verbal numeric pain intensity as

	Beaudoin 2013 – a 34 patient RCT from the US using an 11-point numerical rating scale demonstrating significant ($p < 0.001$) reduction in average numeric pain rating at 4-hours as well as significantly greater levels of pain relief via summed pain intensity score. In addition, the median additional morphine required was reduced from 5 mg to 0 mg using femoral nerve block ($p = 0.028$). ($p = 248-249$) This is the highest quality study among the 7 included in this systematic review with overall low risk of bias.
	Catheter-Placed (Continuous) Femoral Nerve Block
	Murgue 2006 – a 16 patient RCT in France assessing 0-10 verbal numeric rating scale for pain with reduction from 6.5 to 2.1 favoring continuous femoral nerve block. (p 250)
	<u>Luger 2013</u> – a 20 patient RCT from Austria using 0-10 visual analog scale with reduction of mean pain score at 1-hour from 4.7 to 0.8 and lower pain scores extending to 12-hours after nerve block initiated. Cardiovascular instability evaluated by troponin levels was also lower in the femoral nerve block group (p < 0.03). (p 250)
	Szucs 2012 – a 24 patient RCT from Ireland evaluating pain intensity using 0-100 visual analog scale every 6 hours for 72 hours while patients were at rest or mobile. At rest, femoral nerve block scores were significantly lower than control groups (9.5 versus 31, $p = 0.031$). While moving around, femoral nerve block exhibited lower pain scores (31 versus 67) at all time points up to 72 hours. Femoral nerve block patients also had lower morphine use over 72 hours and higher patient satisfaction scores ($p = 0.014$). ($p = 250$)
	The results do not provide details about who (EM, Ortho, Trauma-Surgery, or Anesthesiology) placed the femoral nerve block (or catheter), whether point-of-care ultrasound (POCUS) was used, or the experience level of the individual placing the nerve block. The systematic review provides no details about the local analgesic (lidocaine, bupivacaine) used in the individual trials. The authors also do not elaborate on how adverse events were identified or whether downstream outcomes such as post-operative rehabilitation occurred in the nerve block subset.
How precise are the results?	See 95% Confidence Intervals above. Note that some studies did not report estimates of precision.
Were the results similar from study to study?	Yes, every study demonstrated benefit favoring femoral nerve block. The nerve block was also associated with lower adverse event rates.
Will the results help me in caring for my patients?	
How can I best interpret the results to apply them to the care of my patients?	Low quality randomized controlled trial evidence suggests an immediate and sustained decrease in hip fracture pain at rest and with movement without any increase in adverse events such as respiratory depression or cardiac instability. Without understanding whether POCUS was used, the level of expertise of the physician administering the femoral nerve block, or how adverse events were identified – these results should be applied with caution as significant risk of unacknowledged bias may exist that future research could identify.
Were all patient important outcomes considered?	Severity and duration of pain in the hours to days following the fracture are undoubtedly most patient's highest priority. Additional outcomes such as hospital length-of-stay, duration of rehabilitation, functional recovery, and quality of life would also be important to quantify to develop more holistic shared decision making possible.
Are the benefits worth the costs and potential risks?	Based upon this low-quality evidence, the benefits of femoral nerve block in older hip fracture patients in the ED appear to outweigh the risks. Future research (and systematic reviews) will need to more explicitly define "risks" in conjunction with Ortho-Trauma, Geriatric-Trauma, Anesthesiology, and Physical Medicine-Rehabilitation colleagues.

Limitations:

- 1) Incomplete search strategy that would be difficult to replicate without additional details from the authors (who may be difficult to locate in 30-years after they've switched jobs or retired). Also, unclear if/how non-peer reviewed research abstracts (like Henderson 2008) were identified since Medline and EMBASE do not typically include scientific assembly abstracts (but Web of Science or SCOPUS usually do).
- 2) Inadequate details regarding the intervention. Who performed the femoral nerve block (emergency medicine versus orthopedic surgery versus anesthesiology), how experienced were they with this nerve block, was POCUS used, and what local anesthetic was administered (lidocaine versus bupivacaine)?
- 3) No clear statement (or citation) of adherence to PRISMA reporting standards?
 Without transdisciplinary adherence to EQUATOR Network reporting guidelines, research manuscripts can devolve into a Tower of Babel impeding cross-disciplinary analysis of investigators' findings.
- 4) Inconsistent reporting of confidence intervals, so precision impossible to evaluate.
- 5) No reporting of inter-rater reliability of Cochrane Risk of Bias assessments, so unable to evaluate reproducibility of bias assessments.
- 6) Methods to identify adverse effects of femoral nerve block not explicitly described and no long-term problems such as delayed post-op rehabilitation are contemplated.
- 7) No report of effect on incident delirium, nor other patient-centric outcomes such as functional recovery, quality of life, opioid dependence, or cost-benefit.
- 8) Overall, low quality evidence (i.e. high risk of bias) with inability to conduct metaanalysis because of design-related heterogeneity.

Bottom Line:

Seven ED-based RCT's of overall low quality demonstrate immediate and sustained pain relief with either single femoral nerve block or continuous catheter infused femoral nerve block. In addition, less rescue opioid analgesia is required. For now, the benefits appear to outweigh the risks so femoral nerve blocks merit consideration in the setting of older adult hip fractures. Future researchers and systematic review authors should (a) standardize pain assessment measures and intervals; (b) more holistically report patient characteristics including dementia, frailty, co-morbid illness burden, injury severity, and incident delirium; (c) explicitly characterize femoral nerve block operators use of POCUS and level of expertise/training with femoral nerve blocks; and (d) contemplate additional potential patient-centric (beneficial and adverse) outcomes in conjunction with Geriatric Trauma, Ortho-Trauma, Anesthesiology, and Rehabilitation researchers and clinicians.