Critical Review Form
Therapy

Fletcher AK, Rigby AS, Heyes FL. Three-in-one femoral nerve block as analgesia for fractured neck of femur in the emergency department: a randomized, controlled trial. Ann Emerg Med. 2003 Feb;41(2):227-33.

Objective: **"To assess whether 3-in-1 femoral nerve block is effective when taught to and implemented by ED staff." (p 228)**

Methods: **This was a prospective randomized controlled trial in the emergency department (ED) of Rotherham General Hospital in the United Kingdom. Patients were enrolled for six months from February to August. At the time Rotherham received 65,000 annual visits and were staffed by two senior attending physicians (consultants), four earlier career attending physicians (middle-grade physicians), and 7 senior residents (house officers). With the exception of one senior attending physician, all of these physicians were formally trained in 3-in-1 femoral nerve block without the use of ultrasound. The landmark based 3-in-1 femoral nerve block is demonstrated at about the 6-minute mark of https://www.youtube.com/watch?v=8oOFmGXZSUo. The more contemporaneous ultrasound guided technique is demonstrated here https://www.youtube.com/watch?v=_OugsPA4rxY.**

Training included a 30-minute lesson in anatomy, pharmacology, and local anesthetic toxicity, followed by supervised practice on a mannequin. A 3-in-1 nerve block on a patient was subsequently supervised. Competence was achieved when the supervising practitioner concluded that key safety and technical proficiency were achieved with a satisfactory patient nerve block. (p 228-229)

The authors are not explicit about when enrollment occurred or how patients were identified, but "patients with all types of fractured neck of femur" were eligible. Exclusion criteria included patients with confusion (inability to consent), pre-existing bleeding diathesis or warfarin use, local or systemic infection, or previous hypersensitivity to local anesthestics. Patients were randomized to control arm who received 5-10 mg of intravenous morphine "available hourly until analgesia was achieved" until surgery versus 20 mL of 0.5% bupivacaine using the Winnie technique. The Winnie technique used neither ultrasound nor a peripheral nerve stimulator. A (femoral?) intravenous cannula was placed first and patency confirmed. Then "the femoral pulse was palpated, and the nerve block was inserted 1 cm lateral to the pulse once paresthesia (was) elicited to localize the nerve. The local anesthetic was injected in a cranial direction and with pressure distal to the needle during and shortly after injection to encourage the local anesthetic to track cephalid." (p 229)

A numeric rating scale was used to evaluate discomfort with 0 = no pain, 1 = mild pain, 2 = moderate pain, and 3 = severe pain. Pain was assessed with movement on arrival and at 1,

4, 8, 12, 16, and 24 hours after randomization by ward nurses. These nurses were blinded to whether or not patients received the 3-in-1 block or routine care, as were the admitting orthopedic senior house officers. Patients were not blinded to the intervention "because our research ethics committee considered placebo injection unacceptable." (p 230) A blinded observer abstracted all date including the total morphine dose, fracture type, and time to surgery. With a total study size of 50 patients, the study had 80% power to observe a 40% pain reduction with a (one-sided or two-sided) alpha of 0.05.

	PGY: 2	

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Guide	Comments
Are the results valid?	
Did experimental and control groups being the study with a similar prognosis?	
Were patients randomized?	Yes. "The randomization sequence was derived from a random number generator…" (p 229)
Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be "randomized" to a particular group?	Yes. "…allocation concealment was achieved by means of the sealed opaque envelope method." (p 229)
Were patients analyzed in the groups to which they were randomized?	No clear statement of Intention to Treat analysis, but no reported cross-over patients either. The authors do not report whether patients randomized to 3-in-1 block received morphine before or during the nerve block procedure.
Were patients in the treatment and control groups similar with respect to known prognostic factors?	Probably. Table 1 on page 230 demonstrates very similar distributions of age, gender, fracture type, time to surgery, and initial pain scores. No statistical analyses for significance are reported. Additional demographics of interest would include pre-existing dementia and dementia severity (affects ability to report pain), functional independence, and co-morbid disease burden.
Did experimental and control groups retain a similar prognosis after the study started?	
Were patients aware of group allocation?	Yes. "Patients were not blinded to group allocation because our research ethics committee considered placebo injection unacceptable." (p 230)
Were clinicians aware of group allocation?	No. Allocation concealment was maintained in that "…ward nursing staff blinded to the intervention and (pain assessments) formed part of regular nursing observations" and "the admitting orthopedic senior house officer was also unaware of study intervention". (p 230)
Were outcome assessors aware of group allocation?	No. A "blinded observer (AKF) abstracted all data". (p 230)
Was follow-up complete?	No loss to follow-up reported. "Hospital notes were examined again at 6 months when the incidence of post-operative complications, time to discharge, and death rate were recorded." (p 230) The authors do not consider whether patients would have presented to a different hospital and did not attempt to contact patients for additional information.
What are the results?	
How large was the treatment effect?	14 of the 15 ED staff performed 3-in-1 block and no one physician or grade performed more than 5 nerve blocks among the 50 patients enrolled in this study. The mean age patient was 78 years old and 70% were female. About 60% of fractures were intertrochanteric and the mean time to surgery was 29 hours in the intervention arm versus 27 hours in the control group. The mean pain scores on arrival for the intervention and control were 2.8 and 2.7, respectively. Patients receiving the 3-in-1 block attained maximal pain relief almost 3-hours earlier than morphine-only patients (mean difference 2.93 hours with 95% CI -5.48 to -0.38 hours earlier). (Figure 3, p 231) Patients receiving the 3-in-1 block used less morphine per hour (mean difference -0.68 mg/hour with 95% CI -1.23 to -0.12 mg/hour). (Figure 4, p 230) "No clinically important differences between the groups in respect to pulse rate, oxygen saturation, or respiratory rate at any time interval" were observed. At 6-months follow-up, 3 study patients and 3 control patients had died. Additionally, pneumonia occurred in 2 study patients and 4 control patients, as well as a DVT in 1 study patient and 1 control patient. (p 231)

	No adverse anesthetic effects were noted in any of the 24 patients receiving the 3-in-1 nerve block.
How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?)	See 95% CI above.
How can I apply the results to patient care?	
Were the study patients similar to my patient?	Probably. Older adults in ED with hip fracture related pain. Additional demographic details would add value to assessing external validity to urban American hip fracture patients, including ethnicity, cognitive frailty, baseline functional status, age-related vulnerability via ISAR-like instruments and frailty measures, and underlying co-morbid disease burden including osteoporosis.
Were all clinically important outcomes considered?	No. The authors excluded patients who are most likely to benefit from prompt 3-in-1 nerve blocks – those with "confusion". In this setting, "confusion" likely denotes either acute delirium (secondary to pain) or baseline dementia (in which case assessing pain is challenging and requires a unique approach). Effective and expedient pain relief can prevent incident delirium in the ED, but this study excluded those patients and did not assess for prevalent delirium or incident delirium. Ethical approaches to recruit cognitively impaired patients into research has now been developed because excluding these patients is also unethical. Methods to accurately identify dementia and delirium now exist, as well as transdisciplinary approaches to research in undifferentiated cognitive impairment. Another outcome that is neglected is time to rehabilitation hospital and subsequent time until home. In general, geriatric researchers need to measure and report patient-centric outcomes more carefully in the future.
Are the likely treatment benefits worth the potential harm and costs?	Based upon this small single-center RCT, appropriately trained ED physicians can safely administer 0.5% bupivacaine by landmark approach without unacceptably high risk of adverse medication or procedure side effects with the advantage of maximal pain relief 3-hours faster than with morphine alone. More rapid pain relief is undoubtedly of high priority for patients, but whether femoral nerve blocks delay rehabilitation or adversely impact time until home is not addressed by this study.

Limitations:

1) **Standard of care for femoral nerve block in 2019 includes point-of-care ultrasound (POCUS) guidance, so the landmark based 3-in-1 approach is probably outdated. However, acquiring landmark based skills when POCUS is unavailable should still be a priority for EM training programs.**

2) **Excluding patients with dementia or delirium is problematic since these patients may be most likely to benefit from nerve blocks in terms of reducing unrecognized pain (dementia requires different approach to quantify pain) and/or reducing incident delirium occurrence or prevalent delirium duration/severity. Ethical approaches to recruit cognitively impaired patients into research has now been developed because excluding these patients is also unethical. Methods to accurately identify dementia and delirium now exist, as well as transdisciplinary approaches to research in undifferentiated cognitive impairment.**

Bottom Line:

Landmark-based 3-in-1 nerve blocks by trained ED physicians effectively alleviates hip fracture pain in non-cognitively impaired older adults. These results cannot be extrapolated to patients with dementia or delirium, which is unfortunate since cognitively frail individuals are theoretically more likely to benefit from more efficient analgesia in terms of reduced incident delirium and the corresponding morbidity associated with delirium (increased ED length of stay, operative delay, increased hospital length of stay, higher healthcare costs). In addition, this study cannot address whether ED nerve blocks for hip fracture delay rehabilitation. Since this study was published, alternative nerve block approaches such as the fascia iliaca block have also proven effective and feasible so future research could compare the efficacy and physician-level acceptability of different nerve block techniques.

Finally, the July 2019 issue of EM:RAP reviewed concerns about bupivacaine toxicity with the following recommendations. 1) Withdraw to ensure not in vascular structure before injecting and repeat withdraw after every 5-10 mL to ensure you haven't drifted into a vessel; 2) hydrolocate with POCUS before you inject; 3) be aware that the 20-30 mL of 0.25% to 0.5% bupivacaine required for hip fracture nerve blocks can induce cardiotoxicity including hypotension and seizures – since lidocaine does not have this cardiotoxicity or neurotoxicity consider using lidocaine rather than bupivacaine; and 4) don't use bupivacaine without intralipid nearby (in the ED).