Comparative Effectiveness Review
Number 30

Effective Health Care Program

Pain Management Interventions for Hip Fracture

Executive Summary

Introduction

Hip fractures are a source of significant morbidity and mortality. Incidence increases substantially with age, rising for men and women, respectively, from 22.5 and 23.9 per 100,000 populations at age 50, to 630.2 and 1,289.3 per 100,000 populations by age 80. Short-term mortality rates are high and range from 25 percent for women to 37 percent for men in the first year following a hip fracture. Furthermore, a large proportion of those patients who survive never recover to their prefracture level of function, and approximately 25 to 50 percent of elderly patients with hip fractures have not returned home by 1 year postfracture. Up to 25 percent of hip fractures occur in continuing care facilities (i.e., long-term residential care for dependent people).

Pain following hip fracture has been associated with delirium, depression, sleep disturbance, and decreased response to interventions for other disease states. Therefore, it is important to treat and manage complaints of pain adequately during acute treatment for hip fracture. Furthermore, poorly managed postoperative pain is associated with delayed ambulation, pulmonary complications, and delayed transition to lower levels of care. The patient's self-report of pain is the gold standard for evaluating its character and intensity. However, those with dementia or acute

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The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

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delirium may have difficulty reporting pain levels. The potential for underreporting of pain has direct ramifications for the hip fracture population, as many patients are frail older people with postoperative confusion and an impaired ability to communicate.

Key Questions

Key Question (KQ) 1: In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the effectiveness of pharmacologic and/or nonpharmacologic pain management interventions for controlling acute (up to 30 days postfracture) and chronic pain (up to 1 year postfracture) compared with usual care or other interventions in all settings?

KQ 2: In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the effectiveness of pharmacologic and/or nonpharmacologic pain management interventions on other outcomes up to 1 year postfracture compared with usual care or other interventions in all settings? Other outcomes include:

a. Mortality (30-day and up to 1 year postfracture)

b. Functional status

c. Pain medication use; change in type and quantity

d. Mental status

e. Health-related quality of life

f. Quality of sleep in the hospital

g. Ability to participate in rehabilitation

h. Return to prefracture living arrangements

i. Health services utilization

KQ 3: In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the nature and frequency of adverse effects that are directly or indirectly associated with pharmacologic and nonpharmacologic pain management interventions up to 1 year postfracture compared with usual care or other interventions in all settings?

KQ 4: In older adults (≥50 years) admitted to the hospital following acute hip fracture, how do the effectiveness and safety of pharmacologic and nonpharmacologic pain management interventions vary in differing subpopulations following acute hip fracture up to 1 year after fracture compared with usual care or other interventions in all settings?

Methods

Literature Search

The following bibliographic databases were searched systematically for studies published from 1990 to 2010: AMED (Allied and Complementary Medicine); Global Health; International Pharmaceutical Abstracts; BIOSIS Previews; CINAHL (Cumulative Index to Nursing & Allied Health Literature); Academic Search Elite; Health Source: Nursing and Academic Edition; Cochrane Complementary and Alternative Medicine and Pain Database; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; EBM Reviews – Cochrane Central Register of Controlled Trials; Embase; Global Health Library; MEDLINE; Pascal; PeDRO (The Physical Therapy Evidence Database); ProQuest Dissertations and Theses–Full Text; Scopus; Web of Science; and TOXLINE. Hand searches were conducted to identify literature from proceedings from the following scientific meetings: American Geriatric Society, American Physical Therapy Association, American Society of Regional Anesthesia and Pain Medicine, European Society of Regional Anesthesia, European Society of Anesthesiology, and International Anesthesia Research Society. Ongoing studies were identified by searching clinical trials registers in addition to contacting experts in the field. Reference lists of relevant reviews were searched to identify additional studies. No language restrictions were applied.

Study Selection

Two reviewers independently screened titles and abstracts using general inclusion criteria. The full text publication of all articles identified as “include” or “unclear” were retrieved for formal review. Each full-text article was independently assessed by two reviewers using detailed a priori inclusion criteria and a standardized form. Disagreements were resolved by consensus or by third-party adjudication. Randomized controlled trials (RCTs), nonrandomized controlled trials (nRCTs), cohort studies (prospective or retrospective), and case-control studies were included if they were published in 1990 or later, focused on older

adults (≥ 50 years) who were admitted to the hospital with acute hip fracture due to low-energy trauma, and examined any pharmacological or nonpharmacological pain management therapy, regardless of mode of administration or time point during the care pathway.

Quality Assessment and Rating the Body of Evidence

Two reviewers independently assessed the methodological quality of included studies with disagreements resolved through discussion or third-party adjudication, as needed. The Cochrane Collaboration's Risk of Bias tool was used to assess RCTs and nRCTs. Observational analytic studies were assessed using the cohort and case-control Newcastle Ottawa Scales. In addition, the source of funding was recorded for all studies.

The body of evidence was rated by two reviewers using the Agency for Healthcare Research and Quality GRADE approach (Grading of Recommendations, Assessment, Development, and Evaluation). The strength of evidence was assessed for outcomes identified by the clinical investigators to be most clinically important: acute pain (up to 30 days), chronic pain (up to 1 year), mortality (30-day), and the incidence of serious adverse effects (e.g., delirium, myocardial infarction, renal failure, stroke). The following four major domains were assessed: risk of bias (low, medium, high), consistency (no inconsistency, inconsistency present, unknown, or not applicable), directness (direct, indirect), and precision (precise, imprecise).

Data Extraction

Data were independently double-extracted by two reviewers using a standardized form; discrepancies were resolved by consensus or third-party adjudication. Extracted data included study characteristics, inclusion/exclusion criteria, participant characteristics, interventions, and outcomes.

Data Analysis

Evidence tables and qualitative description of results were presented for all included studies. Comparative studies were considered appropriate to combine in a meta-analysis if the study design, study population, interventions being compared, and outcomes were deemed sufficiently similar. Dichotomous outcomes were combined using the DerSimonian and Laird random-effects model, except in instances where the percentage of participants with an event was less than 1 percent, in which case Peto's odds ratio (OR) was calculated using a fixed-effect model. Continuous outcomes were combined using the mean difference (MD), or standardized mean difference (SMD), where appropriate. Statistical heterogeneity was quantified using the I-squared (I^2) statistic.

Results

Description of Included Studies

The search strategy identified 9,357 citations; 83 unique studies met the eligibility criteria and were included in the review. The studies included 64 RCTs, 5 nRCTs, and 14 cohort studies. The number of participants in the studies ranged from 14 to 1,333 (median = 60 [interquartile range (IQR): 40 to 90]). The mean age of study participants ranged from 59.2 to 86.3 years. Based on the interventions reported in each study, the studies were divided into eight groups: systemic analgesia (n = 3), anesthesia (n = 30), complementary and alternative medicine (CAM) (n = 2), multimodal pain management (n = 2), nerve blocks (n = 32), neurostimulation (n = 2), rehabilitation (n = 1), and traction (n = 11).

Methodological Quality of Included Studies

All but two of the RCTs were considered to have a high or unclear risk of bias. The most common sources of potential bias were inadequate description of the randomization procedure, allocation concealment, and external sources of funding. The methodological quality of the cohort studies was moderate, with a median score of 7 stars on a possible score of 9 (IQR: 6 to 8). Common weaknesses in the design of the studies included lack of independent blind outcome assessment and failure to adequately control for potential confounding factors.

Results of Included Studies

The results of the studies are presented by the type of intervention and by the key questions. A table with the summary of findings for outcomes for each intervention is presented at the end of the executive summary.

Systemic Analgesia

Three RCTs (n = 214) evaluated different types of systemic analgesia. The mean age ranged from 77.2 to 78.5 years; most patients were female.

KQ 1: Acute pain management. All three trials reported acute pain. Acute pain was measured using the 10cm Visual Analogue Scale (VAS); the mean baseline measure was 6.5cm. One trial (n = 90) comparing parecoxib intravenous (IV) versus diclofenac intramuscular (IM) ± meperidine IM found a significant difference in favor of parecoxib IV (MD -0.70; 95% confidence interval [CI] -1.04, -0.36; p <0.0001). The second trial (n = 30) comparing intrathecal isotonic clonidine versus intrathecal hypertonic clonidine reported a significant difference in favor of isotonic clonidine (MD -1.69; 95% CI -2.01, -1.37; p <0.00001). The third trial (n = 94) comparing lysine clonixinate versus metamizole found no significant difference (MD -0.43; 95% CI -1.30, 0.44; p = 0.33). The strength of the evidence was rated as insufficient.

KQ 2: Other outcomes. *Additional pain medication use* was reported in one trial comparing lysine clonixinate versus metamizole and reported no significant difference between groups (OR 3.00; 95% CI 0.30, 29.94; p = 0.35). *Delirium* was reported in one trial comparing lysine clonixinate versus metamizole and found no significant difference (OR 0.96; 95% CI 0.06, 15.77; p = 0.98). The strength of the evidence was rated as insufficient.

KQ 3: Adverse effects. One trial comparing lysine clonixinate versus metamizole reported the number of participants with *any adverse event* and found a significant difference in favor of metamizole (OR 3.50; 95% CI 1.04, 11.81; p = 0.04). Similarly, fewer patients in the metamizole group reported any *gastrointestinal disturbance* (OR 11.84; 95% CI 1.45, 96.75; p = 0.02). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Anesthesia

Twenty-one RCTs and one nRCT (n = 1,062) evaluated anesthesia including neuraxial (i.e., continuous vs. single administration) or neuraxial versus general anesthesia, or another form of anesthesia (i.e., spinal or regional); sample sizes ranged from 20 to 90. Additionally, eight cohort studies (n = 3,086) provided additional data. The mean age of participants ranged from 70 to 86 years; most were female. Acute pain was measured using different scales (numeric rating score [1–5] and 10cm VAS). The studies were grouped as follows: spinal versus epidural or general anesthesia (n = 10); neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil (n = 14); neuraxial anesthesia: different doses or modes of administration (continuous vs. single administration) (n = 13).

KQ 1: Acute pain management. The average baseline VAS pain score was 4.7.

Spinal versus general anesthesia. One RCT (n = 30) reported a statistically significant difference of additional pain relief in favor of spinal anesthesia (MD = -0.86; 95% CI -1.30, -0.42; p = 0.0001). The strength of the evidence was rated as insufficient.

Neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil. Three RCTs compared additional fentanyl (n = 40), morphine (n = 40), and sufentanil (n = 50) versus standard spinal anesthesia. In the studies comparing the addition of fentanyl or sufentanil, no patients reported feeling pain following the procedure. In the study comparing the addition of morphine, there was no significant difference between groups (MD = -0.36; 95% CI -1.11, 0.39; p = 0.35). One RCT and one nRCT (n = 80) comparing additional fentanyl reported acute pain on day 1 and found no significant difference between groups (OR 1.24; 95% CI 0.34, 4.48; p = 0.75). The strength of the evidence was rated as insufficient.

KQ 2: Other outcomes. *Spinal versus general anesthesia or spinal versus epidural anesthesia*. Two RCTs reported 30-day mortality (n = 99) and found no statistically significant difference in mortality rates (OR 1.73; 95% CI 0.53, 5.68; p = 0.36). In two cohort studies (n = 650), pooling was not performed due to marked statistical heterogeneity and conflicting results between the studies. The strength of the evidence was rated as insufficient.

In one RCT (n = 30) that reported *delirium* there was no significant difference between groups (OR 0.76; 95% CI 0.18, 3.24; p = 0.71). The strength of the evidence was rated as insufficient.

Length of stay (LOS) for acute hospitalization was reported in two RCTs (n = 99). LOS was significantly less in the general anesthesia group (MD 1.69; 95% CI 0.38, 3.01; p = 0.01).

Neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil. Additional pain medication use was reported in six RCTs. In one RCT (n = 40) comparing the addition of clonidine versus standard spinal anesthesia, all participants required additional pain medication. The pooled estimate from three trials examining the addition of fentanyl (n = 102) showed no significant difference between groups (OR 5.51; 95% CI 0.25, 122.08; p = 0.28). There was no significant difference in additional pain medication use in one RCT (n = 40) that compared the addition of morphine (OR 0.27; 95% CI 0.07, 1.04; p = 0.06). Similarly, three RCTs (n = 132) that compared the addition of sufentanil found no difference between groups (Peto's OR 7.39; 95% CI 0.15, 372.38; p = 0.32).

Delirium was reported in one RCT (n = 40) comparing the addition of morphine and found no significant difference between groups (OR 3.15; 95% CI 0.12, 82.16; p = 0.49). The strength of the evidence was rated as insufficient.

Neuraxial anesthesia: different doses and modes of administration (continuous vs. single administration). Three RCTs (n = 163) reported *30-day mortality*. In two, there were no deaths. In the third, there was no significant difference between groups (OR 0.46; 95% CI 0.07, 3.02; p = 0.42). Additionally, 30-day mortality was reported in one cohort study (n = 291) that found no significant difference between groups (OR 0.96; 95% CI 0.30, 3.00; p = 0.94). The strength of the evidence was rated as low.

Additional pain medication use was reported in two RCTs (n = 134); there were no events in either group. *LOS for acute hospitalization* was reported in two RCTs (n = 89). There was no significant difference between groups (MD = -0.98; 95% CI -2.06, 0.10; p = 0.07). In two RCTs (n = 134) that reported *delirium*, there was no significant difference between groups (OR 1.27; 95% CI 0.32, 4.99; p = 0.73). The strength of the evidence was rated as low.

Spinal anesthesia (different doses). One cohort study (n = 182) reported that there was no significant difference in *30-day mortality* rates between groups (OR 0.49; 95% CI 0.12, 2.02; p = 0.32). The strength of the evidence was rated as insufficient. Another cohort study (n = 60) reported no significant difference in the incidence of delirium (OR 0.46; 95% CI 0.08, 2.75).

In one RCT (n = 60) that reported on *additional pain medication use*, there was no significant difference between groups at different doses (4 vs. 5mg, 4 vs. 6mg, or 5 vs. 6mg).

KQ 3: **Adverse effects**. *Spinal versus general anesthesia or spinal versus epidural anesthesia*. Two RCTs (n = 73) and one cohort study (n = 335) reported adverse effects. Overall, the RCTs reported no significant differences in the occurrence of hypotension, myocardial infarction, or ST segment depression. The cohort study found no difference in the incidence of headaches and hypotension.

Neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil. Eleven RCTs and one nRCT (n = 490) provided data on adverse effects.

a. *Addition of clonidine*. One trial (n = 40) reported no *damage to surrounding structures, headaches, or infections*.

b. *Addition of fentanyl*. There was no significant difference in the number of participants reporting an *allergic reaction* in four RCTs (n = 164). There was no significant difference in the number of participants reporting *bradycardia* in one RCT

(n = 42). Seven trials (n = 284) reported the frequency of *hypotension*. Results were inconsistent across studies and the pooled results are not reported due to high heterogeneity. Five trials (n = 204) reported *nausea or vomiting* and found no significant difference between groups (OR 1.10; 95% CI 0.06, 20.73; p = 0.95). There were no reports of *neurological complications* in one RCT (n = 40); no reports of *respiratory distress* in three RCTs (n = 124); no reports of *gastrointestinal symptoms* in three RCTs (n = 140); and no reports of *headaches* in one trial (n = 40).

c. *Addition of meperidine*. There were no reports of *headaches* in one RCT (n = 34).

d. *Addition of morphine*. One RCT (n = 40) reported no significant difference in the number of participants reporting *allergic reactions, gastrointestinal symptoms*, or *nausea or vomiting*.

e. *Addition of sufentanil*. There was no significant difference in the incidence of *bradycardia* in one trial. Three trials (n = 132) reported a significantly lower incidence of *hypotension* in participants receiving sufentanil (OR = 0.05; 95% CI 0.01, 0.34). In one RCT (n = 42) there were no reports of *allergic reaction, nausea or vomiting*, or *respiratory distress*.

Neuraxial anesthesia: different modes of administration. In one cohort study (n = 291), there were no reports of adverse effects. In one RCT (n = 60) there was no significant difference in the occurrence of *gastrointestinal symptoms*. In two trials (n = 103) that reported on *hypotension* there was a significant difference between groups in favor of continuous spinal anesthesia (OR 0.12; 95% CI 0.03, 0.51; p = 0.004). Similarly, in one cohort study (n = 291) there was a statistically significant difference in favor of continuous spinal anesthesia (OR 0.08; 95% CI 0.04, 0.14; p < 0.00001). There was no significant difference in *myocardial infarction* in one trial (n = 29). There was no significant difference in the occurrence *ST depression* in one trial (n = 29). In one RCT (n = 74) there were no reports of *bradycardia*, *myocardial ischemia*, or *stroke*, and no reports of *headache* in one trial (n = 60) or one cohort study (n = 291).

Neuraxial anesthesia: different doses. In one cohort study (n = 182), there were no reports of adverse effects. In one RCT (n = 60) there was no significant difference in the occurrence of *allergic reaction* for the different doses of bupivacaine. *Bradycardia* was reported in two trials (n = 120); there was no significant difference among the different doses of bupivacaine or levobupivacaine. *Hypotension* was reported in four RCTs (n = 190). There was a significant difference following 4mg versus 6mg of bupivacaine (OR 0.03; 95% CI 0.00, 0.58; p = 0.02), but not 5 versus 6mg of bupivacaine (OR 0.31; 95% CI 0.08, 1.13; p = 0.08). Three cohort studies reported hypotension (n = 267) and found a significant difference following 2.5mg versus 5mg of bupivacaine (OR 0.08; 95% CI 0.03, 0.23; p <0.00001), 4 versus 12mg of bupivacaine (OR 0.03; 95% CI 0.01, 0.15; p <0.00001), and 0.125 versus 0.5 percent of bupivacaine (OR 0.15; 95% CI 0.03, 0.87; p = 0.03). One cohort study reported a significant difference in the incidence of hypotension following 4mg versus 12mg (OR 0.03; 95% CI 0.01, 0.15; p <0.00001), but no difference in the incidence of *delirium*. There were no reports of *nausea or vomiting* in two trials (n = 100); no reports of *residual sensory deficits or motor weakness, respiratory distress, sedation, or urinary retention* in one RCT (n = 60); no reports of *gastrointestinal symptoms* in two trials (n = 100); and no reports of *headache* in one cohort study (n = 182).

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Complementary and Alternative Medicine

Two RCTs (n = 98) evaluated the administration of CAM interventions versus no or sham intervention. The mean age ranged from 76.8 to 86.3 years; most were female. One trial (n = 38) compared acupressure versus sham control delivered preoperatively. Acute pain was measured using the 10cm VAS; the baseline measure was 6.5cm. The second trial (n = 60) compared the Jacobson relaxation technique (a two-step process of contracting and relaxing specific muscles) versus no intervention. Pain was measured using a 10-point verbal scale; the baseline measure was not reported.

KQ 1: Acute pain. Acupressure reduced pain versus a sham intervention (MD -3.01; 95% CI -4.53, -1.49; p <0.0001). Relaxation also showed a reduction in pain versus no relaxation (MD -1.10; 95% CI -1.43, -0.77; p <0.00001). The strength of the evidence was rated as insufficient.

KQ 2: Other outcomes. In the RCT that examined relaxation, fewer patients in the relaxation group required *additional pain medication* (e.g., meperidine or morphine) versus the control group (MD -8.43; 95% CI -15.11, -1.75; p = 0.01).

KQ 3: Adverse effects. No data were reported.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Multimodal Pain Management

Two cohort studies (n = 226) evaluated multimodal pain management versus standard care. These studies described the use of multiple pain management strategies (sequential or in parallel) as part of the clinical pathway for patients with hip fractures. The mean age was not reported; most participants were female. One study compared a formal postoperative protocol of IV and oral tramadol plus acetaminophen versus standard care. The second compared a formal preoperative protocol of skin traction, morphine and acetaminophen versus standard care.

KQ 1: Acute pain. No data were reported.

KQ 2: Other outcomes. *Mortality* was reported in one study (n = 106). There was no significant difference between groups after 30 days (OR 0.54; 95% CI 0.16, 1.77; p = 0.31), or at 1 year (OR 0.60; 95% CI 0.25, 1.47; p = 0.26). Both studies reported *delirium* and found no significant difference between groups. The strength of the evidence for both outcomes was rated as insufficient.

KQ 3: Adverse effects. Data were reported in one study (n = 106). There were no significant differences between groups.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Nerve Blocks

Twenty-nine RCTs (n = 1,757) evaluated nerve blocks, including 3-in-1 (neurostimulation [NS]/ultrasound-guided [US]), combined lumbar/sacral plexus, fascia iliaca compartment, femoral, lumbar plexus plus sciatic nerve, posterior lumbar plexus, psoas compartment, obutarator, and epidural nerve blocks. These were compared with placebo/standard care, or a different method of nerve blocks. Additionally, three cohort studies (n = 696) evaluated 3-in-1, femoral, and lumbar plexus plus sciatic nerve blocks versus analgesia, or comparing different analgesic medications in femoral lumbar plexus plus sciatic blocks. The mean age of participants ranged from 59.2 to 85.9 years; most were female. Acute pain was measured using different scales (i.e., numeric rating scales and 10cm VAS). Eight studies using the VAS reported mean baseline scores from 1.4cm to 7.3cm. The studies were grouped as follows: nerve blocks versus standard care/placebo; nerve blocks versus neuraxial anesthesia; nerve blocks–ropivacaine versus bupivacaine; nerve blocks–addition of clonidine; and nerve blocks–ultrasound versus neurostimulation.

KQ 1: Acute pain management. *Nerve blocks versus no block*. Acute pain was reported in 13 RCTs (n = 942). There was significant heterogeneity between the study results (I2 = 92 percent) and so pooled results are not reported. Even so, subgroup analyses showed significant results in favor of individual nerve blocks, except 3-in-1 block. Also preoperative nerve blocks seemed to be more effective than postoperative administration. One trial (n = 50) reported a significant difference in postoperative pain on day 1 favoring nerve blocks (OR 0.10; 95% CI 0.03, 0.36; p = 0.0005). The strength of the evidence was rated as moderate.

Nerve blocks versus neuraxial anesthesia. Acute pain was reported in three RCTs (n = 109). There was no significant difference between groups (MD -0.35; 95% CI -1.10, 0.39; p = 0.35). The strength of the evidence was rated as low.

KQ 2: Other outcomes. *Nerve blocks versus no block*. Four RCTs (n = 228) evaluated 30-day mortality; there was no significant difference between groups (OR 0.28; 95% CI 0.07, 1.12; p = 0.07). The strength of the evidence was rated as low. There was no significant

difference in 1-year mortality in two RCTs (n = 112) (OR 0.82; 95% CI 0.25, 2.72; p = 0.74), or in one cohort study (n = 535) (OR 0.73; 95% CI 0.48, 1.10; p = 0.14). Seven RCTs (n = 378) evaluated *additional pain medication use* and found a significant difference favoring nerve blocks (OR 0.32; 95% CI 0.14, 0.72; p = 0.006). Similarly, one cohort study (n = 99) reported a significant difference favoring nerve blocks (OR 0.03; 95% CI 0.00, 0.44; p = 0.01). Pooled results for four RCTs (n = 461) and two cohort studies (n = 634) that provided data on *delirium* showed a significant difference favoring nerve blocks (OR 0.33; 95% CI 0.16, 0.66; p = 0.002 [RCTs]; OR 0.24; 95% CI 0.08, 0.72; p = 0.01[cohort studies]). The strength of the evidence was rated as moderate. *LOS for acute hospitalization* (days) was reported in two cohort studies (n = 634), but the pooled results are not reported due to marked heterogeneity between the original study results. *Quality of sleep* was reported in one RCT (n = 77) that found no significant difference (MD 0.30; 95% CI -0.46, 1.06; p = 0.44).

Nerve blocks versus neuraxial anesthesia. Additional pain medication use was reported in one RCT (n=30); there was no significant difference between groups (OR 2.00; 95% CI 0.38, 10.51; p = 0.41). Delirium was reported in one RCT (n = 29); there was no significant difference between groups (OR 1.20; 95% CI 0.27, 5.40; p = 0.81). The strength of the evidence was rated as insufficient.

Ropivacaine versus bupivacaine. *Additional pain medication use* and *delirium* were reported in one cohort study (n=62). There was no significant difference between groups for either outcome (OR 1.25; 95% CI 0.42, 3.76; p=0.69; OR 1.93; 95% CI 0.17, 22.50; p=0.60, respectively). The strength of the evidence for delirium was rated as insufficient.

KQ 3: Adverse effects. *Nerve blocks versus no block. Respiratory infection* was reported in five RCTs (n=268) and found no significant difference (OR 0.43; 95% CI 0.18, 1.04; p=0.06). There were no significant differences between groups for the following adverse effects: *cardiac complications* (2 RCTs, n=128; 1 cohort study, n=99); *damage to surrounding structures* (3 RCTs, n=224); *deep venous thrombosis* (2 RCTs, n=100); *myocardial infarction* (2 RCTs, n=145; 1 cohort study, n=535); *nausea/vomiting* (6 RCTs, n = 421); *pulmonary embolism* (2 RCTs, n = 128); *surgical wound infection* (2 RCTs, n = 110); *urinary retention* (2 RCTs, n = 62; 1 cohort study, n = 535). There were no reports of infection in two RCTs (n = 184). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

Nerve blocks versus neuraxial anesthesia, ropivacaine versus bupivacaine and addition of clonidine. The reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

US versus NS. Two RCTs (n = 100) reported no significant difference in damage to surrounding structures (OR 0.16; 95% CI 0.02, 1.30; p = 0.09). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. One RCT recruited patients with pre-existing heart disease. There was a significant reduction in pain favoring nerve blocks (MD -0.55; -0.81, -0.29; p <0.0001). There was no significant difference in 30-day mortality (OR 0.10; 95% CI 0.01, 1.90; p = 0.12) or adverse effects. One RCT recruited participants that were independent prior to their hip fracture. There was no significant difference between nerve blocks versus standard care for 30-day mortality (OR 1.00; 95% CI 0.06, 16.76; p = 1.00).

Neurostimulation

Two RCTs (n = 123) evaluated transcutaneous electrical neurostimulation (TENS) versus sham control. One trial administered the TENS preoperatively, and the other postoperatively. The mean age of participants ranged from 71.2 to 80.5 years; most were female. Pain was measured using the VAS; the mean baseline measure was 8.4 to 8.8.

KQ 1: Acute pain. Two RCTs (n = 123) found a significant difference in additional pain relief in favor of TENS (MD -2.79; 95% CI -4.95, -0.64; p = 0.01).

Pain on movement was reported in one trial (n = 60) and found a significant difference in favor or TENS (MD -3.90; 95% CI -6.22, -1.58; p = 0.001). The strength of the evidence was rated as insufficient.

KQ 2: Other outcomes. One RCT (n = 60) provided data on *health-related quality of life (HRQOL)* and *quality of sleep*. TENS provided significant improvement in HRQOL (MD -4.30; 95% CI -6.86, -1.74; p = 0.001) and quality of sleep (MD -3.60; 95% CI -575, -1.45; p = 0.001).

KQ 3: Adverse effects. No data were reported.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Rehabilitation

One RCT (n = 37) evaluated physical therapy (stretching and strengthening of spinal and psoas muscles) versus standard care. The mean age was 67.1; all participants were female. Pain was measured using the 10cm VAS; the mean baseline measure was 7.9cm.

KQ 1: Acute pain. There was a significant difference in additional pain relief following physical therapy (MD -1.39; 95% CI -2.27, -0.51; p = 0.002). The strength of the evidence was rated as insufficient.

KQ 2: Other outcomes. No other outcomes were reported.

KQ3: Adverse effects. No data were reported.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. All participants were female.

Traction

Nine RCTs, four nRCTs, and one cohort study evaluated skin or skeletal traction versus no intervention or other interventions. Sample sizes ranged from 60 to 311. The mean age ranged from 74.0 to 81.0; most participants were female.

KQ 1: Acute pain management. Acute pain was measured using the 10cm VAS; the mean baseline measure ranged from 0.3 to 6.9cm. Eight trials compared skin traction (n = 498) versus no traction (n = 594) and found no significant difference between groups. The strength of the evidence was rated as low. One trial (n = 78) compared skin traction versus skeletal traction and found no difference between groups. The strength of the evidence was rated as insufficient.

KQ 2: Other outcomes: *LOS for acute hospitalization* was reported in two trials (n = 326) comparing skin traction versus no traction and no significant difference was found. *Thirty-day mortality* was reported in one RCT (n = 80) that found no difference between skin and skeletal traction versus no traction. *Additional pain medication use* was reported in one RCT and one nRCT (n = 352). There was no significant difference between groups.

KQ 3: Adverse effects. Seven RCTs (n = 1,043) and one cohort study (n = 134) provided data on adverse effects. The reported adverse effects were from one to two studies, and did not demonstrate any significant statistical differences between the pain management interventions.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Rating the Body of Evidence

Most of the evidence for the key outcomes (acute pain, chronic pain, mortality [30-day]), and the incidence of serious adverse effects (i.e., delirium, myocardial infarction, renal failure, stroke) came from single trials and cohort studies precluding any conclusions. The strength of evidence was low to moderate to support the use of some interventions for alleviating acute pain, preventing delirium, and decreasing the 30-day mortality rate (see Table A). The strength of evidence for the remaining outcomes was classified as insufficient due to lack of an adequate number of studies and study power.

Future Research

Multicenter research studies. Adequately powered multicenter research studies are needed to provide a comprehensive assessment of safe, effective, and appropriate pain management following a hip fracture. Studies need to be large enough to allow subgroup

analyses by age, sex, comorbidities, or functional groups (e.g., independent vs. dependent in ambulation). In addition, researchers need to consider inclusion of common subpopulations of hip fracture patients. In particular, those with altered cognition who make up a substantial proportion of the overall hip fracture patient population should be included in future studies of pain management following hip fracture.

Outcomes. Standardization of outcomes and outcome measures will allow easier and meaningful comparisons across different interventions and among studies. The types of outcomes reported do not reflect the multidimensional nature of pain. Relevant outcomes should include validated pain scores, prescription of opiates and other agents, and adverse effects or complications attributable or related to the intervention. Associated outcomes of pain such as function, quality of life, and time to recovery should also be evaluated. The evaluation of pain should include long-term followup of outcomes beyond the acute hospital setting to determine the pattern of pain recovery and whether early effective pain management techniques affect ultimate recovery levels.

Methods. Future research should seek to minimize bias by blinding outcome assessors, use of validated and standardized outcome assessment instruments, adequate allocation concealment (where applicable), and appropriate handling and reporting of missing data.

Conclusions

For the majority of interventions, sparse data are available, which precludes firm conclusions for any single approach or for the optimal overall pain management following nonpathological hip fracture due to low energy trauma. The dearth of evidence related to long-term outcomes and the fact that the majority of the data is derived from studies of low methodological quality or from study designs associated with higher risk of bias (i.e., cohort studies) further weaken any conclusions. Overall, the evidence shows that most interventions result in improvements in short-term pain scores; however, few differences of long-term clinical importance are noticeable when comparisons between interventions are available. The rates of complication were generally low, and the majority of complications were not significantly different among the interventions. Well-designed and -powered, long-term trials are needed in order to determine the relative effectiveness of pain interventions for hip fracture patients. Until then, pain management in this population will rely heavily on availability of the interventions, staff skills, and training and pre-existing patient comorbidities.

Table A. Summary of evidence for key outcomes for pain management following hip fracture

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Systemic analgesia			
Acute pain	Parecoxib IV vs. diclofenac ± meperidine IM (1 RCT)	Insufficient	Significant effect in favor of parecoxib IV (MD = -0.70; 95% CI -1.04, -0.36)
	Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine (1 RCT)		Significant effect in favor of intrathecal isotonic clonidine (MD = -1.69; 95% CI -2.01, -1.37)
	Lysine clonixinate vs. metamizole (1 RCT)		No significant difference
Acute pain at rest	Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal vs. general anesthesia			
Acute pain	Spinal vs. general anesthesia (1 RCT)	Insufficient	Significant effect in favor of spinal anesthesia (MD = -0.86; 95% CI -1.30, -0.42)
Chronic pain	None	Insufficient	No data
30-day mortality	Spinal vs. general anesthesia (2 RCTs, 2 cohort studies)	Low	No significant difference
Delirium	Spinal vs. general anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	Spinal vs. general anesthesia (2 RCT)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal – continuous vs. single administration			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data

Table A. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Anesthesia: spinal – continuous vs. single administration (continued)			
30-day mortality	Continuous vs. single administration (3 RCTs, 1 cohort study)	Low	No significant difference
Delirium	Continuous vs. single administration (2 RCTs)	Low	No significant difference
Myocardial infarction	Continuous vs. single administration (1 RCT)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	Continuous vs. single administration (1 RCT)	Insufficient	No significant difference
Outcome	Comparison (# studies)	Strength of evidence	Summary
Anesthesia: spinal – addition of other medications			
Acute pain	Addition of fentanyl vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
	Addition of morphine vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
	Addition of sufentanil vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Addition of morphine vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal – different doses			
Acute pain	Bupivacaine 2.5mg vs. 5mg (1 cohort study)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Bupivacaine 4mg vs. 12mg (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data

Table A. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Anesthesia: spinal – different doses (continued)			
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Complementary and alternative medicine			
Acute pain	Acupressure vs. standard care (1 RCT)	Insufficient	No significant difference
	Relaxation vs. standard care (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Multimodal pain management			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Delirium	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Nerve blockade			
Acute pain	Nerve block vs. no nerve block (11 RCTs)	Moderate	Significant effect in favor of nerve block in subgroup analyses
Pain on movement	Nerve block vs. no nerve block (4 RCTs)	Low	Significant effect in favor of nerve block in subgroup analyses
Pain at rest	Nerve block vs. no nerve block (3 RCTs)	Low	Data inconsistent for conclusions to be made
Day 1 pain	Nerve block vs. no nerve block (1 RCTs)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data

Table A. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Nerve blockade (continued)			
30-day mortality	Nerve block vs. no nerve block (4 RCTs)	Low	No significant difference
Delirium	Nerve block vs. no nerve block (3 RCTs, 2 cohort studies)	Moderate	Significant effect in favor of nerve block (ORRCT = 0.36; 95% CI 0.17, 0.74) (ORCohort = 0.24; 95% CI 0.08, 0.72)
Myocardial infarction	Nerve block vs. no nerve block (2 RCTs, 1 cohort study)	Insufficient	No significant difference
Stroke	Nerve block vs. no nerve block (1 RCT, 1 cohort study)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Nerve blockade vs. regional anesthesia			
Acute pain	Nerve block vs. regional anesthesia (3 RCTs)	Low	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Nerve block vs. regional anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Nerve Blocks: ropivacaine vs. bupivacaine			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Ropivacaine vs. bupivacaine (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Neurostimulation			
Acute pain	Neurostimulation vs. standard care (2 RCTs)	Insufficient	Significant effect in favor of neurostimulation (MD = -2.79; 95% CI -4.95, -0.64)
Pain on movement	Neurostimulation vs. standard care (1 RCT)	Insufficient	Significant effect in favor of neurostimulation (MD = -3.90; 95% CI -6.22, -1.58)

Table A. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Neurostimulation (continued)			
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No dataSummary of evidence for key outcomes for pain management following hip fracture (continued)
Rehabilitation			
Acute pain	Physical therapy vs. standard care (1 RCT)	Insufficient	Significant effect in favor of physical therapy (MD = -1.39; 95% CI -2.27, -0.51)
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Traction			
Acute pain	Skin traction vs. no traction (7 RCTs)	Low	No significant difference
	Skin traction vs. skeletal traction (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	Skin traction vs. no traction (1 RCT)	Insufficient	No significant difference
	Skeletal traction vs. no traction (1 RCT)	Insufficient	No significant difference
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data

CI = confidence interval; IM = intramuscular; IV = intravenous; MD = mean difference; OR = odds ratio; RCT = randomized controlled trial

Full Report

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