Comparative Effectiveness of Pain Management Interventions for Hip Fracture: A Systematic Review

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Background: Pain management is integral to the management of hip fracture.

Purpose: To review the benefits and harms of pharmacologic and nonpharmacologic interventions for managing pain after hip fracture.

Data Sources: 25 electronic databases (January 1990 to December 2010), gray literature, trial registries, and reference lists, with no language restrictions.

Study Selection: Multiple reviewers independently and in duplicate screened 9357 citations to identify randomized, controlled trials (RCTs); nonrandomized, controlled trials (non-RCTs); and cohort studies of pain management techniques in older adults after acute hip fracture.

Data Extraction: Independent, duplicate data extraction and quality assessment were conducted, with discrepancies resolved by consensus or a third reviewer. Data extracted included study characteristics, inclusion and exclusion criteria, participant characteristics, interventions, and outcomes.

Data Synthesis: 83 unique studies (64 RCTs, 5 non-RCTs, and 14 cohort studies) were included that addressed nerve blockade (n = 32), spinal anesthesia (n = 30), systemic analgesia (n = 3), traction (n = 11), multimodal pain management (n = 2), neurostimulation (n = 2), rehabilitation (n = 1), and complementary and alternative medicine (n = 2). Overall, moderate evidence suggests that nerve blockades are effective for relieving acute pain and reducing delirium. Low-level evidence suggests that preoperative traction does not reduce acute pain. Evidence was insufficient on the benefits and harms of most interventions, including spinal anesthesia, systemic analgesia, multimodal pain management, acupressure, relaxation therapy, transcutaneous electrical neurostimulation, and physical therapy regimens, in managing acute pain.

Limitations: No studies evaluated outcomes of chronic pain or exclusively examined participants from nursing homes or with cognitive impairment. Systemic analgesics (narcotics, nonsteroidal anti-inflammatory drugs) were understudied during the search period.

Conclusion: Nerve blockade seems to be effective in reducing acute pain after hip fracture. Sparse data preclude firm conclusions about the relative benefits or harms of many other pain management interventions for patients with hip fracture.

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Effective pain management is a primary goal in hip fracture. Patients who experience greater pain are at higher risk for delirium, are slower to mobilize, have longer hospital stays and poorer health-related quality of life (1–4), and report persistent pain 3 to 6 months after hip fracture (3, 5). The ramifications of undertreated pain include increased risks for cardiovascular events, delirium, depression, and sleep disturbances and decreased responses to interventions for other disease states (6–8).

Postoperative pain may be undertreated in older adults (9). Opioid analgesics are often prescribed hesitantly in this population because of fear of adverse events, such as delirium (3, 10). Another challenge to managing pain in this patient population is that a substantial proportion has cognitive impairment (for example, dementia, delirium, and acute confusion) (11, 12). Assessing pain intensity is challenging in patients with cognitive impairment because self-report is the gold standard of pain measurement (3, 10).

To our knowledge, no evidence-based guidelines are available for pain management associated with hip fractures. The objective of this comparative effectiveness review was to analyze the best evidence on the effectiveness and safety of pharmacologic and nonpharmacologic techniques for managing pain in older adults after acute hip fracture compared with usual care or other interventions (**Appendix Figure**, available at www.annals.org).

See also:

Print
Editors' Notes 235

Web-Only
Appendix Tables
Appendix Figure
CME quiz
Conversion of graphics into slides

METHODS

We followed a protocol by using methodological approaches outlined in the Agency for Healthcare Research and Quality Methods Guide for Effectiveness and Comparative Effectiveness Reviews. A technical panel of experts from multiple fields (such as anesthesiology, rehabilitation, and surgery) helped formulate the analytic framework and key questions and reviewed the search strategies and review

methods. This review provides a summary of the methods; details are available in the full report (13).

Data Sources and Searches

We searched electronic databases and clinical trial registries, with no language restrictions, from January 1990 to December 2010 and hand-searched scientific meeting proceedings and reference lists (**Appendix Table 1**, available at www.annals.org). Search terms were selected by scanning search strategies of systematic reviews on similar topics and by examining index terms of potentially relevant studies. A combination of subject headings and text words were adapted for each electronic resource. This included terms for hip fracture (fracture* and [hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck"]) and pain (pain* or heal or healing or therap* or recover* or "quality of life" or rehabilitat* or "drug therapy" or pharmacological or acupunct* or acupress* or traction or "electrical stimulation" or "passive motion" or morphine or acetaminophen or paracetamol or tylenol or anesth* or analges*). We excluded research published before 1990 because surgical procedures and medical care for this patient population have changed substantially since then. We examined all pain management interventions used for hip fracture, including (but not limited to) nerve blockade, systemic analgesics (for example, opiates and nonsteroidal anti-inflammatory drugs [NSAIDs]), anesthetics, and traction.

Study Selection

Two reviewers independently screened titles, abstracts, and the full text of identified articles; disagreements were resolved by consensus or third-party adjudication. Randomized, controlled trials (RCTs); nonrandomized, controlled trials (non-RCTs); cohort studies (prospective or retrospective); and case–control studies were included if they were published in 1990 or later; included adults aged 50 years or older who were hospitalized with acute hip fracture because of low-energy trauma; and examined any pain management intervention, regardless of method of administration or time point during the care pathway.

Data Extraction, Quality Assessment, and Rating the Body of Evidence

Two reviewers independently extracted data, assessed methodological quality, and rated the body of evidence; discrepancies were resolved by consensus or third-party adjudication. Extracted data included study characteristics, inclusion and exclusion criteria, participant characteristics, interventions, and outcomes. We used the Cochrane Collaboration's Risk of Bias tool (14) to assess RCTs and non-RCTs (**Appendix Table 2**, available at www.annals.org) and the Newcastle-Ottawa Scale (15) to assess observational studies.

We assessed the strength of evidence (rated by using the GRADE [Grading of Recommendations Assessment, Development and Evaluation] approach) (16) for outcomes that the clinical investigators had identified as the most clinically important: acute pain (≤30 days), chronic pain (≤1 year), 30-day mortality, and incidence of serious adverse events (delirium, myocardial infarction [MI], renal failure, and stroke) (**Table**). We assessed study design (experimental or observational), risk for bias (low, medium, or high), consistency (no inconsistency, inconsistency present, or unknown), directness (direct or indirect), and precision (precise or imprecise).

Context

Multiple pain management strategies are available for patients after hip fracture.

Contribution

This systematic review found moderate-level evidence that nerve blockades reduced acute pain and delirium after hip fracture and low-level evidence that preoperative traction did not affect pain. Benefits and harms of such interventions as spinal anesthesia, systemic analgesia, multimodal pain management, acupressure, relaxation therapy, transcutaneous electrical neurostimulation, and physical therapy were unclear.

Caution

No or few studies evaluated outcomes of chronic pain or systemic analgesics.

Implication

Nerve blockade reduces acute pain after hip fracture, but the comparative effectiveness of multiple alternative pain management strategies is not known.

—The Editors

Data Synthesis and Analysis

We pooled the studies if the study design, interventions being compared, and outcomes were considered to be similar. Odds ratios (ORs) for dichotomous outcomes were combined by using the DerSimonian and Laird random-effects model (17), except for rare events (<1% incidence), in which case the Peto method was used (18). Continuous outcomes were combined by using the mean difference (MD) or standardized mean difference (SMD) when different scales were used across studies (19). The SMD allows data transformation to a uniform scale by dividing the mean by its SD. Statistical heterogeneity was quantified by using the I^2 statistic (20). When heterogeneity was substantial ($I^2 > 75\%$), we investigated sources of heterogeneity by determining the effect of important modifiers: intervention details (type and quantity), study design and risk for bias, and effect of imputed data. A priori subgroup analyses included sex, age, race, body mass index, marital status, comorbid conditions, prefracture functional ability, and family distress. All analyses were performed with Review Manager, version 5.01 (The Cochrane Collaboration, Copenhagen, Denmark).

Table. **Summary of Evidence for Key Outcomes and Serious Adverse Events***

Outcome	Comparison (Reference)	Strength of Evidence	Summary
NB			
Acute pain	No NB (13 RCTs [23–35])	Moderate	Effect in favor of individual NBs in subgroup analyses: epidural analgesia: SMD, –0.83 (95% CI, –1.17 to –0.49); femoral NB: SMD, –1.01 (CI, –1.46 to –0.57); psoas compartment NB: SMD, –1.05 (CI, –1.72 to –0.39); combined NBs: SMD, –2.68 (CI, –3.22 to –2.14)
Acute pain	Regional anesthesia (3 RCTs [38, 39, 48])	Low	No statistically significant difference (MD, –0.35 [CI, –1.10 to 0.39])
Pain on movement	No NB (4 RCTs [25, 28, 35, 40])	Low	Effect in favor of NB in subgroup analyses: 3-in-1 NB: SMD, –1.02 (CI, –1.83 to –0.21); epidural analgesia: SMD, –2.30 (CI, –2.92 to –1.68); femoral NB: SMD, 0.36 (CI, –0.04 to 0.75)
Pain at rest	No NB (3 RCTs [28, 35, 40])	Low	Inconsistent results: 3-in-1 NB: MD, –0.07 (CI, –0.41 to 0.27); epidural analgesia: MD, –0.55 (CI, –0.81 to –0.29); femoral NB: MD 0.18 (CI, 0.03 to 0.33)
Pain on day 1	No NB (1 RCT [42])	Insufficient	Effect in favor of NB (OR, 0.10 [CI, 0.03 to 0.36])
30-d mortality	No NB (4 RCTs [22, 26, 28, 42])	Low	No statistically significant difference (OR, 0.28 [CI, 0.07 to 1.12])
Delirium	No NB (4 RCTs [22, 29, 30, 41]; 2 cohort studies [50, 52])	Moderate	Effect in favor of NB (OR_{RCT}, 0.33 [CI, 0.16 to 0.66]; (OR_{cohort}, 0.24 [CI, 0.08 to 0.72])
Delirium	Regional anesthesia (1 RCT [38])	Insufficient	No statistically significant difference (OR, 1.20 [CI, 0.27 to 5.40])
Delirium	Ropivacaine vs. bupivacaine (1 cohort study [51])	Insufficient	No statistically significant difference (OR, 1.93 [CI, 0.17 to 22.50])
MI	No NB (2 RCTs [28, 32]; 1 cohort study [52])	Insufficient	No statistically significant difference (OR_{RCT}, 1.00 [CI, 0.06 to 16.67]; Peto OR_{cohort}, 0.69 [CI, 0.09 to 5.53])
Stroke	No NB (1 RCT [26]; 1 cohort study [52])	Insufficient	No statistically significant difference (OR_{RCT}, 3.12 [CI, 0.12 to 80.39]; (OR_{cohort}, 0.25 [CI, 0.03 to 1.99])
Spinal anesthesia			
Acute pain	General anesthesia (1 RCT [57])	Insufficient	Effect in favor of spinal anesthesia (MD, –0.86 [CI, –1.30 to –0.42])
30-d mortality	General anesthesia (2 RCTs [53, 61]; 5 cohort studies [76–78, 80, 81])	Low	No significant difference (OR_{RCT}, 1.73 [CI, 0.53 to 5.68]; OR_{cohort}, 0.87 [CI, 0.45 to 1.67])
Delirium	General anesthesia (1 RCT [57]; 2 cohort studies [78, 80])	Insufficient	No statistically significant difference (OR_{RCT}, 0.76 [CI, 0.18 to 3.24]; OR_{cohort}, NR)
MI	General anesthesia (1 RCT [61]; 1 cohort study [78])	Insufficient	No statistically significant difference (OR_{RCT}, 1.55 [CI, 0.06 to 42.91]; OR_{cohort}, 0.21 [CI, 0.03 to 1.78])
Renal failure	General anesthesia (1 cohort study [80])	Insufficient	No statistically significant difference (OR, 0.49 [CI, 0.04 to 5.50])
Stroke	General anesthesia (2 cohort studies [78, 80])	Insufficient	No statistically significant difference (OR, 0.98 [CI, 0.23 to 4.14])
Spinal anesthesia: continuous administration			
30-d mortality	Single administration (3 RCTs [59, 61, 68]; 1 cohort study [77])	Low	No statistically significant difference (OR_{RCT}, 0.46 [CI, 0.07 to 3.02]; OR_{cohort}, 0.96 [CI, 0.30 to 3.00])
Delirium	Single administration (2 RCTs [59, 68])	Low	No significant difference (OR, 1.27 [CI, 0.32 to 4.99])
MI	Single administration (1 RCT [61])	Insufficient	No statistically significant difference (OR, 0.33 [CI, 0.01 to 8.88])
Stroke	Single administration (1 RCT [68])	Insufficient	No statistically significant difference: no strokes reported for either group (not estimable)
Spinal anesthesia: addition of other medications			
Acute pain	Addition of fentanyl vs. standard spinal anesthesia (1 RCT [66])	Insufficient	No reported significant difference: no reported pain in 1 group (not estimable)
Acute pain	Addition of morphine vs. standard spinal anesthesia (1 RCT [63])	Insufficient	No statistically significant difference (MD, –0.36 [CI, –1.11 to 0.39])
Acute pain	Addition of sufentanil vs. standard spinal anesthesia (1 RCT [70])	Insufficient	No statistically significant difference: no reported pain in 1 group (not estimable)
Pain on day 1	Addition of fentanyl vs. standard spinal anesthesia (2 RCTs [66, 82])	Insufficient	No statistically significant difference (OR, 1.24 [CI, 0.34 to 4.48])
Delirium	Addition of morphine vs. standard spinal anesthesia (1 RCT [63])	Insufficient	No statistically significant difference (OR, 3.15 [CI, 0.12 to 82.16])

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Table —Continued

Outcome	Comparison (Reference)	Strength of Evidence	Summary
Spinal anesthesia: dose			
30-d mortality	Bupivacaine, 2.5 mg vs. 5 mg (1 cohort study [77])	Insufficient	No statistically significant difference (OR, 0.49 [CI, 0.12 to 2.02])
Delirium	Bupivacaine, 4 mg vs. 12 mg (1 cohort study [75])	Insufficient	No statistically significant difference (OR, 0.46 [CI, 0.08 to 2.75])
Systemic analgesia			
Acute pain	IV parecoxib vs. diclofenac ± IM meperidine (1 RCT [83])	Insufficient	Effect in favor of IV parecoxib (MD, –0.70 [CI, –1.04 to –0.36])
Acute pain	Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine (1 RCT [84])	Insufficient	Effect in favor of intrathecal isotonic clonidine (MD, –1.69 [CI, –2.01 to –1.37])
Acute pain	Lysine clonixinate vs. metamizole (1 RCT [85])	Insufficient	No statistically significant difference (MD, –0.43 [CI, –1.30 to 0.44])
Acute pain at rest	Lysine clonixinate vs. metamizole (1 RCT [85])	Insufficient	No statistically significant difference (MD, –0.43 [CI, –1.30 to 0.44])
Delirium	Lysine clonixinate vs. metamizole (1 RCT [85])	Insufficient	No statistically significant difference (OR, 0.96 [CI, 0.06 to 15.77])
Multimodal pain management			
30-d mortality	Standard care (1 cohort study [87])	Insufficient	No statistically significant difference (OR, 0.54 [CI, 0.16 to 1.77])
Delirium	Standard care (2 cohort studies [86, 87])	Insufficient	No statistically significant difference (protocol 1: OR, 0.82 [CI, 0.34 to 1.96]; protocol 2: OR, 0.45 [CI, 0.04 to 5.16])
MI	Standard care (1 cohort study [87])	Insufficient	No statistically significant difference (OR, 0.45 [CI, 0.04 to 5.16])
Stroke	Standard care (1 cohort study [87])	Insufficient	No statistically significant difference (Peto OR, 0.13 [CI, 0.00 to 6.32])
Traction			
Acute pain	Skin vs. no traction (8 RCTs [88, 90–92, 94, 95, 97, 98])	Low	No statistically significant difference (MD, 0.20 [CI, –0.24 to 0.65])
Acute pain	Skin vs. skeletal traction (1 RCT [93])	Insufficient	No statistically significant difference (MD, 0.10 [CI, –0.60 to 0.80])
30-d mortality	Skin vs. no traction (1 RCT [89])	Insufficient	No statistically significant difference (OR, 0.16 [CI, 0.01 to 4.14])
30-d mortality	Skeletal vs. no traction (1 RCT [89])	Insufficient	No statistically significant difference (OR, 0.13 [CI, 0.00 to 3.43])
TENS			
Acute pain	Standard care (2 RCTs [99, 100])	Insufficient	Effect in favor of neurostimulation (MD, –2.79 [CI, –4.95 to –0.64])
Pain on movement	Standard care (1 RCT [99])	Insufficient	Effect in favor of neurostimulation (MD, –3.90 [CI, –6.22 to –1.58])
Rehabilitation			
Acute pain	Stretching and strengthening vs. standard care (1 RCT [101])	Insufficient	Effect in favor of stretching and strengthening program (MD, –1.39 [CI, –2.27 to –0.51])
CAM			
Acute pain	Acupressure vs. standard care (1 RCT [102])	Insufficient	Effect in favor of acupressure (MD, –3.01 [CI, –4.53 to –1.49])
Acute pain	Relaxation vs. standard care (1 RCT [103])	Insufficient	Effect in favor of relaxation (MD, –1.10 [CI, –1.43 to –0.77])

CAM = complementary and alternative medicine; IM = intramuscular; IV = intravenous; MD = mean difference; NB = nerve blockade; NR = not reported (owing to high heterogeneity among included studies); OR = odds ratio; RCT = randomized, controlled trial; SMD = standardized mean difference; TENS = transcutaneous electrical nerve stimulation.

* Key outcomes that are not presented did not have any data, and the strength of evidence was rated as insufficient.

Role of the Funding Source

The Agency for Healthcare Research and Quality suggested the initial questions and approved copyright assertion for the manuscript but did not participate in the literature search, data analysis, or interpretation of the results.

RESULTS

We identified 9357 citations and included 83 unique studies (64 RCTs, 5 non-RCTs, and 14 cohort studies) with 14 to 1333 participants (median, 60 participants; interquartile range, 40 to 90 participants]) (**Figure 1**). The full report (13) includes the search strategies and details of the included and excluded studies.

Studies were published between 1990 and 2010 (median year, 2003; interquartile range of years, 1998 to 2007), and nearly all were published in peer-reviewed journals. Most were RCTs performed in single-university settings in Europe, which investigated pre- or intraoperative

pain management interventions in the acute care setting, and none was from institutional settings (such as nursing homes). Five of the 83 studies were from North America, and 55 were from Europe.

The mean age of study participants ranged from 59 to 86 years. Most participants were female (74%). Almost one half of the studies ($n = 31$) excluded participants with cognitive impairment or delirium. Pain, the primary outcome, was measured with an array of validated visual and numerical pain scales (for example, visual analogue scale).

Of the RCTs, only 2 (21, 22) were considered to be at low risk for bias (**Appendix Table 3**, available at www.annals.org). The methodological quality of the cohort studies was moderate (median, 7; interquartile range, 6 to 8). Interventions were divided into 8 groups (**Table** and **Appendix Table 4**, available at www.annals.org): nerve blockade ($n = 32$) (21–52), anesthesia ($n = 30$) (53–82), systemic analgesia ($n = 3$) (83–85), multimodal pain management ($n = 2$) (86, 87), traction ($n = 11$) (88–98), neurostimulation ($n = 2$) (99, 100), physical therapy regimens ($n = 1$) (101), and complementary and alternative medicine ($n = 2$) (102, 103).

Most of the evidence for key outcomes and serious adverse events came from single trials and cohort studies. The strength of evidence was low to moderate for some interventions in alleviating acute pain, preventing delirium, and decreasing the 30-day mortality rate (**Table**). The strength of evidence for the remaining outcomes was insufficient because of inadequate numbers of studies and study power.

Nerve Blockade

Twenty-nine RCTs (21–49) evaluated nerve blockades, including 3-in-1, combined lumbosacral plexus, fascia iliaca compartment, femoral nerve, lumbar plexus plus sciatic nerve, posterior lumbar plexus, psoas compartment, obturator nerve, epidural, and combined blockades. These blockades were compared with placebo, standard care, or another method of nerve blockade. Three cohort studies (50–52) evaluated 3-in-1, femoral nerve, and lumbar plexus plus sciatic nerve blockades versus systemic analgesia or compared analgesic medications in femoral lumbar plexus plus sciatic blockade.

Acute pain was reported in studies comparing various nerve blockades with no blockade (**Figure 2**), but pooled results were not reported because of significant heterogeneity ($I^2 = 92\%$). Sensitivity analyses showed statistically significant results in favor of each type of blockade except 3-in-1 and fascia iliaca blockades (**Table**). When blockades were used, pain on movement and at rest were inconsistent and dependent on the type of blockade (**Table**), but less use of

Figure 1. **Summary of evidence search and selection.**

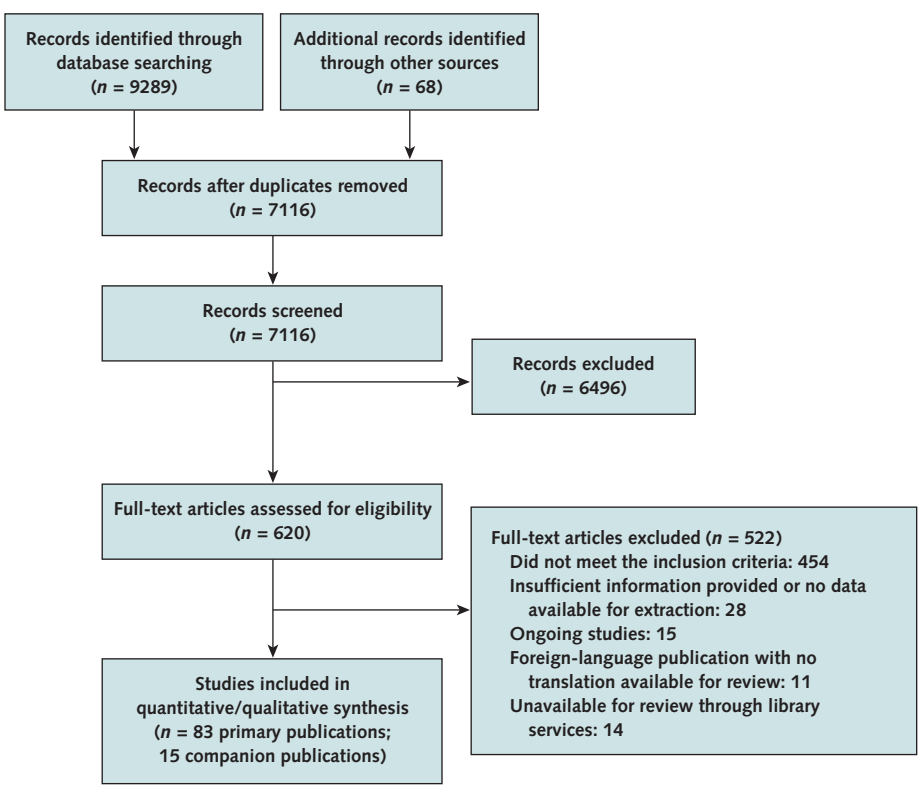
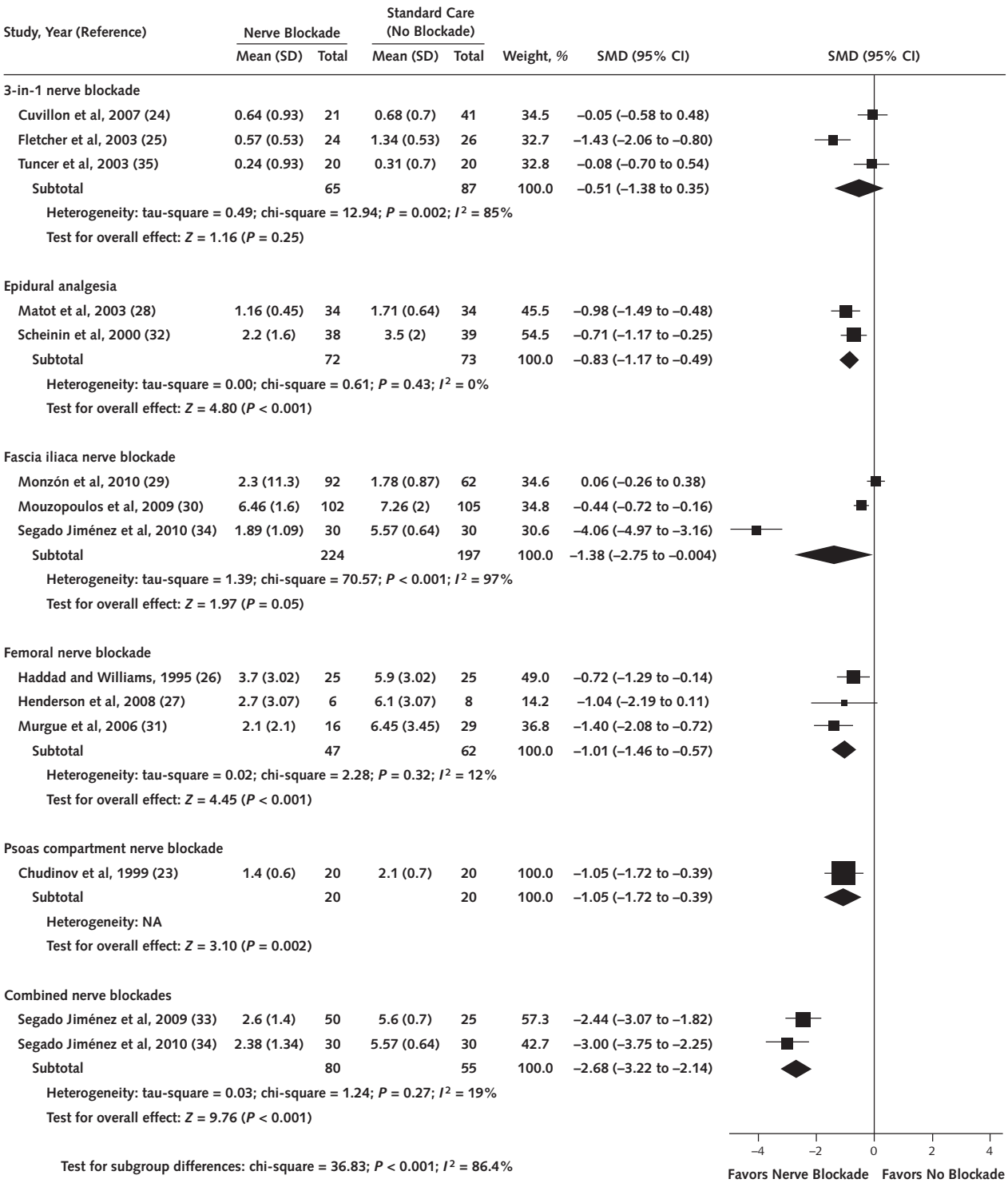


Figure 2. **Nerve blockade versus no blockade: acute pain (posttreatment).**



NA = not applicable; SMD = standardized mean difference.

supplemental pain medication was reported in 7 RCTs (OR, 0.32 [95% CI, 0.14 to 0.72]) (21, 23, 25, 35, 37, 40, 42) and 1 cohort study (OR, 0.03 [CI, 0.00 to 0.44]) (50).

The incidence of delirium, a common complication of hip fracture, was statistically significantly decreased with nerve blockades compared with no blockade. Other than

reducing the incidence of delirium, nerve blockades offered no advantage in preventing cardiac complications (22, 28, 50), deep venous thrombosis (25, 26), MI (**Table**), nausea or vomiting (21, 24, 29, 35, 40, 47), pulmonary embolism (22, 28), respiratory infection (22, 25, 26, 28, 49), stroke (**Table**), surgical-wound infection (22, 26), urine retention (24, 47, 52), or urinary tract infection (26, 52). Nerve blockade reduced the length of acute hospitalization (50, 52); however, pooled results were not reported because of marked heterogeneity (I^2 = 93%). Mortality rates were unchanged at 30 days or 1 year (24, 25, 52) (**Table**) with the use of nerve blockades. Similar mortality results were found in participants with preexisting heart disease (OR, 0.10 [CI, 0.01 to 1.90]) or who were living independently before hip fracture (OR, 1.00 [CI, 0.06 to 16.76]).

Nerve blockade and neuraxial anesthesia had similar results in terms of acute pain, use of additional pain medications (48), and delirium (**Table**). No outcome differences were attributable to any nerve blockade in trials that assessed the use of bupivacaine versus ropivacaine (46) or the addition of clonidine to the injectate (43).

Anesthesia

Anesthesia techniques for hip fracture surgery were evaluated in 21 RCTs (53–73), 1 non-RCT (82), and 8 cohort studies (74–81). One RCT (57) reported that spinal anesthesia provided a small benefit for pain relief relative to general anesthesia; however, 30-day or 1-year mortality rates did not statistically significantly differ (53, 61, 76–78, 80, 81) (**Table**). Furthermore, 1 cohort study (77) reported a higher incidence of hypotension in patients receiving general anesthesia compared with single-shot spinal anesthesia (OR, 0.04 [CI, 0.01 to 0.13]) but not incremental spinal anesthesia. No statistically significant differences in hypotension, hypothermia, MI, or ST-segment depression were reported in RCTs comparing spinal with general anesthesia (56, 57, 61). Cohort studies (77, 78, 80, 81) found no difference in the incidence of angina, congestive heart failure, exacerbations of chronic obstructive pulmonary disease, gastrointestinal bleeding, headache, MI, pleural effusion, pneumonia, pulmonary embolism, respiratory distress, renal failure, stroke, or thrombophlebitis. Patients who received general anesthesia had significantly shorter lengths of stay for acute hospitalization than did those who received spinal anesthesia (MD, 1.69 days [CI, 0.38 to 3.01 days]) (reported in 2 RCTs [53, 61]).

Several studies explored the effect of different doses (58, 60, 69, 71, 72, 74, 75, 77) and methods of administration (single shot vs. continuous) (59, 61, 62, 68, 77, 79) of neuraxial anesthetic agents. No statistically significant differences in acute pain, the need for additional postoperative pain medication, mortality rates, adverse events (including delirium), or length of stay were observed (**Table**).

The addition of clonidine, fentanyl, meperidine, morphine, or sufentanil (54, 55, 62–67, 70, 73, 82) to standard spinal local anesthesia did not statistically significantly improve postoperative pain relief (**Table**). The addition of fentanyl also did not statistically significantly increase the incidence of allergic reaction (64–66, 82), bradycardia (64), neurologic complications (82), respiratory distress (64, 65, 82), gastrointestinal symptoms (55, 64–66, 71, 82), or headache (82). Seven trials (54, 55, 64–66, 73, 82) reported the frequency of hypotension after the addition of fentanyl, but the results were inconsistent across studies and pooled results were not reported. Supplementation of spinal local anesthetic agents with morphine did not statistically significantly increase the incidence of delirium, allergic reactions, nausea or vomiting, or other gastrointestinal symptoms in 1 RCT (63).

When spinal anesthetic agents were supplemented with sufentanil, 3 trials (64, 70, 73) reported a significantly lower incidence of hypotension in patients receiving sufentanil (OR, 0.05 [CI, 0.01 to 0.34]); 1 study reported no increase in the incidence of allergic reaction, bradycardia, nausea or vomiting, or respiratory distress (64).

Compared with single-shot techniques, continuous spinal anesthesia resulted in less hypotension in 2 RCTs (61, 68) (OR, 0.12 [CI, 0.03 to 0.51]) and 1 cohort study (77) (OR, 0.08 [CI, 0.04 to 0.14]). No differences in the occurrence of gastrointestinal symptoms (59), ST-segment depression (61), MI (61), bradycardia (68), myocardial ischemia (68), stroke (68), and headache (59, 77) were reported.

The incidence of hypotension was the only consistent difference observed with increasing the dose of local spinal anesthetic. One RCT (60) found a significant difference after 4 mg versus 6 mg of bupivacaine (OR, 0.03 [CI, 0.00 to 0.58]). Cohort studies (74, 75, 77) found a significant difference after 2.5 mg versus 5 mg of bupivacaine (OR, 0.08 [CI, 0.03 to 0.23]), 4 mg versus 12 mg of bupivacaine (OR, 0.03 [CI, 0.01 to 0.15]), and 0.125% versus 0.5% bupivacaine (OR, 0.15 [CI, 0.03 to 0.87]). The incidence of bradycardia (58, 60) or delirium (75) did not significantly differ among the doses of bupivacaine or levobupivacaine. No cases of nausea or vomiting (60, 71); residual sensory deficits or motor weakness, respiratory distress, sedation, or urine retention (58, 60); or headache (77) were reported with differing anesthesia doses.

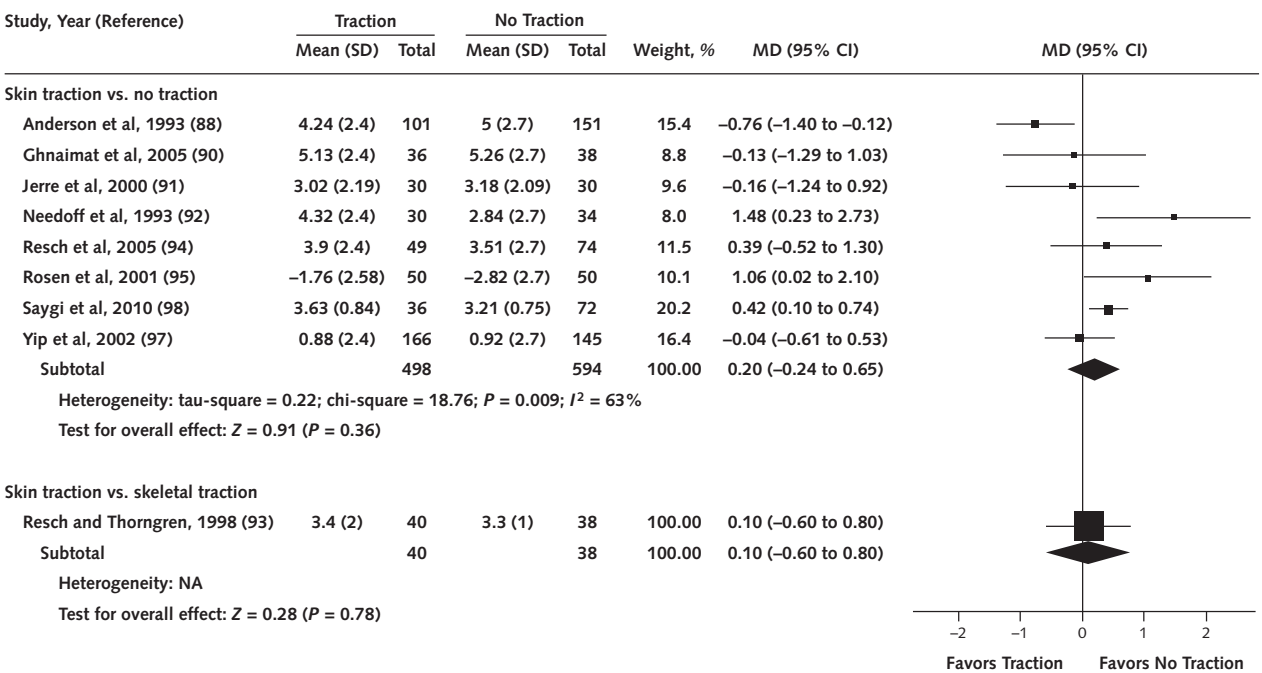
Systemic Analgesia

Of 3 RCTs comparing systematic analgesics (**Table**), 1 (83) reported that intravenous parecoxib is more effective than the combination of intramuscular diclofenac and meperidine. A second RCT (84) reported that intrathecal isotonic clonidine was more effective than hypertonic clonidine.

Multimodal Pain Management

Two cohort studies described the use of multiple pain management strategies (sequential or in parallel) as part of a clinical pathway. One study (86) compared a postoperative protocol of tramadol plus acetaminophen compared with standard care. The other study (87) compared a preoperative protocol of skin traction, morphine, and acetaminophen with standard care and reported no difference

Figure 3. **Traction versus no traction: acute pain (posttreatment).**



MD = mean difference; NA = not applicable.

between groups for 30-day or 1-year mortality or for adverse events. Both studies reported no difference in the incidence of delirium (**Table**).

Physical Modalities and Physical Therapy Regimens

Yielded acute pain, length of acute hospitalization (88, 90), or use of additional analgesic medication (88, 95) did not statistically significantly differ between preoperative skin traction and no traction (**Table** and **Figure 3**). Thirty-day mortality did not statistically significantly differ between skin and skeletal traction (**Table**).

Transcutaneous electrical nerve stimulation (TENS) was compared with a sham control in 2 studies, 1 before (100) and 1 after (99) surgery. Both studies reported pain relief with TENS (**Table**). When TENS was applied after surgery, pain on movement was reduced (**Table**) and health-related quality of life (MD, −4.30 [CI, −6.86 to −1.74]) and quality of sleep (MD, −3.60 [CI, −575 to −1.45]) improved. One RCT (101) demonstrated that stretching and strengthening of spinal and psoas muscles provided more pain relief than standard care (**Table**).

Complementary and Alternative Medicine

Acupressure provided short-term pain relief compared with a sham intervention (**Table**). The Jacobson relaxation technique (a 2-step process of contracting and relaxing specific muscles) also provided short-term pain relief (**Table**) and reduced the need for additional pain medication (MD, −8.43 [CI, −15.11 to −1.75]).

DISCUSSION

Hip fracture is associated with substantial pain, but the evidence on pain management after hip fracture was surprisingly sparse. We identified only 83 studies that met the inclusion criteria, precluding firm conclusions for any single approach or for optimal overall pain management. Most studies were RCTs conducted in single-university settings in Europe, with few studies from North America. Studies primarily evaluated pharmacologic management of postoperative pain in the acute care setting, including documentation of adverse events and short-term mortality. Most studies focused on a single discipline (for example, anesthesiology or rehabilitation), despite supporting evidence that optimal pain management is multidisciplinary (104, 105). No included study examined pain beyond 30 days. More often than not, functional recovery, health-related quality of life, and health services utilization were underreported. Despite these limitations, at least 5 general conclusions can be made.

First, nerve blockade seems to be more effective than standard care. It reduced the need for supplemental systemic analgesia and lowered the risk for delirium, although most studies did not report on how nerve blockades may affect ambulation or rehabilitation. Several technically different blockade approaches have been studied in this context, and most were found to be beneficial. The evidence does not support a preference for more complex techniques (for example, catheter-based, continuous epidural infusions) over simpler, safer approaches (for example, single-

shot femoral blockade). Nerve blockade is within the repertoire of most practicing anesthesiologists, but many clinicians do not perform it routinely because they believe the additional time, effort, and supervision required may outweigh the benefits (106). On the contrary, the evidence would suggest that blockade may be beneficial.

Second, spinal anesthesia, although effective and safe, does not demonstrably differ from general anesthesia in rates of mortality, delirium, or other medical complications. This is in contrast to other recent reviews (107, 108), which show a greater benefit for regional anesthesia than general anesthesia. The discrepancy may reflect improvements in the safety and adverse-effect profile of general anesthesia or in the medical care of older participants in the past 2 decades (because the aforementioned reviews included studies dating back to 1977).

Adding other agents to plain local anesthesia for spinal anesthesia does not seem to affect outcomes outside the operating room. Furthermore, larger doses of a spinal anesthetic may cause more hypotension without improving pain control or other outcomes (109). Evidence was insufficient to show that multimodal analgesia yields improvements over single modalities.

Third, surprisingly few studies focused on systemic analgesics, opiates, or traditional NSAIDs. Because most NSAID trials are for short-term treatment of chronic pain and given the risks associated with NSAIDs (for example, gastrointestinal damage, bleeding, and drug interactions), NSAID use in this population has not been aggressively pursued. However, it is surprising that given the regular daily use of NSAIDs for acute, surgical, and arthritis pain, we identified only 3 trials of systemic analgesia in hip fracture published since 1990. Of these, 1 small trial of intravenous parecoxib (an agent not available in North America) compared with diclofenac and meperidine reported a significant finding. Because meperidine use is discouraged among older populations owing to its association with delirium (110), this study may have even further limited clinical utility.

Fourth, preoperative traction does not reduce pain or complications compared with no traction. These results are consistent with those of a Cochrane review (111).

Finally, only 4 nonpharmacologic interventions were identified: acupressure, relaxation therapy, TENS, and physical therapy. Although these interventions were based on limited evidence, they seem to be safe and may result in clinically meaningful reductions in pain. A consideration of nonpharmacologic interventions is that, similar to nerve blockade, proper application and instruction may require additional time and training of allied health professionals.

A strength of this review is the comprehensiveness of the search, which included 25 electronic databases, conference proceedings, and forward-searching of included studies. Language was not an exclusion criterion, and we included studies published in 8 languages. The main limitations relate to the quantity, quality, and external validity of the available evidence. First, important subgroups of patients with hip fracture were frequently excluded. Almost one half of the studies ($n = 31$) excluded patients with cognitive impairment or who could not cooperate. With approximately 30% to 60% (11, 12) of the elderly population with hip fracture having some degree of cognitive impairment, this represents a significant selection bias. Furthermore, approximately 25% of patients with hip fracture are from nursing homes (112, 113), and none of the included studies examined this population exclusively.

Second, because our literature search included studies only from 1990 onward, we may not have identified older studies of systemic analgesics and anesthetics. Even so, with the changes in hip fracture care over the past 20 years, evidence found before 1990 may not apply to current care standards that focus on early patient mobility.

Third, the lack of standardized outcomes limits the interpretation and applicability of the results. Although pain and function are correlated (3), most studies focused on pain relief and did not evaluate an intervention's effects on the patient's ability to mobilize after surgery, a factor linked to recovery levels after hip fracture (114).

Fourth, we found minimal evidence about managing pain after hospital discharge or assessment of the long-term effects of early postoperative pain management on subsequent recovery. Finally, because of the low incidence of postoperative complications, no individual study had adequate power to detect adverse events.

For future studies, we suggest a conditional set of minimal scientific criteria to guide the next generation of trials on pain management of hip fracture to provide more valid and clinically useful information. Adequately powered, multicenter studies that assess safety, effectiveness, and appropriateness of pain management after hip fracture should include, at the least, subgroup analyses comparing patients with and without cognitive impairment and community-dwelling versus nursing home residents. Study follow-up should extend beyond the acute care setting and should evaluate patients at least 6 months after fracture (3). Standardized and validated outcome measures should be selected to allow meaningful comparisons across interventions and studies. Relevant outcomes include validated pain scores, prescription of analgesics, and adverse events. Given how common impaired cognition occurs in this patient population, nonverbal pain assessment scales are recommended (107, 115, 116). Outcome measures should also include functional status, health-related quality of life, and health service utilization.

In summary, the evidence showed that most pain management interventions improved short-term pain, but few studies of long-term clinical importance were available. Until more rigorous evidence is generated, the review summarizes what should be considered the current state of the evidence for managing hip fracture pain.

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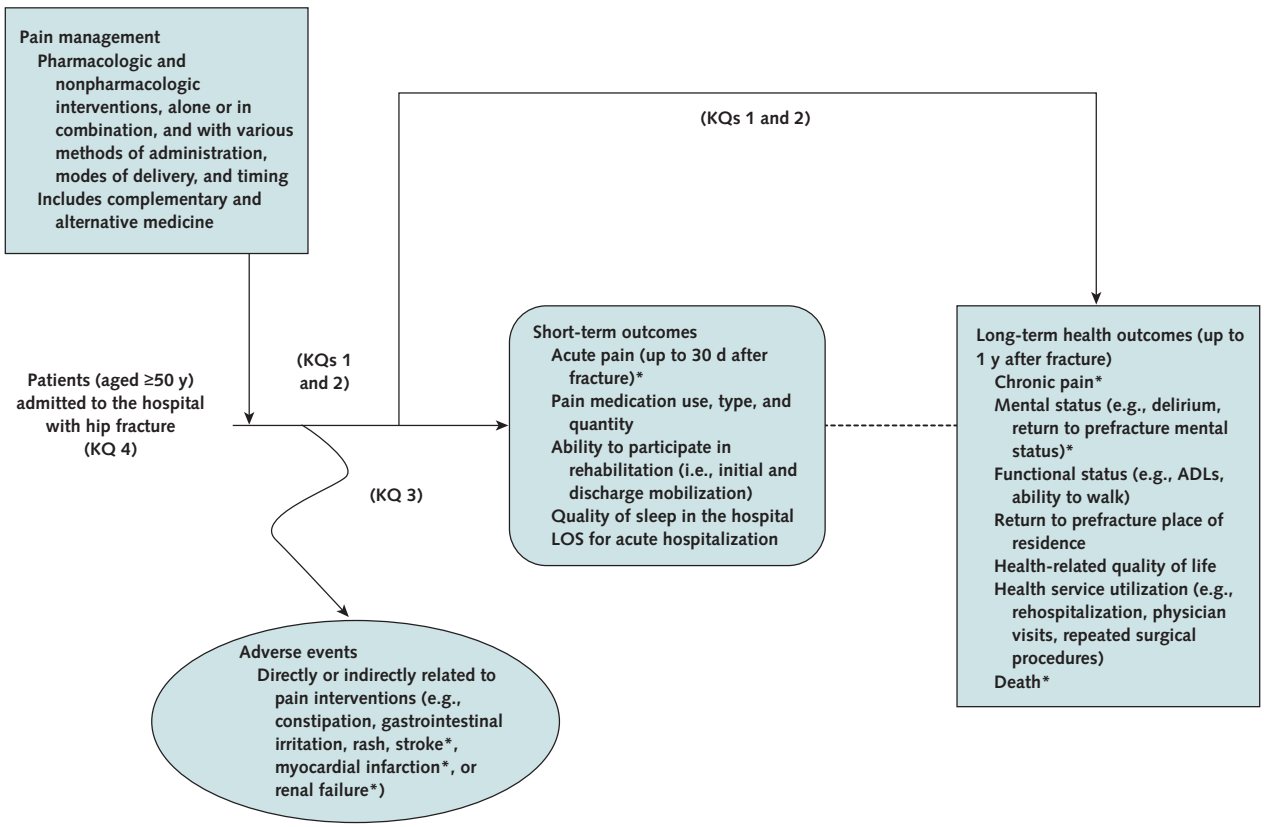
Appendix Figure. **Analytic framework for pain management interventions for hip fracture.**



ADL = activity of daily living; KQ = key question; LOS = length of stay.
* Body of evidence rated by using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach.

Appendix Table 1. Literature Search

Bibliographic databases

AMED (Allied and Complementary Medicine), Global Health, and International Pharmaceutical Abstracts—Ovid version
BIOSIS Previews, Institute for Scientific Information, Thomson Reuters
CINAHL, Academic Search Elite, and Health Source: Nursing and Academic Edition—Ebsco version
Cochrane Complementary Medicine Trials Register and Complementary and Alternative Medicine and Pain Database (grant R24-AT001293 from the National Center for Complementary and Alternative Medicine)
Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects—Wiley version
EBM Reviews, Cochrane Central Register of Controlled Trials—Ovid version
EMBASE—Ovid version
Global Health Library, World Health Organization
MEDLINE—Ovid version
PASCAL—Ovid version
PEDro (Physiotherapy Evidence Database)
ProQuest Dissertations and Theses—full text
Scopus, Elsevier
TOXLINE, ProQuest
Web of Science, Institute for Scientific Information, Thomson Reuters

Conference proceedings

Conference Papers Index, ProQuest
OCLC PapersFirst, OCLC FirstSearch
ScienceDirect tables of contents

Trial registries

ClinicalStudyResults.org
ClinicalTrials.gov, National Institutes of Health
Current Controlled Trials, BioMed Central
ICTRP Search Portal, World Health Organization
IFPMA Clinical Trials Portal
UMIN-CTR

Conference proceedings (hand-search)

American Geriatrics Society
American Physical Therapy Association
American Society of Regional Anesthesia and Pain Medicine
European Society of Regional Anesthesia
European Society of Anaesthesiology
International Anesthesia Research Society

ICTRP = International Clinical Trials Registry Platform; IFPMA = International Federation of Pharmaceutical Manufacturers & Associations; UMIN-CTR = University Hospital Medical Information Network Clinical Trials Registry.

Appendix Table 2. Risk for Bias Assessment for Randomized and Nonrandomized, Controlled Trials

Guideline	Decision Rule
Sequence generation	
If computer-generated, random-number list, flipping coins, randomly picking envelopes, etc., is specified	Yes
If the description includes only "random," "randomly generated," "randomized," etc., do not assume additional details	Unclear
If the description is quasi-randomized (e.g., alternate randomization, day of the year, day of the month, birth date, birth month, beginning letter of last name, availability of investigator or specialist)	No
Allocation concealment*	
If the assignment is conducted by central telephone, pharmacy, etc.	Yes
If dark (or opaque), sealed, and sequentially numbered envelopes are used	Yes
If the envelopes are not stated as dark and sealed or sequentially numbered	Unclear
Blinding	
If the study states to be blinded (masked), and the blinding is considered to be possible and not likely to be broken	Yes
If the study states only to be blinded, double-blinded, double-dummy, etc., without any further details	Unclear
If the study states the use of a placebo (dummy) with no further details	Unclear
If no mention of blinding	No
Incomplete outcome data	
Look for ITT analysis (all randomly assigned patients are analyzed)	Yes
If all participants were accounted for (i.e., no dropouts or censored analysis conducted)	Yes
If the numbers and reasons for withdrawals/dropouts were described and similar across groups (and ≤10%)	Yes
If there is a dropout rate between 10% and 30% and no ITT analysis	Unclear
If there is a >30% dropout rate and no ITT analysis	No
Selective outcome reporting	
If the study protocol is available (referenced in the article), and the outcomes reported in the publication match those specified in the protocol	Yes
If the study protocol is available (referenced in the article), and the outcomes reported in the publication do not match those specified in the protocol but there is reference to another publication in which this information presented	Yes
If the study protocol is not available, and the outcomes reported in the Methods and Results sections match	Yes
Other sources of bias	
Assess for baseline imbalances that could have biased the results (or were not accounted for)	
Assess for early stopping for benefit	
Assess for appropriateness of crossover design (e.g., inadequate wash-out period)	
Assess for inappropriate influence of funders that could have biased the results:	
If sponsor is acknowledged, and there is a clear statement regarding no involvement of sponsor in trial conduct or data management or analysis or coauthorship	Yes
If sponsor is acknowledged with no further information provided, or author or coauthor works for a pharmaceutical company	No
If funding source is not mentioned	Unclear
Note any "other" sources of bias	

ITT = intention-to-treat.

* Sequential numbering of the envelopes is required for adequate allocation concealment only if the method of randomization was anything other than randomly picking envelopes (i.e., the envelopes were used only for allocation concealment and not as part of the randomization process).

Appendix Table 3. **Summary Risk for Bias Assessment for Randomized and Nonrandomized, Controlled Trials***

Domain	High	Unclear	Low
Pharmacologic analgesia			
Adequate sequence generation	0 (0)	3 (100)	0 (0)
Allocation concealment	0 (0)	3 (100)	0 (0)
Blinding	0 (0)	1 (33.33)	2 (66.67)
Incomplete outcome data addressed	0 (0)	1 (33.33)	2 (66.67)
Free of selective reporting	0 (0)	1 (33.33)	2 (66.67)
Free of other bias	0 (0)	2 (66.67)	1 (33.33)
Anesthesia			
Adequate sequence generation	2 (9.09)	17 (77.27)	3 (13.64)
Allocation concealment	1 (4.55)	17 (77.27)	4 (18.18)
Blinding	1 (4.55)	10 (45.45)	11 (50.00)
Incomplete outcome data addressed	2 (9.09)	3 (13.64)	17 (77.27)
Free of selective reporting	0 (0)	0 (0)	22 (100)
Free of other bias	0 (0)	19 (86.36)	3 (13.64)
Complementary and alternative medicine			
Adequate sequence generation	0 (0)	1 (50)	1 (50)
Allocation concealment	0 (0)	2 (100)	0 (0)
Blinding	1 (50)	0 (0)	1 (50)
Incomplete outcome data addressed	0 (0)	0 (0)	2 (100)
Free of selective reporting	0 (0)	0 (0)	2 (100)
Free of other bias	0 (0)	2 (100)	0 (0)
Nerve blockade			
Adequate sequence generation	0 (0)	19 (65.52)	10 (34.48)
Allocation concealment	0 (0)	23 (79.31)	6 (20.69)
Blinding	7 (24.14)	13 (44.83)	9 (31.03)
Incomplete outcome data addressed	3 (10.35)	3 (10.35)	23 (79.31)
Free of selective reporting	4 (13.79)	0 (0)	25 (86.21)
Free of other bias	1 (3.45)	21 (72.41)	7 (24.14)
Neurostimulation			
Adequate sequence generation	0 (0)	1 (50)	1 (50)
Allocation concealment	0 (0)	1 (50)	1 (50)
Blinding	0 (0)	0 (0)	2 (100)
Incomplete outcome data addressed	1 (50)	0 (0)	1 (50)
Free of selective reporting	0 (0)	0 (0)	2 (100)
Free of other bias	1 (50)	1 (50)	0 (0)
Rehabilitation			
Adequate sequence generation	0 (0)	0 (0)	1 (100)
Allocation concealment	0 (0)	1 (100)	0 (0)
Blinding	1 (100)	0 (0)	0 (0)
Incomplete outcome data addressed	0 (0)	0 (0)	1 (100)
Free of selective reporting	0 (0)	0 (0)	1 (100)
Free of other bias	0 (0)	1 (100)	0 (0)
Traction			
Adequate sequence generation	4 (40)	4 (40)	2 (20)
Allocation concealment	4 (40)	6 (60)	0 (0)
Blinding	10 (100)	0 (0)	0 (0)
Incomplete outcome data addressed	1 (10)	0 (0)	9 (90)
Free of selective reporting	1 (10)	0 (0)	9 (90)
Free of other bias	0 (0)	5 (50)	5 (50)

* Values reported are numbers (percentages) of studies.

Appendix Table 4. Description of Interventions

Pain Intervention	Summary	Timing of intervention
Nerve blockade	Includes lateral cutaneous nerve of the thigh, femoral nerve, sciatic nerve, 3-in-1 nerve blockade (femoral, obturator, sciatic nerves), psoas (lumbar plexus), or continuous epidural blockade Local anesthetics (e.g., bupivacaine) used in regional nerve blockades to prevent generation and conduction of nerve impulses to the spinal column and brain Additional medications used with nerve blockades include clonidine, morphine, fentanyl, and sufentanil	Preoperative Intraoperative Postoperative
Systemic analgesia: NSAIDs (e.g., diclofenac)	Used for their analgesic properties and act by inhibiting both COX isoenzymes (COX-1 and COX-2) Acetaminophen, a commonly used analgesic, has minimal inhibition of COX-1 and COX-2 but appreciable inhibition of central COX-3; the precise mechanism for analgesia has not been confirmed	Preoperative Intraoperative Postoperative
Systemic analgesia: opioids (e.g., morphine)	Can be used to treat mild to severe pain Fentanyl primarily targets the μ-receptors in the brain and spinal cord and is used to treat severe pain Sufentanil is 5 to 10 times more potent than fentanyl; it is ideal for short, quick action because of its immediate onset of action and limited accumulation	Preoperative Intraoperative Postoperative
Anesthesia	General and neuraxial (i.e., spinal and epidural anesthesia) Pain management during general anesthesia is usually accomplished by systemic analgesia (e.g., opioids) During neuraxial anesthesia, injection of a local anesthetic into the epidural or subarachnoid space (e.g., spinal anesthesia) causes pain relief and often does not require additional pain medications	Intraoperative
TENS	Uses electrodes to apply electrical energy to peripheral nerves to treat acute and chronic musculoskeletal pain Electrical stimulation is administered at varying amplitudes and frequencies, depending on the indication	Preoperative Postoperative
Physical therapy	Rehabilitation is a standard part of postoperative care to increase mobility and reduce pain; the goal is to increase muscle strength and range of motion as soon as possible after hip fracture	Postoperative
Traction	By providing 5 to 10 lb of traction to the lower limb, intracapsular pressure is decreased and fracture reduction made easier Skin traction is applied by using adhesive tape, bandaging the limb, and placing it on a traction sled with an appropriate weight hung from it Skeletal traction involves passing a metal pin through the proximal tibia or distal femur, under local anesthesia; traction is applied by using ropes and weights attached to the end of the pin	Preoperative
Multimodal pain management	Use of multiple pain management strategies (consecutively or in parallel) as part of the clinical pathway for patients with hip fractures; goal is to decrease pain to a greater extent than with 1 intervention alone	Preoperative Intraoperative Postoperative
Acupressure	Auricular acupressure involves placing tiny beads onto the outer ear at acupuncture points, thereby stimulating the corresponding acupuncture points; it is performed at sites known to decrease pain and anxiety	Preoperative Postoperative
Jacobson relaxation technique	Two-step process of contracting and relaxing specific muscles; with practice, the patient learns which muscles are related to pain and relaxes them	Preoperative Postoperative

COX = cyclooxygenase; NSAID = nonsteroidal anti-inflammatory drug; TENS = transcutaneous electrical nerve stimulation.