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Review Article

REGIONAL ANAESTHESIA

Systematic review of the effects of fascia iliaca compartment block on hip fracture patients before operation

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Abstract

Background: Fascia iliaca compartment block is used for hip fractures in order to reduce pain, the need for systemic analgesia, and prevent delirium, on this basis. This systematic review was conducted to investigate the analgesic and adverse effects of fascia iliaca block on hip fracture in adults when applied before operation.
Methods: Nine databases were searched from inception until July 2016 yielding 11 randomised and quasi-randomised controlled trials, all using loss of resistance fascia iliaca compartment block, with a total population of 1062 patients. Meta-analyses were conducted comparing the analgesic effect of fascia iliaca compartment block on nonsteroidal anti-inflammatory drugs (NSAIDs), opioids and other nerve blocks, preoperative analgesia consumption, and time to perform spinal anaesthesia compared with opioids and time for block placement.
Results: The analgesic effect of fascia iliaca compartment block was superior to that of opioids during movement, resulted in lower preoperative analgesia consumption and a longer time for first request, and reduced time to perform spinal anaesthesia. Block success rate was high and there were very few adverse effects. There is insufficient evidence to conclude anything on preoperative analgesic consumption or first request thereof compared with NSAIDs and other nerve blocks, postoperative analgesic consumption for preoperatively applied fascia iliaca compartment block compared with NSAIDs, opioids and other nerve blocks, incidence and severity of delirium, and length of stay or mortality.
Conclusions: Fascia iliaca compartment block is an effective and relatively safe supplement in the preoperative pain management of hip fracture patients.

Keywords: analgesia; fascia iliaca compartment block; hip fractures; nerve block; preoperative care

Fascia iliaca compartment block (FIC) has been used before operation for hip fractures[1–15] and is widely believed to offer fast and adequate pain relief with fewer adverse effects than systemic analgesia, especially in the elderly.[16,17] FIC can be performed either guided by ultrasound[1,12,15,18] or with a loss of resistance (LOR) technique. Modification can be performed by angling the cannula cranially[3,7,19] or by placing a catheter for continuous infusion.[1,15,19,20]

A systematic review from 2011 concluded that regional nerve blockades, including FIC, seemed to be effective in reducing pain and decreased the incidence of delirium[21] in patients with hip fractures. Two other reviews have been previously conducted to examine the effect of FIC, but all have either included a very limited number of studies or low level of evidence and none have performed a meta-analysis of the available data.[16,17] The preoperative role of FIC in patients with

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Editor's key points

- The use of fascia iliaca block in the preoperative management of the pain of hip fracture was systematically reviewed.
- Meta-analysis showed improved analgesia and faster placement of spinal anaesthesia when fascia iliaca block was used. Postoperative delirium also appeared to be decreased.

hip fractures therefore remains poorly defined. The aim of this review is to determine what the analgesic and adverse effects of FIC are for hip fractures, when applied before operation, by performing a systematic review and a meta-analysis comparing FIC with other types of analgesia.

Methods

Protocol and registration

A protocol for this review has been registered with PROSPERO International prospective register of systematic reviews under the registration number: CRD42016041545.

Eligibility criteria

Eligible studies included comparative studies, either randomised or quasi-randomised controlled trials, enrolling adult patients (≥18 yr) with hip fracture. Only studies comparing FIC with non-intervention, placebo, paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, or other nerve blockades directly were eligible. For the purposes of this review, all forms of FIC were included (single dose or continuous catheter infusion, different types and dosage of local anaesthetics). Outcomes of interest included analgesic effects [visual analogue scale (VAS), numeric rating scale (NRS), additional analgesic usage, and first request for additional analgesia], incidence and severity of delirium, adverse effects, damage to structures surrounding the block site, allergic reactions, length of hospitalisation, and mortality. Only studies published in peer-review journals were eligible and ongoing trials or unpublished data were excluded.

Information sources and search

Both electronic and hand-searching techniques were used to identify studies. Nine databases: PubMed, Cochrane Library, EMBASE, CINAHL, Scopus, Web of Science, EBSCO, ProQuest, and Global Index Medicus, were all queried from database inception until July 1, 2016 without any language restriction or limits to publication type. Free text keyword searches were conducted using the following search words and Boolean operators: '*(hip fracture OR hip surgery OR femur fracture) AND (Fascia iliaca block OR Fascia iliaca nerve block OR Fascia iliaca compartment block OR Fascia iliaca compartment nerve block OR Fascia iliac block OR Fascia iliac nerve block OR Fascia iliac compartment block OR Fascia iliac compartment nerve block OR Fascia-iliaca block OR Fascia-iliaca nerve block OR Fascia-iliaca compartment block OR Fascia-iliaca compartment nerve block OR Fascia-iliac block OR Fascia-iliac nerve block OR Fascia-iliac compartment block OR Fascia-iliac compartment nerve block OR FICB OR FIC OR FIB)*'.

PubMed, Cochrane Library, EMBASE, CINAHL, and Global Index Medicus were also searched with the Medical Subject Headings (MeSH) terms and Boolean operators; '*Hip fractures AND (Nerve Block OR Fascia)*', as a specific MeSH term for FIC does not exist. Web of Science, Scopus, EBSCO, and ProQuest does not allow for a MeSH terms search. The reference lists of all articles examined by full text and similar reviews were hand searched.

Study selection

Decisions for inclusion were based on review of each abstract performed by one reviewer (J.S.). Eligibility of potential studies underwent full text review by the same author. Studies were excluded if they did not meet the inclusion criteria.

Data collection process

Two reviewers extracted all relevant data from the full text versions of eligible studies using a predefined data extraction form. One reviewer (J.S.) extracted the data and a second reviewer (A.M.) independently checked the completeness by reviewing the full text articles. Disagreement between the two researchers was resolved by discussion, and if necessary by arbitration of the senior researcher (A.M.). Study characteristics included author, publication year, study design, sample size, inclusion and exclusion criteria, type of intervention and control, performer of block, outcome data, and authors' main conclusions.

Statistical analysis

To facilitate meta-analysis, studies which reported skewed data, and hence medians and inter-quartile range and 10th and 90th percentiles, were transformed by setting median equal to mean and estimating standard deviation by dividing inter-quartile range and 10th and 90th percentile range with 1.35 and 1.28, respectively, if full datasets could not be obtained. The 11 point NRS was converted to a 100-mm VAS scale by multiplying by 10, as these tend to correlate.[22] Forest plots were used to show point estimates and 95% confidence intervals (CIs) of individual included studies and results. Data analyses abided by the guidelines set out by the Cochrane Collaboration regarding statistical methods. In all instances, two-tailed P-values <0.05 were considered significant. Relative risks and the standardised mean difference (SMD) for continuous outcomes were also calculated. Considering the expected heterogeneity across studies, it was decided to use an inverse variance random-effects model to evaluate outcomes. Subgroup analyses were performed as a means of investigating heterogeneous control interventions and data collection points. Intervention types were pooled into the following subgroups; NSAIDs, opioids, and other nerve blockades, in order to gain sufficient data to perform a meta-analysis. The decision to perform subgroup analysis was taken in the data collection phase of this review, as was the decision on how to pool data at different time intervals. Subgroup analysis based on the risk of bias was not conducted, because of a limited number of included studies. Subgroup analyses based on the type of fracture and surgery, type of drug and dosage of intervention, and dosage of control were not performed because of the limited available data. As a result of the expected problem of assessing the variation in rescue analgesia, no method of analysis was selected before the publication of the protocol. Heterogeneity was assessed using the I^2 statistic, where values >50% are consistent with large heterogeneity,[23] and using heterogeneity P-value, where values <10% are consistent with large heterogeneity.[23] No funnel plots were

Table 1 Study characteristics for all included studies in this review. FIC, fascia iliaca compartment block; FNB, femoral nerve blockade; LOR, loss of resistance; NRS, numeric rating scale; NSAIDs, non-steroidal anti-inflammatory drugs; qRCT, quasi randomised controlled trial; RCT, randomised controlled trial; SA, spinal anaesthesia; VAS, visual analogue scale. *Includes femur shaft fractures, †83 participants received 3-in-1 block (anatomically guided=31, nerve stimulator guided=18, ultrasound guided=34)

Author (and year)	Study type	Participants	Inclusion criteria	Exclusion criteria	Intervention	Control	Outcome of interest	Main conclusion
Mouzopoulos and colleagues[40] (2009)	RCT	*n*=207 FIC=102 Placebo=105	Age≥70 yr with intermediate or high risk for developing delirium	Allergy to local anaesthetics, delirium at admission, metastatic hip cancer, use of cholinesterase inhibitors, severe coagulopathy, Parkinsonism, epilepsy, levodopa treatment, delay of surgery of more than 72 h after admission, and inability to participate in interviews	LOR FIC with bupivacaine 0.25% (0.3 ml kg^{-1}) on admission and repeated daily every 24 h	Placebo FIC with saline 0.9%	Additional analgesic consumption, adverse effects, and incidence of delirium	Lower risk, severity, and duration of delirium for FIC
Hanna and colleagues[41] (2014)	qRCT	*n*=104 FIC=52 Standard care=52	Radiographically confirmed proximal femur fracture	Bleeding diatheses, femoral grafts in the affected limb, inflammation at injection site, or allergy to local anaesthetics	LOR FIC with levobupivacaine0.25% (<40 kg 20 ml, 40–80 kg 30 ml or >80 kg 40 ml)	Unspecified dosage of codeine and paracetamol, and opioids if operation was delayed by more than 24 h (same as FIC group received)	Analgesic effect, additional analgesic consumption, adverse effects, and block success rate	Lower VAS score at 2 and 8 h and lower additional analgesic usage for FIC. No significant difference on VAS at 15 min, 16 or 24 h
Williams and colleagues[42] (2016)	qRCT	*n*=119 FIC=50 Standard care=69	Femoral neck fracture	Patients with subtrochanteric fractures that required application of a splint or traction, prescribed warfarin, dementia, any overlying skin infection, previous femoral bypass surgery, or local anaesthetic allergy	LOR FIC with levobupivacaine 0.25% (<50 kg 30 ml, >50 kg 40 ml)	Paracetamol 1g 4 times a day, codeine 60 mg 4 times a day and opioid 10 mg 2 hourly as required (same as FIC group received)	Analgesic effect, additional analgesic consumption, and block success rate	Lower VAS score and lower additional opioids usage for FIC
Fujihara and colleagues[43] (2013)	qRCT	*n*=56 FIC=31 NSAIDs=25	Clinical diagnosis of a proximal femur fracture confirmed radiologically after intervention	Not described in article	LOR FIC with ropivacaine 0.75%, 10 ml and mepivacaine 2%, 10 ml	25 mg diclofenac sodium suppository	Analgesic effect and additional analgesic consumption	Lower VAS score and lower additional NSAID request for FIC
Godoy Monzón and colleagues[44] (2010)	RCT	*n*=154 FIC=92 NSAIDs=62	Proximal femur fracture and age >65 yr	Anatomical abnormalities in the inguinal area different from fracture, known coagulation disorders, and allergy to used analgesia	LOR FIC with bupivacaine 0.25% (0.3 ml kg^{-1}) and dextrose i.v. 5% (3–5 ml)	Placebo FIC with 0.9% saline and i.v. NSAIDs (diclofenac or ketorolac)	Analgesic effect, adverse effects, and incidence of delirium	Similar effects on VAS scores but faster effect for FIC and more prolonged action for NSAIDs. Lowest incidence of delirium, nausea, and vomiting for FIC
Diakomi and colleagues[45] (2014)	RCT	*n*=41 FIC=21 Opioids=20	Patients undergoing surgery for proximal femur fracture	Contraindications for central nervous blockade, impaired cognition or dementia, multiple fractures, and any previous analgesic	Modified LOC FIC (60 degree cranial angling) with ropivacaine 0.5%, 40 ml	I.V. fentanyl 1.5 μg kg^{-1}	Analgesic effect, additional analgesic consumption,	Lower NRS, lowest time to achieve spinal anaesthesia, better quality of position, lower postoperative morphine consumption,

Continued

Table 1 Continued

Author (and year)	Study type	Participants	Inclusion criteria	Exclusion criteria	Intervention	Control	Outcome of interest	Main conclusion
				administration in the last 12 h before surgery			time to SA, and adverse effects	longer time to first analgesic demand, and higher patient satisfaction in FIC
Foss and colleagues[46] (2007)	RCT	*n*=48 FIC=24 Opioids=24	Clinical diagnosis of a proximal femur fracture, confirmed radiologically after intervention and intact cognitive status	Previous surgery in the affected hip, regular pre-fracture opioid or glucocorticoid therapy, alcohol or substance abuse, infection at the injection site, morphine intolerance, or any previous opioid administration for the acute pain	LOR FIC with mepivacaine 1.0%, 40 ml with 1:200,000 epinephrine and contralateral i.m. saline (0.02 ml kg^{-1})	Placebo FIC with 0.9% saline and contralateral i.m. morphine 5.0 mg ml^{-1}, 0.1 mg kg^{-1} (0.02 ml kg^{-1})	Analgesic effect, additional analgesic consumption, adverse effects, block success rate, and time to perform block	Largest reduction in VAS score, lower rate of sedation, and lowest morphine consumption for FIC
McRae and eolleagues[47] (2015)*	RCT	*n*=24 FIC=11 Opioids=13	Clinical diagnosis of hip or femur fracture	Communication barriers, cognitive impairment, weight <50 kg, local infection at injection site, pre-existing neurological deficit to the affected limb, inability to identify the anatomical landmarks, hemodynamic instability, hypersensitivity to used analgesia, or known coagulation disorders	Modified LOR FIC with lidocaine 2%, 20 ml with epinephrine 1:200,000 diluted with saline 0.9%, 20 ml to a total solution volume of 40 ml (50–70 kg 30 ml or >70 kg 40 ml)	I.V. morphine sulphate (2.5 mg every 2 min) until pain was controlled (maximum dose 0.5 mg kg^{-1})	Analgesic effect, additional analgesic consumption, adverse effects, block success rate, and time to perform block	Lower VAS for FIC at 15 min and during transfer to bed, and lower additional opioid consumption for FIC
Yun and colleagues[48] (2009)	RCT	*n*=40 FIC=20 Opioids=20	Isolated femur neck fracture	Allergy to local anaesthetics, haemorrhagic diathesis, peripheral neuropathy, mental disorders, or block failure (none were excluded because of block failure)	LOR FIC with 30 ml 3.75 mg ml^{-1} ropivacaine (112.5 mg)	I.V. alfentanil 10 mg kg^{-1} followed by continuous infusion of 0.25 mg kg^{-1}	Analgesic effect, additional analgesic consumption, time to SA, adverse effects, and block success rate	Lower VAS score, lower time to achieve spinal anaesthesia, and better patient acceptance for FIC
Newman and colleagues[49] (2013)	RCT	*n*=107 FIC=56 FNB=51	Isolated femur neck fracture and mini-mental score of ≥8/10	Diminished mental capacities, coagulation disorders, allergy to local anaesthetic, infection at injection site, and previous femoral vascular surgery	LOR FIC with levobupivacaine 0.5% (>70 kg 30 ml, 50–70 kg 25 ml, or <50 kg 20 ml)	Nerve stimulator guided FNB with levobupivacaine 0.5% (>70 kg 30 ml, 50–70 kg 25 ml, or <50 kg 20 ml)	Analgesic effect and additional analgesic consumption	Largest reduction in VAS score and lowest morphine consumption for FNB
Reavley and colleagues[50] (2015)†	RCT	*n*=162 FIC=79 3-in-1=83	Radiographically confirmed femur neck fracture	Mini-mental state examination of ≤7/10, other distracting painful pathology, contraindication to local anaesthetic agents, communication barriers, or injury less than 24 h previously	LOR FIC bupivacaine 0.5% (2 mg kg^{-1}) solution up to a maximum of 150 mg diluted with saline 0.9%	3-in-1 block with bupivacaine 0.5% (2 mg kg^{-1}) solution up to a maximum of 150 mg diluted with saline 0.9%	Analgesic effect, additional analgesic consumption, and length of stay	No significant differences in analgesic effect measured with VAS score, but longer length of hospitalisation in the FIC group

conducted to detect publication bias because of the low number of studies. All analyses were conducted using Review Manager (RevMan; version 5.3), Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Risk of bias in individual studies

Two reviewers assessed risk of bias in individual studies based on criteria adapted from the Cochrane 'Risk of Bias' assessment tool.[24] A study was rated overall as high risk for bias if there were important imbalances at baseline, if there was improper randomisation, failure of blinding of outcome assessors, or if there was significant (>15%) loss to follow-up.

Results

Study selection

The database search yielded 538 studies. A total of 278 abstracts were screened after removal of duplicates. After screening, 41 full text articles were assessed for eligibility. The majority were excluded either because they were found not to be relevant for this review, 15 studies,[19,25–39] or because of an inappropriate study design (15 studies).[1–15] The reference lists of all articles examined by full text and similar reviews were hand searched, but yielded no additional articles. In total, 11 studies met inclusion criteria.[40–50] Included studies date from 2007 to 2016. FIC was provided to 538 patients, whereas 524 patients received a different form of analgesia for hip fractures. We attempted to obtain fuller data from McRae and colleagues[47] by mail and email but were unsuccessful.

Study characteristics

Table 1 presents highlighted study features. Eight studies[40,44–50] were randomised controlled trials and three studies[41–43] were quasi randomised controlled trials. All 11 studies[40–50] used bolus LOR FIC. Four of the included studies used opioids as control,[45–48] NSAIDs were used in two,[43,44] as were other forms of nerve blockades,[49,50] one study[40] used placebo FIC, and two studies[41,42] used standard care; paracetamol, codeine, and possibly other opioids (in one study[41] the dosages were unspecified), see Table 1.

Ten studies[41–50] provided data on analgesic effect. Ten studies[40–43,45–50] provided data on additional analgesic consumption. Two studies[45,48] measured time to perform spinal anaesthesia. Seven studies[40,41,44–48] provided data on adverse effects. Two studies[40,44] reported data on incidences of delirium. One study[50] provided data on length of stay and no studies provided data on mortality. Five studies[41,42,46–48] provided data on block success rate, and two studies[46,47] measured time to perform block.

Risk of bias within studies

Three of the included randomised controlled trials[40,44,45] were rated with overall low risk of bias and five[41–43,46–50] were rated as high risk of bias, as were the three quasi randomised controlled trials,[41–43] based on criteria adapted from the Cochrane 'Risk of Bias' assessment tool,[24] see Table 2. Three studies[41–43] had a significant risk of selection bias; all quasi randomised controlled trials. Most of the studies[41–43,47–50] included in this review, seven, did not provide a satisfactory description of their blinding processes to be deemed low risk of bias, although most included some form of blinding. While two studies[41,43] had unclear or incomplete descriptions of their outcome data, this was considered a minor source of bias. None of the studies reported a loss to follow-up >15%. Four studies[45–47,50] provided information on protocols published before the study, while seven[40–44,48,49] did not. One study[46] had important imbalances at baseline including a statistically significant lower VAS score at rest in the control group (P=0.04).

Results of individual studies

Primary outcomes

The two studies[41,42] comparing the analgesic effect of FIC to standard care showed mixed results, where most measurements showed a statistically significant greater analgesic effect for FIC while some were non-significant. The one study[42] which also measured VAS during movement showed a statistically significant greater analgesic effect for FIC for all measurements during movement, see Table 3 for CIs and P-values.

Table 2 Risk of bias within studies based on criteria adapted from the Cochrane 'Risk of Bias' assessment tool. *Does not state if observers were blinded although assessments were performed at another unit, † important differences at baseline

Author (and year)	Selection bias		Performance bias	Detection bias	Attrition bias	Other bias	Overall rating
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Anything else	
Mouzopoulos and colleagues[40] (2009)	Low	Low	Low	Unclear*	Low		Low
Hanna and colleagues[41] (2014)	High	High	High	High	Unclear		High
Williams and colleagues[42] (2016)	High	High	High	High	Low		High
Fujihara and colleagues[43] (2013)	High	High	High	High	Unclear		High
Godoy Monzón and colleagues[44] (2010)	Low	Low	Low	Low	Low		Low
Diakomi and colleagues[45] (2014)	Low	Low	High	Low	Low		Low
Foss and colleagues[46] (2007)	Low	Low	Low	Low	Low	High	High
McRae and colleagues[47] (2015)	Low	Low	High	High	Low		High
Yun and colleagues[48] (2009)	Low	Low	High	High	Low		High
Newman and colleagues[49] (2013)	Low	High	High	High	Low		High
Reavley and colleagues[50] (2015)	Low	Low	High	High	Low		High

Table 3 Results of individual studies on analgesic effect reported in millimetres visual analogue scale (VAS) or numeric rating scale (NRS). Data are median (inter-quartile range), mean [95% confidence interval], mean (standard deviation). FIC, fascia iliaca compartment block; FNB, femoral nerve blockade; LOR, loss of resistance. *Includes femur shaft fractures

Author (and year)	Intervention	Control	Time of measurement	FIC	Control	P-value
Hanna and colleagues[41] (2014)	LOR FIC with levobupivacaine 0.25% (<40 kg 20 ml, 40–80 kg 30 ml, or >80 kg 40 ml)	Unspecified dosage of codeine and paracetamol, and opioids if operation was delayed by more than 24 h (same as FIC group received)	Baseline	8	8	0.54
			15 min	6	6	0.11
			2 h	4	7	0.03
			8 h	3	7	0.01
			16 h	3	6	0.10
			24 h	3	6	0.13
Williams and colleagues[42] (2016)	LOR FIC with levobupivacaine 0.25% (<50 kg 30 ml, >50 kg 40 ml)	Paracetamol 1 g 4 times a day, codeine 60 mg 4 times a day, and opioid 10 mg 2 hourly as required (same as FIC group received)	During rest			
			Baseline	7.9 [7.7–8.2]	8.0 [7.9–8.2]	0.48
			15 min	5.8 [4.9–6.1]	7.7 [6.1–8.1]	0.004
			2 h	4.1 [3.9–4.3]	6.1 [5.2–7.4]	0.003
			8 h	4.0 [3.8–4.2]	5.6 [5.0–6.3]	0.20
			During moment			
			Baseline	9.6 [9.5–9.7]	9.5 [9.5–9.8]	0.32
			15 min	8.0 [7.8–8.2]	9.2 [9.0–9.5]	<0.001
			2 h	6.0 [5.9–6.3]	9.0 [8.7–9.3]	<0.001
			8 h	6.1 [6.0–6.2]	8.9 [8.6–9.2]	<0.001
Fujihara and colleagues[43] (2013)	LOR FIC with ropivacaine 0.75%, 10 ml and mepivacaine 2%, 10 ml	25 mg diclofenac sodium suppository	Baseline	91 (5.7)	92 (6.3)	0.536
			10 min	31 (18.2)	92 (6.3)	<0.001
			12 h	36 (19.0)	81 (7.8)	<0.001
Godoy Monzón and colleagues[44] (2010)	LOR FIC with bupivacaine 0.25% (0.3 ml $kg^{-1)}$ and dextrose i.v. 5%, 3–5 ml	Placebo FIC with saline 0.9% and i.v. NSAID (diclofenac or ketorolac)	Baseline	85 (7.2)	76 (2.2)	0.411
			15 min	29 (1.6)	62.4 (1.7)	<0.001
			2 h	23 (11.6)	17.8 (1.1)	0.764
			8 h	44 (9.1)	20.3 (1.2)	0.083
Diakomi and colleagues[45] (2014)	Modified LOC FIC (60 degree cranial angling) with ropivacaine 0.5%, 40 ml	I.V. fentanyl 1.5 μg kg^{-1}	Baseline	8 (1.9)	7.6 (2.3)	0.546
			Before positioning	2.2 (2.3)	5.2 (2.1)	<0.001
			During positioning	3.2 (1.8)	7.5 (2.4)	<0.001
			After positioning	1.6 (1.6)	5.5 (2.4)	<0.001
Foss and colleagues[46] (2007)	LOR FIC with mepivacaine 1.0%, 40 ml with 1:200,000 epinephrine and contralateral i.m. saline (0.02 ml kg^{-1})	Placebo FIC with 0.9% saline and contralateral i.m. 5.0 mg ml^{-1}, 0.1 mg kg^{-1} morphine (0.02 ml kg^{-1})	During rest			
			Baseline	5 (2–7)	2 (0–4.5)	0.04
			30 min	3 (1–7)	2 (0–4)	0.28
			1 h	2.5 (0–4)	2 (0–4)	0.81
			3 h	2 (0–3)	1 (0–4)	0.64
			During moment			
			Baseline	9 (7–10)	9 (8–10)	1.00
			30 min	8 (6–9)	8 (8–9.5)	0.34
			1 h	6.5 (5–8)	8 (7–9.5)	0.05
			3 h	5.5 (5–8)	8 (7–9)	0.01
McRae and colleagues[47] (2015)*	Modified LOR FIC with lidocaine 2%, 20 ml with epinephrine 1:200,000 diluted with saline 0.9%, 20 ml to a total solution volume of 40 ml (50–70 kg 30 ml or >70 kg 40 ml)	I.V. morphine sulphate (2.5 mg every 2 min) until pain was controlled (maximum dose 0.5 mg kg^{-1})	Baseline	10 (6–10)	9 (8–10)	1.00
			15 min	3 (1–5)	7 (4–8)	0.047
			Arrival ED	1 (0–4)	3 (1–6)	0.21
			At triage	2 (0–2)	4 (1–6)	0.18
			Transfer to bed	2 (0–2)	5 (3–6)	0.006
			2 h	1 (0–2)	3 (0–6)	0.095

Continued

Table 3 Continued

Author (and year)	Intervention	Control	Time of measurement	FIC	Control	P-value
Yun and colleagues[48] (2009)	LOR FIC with ropivacaine 30 ml, 3.75 mg ml^{-1} (112.5 mg)	I.V. alfentanil 10 mg kg^{-1} followed by continuous infusion of 0.25 mg kg^{-1}	Baseline	66 (7)	66 (6)	1.00
			Before positioning	20 (6)	21 (7)	0.630
			During positioning	21 (9)	40 (1)	<0.001
Newman and colleagues[49] (2013)	LOR FIC with levobupivacaine 0.5% (>70 kg 30 ml, 50–70 kg 25 ml or <50 kg 20 ml)	Nerve stimulator guided FNB with levobupivacaine 0.5% (>70 kg 30 ml, 50 –70 kg 25 ml, or <50 kg 20 ml)	Baseline	82 (17)	81 (15)	0.749
			2 h	54 (24)	44 (26)	0.047
Reavley and colleagues[50] (2015)	LOR FIC bupivacaine 0.5% (2 mg kg^{-1}) solution up to a maximum of 15 mg diluted with saline 0.9% solution up to a maximum of 150 mg diluted with saline 0.9%	3-in-1 block with bupivacaine 0.5% (2 mg kg^{-1})	Baseline	65 (26)	64 (26)	0.80
			30 min	44 (26)	45 (24)	0.85
			1 h	38 (25)	35 (25)	0.44

Of the two studies comparing the analgesic effect of FIC to NSAIDs, both demonstrated a statistically significant greater analgesic effect for FIC after 10–15 min,[43,44] but at 2 h one study[44] could not demonstrate any significant difference, and at 8–12 h one study[43] showed a significant effect in favour of FIC while the other[44] was in favour of NSAIDs.

Of the four studies comparing the analgesic effect of FIC to opioids, two[45,47] demonstrated a statistically significant greater analgesic effect for FIC during rest in the first half hour, while the other two studies could not demonstrate a statistically significant difference.[46,48] At 1–3 h, two studies[46,47] could not demonstrate any significant difference and the other two[45,48] had no measurements. During movement, three studies[45,47,48] comparing FIC to opioids were in favour of FIC, while one failed to demonstrate any statistically significant difference[46] in the first 30 min after intervention. Up to 2 h after intervention, two studies[46,47] demonstrated a significant difference in favour of FIC, although one out of two measurements in one study[46] was not significant. At 3 h, one study[46] found a greater analgesic effect in favour of FIC, while the other three[45,47,48] had no measurements.

Of the two studies which compared the analgesic effect of FIC to other forms of nerve blockade, one showed a lesser analgesic effect for FIC,[49] while one[50] could not demonstrate a statistically significant difference.

The one study[40] comparing the analgesic sparing effect of FIC to placebo and the two studies[41,42] comparing FIC to standard care (paracetamol, codeine, and possibly other opioids) all reported lower usage of additional analgesia. In two studies[40,41] the authors did not provide any information as to whether this was statistically significant and calculations could not be performed from the data published. In the third study[42] FIC reduced the mean dose of oral morphine sulphate from 15.5 to 5.0 mg ($P<0.01$; no CIs could be calculated).

In the studies comparing FIC to NSAIDs, only one[43] used additional analgesia as an outcome and the proportion of patients who requested additional NSAIDs was 21% compared with 82% in the control group ($P<0.05$).

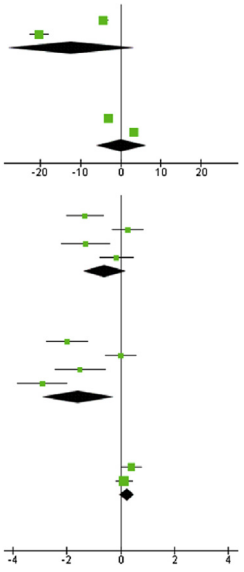
Most of the studies included in this review comparing FIC to opioids demonstrated a statistically significant lower usage of additional opioids analgesia in the FIC groups.[45–48] Three studies reported the mean dosage of additional i.v. morphine for FIC *vs* the control; 4.11 mg (95% CI; 2.61, 5.61) *vs* 7.42 mg (95% CI; 5.24, 9.60) ($P=0.03$),[45] 0 mg (95% CI; 0, 0) *vs* 6 mg (95% CI; 5.38, 6.62) ($P<0.01$),[46] and 0 mg (95% CI; −1.24, 1.24) *vs* 5 mg (95% CI; 2.20, 7.80) ($P=0.03$).[47] While one study[48] could not demonstrate any significant difference between the mean dosage of additional i.m. Demerol for FIC compared with the control group before operation; 12.5 mg (95% CI; 3.60, 21.4) *vs* 15 mg (95% CI; 5.40, 24.6) ($P=0.69$).

Compared with other forms of nerve blockade, one study showed a significant higher consumption of morphine for FIC[49] with 46% *vs* 61% ($P=0.04$) receiving 0 mg morphine 12 h after the block compared with the control group. Another study[50] did not demonstrate any significant difference for i.v. paracetamol; 1 g (95% CI; −1.91, 3.91) *vs* 1 g (95% CI; 1.00, 1.00) ($P=1.00$), for oral paracetamol; 3 g (95% CI; 2.64, 3.36) *vs* 3 g (95% CI; 2.64, 3.36) ($P=1.00$), for oral codeine; 180 mg (95% CI; 120, 240) *vs* 120 mg (95% CI; 71.7, 168) ($P=0.11$), or i.v. morphine 5 mg (95% CI; −7.28, 17.3) *vs* 8 mg (95% CI; −17.4, 33.4) ($P=0.78$).

Two studies[45,48] reported on the first request for additional analgesia for FIC *vs* opioids; 245 min (95% CI; 205, 285) *vs* 145 min (95% CI; 14.9, 275) ($P=0.12$)[45] and 516 min (95% CI; 437, 594) *vs* 270 min (95% CI; 189, 351) ($P<0.01$).[48]

Table 4 Meta-analysis comparing analgesic effect of FIC with NSAID, opioids, and other forms of nerve blockades. Please note that a larger scale is used for NSAID than for opioids and nerve blockades. CI, confidence interval; FIC, fascia iliaca compartment block; NSAIDs, non-steroidal anti-inflammatory drugs; SD, standardised difference; SMD, standardised mean difference

Study or subgroup	FIC			Control			Weight	SMD (95% CI)	SMD (95% CI)
	Mean	SD	Total	Mean	SD	Total			
NSAIDs after 10–15 min									
Fujihara and colleagues[43] (2003)	31	18.2	31	92	6.3	25	50.2%	−4.24 (−5.20, −3.27)	
Godoy Monzón and colleagues[44] (2010)	29	1.6	92	62.4	1.7	62	49.8%	−20.25 (−22.57, −17,94)	
Subtotal			123			87	100.0%	−12.21 (−27,91, 3.49)	
Heterogeneity:	Tau^2=127.48, χ^2=156.61, df=1 (P<0.001), I^2=99%								
Test for overall effect:	Z=1.52 (P=0.13)								
NSAIDs after 8–12 h									
Fujihara and colleagues[43] (2003)	36	19	31	81	7.8	25	49.9%	−2.94 (−3.71, −2.17)	
Godoy Monzón and colleagues[44] (2010)	44	9.1	92	20.3	1.2	62	50.1%	3.33 (2.83, 3.83)	
Subtotal			123			87	100.0%	0.20 (−5.94, 6.35)	
Heterogeneity:	Tau^2=19.55, χ^2=179.34, df=1 (P<0.001), I^2=99%								
Test for overall effect:	Z=0.06 (P=0.95)								
Systemic opioids during rest within 30 min									
Diakomi and colleagues[45] (2014)	22	23	21	52	21	20	25.2%	−1.33 (−2.02, −0.65)	
Foss and colleagues,[46] 2007	30	44.4	24	20	29.6	24	26.7%	0.26 (−0.31, 0.83)	
McRae and colleagues[47] (2015)	30	29.6	11	70	29.6	13	22.2%	−1.30 (−2.20, −0.41)	
Yun and colleagues[48] (2009)	20	6	20	21	7	20	26.0%	−0.15 (−0.77, 0.47)	
Subtotal			76			77	100.0%	−0.59 (−1.40, 0.21)	
Heterogeneity:	Tau^2=0.54, χ^2=16.80, df=3 (P<0.001), I^2=82%								
Test for overall effect:	Z=1.45 (P=0.15)								
Systemic opioids during movement within 120 min									
Diakomi and colleagues[45] (2014)	32	18	21	75	24	20	25.2%	−1.99 (−2.76, −1.23)	
Foss and colleagues[46] (2007)	80	22.2	24	80	11.1	24	26.2%	0.00 (−0.57, 0.57)	
McRae and colleagues,[47] 2015	20	14.8	11	50	22.2	13	24.2%	−1.51 (−2.44, −0.58)	
Yun and colleagues[48] (2009)	21	9	20	40	1	20	24.3%	−2.91 (−3.82, −1.99)	
Subtotal			76			77	100.0%	−1.58 (−2.90, −0.25)	
Heterogeneity:	Tau^2=1.67, χ^{22}=35.31, df=3 (P<0.001), I^2=92%								
Test for overall effect:	Z=2.33 (P=0.02)								
Nerve blockades after 1–2 h									
Newman and colleagues[49] (2013)	54	24	56	44	26	51	41.3%	0.40 (0.01, 0.78)	
Reavley and colleagues[50] (2015)	38	25	79	35	25	83	58.7%	0.12 (−0.19, 0.43)	
Subtotal			135			134	100.0%	0.23 (−0.03, 0.50)	
Heterogeneity:	Tau^2=0.01, χ^2=1.23, df=1 (P<0.27), I^2=19%								
Test for overall effect:	Z=1.71 (P=0.09)								



One study[48] reported the proportions of patients who requested additional use of i.v. alfentanil during positioning for spinal anaesthesia; 0% for FIC compared with 30.7% (P<0.01) in the opioid control group.

One study[45] only reported a significant lower proportion of patients who requested additional use of i.v. morphine with 42.9% *vs* 94.7% (P<0.01) for FIC *vs* the opioids control group after operation. Another study[48] did not find any significant difference between the dosage of additional i.m. Demerol at 6 and 24 h after operation; 20 mg (95% CI; 8.30, 31.7) *vs* 48 mg (95% CI; 19.0, 77.0) (P=0.07) and 41 mg (95% CI; 18.5, 63.5) *vs* 72 mg (95% CI; 39.7, 104) (P=0.11), respectively.

Secondary outcomes

Two studies[45,48] measured time to perform spinal anaesthesia for patients receiving FIC compared with opioids and both found statistically significant shorter times to perform spinal anaesthesia in the FIC group; 2.88 min (95% CI; 2.34, 3.42) *vs* 5.02 min (95% CI; 4.06, 5.98) (P<0.01)[45] and 6.9 min (95% CI; 5.63, 8.16) *vs* 10.8 min (95% CI; 8.18, 13.4) (P<0.01).[48]

Of the 11 studies included in this review; three[43,49,50] did not address adverse effects and one[45] reported no differences in adverse effects between groups without including any additional information. The remaining seven studies included

Table 5 Meta-analysis comparing additional preoperative opioid analgesia usage for FIC with opioids. CI, confidence interval; FIC, fascia iliaca compartment block; SD, standardised difference; SMD, standardised mean difference

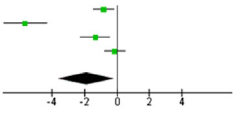
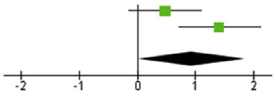
Study or subgroup	FIC			Control			Weight	SMD (95% CI)	SMD (95% CI)
	Mean	SD	Total	Mean	SD	Total			
Diakomi and colleagues[45] (2014)	4.11	3.3	21	7.42	4.65	20	25.8%	−0.81 (−1.45, −0.17)	
Foss and colleagues[46] (2007)	0	0.01	24	6	1.48	24	23.3%	−5.64 (−6.95, −4.33)	
McRae and colleagues[47] (2015)	0	1.85	11	5	4.63	13	25.0%	−1.33 (−2.23, −0.42)	
Yun and colleagues[48] (2009)	12.5	19	20	15	20.5	20	25.9%	−0.12 (−0.74, 0.50)	
Total			76			77	100.0%	−1.89 (−3.63, −0.14)	
Heterogeneity:	Tau^2=2.96, χ^2=56.88, df=3 (P<0.001), I^2=95%								
Test for overall effect:	Z=2.12 (P=0.03)								Favours FIC Favours control

Table 6 Meta-analysis comparing time for first request for analgesia of FIC with opioids. CI, confidence interval; FIC, fascia iliaca compartment block; SD, standardised difference; SMD, standardised mean difference

Study or subgroup	FIC			Control			Weight	SMD (95% CI)	SMD (95% CI)
	Mean	SD	Total	Mean	SD	Total			
Diakomi and colleagues[45] (2014)	245	88	21	145	278	20	51.6%	0.48 (−0.14, 1.10)	
Yun and colleagues[48] (2009)	516	168	20	270	174	20	48.4%	1.41 (0.71, 2.11)	
Total			41			40	100.0%	0.93 (0.02, 1.84)	
Heterogeneity:	Tau^2=0.32, χ^2=3.78, df=1 (P=0.05), I^2=74%								
Test for overall effect:	Z=2.00 (P=0.05)								Favours FIC Favours control

351 patients receiving FIC. The only adverse effects reported in these studies were local hematomas at injection site (1.7%), nausea, and a single case of hematemesis for FIC. Neither nausea and vomiting nor hematemesis was attributable to FIC according to the authors.

Two studies[40,44] measured rates of delirium and found FIC to have a statistically significant protective effect; relative risk of 0.45 (95% CI; 0.23, 0.87)[40] and an incidence of 0% *vs* 6.45%.[44] One study[40] also measured severity and duration of delirium and likewise found FIC to have a protective effect; severity of delirium according to the highest value of the DRSR-98 was 14.3 *vs* 18.6, mean difference 4.27 (95% CI; 1.80, 5.64) (P<0.01) with a mean duration of 5.22 days *vs* 11.0 days (95% CI; 3.87, 7.62) (P<0.01).

One study comparing FIC to other blocks[50] measured length of stay and found a significant longer stay for the FIC group with 0.26 days (95% CI; 0.07, 0.45) (P<0.01). The authors did not attribute this to FIC itself, but could not offer any explanation to this. No studies included in this review examined mortality rate.

Five studies reported on partial or complete block success rate, however several measures have been used to define it; from an absence in cold perception in some or all of the areas innervated by the affected nerves to a reduction in different pain scores or confirmation of placement using ultrasound. The self-reported successful block placement for articles included in this review ranged from 40% to 84%.[41,42,46–48] One study[48] reported partial successful block placement; if partial blocks are considered successful, then the range is 65–100%. Two studies[46,47] measured time to perform block; 4 min (95% CI; 3.30–4.69)[46] and 11 min (95% CI; 7.52–14.5).[47]

Synthesis of results

Primary outcome

In order to achieve sufficient data points to perform a meta-analysis, only the following measurements in time and activity were included: FIC *vs* NSAIDs at rest 10–15 min after intervention, FIC *vs* NSAIDs at rest 8–12 h after intervention, FIC *vs* opioids at rest within the first 30 min of intervention, FIC *vs* opioids at movement within 2 h of intervention, and FIC *vs* other forms of nerve blockades 1–2 h after intervention. As only a single study out of two comparing FIC to standard care included standard deviations or CIs, it was not possible to include standard care in the meta-analysis.

Compared with opioids during movement, FIC had a greater analgesic effect with an SMD of −1.58 (95% CI; −2.90, −0.25) (P=0.02) (heterogeneity: tau^2=1.67, P<0.01, I^2=92%), see Table 4.

No statistically significant difference between FIC and opioids could be demonstrated during rest, with an SMD of −0.59 (95% CI; −1.40, 0.21) (P=0.15) (heterogeneity: tau^2=0.54, P<0.01, I^2=82%). No statistically significant difference in effect could be found between FIC and NSAIDs at 10–15 min with an SMD of −12.2 (95% CI; −27.9, 3.49) (P=0.13)

(heterogeneity: tau^2=127, P<0.01, I^2=99%), or at 8–12 h with an SMD of 0.20 (95% CI; −5.94, 6.35) (P=0.95) (heterogeneity: tau^2=19.55, P<0.01, I^2=99%). Likewise, no statistically significant effect could be demonstrated between FIC and other forms of nerve blockades with an SMD of 0.23 (95% CI; −0.03, 0.50) (P=0.09) (heterogeneity: tau^2=0.01, P=0.27, I^2=19%).

Because of variable methods of reporting final outcome results, missing statistics and clinical heterogeneity between studies, it was only possible to conduct a meta-analysis on the preoperative use of additional opioid analgesia and time for first analgesic request for FIC compared with controls using opioids. A meta-analysis on the possible additional non-opioid and postoperative analgesic sparing effect of FIC could not be performed.

Compared with opioids, FIC had a lower additional preoperative opioid analgesia usage with an SMD of −1.89 (95% CI; −3.63, −0.14) (P=0.03) (heterogeneity: tau^2=2.96, P<0.01, I^2=95%), see Table 5.

Compared with opioids, FIC was found to have a significantly longer time for first request for additional analgesia with an SMD of 0.93 (95% CI; 0.02, 1.84) (P=0.05) (heterogeneity: tau^2=0.32, P=0.05, I^2=74%), see Table 6.

Secondary outcomes

Compared with opioids, FIC was found to have a significantly shorter time to perform spinal anaesthesia with an SMD of −1.06 (95% CI; −1.53, −0.59) (P<0.01) (heterogeneity: tau^2=0.00, P=0.41, I^2=0%). The time to perform an FIC was calculated to be 6.2 min (95% CI; 4.7, 7.7). Because of variable methods of reporting final outcome results, missing statistics, and clinical heterogeneity between studies, a meta-analysis could not be performed on the effects on delirium, length of stay, and mortality.

Discussion

Summary of evidence

This systematic review and meta-analysis demonstrated that FIC had a superior analgesic effect compared with opioids during movement, but did not demonstrate any statistical difference between NSAIDs, opioids at rest, or other forms of nerve block.

The meta-analysis did not demonstrate any statistically significant difference between the analgesic effect of FIC and NSAIDs after 10–15 min. While both included studies individually demonstrated a superior effect for FIC, the differences in results resulted in a large CI. At 8–12 h, one was in favour of FIC. The study with measurements 12 h after intervention reported statistically significant higher VAS at 12 h compared with 15 min and 2 h, possibly indicating that the effects of the FIC had worn off. When examining both the heterogeneity P-value and I^2, we found substantial heterogeneity, which reduced the reliability of the results.

Compared with opioids at rest, the meta-analysis did not demonstrate any difference. Two of the four studies individually were in favour of FIC and one was not statistically significant. The fourth study had a lower VAS score at baseline for the control group. The authors themselves decided, based on this, to use ΔVAS as a measurement instead of comparing the FIC and control group directly. When this analysis was carried out, the study was in favour of FIC. This form of analysis is, however, just as problematic because of the exceptional low baseline scores of the control group. During movement, three of the four studies showed a statistically significant difference in favour of FIC, while one demonstrated no difference. The meta-analysis did, however, demonstrate a statistically significant effect in favour of FIC during movement. Both the heterogeneity P-value and I^2 demonstrated large heterogeneity both during rest and movement, which reduces the reliability of the results. In the meta-analysis excluding skewed data there was a homogeneity during movement, but only when examining the heterogeneity P-value, but not for I^2.

While no statistically significant difference could be demonstrated between FIC and other forms of nerve blockades in the meta-analysis, only two studies were included and combined, and these had an SMD of 0.23 (95% CI; −0.03, 0.50) (P=0.087) indicating that FIC might be less effective than other forms of nerve blockades. It is worth mentioning that femoral nerve and 3-in-1 blocks were grouped together because of the limited number of studies and that the studies individually demonstrated a lower effect for FIC compared with a femoral nerve block and almost no difference between FIC and 3-in-1 block. The test for heterogeneity showed low heterogeneity across the studies.

Of the 15 cohorts and retrospective studies studied in full text, which was relevant for this review, but not included because of study design, all showed an effect of FIC on hip fractures,[1–15] also during movement and positioning.[4,6–8] There seems to be an effect of at least 8 h for bolus FIC, when long-lasting local anaesthesia such as bupivacaine is used.[3,10–12] There is, however, a high risk for publication bias and confounding factors such as additional analgesia for these studies.

The meta-analysis demonstrated that FIC had lower preoperative additional opioid analgesia usage and a significantly longer time for first request for additional analgesia, compared with opioids. When examining I^2, we found substantial heterogeneity, but not for the heterogeneity P-value. While it was not possible to perform a meta-analysis on preoperative analgesic consumption for FIC compared with placebo, standard care, or NSAID, all included studies report significant lower consumption, but additional data are necessary. Compared with other forms of nerve blockade, there were mixed results. Postoperative analgesia consumption likewise showed mixed results. The meta-analysis demonstrated that FIC resulted in a significantly shorter time to perform spinal anaesthesia compared with opioids, which could be because of superior analgesic effect during movement.

Of the articles included in this review, none found any adverse effects attributed to FIC besides hematomas at the injection site with an incidence rate of 1.7%. In order to investigate adverse effects further, the 15 cohorts and retrospective studies examined by full text and deemed relevant for this review were searched for adverse effects. Of these, only eight[3,4,6,7,10,12,14,15] reported adverse effects. These eight studies included 2179 patients; four instances of anaesthetic toxicity (risk of 0.18%)[3,4] and two hematomas at injection site (risk of 0.09%)[10] were reported. There is, however, most likely an under-reporting of, at least, minor adverse effects. The two hematomas at the injection site were both reported in the same study where 63 FIC were performed, resulting in an incidence of 3.2% which is close to the rate of 1.7% reported in the studies included in this review.

It was not possible to perform a meta-analysis on incidence and severity of delirium, length of stay, or mortality, because of the limited available data. The two included studies measuring incidence of delirium compared placebo and NSAID; both found a protective effect of FIC, and the one study

comparing FIC with placebo also reported a significant reduction in severity and duration, but more data are needed. One study comparing FIC with other blockades measured length of stay and found a significant longer stay for the FIC; the authors, however, did not attribute this to FIC itself, but could not offer any explanation. No studies included in this review examined mortality rate.

The average time for block placement was calculated to be 6.2 min. The reported block success rate for studies included in this review is in the range of 65–100% (including partial successfully blocks),[41,42,46–48] which correlates well with other studies.[7,9,11,15,20,26,51] FIC can generally be performed with minimal training[2,4,11] and by non-medical practitioners.[5–7,17,47] FIC is generally safe to use and patient satisfaction is generally high.[7,45–48] There is, however, a small chance of local anaesthetic intoxication and hematoma at the injection site.[2–4,6,7,9–12,14,15,40,43] There are also, in the literature described, case reports of pneumoretroperitoneum using continuous infusion,[52] bladder puncture with a modified block under very special conditions,[53] and postoperative neuropathy.[54]

Limitations

The protocol was changed during the literature search phase to include quasi-randomised, controlled trials in order to perform this review on sufficient data. Screening for eligibility was performed by a single reviewer instead of two or more. Only 11 articles met the inclusion criteria set forward in this review, and only six of those included 100 patients or more, none more than 207 in total, and most studies had a high risk of bias resulting in a limited basis for a systematic review. In addition, there may be a risk of reporting bias, mainly in the form of publication bias, because of the limited number of trials with a large study population and low proportion of null results. In the meta-analyses comparing the analgesic effect, there was a large heterogeneity in all but one subgroup in the meta-analysis including skewed data, when examining the heterogeneity *P*-value. This could, however, be attributable to the low number of studies included. When calculating I^2, all subgroups except one had large heterogeneity, which reduces the confidence of this review's recommendations of FIC.

Conclusion

This review revealed a superior analgesic effect of FIC compared with opioids during movement and an equivalent effect compared with NSAIDs, opioids, and other nerve blocks in hip fracture patients before operation. FIC had lower preoperative analgesia consumption and a longer time for first request compared with opioids. FIC reduced time to perform spinal anaesthesia. Block success rate was found to be high and there were very few adverse effects. There is insufficient evidence to conclude anything on preoperative analgesic consumption or first request compared with NSAIDs and other nerve blocks, postoperative analgesic consumption for preoperative applied FIC compared with NSAIDs, opioids and other nerve blocks, incidence and severity of delirium, length of stay, or mortality.

Authors' contributions

Protocol design: both authors.
Conducted literature search and study selection: J.S.
Supervised literature search and study selection: A.M.M.
Performed data extraction and assessment of risk of bias: both authors.
Conducted meta-analysis: J.S.
Supervised meta-analysis: A.M.M.
Wrote first draft of the manuscript: J.S.
Complied with the International Committee of Medical Journal Editors recommendations including final approval of this review: both authors.

Declaration of interest

The authors have no competing interest to declare.

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