

REVIEW ARTICLES



Epidural analgesia compared with peripheral nerve blockade after major knee surgery: a systematic review and meta-analysis of randomized trials

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> The relative analgesic efficacy and side-effect profile of peripheral nerve blockade (PNB) techniques compared with lumbar epidural analgesia for major knee surgery is unclear. We undertook a systematic review and meta-analysis of all randomized trials comparing epidural analgesia with PNB for major knee surgery. Eight studies were identified that had enrolled a total of 510 patients of whom 464 (91%) had undergone total knee joint replacement. All were small trials and none was blinded (ladad score I-3). PNB technique was variable: in addition to a femoral catheter (n=5), femoral single shot (n=2), or lumbar plexus catheter (n=1) techniques, sciatic blockade was performed in three trials. There was no significant difference in pain scores between epidural and PNB at 0-12 or 12-24 h, WMD 0.22 (95% CI: -0.36, 0.81), 0.05 (-1.01, 0.91), respectively, and no clinically significant difference at 24-48 h, WMD -0.35 (-0.64, -0.02). There was also no difference in morphine consumption (mg) at 0-24 h, WMD -6.25 (-18.35, 5.86). Hypotension occurred more frequently among patients who received epidurals [OR 0.19 (0.08, 0.45)], but there was no difference in the incidence of nausea and vomiting. Two studies reported a higher incidence of urinary retention in the epidural group. Patient satisfaction was higher with PNB in two of three studies which measured this, although rehabilitation indices were similar. PNB with a femoral nerve block provides postoperative analgesia which is comparable with that obtained with an epidural technique but with an improved side-effect profile and is less likely to cause a severe neuraxial complication.

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Major knee surgery such as total knee joint replacement (TKJR) and anterior cruciate ligament reconstruction (ACLR) is associated with moderate to severe postoperative pain which can contribute to immobility-related complications, delay in hospital discharge, and interfere with functional outcome. ^{8 37} These lower limb procedures are amenable to regional anaesthesia techniques which reduce neuroendocrine stress responses, central sensitization of the nervous system and muscle spasms which occur in response to pain stimuli. ^{1 26}

Epidural analgesia has been popular over recent decades as there is evidence for reduced blood loss and fewer thromboembolic complications using neuraxial techniques in orthopaedic surgery. A recent systematic review

comparing lumbar epidural blockade with systemic opioid analgesia reported better dynamic pain scores in the epidural group but no difference in the incidence of side-effects overall.¹² Patients who received epidurals had more frequent hypotension, urinary retention, and pruritis whereas systemic opioids caused more sedation (but no difference was found with respect to respiratory depression or postoperative nausea and vomiting). More importantly, there is evidence that patients undergoing TKJR are at increased risk of serious neurological complications as a result of epidural blockade. This is most likely to be related to degenerative spinal changes and anticoagulant therapy.³²

An alternative regional anaesthesia technique is peripheral nerve blockade (PNB) of one or more major nerves

supplying the lower limb. PNB may provide effective unilateral analgesia with a lower incidence of opioid-related and autonomic side-effects, less motor block, and fewer serious neurological complications compared with epidural analgesia. In contrast to epidural analgesia, continuous PNB techniques do appear to provide pain relief superior to systemic opioid analgesia but with a lower incidence of side-effects. Advances in nerve localization such as ultrasound imaging and continuous catheter technology have also helped to increase interest in PNB for lower limb surgery. Is 19

Most previous studies comparing PNB with epidural analgesia for major knee surgery have demonstrated equivalent analgesia and an improvement in side-effect profile associated with PNB. However, the number of patients enrolled in each study is small and statistical significance is not reached across all variables and all time periods measured. The aim of this study was to undertake a systematic review and meta-analysis of randomized trials of epidural analgesia and PNB in adults undergoing major knee surgery, including comparison of analgesic efficacy, side-effects/complications, patient satisfaction, and rehabilitation indices.

Methods

A systematic review of randomized trials comparing epidural analgesia with PNB for postoperative analgesia after major knee surgery in adults was conducted. The MEDLINE, EMBASE, Pubmed, and CINAHL databases, Bandolier, and the Cochrane Controlled Trials Register (CCTR) were searched from their inception to April 2007 by two of the authors (S.J.F. and S.S.). Abstracts and conference proceedings of the American Society of Anesthesiologists (ASA), International Anesthesia Research Society (IARS), and European Society of Anesthesiology (ESA) were searched manually from 2000 onwards to identify unpublished studies. In addition, we undertook a Google search and contacted several researchers in the field. Prospective randomized trials were searched using the following combinations of terms: total knee replacement/major knee surgery/knee/cruciate ligament, plus epidural/extradural/peridural/combined spinal epidural, plus nerve block/ femoral/sciatic/lumbar plexus/ local anaesthesia. Language restrictions were not applied. The reference lists of retrieved papers were scrutinized to identify further studies for inclusion. Reports were included if the study was a prospective randomized trial comparing continuous lumbar epidural analgesia with local anaesthetic agent compared with any peripheral nerve block (single shot or continuous administered before or after operation) in patients undergoing major knee surgery. Exclusion criteria were opioid-only epidural, single-shot epidural, and intrathecal-only techniques. A total of 12 studies were identified but only eight papers were included in the analysis. Three were clearly multiple publications of the same research, although the methodology reported was variable. ¹⁶ ²¹ ³⁹ One prospective, randomized study of patients undergoing ACLR was retrieved from the search of unpublished conference abstracts, ⁵ but little data were presented in this negative study and further details could not be obtained from the authors. None of the included studies was double-blind, reflecting the ethical issues surrounding the use of placebo catheters.

The studies were examined by two of the authors (S.J.F. and J.S.) for measures that could be meaningfully compared between the studies. If data were not available in the original paper, the authors were contacted by e-mail to request further information. The quality of individual trials was quantified using the Jadad scale²⁴ using five criteria: (i) randomization, (ii) description of randomization, (iii) blinding, (iv) adequacy of blinding, and (v) withdrawals documented.

Outcome measures included: (i) analgesic efficacy, visual analogue dynamic pain scores on the day of surgery and the first and second days after surgery, morphine consumption in the first 24 h after operation; (ii) adverse effects, nausea and vomiting, hypotension, pruritis, urinary retention, sedation, and motor block; (iii) patient satisfaction; and (iv) rehabilitation indices. We also reported other outcome data, including neurological complications, blood loss, time to perform regional block, cardiovascular and surgical complications, and local anaesthetic plasma levels. All data were independently extracted and verified by two of the authors (J.S. and S.S.) and differences resolved by consensus.

Where pain scores were given but it was unclear whether these were at rest or on movement, the worst pain score for that time period was used. Where both nausea and vomiting were reported, we used only the data for vomiting, assuming that all patients who vomited would have experienced nausea as well. Where nausea and vomiting was reported as mild, moderate, or severe, the worst score was used. Visual analogue pain scores were converted to a standardized 0–10 scale. Variables which were not reported numerically were estimated by manual measurements from the published figures.

When no standard deviation (SD) was given for continuous data, the SD was estimated as half the mean value. When data were presented as 95% confidence intervals (CI), the SD was calculated from the formula (SD=95% CI/ $1.96 \times \sqrt{n}$). When the median and range were reported for continuous outcomes, the mean and SD were estimated by assuming that the mean was equivalent to the median and that the SD was a quarter of the range.

Meta-analysis was undertaken using Review Manager (RevMan for Windows version 4.2.9, The Cochrane Collaboration, Oxford, UK) when sufficient data existed in three or more studies. This software calculates the weighted mean difference and 95% CI (by study size and SD) between treatment arms for numerical data in each study and estimates the overall pooled effect.

For dichotomous data, RevMan calculates odds ratio and 95% CI. If heterogeneity was significant ($P \le 0.05$), a random effects model was used. If heterogeneity was non-significant (P > 0.05), a fixed effects model was used. Those parameters which were unsuitable for meta-analysis or reported in a single study were discussed in the text.

Subgroup analysis was performed for the five studies using femoral blockade alone in an attempt to detect a difference in quality of analgesia compared with combined sciatic and femoral/lumbar plexus block. We were unable to perform a subanalysis comparing quality of analgesia with single-shot *vs* continuous blocks as there were little data after the first 12 h after operation. Likewise, analysis of TKJR compared with other types of major knee surgery was not possible as we were unable to obtain subgroup data in those papers which included other procedures.^{2 9}

One of the studies compared pain scores and surgical stress hormones only in the very early postoperative period only (0-3 h) but was included in the analysis.¹ In another study, which was also included, both groups received an epidural as the primary anaesthetic technique in the operating theatre and this was replaced at the end of surgery by a femoral nerve catheter in one study group.²⁷

Results

Of the eight studies included in this systematic review (Table 1), ¹ ² ⁶ ⁹ ¹⁷ ²⁷ ⁴⁶ ⁵⁴ five originated from Europe. There were 510 patients in total included in the analysis, of whom 464 (91%) had undergone TKJR. Other procedures were ACLR (*n*=28; 5.5%) and arthrolysis (*n*=18; 3.5%). The peripheral nerve block technique used was variable (Table 2)—the most common technique was a femoral sheath catheter alone (four studies), ⁶ ⁹ ²⁷ ⁴⁶ then a single-shot femoral block in two studies, ¹ ¹⁷ and continuous lumbar plexus blockade in one study. ² Sciatic nerve blockade was used in three of the eight studies of which two were single-shot techniques ² ¹⁷ and one a continuous catheter. ⁵⁴ The primary anaesthetic technique was general anaesthesia in six studies and in the remaining two studies, spinal anaesthesia, ⁶ and epidural/PNB² were used.

When all studies were combined, there was no difference in visual analogue pain scores between the epidural and the PNB during the first two time periods (0–12 and 12–24 h) after operation (Figs 1 and 2). Subanalysis of studies with or without sciatic block did not change the results. Lower pain score at 24–48 h in the epidural group reached statistical significance [WMD -0.35 (95% CI: -0.64, -0.02); P=0.04] (Fig. 3). Analysis of three studies showed no difference in morphine consumption (mg) at 0–24 h^{21 22 24} [WMD -6.25 mg (95% CI: -18.35, 5.86)]. Opiate consumption in two other studies which were not suitable for meta-analysis was also similar between the groups. 9 46

Hypotension occurred more frequently (P=0.0001) in patients who received an epidural (Fig. 4). There was no difference between the groups in the rate of nausea and vomiting (Fig. 5). The total number of patients with urinary retention, pruritis, or sedation was low (<50 patients in each treatment arm). However, both studies $^{46.54}$ that assessed urinary retention reported that this occurred more often among patients with epidurals [combined OR 0.07 (95% CI: 0.02, 0.27; P<0.0001)]. No difference in the incidence of pruritis or sedation was found in two studies. 9 There was no apparent bias on funnel plot analysis of adverse event data.

Of the three studies reporting patient satisfaction, ¹ ² ¹⁷ two stated that patient satisfaction was higher in the PNB group. ² ¹⁷ Mobilization or rehabilitation was described in six studies. ⁶ ⁹ ¹⁷ ²⁷ ⁴⁶ ⁵⁴ Rehabilitation indices varied but outcomes were generally similar except in one study which reported that better walking distance (day 0 and day 1) and knee extension (day 2, day 3, and at discharge) were obtained in patients with an epidural as a result of quadriceps weakness associated with PNB. ²⁷ However, the data with respect to motor block on the operative side in two other studies were conflicting. ⁶ ⁵⁴ There was no difference between the groups in range of knee movement at 6 months.

one major neurological complication was Only reported—a patient who received an epidural developed foot drop and sphincteric disturbance after operation but the aetiology was not stated. 17 In another study, paraesthesia and numbness occurred more frequently in the epidural group but no further details were given.9 There was no difference between the groups in any of the three studies measuring perioperative blood loss, ^{2 6} ¹⁷ nor was there a difference in the number of cardiovascular complications overall. 6 54 In one study, three patients in the PNB group required re-operation for closed manipulation (n=2) or wound dehiscence.²⁷ The study which reported plasma catecholamine and stress hormone levels concluded that epidural analgesia provides the greatest reduction in sympatho-adrenergic stress response in the early postoperative period, although analgesia and adverse effects were judged to be similar. In this study, plasma bupivacaine concentrations in 21 patients who received femoral nerve block using bupivacaine 150 mg remained well below toxic limits 15–180 min after administration.¹

Inadequate or failed block was described in four studies. Overall, there were 10 of 130 (7.7%) patients in the epidural group and four of 133 (3.0%) patients in the PNB group who had treatment failure, although only one study included these patients in the analysis (intention-to-treat). One study found no difference in block insertion times (mean 13 min in epidural and 12.5 min in combined femoral-sciatic single shot block groups; P=0.92) and time in the anaesthetic room (29.6 and 7.1 min; P=0.34), but in another study there were more catheter problems in the epidural group such as

Table 1 Summary of randomized trials included in the meta-analysis. TKJR, total knee joint replacement; ACLR, anterior cruciate ligament repair; VAS, visual analogue score; GA, general anaesthetic; SE, side-effects; PCA, patient-controlled analgesia; IA, intraarticular

Study/Country	Type of surgery (Jadad score)	No. of patients/groups	Techniques		Duration	Other group	Additional	
			Intraoperative	Epidural	PNB			analgesics
Zaric and colleagues ⁵⁴ / Denmark	TKJR (3)	49/2	GA	Ropivacaine 0.75% boluses to block level T10 preop+infusion ropivacaine 0.25% with sufentanil postop	Femoral and sciatic catheters: preop bolus ropivacaine 0.75% 30 ml each catheter+infusion ropivacaine 0.2% with sufentanil (femoral) and ropivacaine 0.05% (sciatic) postop	55 h postop		PCA morphine ± acetaminophen
Barrington and colleagues ⁶ /Australia	TKJR (3)	108/2	Spinal	Ropivacaine 0.2% with fentanyl infusion postop	Femoral catheter: preop bolus bupivacaine 0.25% with adrenaline 25 ml+infusion bupivacaine 0.2% with PCA bolus postop	Postop D3		Oxycodone ± rofecoxib ± morphine infusion
Davies and colleagues 17/UK	TKJR (3)	59/2	GA	Bupivacaine 0.5% bolus preop+infusion bupivacaine 0.25% postop		Postop D2		PCA morphine
Singelyn and colleagues ⁴⁶ /Belgium	TKJR (2)	45/3	GA	Bupivacaine 0.25% with epinephrine and sufentanil bolus preop+infusion bupivacaine 0.125% with sufentanil and clonidine postop	Femoral catheter: preop bolus bupivacaine 0.25% with adrenaline 37 ml+infusion bupivacaine 0.125% with sufentanil and clonidine postop	48 h postop	PCA morphine	Propacetamol \pm piritramide
Adams and colleagues 1/Germany	TKJR (1)	63/3	GA	Bupivacaine 0.375% bolus postop	Single-shot femoral block: postop bolus bupivacaine 0.375%	3 h postop	PCA pirinitramide	Diclofenac (PCA group)
Capdevila and colleagues ⁹ /France	TKJR and arthrolysis (1)	38 TKJR and 18 arthrolysis/3	GA	Lidocaine 2% with epinephrine and morphine 2 mg to block level T10 bolus postop+infusion 1% lidocaine with clonidine and morphine		Postop D3	PCA morphine	Propacetamol ± ketoprofen ± s.c. morphine prn
Aldahish and colleagues ² /Egypt	TKJR and ACLR (2)	32 TKJR and 28 ACLR/2	Regional	Bupivacaine 0.5% bolus preop+infusion bupivacaine 0.125% postop	Lumbar plexus catheter and single-shot sciatic block: preop bolus bupivacaine 0.5%+infusion bupivacaine 0.125% postop (lumbar plexus only)	48 h postop		
Long and colleagues ²⁷ / USA	TKJR (2)	70/2	GA+Epidural	Ropivacaine 1% bolus preop+infusion ropivacaine 0.2% postop	Femoral catheter: postop bolus+infusion ropivacaine 0.2%	36 h postop		Acetaminophen ± COX-2 inhibitor ± oxycodone ± IA ropivacaine with methylprednisolone and morphine ± hydrocodone ± ketorolac ± tramadol prn

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Table 2 Summary of peripheral block techniques employed in the eight included studies

No. of studies	Femoral single shot	Femoral catheter	Lumbar plexus catheter	Total
No sciatic block	1	4		5
Sciatic single-shot	1		1	2
Sciatic catheter Total	2	1 5	1	1 8

kinking and lateralization to the non-operative side (P < 0.001). 46

Discussion

The principal finding of this systematic review is that a PNB technique using femoral nerve blockade provides analgesia which is comparable with that obtained with an epidural but with a lower incidence of hypotension. This is consistent with the findings of two previous meta-analyses which compared systemic opioid analgesia with epidural analgesia ¹² and continuous PNB, ³⁸ respectively, and also with a previous report in patients undergoing hip surgery. ⁵⁰ We did not detect any benefit from the addition of a sciatic block to a femoral nerve blockade at 0–24 h after operation. The marginal improvement in pain score at 24–48 h in patients receiving epidural analgesia is unlikely to be clinically significant. Although the number of patients in the analysis was small (n=79), there was a

reduction in the incidence of urinary retention using PNB (P<0.0001). This finding is consistent with previous systematic reviews¹² ³⁸ and also with the pharmacology of local anaesthetic administered into the epidural space.

Limitations of the study

There were no large ($n \ge 1000$) randomized trials comparing PNB with epidural analgesia. We identified eight relevant studies so that the meta-analysis included 510 patients but only two studies defined a primary outcome measure. Variable reporting of end points and inconsistent definitions meant that we were unable to include every study for each outcome, despite attempting to contact authors. Although pooling of results increases statistical power, the findings need to be interpreted with caution as there were only a small number of patients identified for some variables. For example, any difference in the rate of pruritis and sedation would be difficult to detect as there were less than 50 patients in each arm of the meta-analysis.

There was also clinical heterogeneity among the studies. For example, there was wide variation in the type of PNB and different techniques such as femoral, combined femoral–sciatic, lumbar plexus, single-shot, and continuous blocks were all treated as one group. There was also variation in the drug, additives, and doses used in both arms of this systematic review (Table 1).

It is important to note that none of the studies reported improved long-term outcome with PNB, which is likely as the choice of analgesic technique is only one component of quality postoperative care, which must include expert physiotherapy and nursing care. Routine hospital discharge

neview.	Kilee Surgery meta-analysis
Comparison:	02 VAS 0-12 h
Outcome:	01 VAS 0-12 h

Study or subcategory	Ν	PNB mean (sd)	N	Epidural mean (sd)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
1 VAS 0-12 all studies							
Adams and colleagues	21	0.80 (0.75)	21	0.70 (0.75)	÷	20.74	0.10 (-0.35, 0.55)
Aldahish and colleagues	30	2.30 (1.15)	30	2.40 (1.20)	+	17.62	-0.10 (-0.69, 0.49)
Davies and colleagues	30	2.15 (0.17)	29	1.50 (0.28)	×	26.92	0.65 (0.53, 0.77)
ong and colleagues	35	1.70 (1.70)	35	2.90 (2.00)	-	12.51	-1.20 (-2.07, -0.33)
Singelyn and colleagues	15	4.80 (2.00)	15	2.00 (2.10)		6.23	2.80 (1.33, 4.27)
aric and colleagues	26	0.00 (1.08)	23	0.00 (1.30)	÷	15.98	0.00 (-0.67, 0.67)
Subtotal (95% CI)	157	()	153	()	•	100.00	0.22 (-0.36, 0.81)
Test for heterogeneity: $X^2=38$	8.22. df=5	P<0.00001), P=86.99	6		T .		(,
Test for overall effect: Z=0.75							
VAS 0-12 h with sciatic blo	ock						
Idahish and colleagues	30	2.30 (1.15)	30	2.40 (1.20)	÷	29.12	-0.10 (-0.69, 0.49)
avies and colleagues	30	2.15 (0.17)	29	1.50 (0.28)	la la	44.47	0.65 (0.53, 0.77)
aric and colleagues	26	0.00 (1.08)	23	0.00 (1.30)	+	26.41	0.00 (-0.67, 0.67)
Subtotal (95% CI)	86	()	82	,	•	100.00	0.25 (-0.32, 0.82)
est for heterogeneity: $X^2=9$.	04. df=2 (A	P<0.01) P=77.9%	17.77		Γ	115.555.55	
est for overall effect: Z=0.86							
VAS 0-12 without sciatic b	lock						
dams and colleagues	21	0.80 (0.75)	21	0.70 (0.75)		52.55	0.10 (-0.35, 0.55)
ong and colleagues	35	1.70 (1.70)	35	2.90 (2.00)	-	31.68	-1.20 (-2.07, -0.33)
ingelyn and colleagues	15	4.80 (2.00)	15	2.00 (2.10)		15.77	2.80 (1.33, 4.27)
Subtotal (95% CI)	71	,=/	71			100.00	0.44 (-1.19, 2.06)
lest for heterogeneity: $X^2=2^{-1}$		P<0.0001) P=90.7%				. 30.00	3(3, L .00)
est for overall effect: $Z=0.53$		(1 30.0001), 1 = 30.1 /0					
Cot for Otoran effect. Z=0.00	(, =0.00)						
					-10 -5 0 5	10	
					Favours PNB Favours Epid	ural	

Fig 1 A meta-analysis of trials comparing PNB with epidural on visual analogue pain scores at 0-12 h including sub-analysis with and without sciatic block.

Review: Knee Surgery meta-analysis Comparison: 03 VAS 12–24 h Outcome: 01 VAS 12–24 h

Study or subcategory	N	PNB mean (sd)	N	Epidural mean (sd)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
1 All studies							
Aldahish and colleagues	30	4.30 (2.15)	30	4.10 (2.05)	→	12.83	0.20 (-0.86, 1.26)
Barrington and colleagues	53	2.00 (1.95)	55	1.70 (1.85)	+	15.35	0.30 (-0.42, 1.02)
Capdevilla and colleagues	20	2.70 (1.35)	17	1.90 (1.25)	-	14.48	0.80 (-0.04, 1.64)
Davies and colleagues	30	4.00 (0.28)	29	5.50 (0.35)	*	18.19	-1.50 (-1.66, -1.34)
Long and colleagues	35	2.50 (1.70)	35	3.90 (1.40)	-	15.27	-1.40 (-2.13, -0.67)
Singelyn and colleagues	15	3.60 (1.10)	15	3.30 (2.30)	-	11.23	0.30 (-0.99, 1.59)
Zaric and colleagues	26	4.00 (2.00)	23	2.70 (1.88)		12.66	1.30 (0.21, 2.39)
Subtotal (95% CI)	209		204		•	100.00	-0.05 (-0.91, 0.91)
Test for heterogeneity: X2=84	.01, df=6 (P<0.00001), P=92.9	%		1		
Test for overall effect: Z=0.10	(P=0.92)						
2 VAS 12-24 h with sciatic blo	ock						
Aldahish and colleagues	30	4.30 (2.15)	30	4.10 (2.05)	-	29.37	0.20 (-0.86, 1.26)
Davies and colleagues	30	4.00 (0.28)	29	5.50 (0.35)	H	41.65	-1.50 (-1.66, -1.34)
Zaric and colleagues	26	4.00 (2.00)	23	2.70 (1.88)	-	28.98	1.30 (0.21, 2.39)
Subtotal (95% CI)	86	A STATE OF THE PARTY OF THE PAR	82		•	100.00	-0.06 (-1.91, 1.79)
Test for heterogeneity: X2=33		(P<0.00001), P=94.1	%				
Test for overall effect: Z=0.06	(<i>P</i> =0.95)						
3 VAS 12-24 without sciatic b							
Barrington and colleagues	53	2.00 (1.95)	55	1.70 (1.85)	+	27.26	0.30 (-0.42, 1.02)
Capdevilla and colleagues	20	2.70 (1.35)	17	1.90 (1.25)	-	25.71	0.80 (-0.04, 1.64)
Long and colleagues	35	2.50 (1.70)	35	3.90 (1.40)	-	27.10	-1.40 (-2.13, -0.67)
Singelyn and colleagues	15	3.60 (1.10)	15	3.30 (2.30)	-	19.93	0.30 (-0.99, 1.59)
Subtotal (95% CI)	123		122		•	100.00	-0.03 (-1.08, 1.03)
Test for heterogeneity: X ² =18		(P=0.0004), P=83.5%	6				
Test for overall effect: Z=0.05	(P=0.96)					4	
					-10 -5 0 5	10	
					Favours PNB Favours Epic	A 100 TO 100	

Fig 2 A meta-analysis of trials comparing PNB with epidural on visual analogue pain scores at 12-24 h including sub-analysis with and without sciatic block.

and rehabilitation after major knee surgery is very variable between countries and institutions. A limitation of all systematic reviews is that negative studies are less likely to be submitted or accepted for publication. Despite these weaknesses, meta-analysis is considered a reliable source of evidence.

Comparison with other studies

The findings of several larger non-randomized series comparing PNB with epidural analgesia for lower limb surgery have been published which are consistent with the results of our study. 11 47 48 Singelyn and Gouverneur 47 reported that 540 patients undergoing major knee surgery who received either continuous '3-in-1' block (n=415) or epidural analgesia (n=125) had similar dynamic pain scores with fewer side-effects and block failures in the PNB group. In another report, these authors reiterated that PNB was the technique of choice. 48 Chelly and colleagues compared i.v. PCA morphine, continuous femoral with singleshot sciatic blockade and epidural analgesia in a cohort study of 92 patients undergoing TKJR. Patients who received PNB had improved pain control, less cardiovascular instability during surgery, and less nausea and vomiting compared with those who had epidurals or PCA. PNB also allowed better toleration of continuous passive motion with earlier mobilization and hospital discharge. 11 Hebl and colleagues²² and Horlocker and colleagues²³ described a 'total joint regional anaesthesia clinical pathway' used at their institution which emphasizes continuous lumbar plexus block along with single-shot sciatic block as part of a multimodal analgesia regimen after TKJR and have reported improved outcome compared with matched historical controls. Interestingly, PNB may also improve the quality of analgesia when added to epidural blockade after TKJR.⁵³ 55

PNB of the lower limb

The femoral nerve along with contributions from the sciatic and obturator nerves at the posterior and medial aspects, respectively, provide sensory innervation of the knee and these are the three terminal nerves are targeted by PNB techniques for major knee surgery.

With the exception of one, all the studies included in our meta-analysis used an anterior infra-inguinal femoral nerve block which is easily performed with the patient in the supine position. This approach is less invasive than lumbar plexus block and is correspondingly associated with fewer serious complications. 4 18 45 Although the obturator nerve is far more consistently involved with lumbar plexus blocks than with either infra-inguinal technique, 18 it is not clear that obturator block translates into improved patient recovery after TKJR. 25 28 31 MRI studies suggest that the local anaesthetic solution spreads predominantly caudally after '3-in-1' block using a peripheral nerve stimulator, blocking the femoral and lateral femoral cutaneous nerves and the anterior branch of the obturator nerve, 30 although there is some evidence that the latter nerves are more reliably blocked with the more lateral, blind, 'double-pop' fascia iliaca block.³³

Review: Knee Surgery meta-analysis Comparison: 04 VAS 24–28 h Outcome: 01 VAS 24–28 h

Study or subcategory	N	PNB mean (sd)	N	Epidural mean (sd)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
Aldahish and colleagues Barrington and colleagues Capdevilla and colleagues Long and colleagues Singelyn and colleagues Zaric and colleagues	30 53 20 35 15 26	4.60 (2.30) 0.80 (0.83) 2.20 (1.18) 3.60 (1.50) 2.50 (1.20) 3.70 (2.33)	30 55 17 35 15 23	4.80 (2.40) 1.10 (1.90) 3.00 (1.15) 3.70 (1.40) 3.00 (2.50) 4.00 (2.50)	*	7.86 36.80 19.63 24.05 5.64 6.02	-0.20 (-0.39, 0.99) -0.30 (-0.85, 0.25) -0.80 (-1.55, -0.05) -1.10 (-0.78, 0.58) -0.50 (-1.90, 0.90) -0.30 (-1.66, 1.06)
Total (95% CI) Test for heterogeneity: X ² =2.1 Test for overall effect: Z=2.08		2=0.84), <i>P</i> =0%	175		-10 -5 0 5	100.00	-0.35 (-0.69, -0.02)
					Favours PNB Favours Epi	idural	

Fig 3 A meta-analysis of trials comparing PNB with epidural on visual analogue pain scores at 24-48 h.

Of the three studies which used sciatic blockade, two performed the blocks using the classical Labat approach and one with an anterior approach. Since the earlier publication of one small negative study,³ trials have shown that the addition of sciatic nerve block improves the quality of analgesia by reducing posterior knee and calf pain after major knee surgery, corresponding to the area innervated by the nerve. ^{7 13} 15 34 52 However, our analysis of patients without sciatic block failed to demonstrate inferior analgesia in this subgroup between 0 and 24 h after operation.

Neurological complications

It was not a goal of our systematic review to calculate an incidence figure for serious neurological complications as much larger numbers of patients are needed to contribute meaningful data. However, we did identify one case of a unilateral foot drop with sphincteric disturbance in approximately 250 patients who received an epidural. No neurological complications were reported in the PNB group.

Spinal haematoma after epidural blockade is more likely when patient 'red flags' are present (e.g. older age, degenerative spinal disorders, anticoagulation) or after traumatic insertion,⁵¹ a common scenario in older patients undergoing lower limb orthopaedic surgery. The incidence

of intravertebral haematoma in female patients undergoing TKJR with an epidural in Sweden during the 1990s was 1:3600.³² This is in close agreement with the estimated reporting rate in the USA during the mid-1990s, 41 despite the utilization of lower routine doses of anticoagulation.⁴⁹ Hypotension associated with epidural analgesia may contribute to end organ ischaemia or infarction in this group of patients if left untreated.³⁵ Because of the problems which may occur, epidural analgesia is not appropriate in the ward setting in every institution. If general anaesthesia is not desirable, single-shot spinal anaesthesia can be combined with PNB44 and should be considered as the incidence of neuraxial complications is lower using this technique than with an epidural in this subpopulation.³²

A major benefit of PNB is that the neurological complications are usually less disastrous than those associated with neuraxial blockade. In the most comprehensive prospective study published to date, peripheral neuropathy occurred at a rate of 1:3763 femoral or sciatic block procedures (95% CI 0-8/10 000). Symptoms persisted after 6 months in more than half of patients who had a nerve injury, and the actual rate may be higher as many practitioners were regional anaesthesia enthusiasts (volunteer bias). A recent editorial estimated that the true rate of neuropathy attributable to PNB is probably around

Knee Surgery meta-analysis Review: Comparison: 07 Hypotension Outcome: 07 Hypotension

Study	PNB	Epidural	OR (fixed)	Weight	OR (fixed)
or subcategory	n/N	n/N	95% CI	%	95% CI
Aldahish and colleagues	3/30	18/30		63.17	0.07 (0.02, 0.30)
Barrington and colleagues	1/53	1/55		3.76	1.04 (0.06, 17.04)
Capdevilla and colleagues	10/20	13/17		27.40	0.31 (0.07, 1.28)
Singelyn and colleagues	0/15	1/15		5.67	0.31 (0.01, 8.28)
Total (95% CI) Total events: 14 (PNB), 33 (epidural) Test for heterogeneity: X ² =3.69, df=3 Test for overall effect: Z=3.79 (P=0.00	118 (<i>P</i> =0.30), <i>P</i> =18.7% 01)	117	•	100.00	0.19 (0.08, 0.45)

Fig 4 A meta-analysis of trials comparing PNB with epidural on rate of hypotension after surgery expressed as odds ratio (OR).

Review: Knee Surgery meta-analysis Comparison: 05 Nausea and vomiting Outcome: 01 Nausea or vomiting

Study or subcategory	PNB n/N	Epidural n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
Adams and colleagues Aldahish and colleagues Capdevilla and colleagues Singelyn and colleagues Zaric and colleagues	3/21 0/30 0/20 5/15 2/26	5/21 1/30 — 1/17 — 4/15 3/23		33.11 11.40 12.18 20.60 22.70	0.53 (0.11, 2.59) 0.32 (0.01, 8.24) 0.27 (0.01, 7.03) 1.38 (0.29, 6.60) 0.56 (0.08, 3.66)
Total (95% CI) Total events: 10 (PNB), 14 (epidural) Test for heterogeneity: X^2 =1.42, df=4 (P =(Test for overall effect: Z =0.96 (P =0.34)	112 0.84), <i>P</i> =0%	106	•	100.00	0.66 (0.28, 1.55)
		0.0	01 0.1 1 10 Favours PNB Favours E	100 pidural	

Fig 5 A meta-analysis of trials comparing PNB with epidural on rate of postoperative nausea and vomiting after surgery expressed as odds ratio (OR).

1:500-1:1000.43 Two series of continuous PNB techniques including 211¹⁴ and 777¹⁰ femoral catheters have been published which reported success rates and technical, infectious, and neurological complications. The rate of neuropraxia after femoral catheter techniques was very similar in these studies: 1/211¹⁴ and 3/683.¹⁰ Although neuropraxia occurred frequently, most of these injuries were patchy sensory deficits and all except one had resolved within a year. In these two studies, 28.6-56% of femoral catheters had bacterial colonization at >48. There were no clinically significant local or surgical infectious complication in the first study, ¹⁴ but in the second study, a psoas abscess was diagnosed in a diabetic woman after a femoral catheter. 10 Placement was difficult in 9.5% of 211 catheters in the first study¹⁴ (with vascular puncture occurring in 5.6%) whereas in the other study, ¹⁰ catheter-related problems (e.g. kinking, leakage, blockage, and dislodgement) occurred in 17.9% of 1416 patients. Salinas and colleagues⁴⁰ reported better analgesia but a higher rate of nerve injury and infectious complications and no improvement in overall outcome with continuous catheters compared with single-shot femoral blocks. Unfortunately, we were unable to compare catheter vs single-shot techniques; therefore, it is not possible to state which is preferable.

The overall effect of quadriceps weakness associated with femoral nerve block on the operative side on recovery and patient satisfaction is unclear from the studies included in this systematic review. One group reported better mobilization with epidural analgesia, 27 and in our own experience some patients find the leg weakness from femoral block unsettling. However, others comment that reduction of pain from significant quadriceps spasm which occurs after TKJR8 is central to the efficacy of PNB6 and improves toleration of continuous passive motion.⁹ Rehabilitation indices were similar in both groups, although patient satisfaction appears to be higher with PNB. Ropivacaine appears attractive as an agent because of reduced cardiotoxicity and motor block compared with bupivacaine. The optimal concentration appears to be around 0.2-0.25%. 20 36

Success rates

The estimated success rate of 97% for PNB among the four studies⁶ 17 46 54 included in this systematic review which reported block failures may reflect the expertise of the investigators and may not be reproducible if used by practitioners with less experience. Although this success rate is in close agreement with that reported by Capdevila and colleagues¹⁰ in a series of 1416 continuous PNB catheters, it is at the upper end of previously published success rates for femoral (86-100%) and sciatic block (94-100%). 18 Similarly, although the mean insertion time for combined blocks of 12.5 min reported by Davies and colleagues¹⁷ is in close agreement with the insertion time reported by Hebl's group, 22 this may not be generally reproducible. Identification of the femoral and sciatic nerves using ultrasound guidance is relatively easy and rapid onset of block with success rates near 100% have been reported in experienced hands.²⁹

Conclusion

A PNB technique which includes femoral block represents the best balance between analgesia and side-effects as a choice of postoperative analgesic technique for major knee surgery such as TKJR, especially as the risk of injury to the neuraxis is negligible. Data are urgently required comparing efficacy and morbidity of single-shot blocks compared with perineural catheter techniques, preferably with a large randomized controlled trial so that a meaningful comparison of less common complications can be undertaken. More work is also needed to prove that newer techniques offer important advantages such as faster return to normal daily activities, decreased morbidity, and improved patient satisfaction. As with all anaesthetic procedures, complication rates reflect in part the skills and judgement of the operator and the risk of system error. It is important to consider risk-benefit on a patient-by-patient basis and tailor the analgesic technique accordingly. Overall, however, we believe that there is now sufficient evidence

that lumbar epidural analgesia should not be used routinely and that PNB is appropriate for multimodal analgesia care after routine major knee surgery.

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