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ORIGINAL ARTICLE

Postoperative outcome in Chinese patients having primary total knee arthroplasty under general anaesthesia/intravenous patient-controlled analgesia compared to spinal-epidural anaesthesia/analgesia

比較華裔病人在全麻／病人靜脈自控鎮痛或腰硬膜外麻醉／鎮痛的情況下接受全膝關節置換手術後的效果

Objective. To compare postoperative outcomes in patients having primary total knee arthroplasty receiving general or regional anaesthesia.

Design. Randomised prospective study.

Setting. Regional hospital, Hong Kong.

Patients. Patients having primary total knee replacement were randomised to either general anaesthesia followed by postoperative intravenous patient-controlled analgesia with morphine, or combined spinal-epidural anaesthesia followed by postoperative epidural infusion of bupivacaine 0.1% with fentanyl 2 µg/mL.

Main outcome measures. Visual analogue scale pain scores, perioperative blood loss, time to first meal and ambulation, and prevalence of postoperative complications.

Results. Sixty consecutive patients were enrolled in this study. Postoperative median pain scores were consistently lower at 1 (P<0.0001), 6 (P=0.08), 12 (P=0.003), 24 (P=0.14), and 48 hours (P=0.007) in those given regional anaesthesia. Although there was a trend towards fewer complications in the latter group, there were no statistically significant differences between the two groups with respect to the incidence of postoperative blood loss, haemodynamic instability, pruritus, nausea, vomiting, urinary retention, or other surgical/medical complications. Postoperatively, patients given regional anaesthesia also resumed meals earlier (P<0.0001), and showed a trend towards earlier ambulation and hospital discharge.

Conclusion. Chinese patients undergoing total knee arthroplasty with regional anaesthesia/regionally delivered analgesia enjoyed better postoperative pain relief and resumed meals earlier than those receiving general anaesthesia/intravenous patient-controlled analgesia. The former also showed trends towards less adverse effects, postoperative complications, earlier ambulation, and earlier hospital discharge.

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目的：比較在全身麻醉或局部麻醉的情況下接受全膝關節置換手術後的效果。

設計：隨機的前瞻性研究。

安排：分區醫院，香港。

患者：隨機安排需要進行全膝關節置換手術的病人分別接受兩種不同的麻醉／鎮痛。第一組全麻，術後採用嗎啡靜脈輸注病人自控鎮痛；第二組腰硬膜外聯合麻醉，術後採用布比卡因（0.1%）及芬太尼（2 µg/mL）硬膜外輸注鎮痛。

主要結果測量：採用視覺模擬量表評量疼痛程度、圍手術期失血、術後首次進食和步行，以及術後出現併發症的普遍程度。

結果：連續60位病人參與是次研究。接受局部麻醉病人的術後疼痛中位數，在術後1小時（P<0.0001）、6小時（P=0.08）、12小時（P=0.003）、24小時（P=0.14）、48小時（P=0.007）持續低下。雖然第二組傾向較少併發症，兩組病

人在圍手術期失血、血流動力學不穩定、瘙癢、噁心嘔吐、尿瀦留及其他內外科併發症方面並無統計上的明顯差異。此外，他們在術後較快能首次進食（P<0.0001），也能較早步行和出院。

結論：對接受全膝關節置換手術的華裔病人來說，局部麻醉／硬膜外鎮痛比全身麻醉／病人自控鎮痛能減少術後鎮痛、更快於術後進食，不良後果和術後併發症都較少，可以更早步行和出院。

Introduction

Combined spinal-epidural anaesthesia offers rapid induction of surgical anaesthesia and allows prolongation of neuro-axial blockade through the epidural catheter. The latter catheter has been used to administer medications for postoperative epidural analgesia to provide pain relief after total knee arthroplasty (TKA).[1]

Epidural anaesthesia and analgesia after TKA is claimed to decrease the incidence of proximal deep vein thrombosis, improve postoperative pain relief, allow early joint mobilisation and rehabilitation, and reduce the length of hospital stay.[2-6] However, other studies have reported contradictory results. Moiniche et al[7] have shown that there may not be any advantage from regional techniques. Moreover, spinal and epidural anaesthesia and analgesia may cause hypotension, motor blockade, urinary retention, and pruritus.[6,8] Complications from the epidural technique such as accidental dural puncture and neurological injury are also possible. There is also the possibility that the antithrombotic mechanism of the regional technique may lead to greater perioperative blood loss.[9,10] Adverse effects and complications resulting from spinal-epidural techniques may therefore outweigh the advantages, delaying hospital discharge, and increasing patient discomfort. It is therefore important to justify the benefit of spinal-epidural techniques in this group of patients.

This study in Chinese patients undergoing TKA therefore set out to compare such outcomes in patients undergoing general anaesthesia followed by postoperative intravenous patient-controlled analgesia (GA/PCA) versus combined spinal-epidural anaesthesia followed by postoperative epidural infusion analgesia (CSE/EA).

Methods

Following approval by the local institutional Research Ethics Committee, the entire study was conducted according to recommendations in the Declaration of Helsinki. Written informed consent was obtained from all patients, who were instructed that participation in the study did not in any way alter other aspects of their perioperative care and treatment, and that they were free to withdraw from it at any time.

Power analysis was performed using data from study of Singelyn et al[4] with a visual analogue scale (VAS) pain score of mean (standard deviation) of 45 (18) for postoperative PCA analgesia. A sample of 30 patients were required in each group in order to detect a 30% change in postoperative pain relief for a power=0.8 and an α=0.05. Consecutive patients scheduled for elective primary TKA were invited to participate in the study. Exclusion criteria were: bilateral knee arthroplasty, revision knee arthroplasty, patient refusal, abnormal coagulation profile, systemic or local infection, allergy to study drugs, abnormal mental status, and physical disability to operate the PCA device. After the preoperative anaesthetic assessment and obtaining of informed consent, each patient was randomised to either GA/PCA with morphine, or CSE/EA. Randomisation was according to a predetermined sequence revealed to the designated attending anaesthesiologist for that patient, though he or she was not involved in any outcome assessments.

All patients in group GA/PCA received fentanyl 2 µg/kg, thiopentone 4 mg/kg, and cisatracurium 0.15 mg/kg at the induction of general anaesthesia, and maintained on isoflurane in oxygen-nitrous oxide mixture. Morphine was given intravenously at skin incision (0.1 mg/kg) and as indicated clinically during the intra-operative period. At the end of surgery, an intravenous (IV) PCA (Graesby 3300; Graesby Medical Ltd, Herts, UK) with morphine was provided to the patient in the recovery room. The PCA programme was set at 1 mg per bolus with a 6-minute lockout interval.

All patients in CSE/EA group received combined spinal-epidural anaesthesia using a needle through needle technique (Portex Combined Spinal/Epidural MiniPak; SIMS Portex, Kent, UK). The epidural space was first located at L3-5 level using a 16G Tuohy needle using a loss of resistance technique, followed by the administration of spinal anaesthesia with 2.6 mL 0.5% plain bupivacaine through a 27G pencil-point needle. The epidural catheter was then inserted via the Tuohy needle after the withdrawal of the spinal needle. Four centimetres of catheter was left in the epidural space. The catheter was connected to a bacteria filter primed with normal saline and then flushed with 0.5 mL of saline. Epidural analgesia with a continuous infusion of bupivacaine 0.1% and fentanyl 2 µg/mL was started just after application of cement and continued into the postoperative period. Where the epidural insertion failed, the patient was given the choice of spinal or general anaesthesia followed by postoperative IV PCA and excluded from the study.

Both the IV PCA and epidural infusion were continued for at least 48 hours and then terminated as clinically indicated. Pain was measured by the VAS (11 points from 0-100). As the wounds were heavily bandaged and the patients immobilised for the first 48 hours, only static

Table 1. Definition of postoperative complications

Complications	Definitions
Arrhythmia	Electrocardiographic (ECG) changes 'requiring' treatment
Myocardial ischaemia	ECG changes and 'requiring' treatment
Myocardial infarction	ECG changes and 'requiring' treatment
Bronchospasm	Clinical wheeze on auscultation or grossly audible wheeze 'requiring' treatment
Collapse of lung	Chest X-ray (CXR) changes
Pneumonia	CXR changes or positive sputum culture or both, 'requiring' antibiotic treatment
Pulmonary embolism	Ventilation-perfusion scan/ echocardiogram/pulmonary arteriogram abnormalities
Cerebrovascular accident	Clinical neurological deficit
Deep vein thrombosis (DVT)	Clinical diagnosis of DVT with or without confirmation by venogram or Doppler ultrasound
Metabolic disturbances	Arterial blood pH <7.3 and base excess <5 mEq/L or glucose level out of the normal range (3.3-6.2 mmol/L)
Septicaemia	Positive blood culture
Wound infection	Positive wound culture

Table 2. Demographic and surgical details*

	GA/PCA group, n=30	CSE/EA group, n=30
Median age (IQR[†]) [years]	69 (62.5-74.0)	65 (61.7-68.2)
ASA[‡] classification		
1	21 (70%)	22 (73%)
2	9 (30%)	6 (20%)
3	0	2 (7%)
No. of patients receiving various prosthesis		
IB2 (Insall/Burstein II)	11 (37%)	8 (27%)
SAL (Self Aligning)	4 (13%)	6 (20%)
CCK (Constrained Condylar Knee)	1 (3%)	3 (10%)
PFC (Press Fit Condylar)	14 (47%)	13 (43%)
Median duration of surgery (IQR) [minutes]	146 (130-163.7)	135 (120-160)
Median intra-operative surgical bleeding (IQR) [mL]	200 (100-212.5)	200 (5-300)

* GA/PCA denotes general anaesthesia followed by postoperative intravenous patient-controlled analgesia, and CSE/EA combined spinal-epidural anaesthesia followed by postoperative epidural infusion analgesia
† IQR denotes interquartile range
‡ ASA denotes American Society of Anesthesiologists

pain scores were taken. All patients who did not receive adequate analgesia using the study methods of pain relief had the PCA programme adjusted to their requirements or had the epidural converted to IV PCA as appropriate. Oral paracetamol 1 g every 6 hours was prescribed to all patients from postoperative day 1 to 3, unless contraindicated. No rescue analgesia was to be used in either group. Metoclopramide 10 mg IV/intramuscular (IM) every 6 hours and chlorpheniramine 5 mg IM every 8 hours were allowed as required to combat nausea and vomiting, and pruritus respectively.

Blinding during postoperative outcome assessment was not possible because the anaesthesia/analgesia modality together with their effects, and the mechanical mode of delivery of postoperative analgesia were essentially different. However, the process of data analysis was blinded as both groups were coded during data entry.

All TKA operations were performed by the same team of surgeons. A urinary catheter was not inserted routinely. A redivac drain was left in-situ at the wound at the end of the operation for 2 to 3 days. All patients received postoperative prophylactic low-molecular-weight heparin for 1 week. Both patient groups also participated in an identical physiotherapy programme. On postoperative day 2 continuous passive motion machines were applied to both groups of patients. The patient was discharged to a rehabilitation centre if he/she was medically stable, had no major surgical complication, and able to achieve an adequate degree of mobility (ie able to transfer in/out of bed with minimal help and walk with aids).

Data collection and statistical analysis
Patients' demographic data, the duration of the operation, and the amount of intra-operative blood loss were recorded.

Subjects were followed up postoperatively until discharge from hospital. In the postoperative period, the following parameters were assessed at 1, 8, 12, 24, and 48 hours: blood loss, pain, nausea and vomiting, pruritus, urinary retention requiring catheterization, blood pressure, pulse rate, and pulse oximetry readings. Hypotension and hypertension were defined as blood pressures less than and greater than 20% of the baseline value respectively. Tachycardia was defined as a heart rate of more than 100 beats/min and oxygen desaturation as a pulse oximetry reading of less than 90% for longer than 1 minute. The time to the first drink and meal, the day when the patient was first able to walk a standardised distance (10 steps), and the time to discharge from hospital were recorded. The incidence of complications such as deep vein thrombosis, any cardiac event, and the presence of infective complications were recorded. All complications were defined according to the criteria in Table 1 and recorded till discharge from the hospital.

Non-parametric data were analysed using the Mann Whitney U test and categorical data with Chi squared test. A P value of less than 0.05 was considered statistically significant. Bonferroni correction was utilised in the VAS pain score analysis to address the issue of multiplicity with the statistical significance set at P<0.01. The VAS pain score results were analysed according to the intention-to-treat principle.

Results

A total of 60 patients were recruited over a period of 8 months. Their demographic and surgical data are summarised in Table 2. Figure 1 shows the randomisation and analysis process. Two patients in CSE/EA group were converted to IV PCA for pain relief because of dislodgement and occlusion of the epidural catheter,
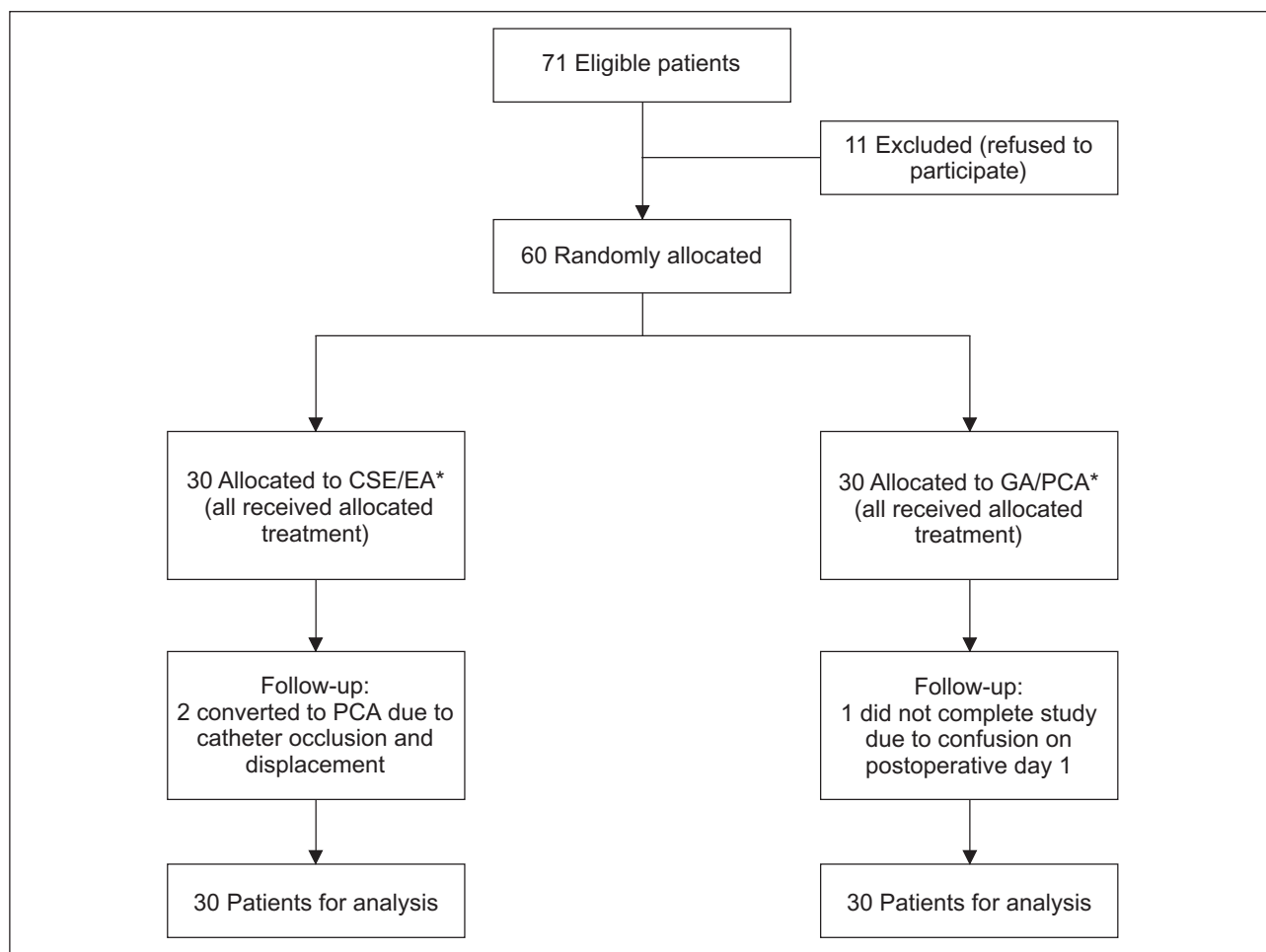
* CSE/EA denotes combined spinal-epidural anaesthesia followed by postoperative epidural infusion analgesia, and GA/PCA general anaesthesia followed by postoperative intravenous patient-controlled analgesia

Fig 1. Flow diagram of patient participation and intention-to-treat analysis

respectively. One patient in GA/PCA did not complete the study because of confusion on the first postoperative day.

The CSE/EA group had consistently lower corresponding median postoperative VAS pain scores than the GA/PCA group at all postoperative pain observations (Fig 2). The findings were similar even if the abovementioned three patients (two in CSE/EA and one in GA/PCA) were excluded from the analysis; differences at postoperative time points 1, 12, and 48 hours attained statistical significance ($P<0.01$).

During the first 48 postoperative hours, corresponding incidences of nausea, vomiting, urinary retention, hypotension, tachycardia, and desaturation were higher in the GA/PCA group than in the CSE/EA group, though they did not reach statistical significance. Pruritus was more common in the CSE/EA group (Table 3).

The CSE/EA group resumed meals earlier ($P<0.0001$); within 24 hours post-surgery (Table 4). There was no difference between the two groups in terms of other postoperative outcomes. Two patients developed
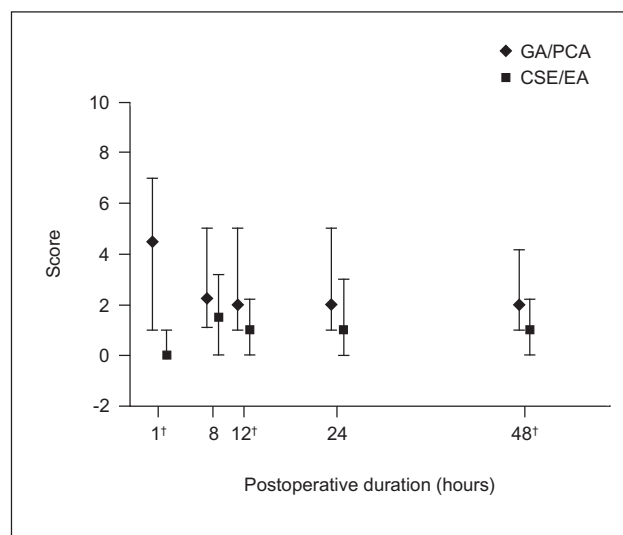
* Median with IQR (error bars) are shown; GA/PCA denotes general anaesthesia followed by postoperative intravenous patient-controlled analgesia, and CSE/EA combined spinal-epidural anaesthesia followed by postoperative epidural infusion analgesia

† $P<0.05$

Fig 2. Visual analogue scale (VAS) pain score*

Table 3. Postoperative complications within 48 hours of surgery*

	GA/PCA group, n=30	CSE/EA group, n=30	P value
Nausea	12 (40%)	9 (30%)	0.42
Vomiting	10 (33%)	7 (23%)	0.39
Itchiness	3 (10%)	6 (20%)	0.28
Urinary retention	13 (43%)	8 (27%)	0.18
Hypotension	19 (63%)	16 (53%)	0.43
Tachycardia	2 (7%)	0	0.15
Oxygen desaturation	2 (7%)	1 (3%)	0.55

* GA/PCA denotes general anaesthesia followed by postoperative intravenous patient-controlled analgesia, and CSE/EA combined spinal-epidural anaesthesia followed by postoperative epidural infusion analgesia

Table 4. Postoperative outcomes*

	GA/PCA group, n=30	CSE/EA group, n=30	P value
Mean (SD) blood loss in first 48 hours (mL)	400 (197.5-530)	385 (275-560)	0.56
No. of days after surgery to first drink[†]	0 (0-0.2)	0 (0-0)	0.17
No. of days after surgery to first meal[†]	1 (0-1)	0 (0-0)	<0.0001
No. of days after surgery to first 10 steps[†]	7 (5-7)	6 (4-7)	0.06
No. of days of acute pain service[†]	3 (3-5)	4 (3-4)	0.83
No. of days of hospital stay[†]	9 (7-10)	7.5 (6-11)	0.32
Mean (SD) No. of postoperative surgical/medical complications	4 (13.3)	2 (6.67)	0.503

* GA/PCA denotes general anaesthesia followed by postoperative intravenous patient-controlled analgesia, and CSE/EA combined spinal-epidural anaesthesia followed by postoperative epidural infusion analgesia
[†] Values are shown as median (interquartile range)

postoperative pneumonia in the GA/PCA group. In the CSE/EA group, a diabetic patient experienced difficult blood sugar control. Surgical complications occurred in two patients (wound infection and swelling) in the GA/PCA group and in one (wound infection) in the CSE/EA group. All three patients were treated conservatively (no surgical intervention). There were no recorded cardiac events or episodes of deep vein thrombosis. The median duration of hospital stay in the GA/PCA and CSE/EA groups was 9 (IQR, 7-10) and 7.5 (IQR, 6-11) days, respectively (P=0.32).

Discussion

Total knee arthroplasty gives rise to severe postoperative pain. Intravenous patient-controlled analgesia has been shown to be effective in relieving such pain.[11,12] However, the side-effects of IV morphine may preclude its effective use. Combined spinal-epidural anaesthesia and analgesia provide effective and continuous pain relief throughout the perioperative period. Our findings also reflected the effectiveness of epidural analgesia, in that during the first 48 hours the VAS scores at all measurement times were lower in the CSE/EA than GA/PCA group. Singelyn et al[4] had previously showed similar results with epidural analgesia during the immediate postoperative period. Although only static pain scores were compared in this study, our findings are nevertheless informative as tight bandaging can cause considerable rest pain.

Side-effects such as hypotension may occur with epidural infusion of local anaesthetic due to sympathetic blockade and relative hypovolaemia secondary to blood loss or inadequate fluid replacement. Indeed, Capdevila et al[3] reported that hypotension occurred significantly more often in patients receiving GA/epidural analgesia than GA/PCA, though in our study there was no difference in the incidence of postoperative hypotension between our two groups. In fact, there was a trend towards a slightly higher incidence of hypotension in our GA/PCA group. As postoperative blood loss in the two groups was similar, intra-operative IV fluid preloading in the regional technique group may have had a protective effect against

postoperative hypotension. However, this explanation may be speculative, as the extent of intra-operative fluid intake was not documented.

Epidural anaesthesia has been reported to reduce blood loss associated with major joint arthroplasty,[13,14] but other studies refute this finding.[5,15] The anti-thrombotic effect of epidural anaesthesia may lead to more bleeding by increasing the blood flow to the lower limb and inhibiting platelet aggregation.[9,10] On the other hand, in clinical settings, epidural anaesthesia does not appear to affect normal platelet aggregation and the coagulation process.[16] Early mobilisation due to superior analgesia has also been implicated as a cause of greater blood loss in epidural analgesia.[6] This phenomenon may be due to earlier mobilisation leading to decreased formation of thrombosed intra-articular haematomas, and the fact that uncongealed blood is more amenable to removal by suction drainage. In this study, the timing of mobilisation did not differ in either group as it was standardised; all patients were attached to continuous passive motion machines on the second postoperative day. We found the blood loss during the first postoperative 48 hours was actually slightly lower in the CSE/EA group, though the difference did not reach statistical significance. Thus, epidural anaesthesia and analgesia did not cause more postoperative bleeding in TKA when compared to GA/PCA.

With the exception of pruritus, all reported side-effects and complications were more common in the GA/PCA group, though none of the differences attained statistical significance. Whilst it is generally assumed that regional anaesthesia causes less postoperative nausea and vomiting

(PONV) than general anaesthesia, these symptoms are nevertheless quite common.[17,18] In our study, the incidence of nausea and vomiting were 30% and 23% respectively in the CSE/EA group and 40% and 33% respectively in the GA/PCA group. We therefore recommend that anti-emetics should be prescribed to all patients during epidural analgesia or IV PCA, at least on an on-demand basis. Pruritus is another common complaint after IV or epidural opioids. The higher incidence of pruritus we encountered in the CSE/EA group was consistent with the results of a recent meta-analysis.[18] However, the intensity of pruritus and PONV were mild and all those affected were able to tolerate these symptoms without stopping their epidural infusion or PCA. Though not statistically significant, we also encountered a higher incidence of urinary retention in the GA/PCA group, possibly related to the known actions of morphine, on detrusor muscle activity and the tone of urinary sphincter.

Two patients in the GA/PCA group (but none in the CSE/EA group) suffered from pneumonia, which is consistent with better preserved respiratory function with the latter type of anaesthesia/analgesia.[19] Our sample size was calculated based on the VAS pain scores and therefore could not be expected to detect differences in the rate of relatively uncommon postoperative complications, such as acute coronary syndrome and pulmonary embolism and pneumonia.

Fast-track surgery is a means of maximising hospital resources. Accordingly, epidural analgesia can hasten rehabilitation and shorten the hospital stay for TKA patients.[3,5] Thus, the time to resume meals was significantly shorter in the CSE/EA than GA/PCA group. This is important, as early feeding has been reported to speed recovery.[20]

There were no statistically significant differences between the two groups with respect to the results of our functional performance indicators ('walk-ten-steps' and the length of stay in hospital tests). Nevertheless the trends were more favourable for CSE/EA group. Arguably, the 'walk-ten-step' test by itself may not be a very sensitive measure of rehabilitation, but combining it with the range of knee joint motion indicators could be more useful.[3,5] Limitations due to our small sample size may also compound these deficiencies. Although we did not show a statistically significant difference in the length of hospital stay between the two groups, the fact that the CSE/EA group stayed for about 1.5 days less, could translate into a significant financial saving.

In conclusion, we found that CSE/EA provided superior postoperative pain relief and achieved a shorter time to the first meal compared to GA/PCA. Although there were no statistically significant differences with respect to the incidence of most side-effects and complications in the two groups, for the majority of such outcomes

there was a trend in favour of the former.

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