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Efficacy and Safety of 3 Different Anesthesia Techniques Used in Total Hip Arthroplasty

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Background: This study compared the efficacy and safety of 3 different anesthesia techniques used in total hip arthroplasty (THA).

Material/Methods: We allocated 198 patients preparing to undertake THA into 3 groups: general anesthesia group (GA group, n=66), caudal epidural anesthesia group (CEA group, n=66), and spinal-epidural anesthesia group (SEA group, n=66). We compared postoperative adverse effects occurring in patients of the 3 anesthesia groups. The Visual Analog Scale (VAS) score, Minimum Mental State Examination (MMSE) score, and β-amyloid (Aβ) expression were calculated to determine the effects of different anesthesia on the postoperative pain and cognitive dysfunction of patients.

Results: The CEA and SEA groups had lower rates of perioperative adverse effects than in the GA group. Patients in the GA group required significantly higher administration of analgesics after the surgery than those in CEA and SEA groups. Higher Aβ expression levels and VAS scores, as well as lower MMSE scores, were also seen in the GA group compared with the other 2 groups.

Conclusions: CEA and SEA were more effective than GA in THA, and CEA seemed to be a better anesthesia technique than SEA.

MeSH Keywords: **Anesthesia, Epidural • Anesthesia, General • Anesthesia, Spinal • Arthroplasty, Replacement, Hip**

Abbreviations: **THA** – total hip arthroplasty; **GA** – general anesthesia; **CEA** – caudal epidural anesthesia; **SEA** – spinal-epidural anesthesia; **POCD** – postoperative cognitive dysfunction; **MMSE** – Mini-Mental State Examination; **VAS** – Visual Analog Scale; **ELISA** – enzyme-linked immunosorbent assay; **Aβ** – β-amyloid; **RCTs** – Randomized Controlled Trial

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2784 6 — 43

Background

Total hip arthroplasty (THA) has become one of the most common surgical operations since 1960 and is regarded as a revolutionary technique significantly improving the outlook for patients with degenerative osteoarthritis, rheumatoid arthritis, proximal femoral fractures, or other damaged hip joints [1]. This technique replaces the dysfunctional joint surface with an artificial prosthesis so that severe pain can be alleviated and normal joint functions can be restored [2,3]. However, THA is usually associated with severe pain during the perioperative period, so it may not be ideal for older patients who often have higher risk of hypertension, renal dysfunction, or ischemic heart disease. As a result, researchers have begun to pursue an effective anesthesia technique to enhance the effectiveness of THA [4–6]. Various anaesthetic and analgesic approaches have been used in conjunction with THA; classical approaches include general anesthesia (GA), caudal epidural anesthesia (CEA), and spinal-epidural anesthesia (SEA) [7–10]. Many studies have suggested that neuraxial anesthesia (epidural or spinal anesthesia) is effective for improving perioperative outcomes, particularly among orthopedic patients [11]. GA has been considered the "gold standard" for the majority of hip procedures and is able to induce fast and thorough anesthesia effects in patients preparing to undergo surgeries [12,13]. However, more recently, regional anesthesia has attracted attention, as it has tremendous potential advantages over GA, allowing for administration to the affected area specifically. Moreover, regional anesthesia is associated with a reduced risk of severe complications such as deep venous thrombosis and surgical site infection [9,12,14]. The implementation of regional analgesia can be achieved through epidural, spinal, or combined approaches [15]. If regional analgesia is implemented in an epidural approach, pain-relieving drugs are injected into the epidural space through a catheter [16]. For spinal anesthesia, the drugs are injected directly into the cerebrospinal fluid around the nerves, taking less time to achieve the corresponding anesthesia effects [17]. There is also a combined technique that has been introduced into clinical practice, which uses a single spinal injection, which is further assisted by an epidural catheter so that pain relief can be achieved continuously [15,18,19]. Several reports have indicated that spinal-epidural anesthesia has superior effectiveness, and patients treated with this approach have lower risk of adverse outcomes compared with conventional regional analgesia techniques [15,20–22]. However, a comprehensive comparison of these anesthesia techniques for THA has not been carried out to date.

Multiple measurements have been established for assessing the effectiveness and safety of anesthesia techniques, including onset time of anesthesia, duration of anesthesia efficacy, analgesic dosage required, postoperative pain scores-Visual Analog Scale (VAS), length of hospital stay, and rate of adverse effects [4,5,23]. Apart from these, postoperative cognitive dysfunction (POCD) following anesthesia in conjunction with THA, a prevailing complication that may affect cognitive functions and trigger short-term memory loss [24–26], is also taken into consideration when assessing the efficacy of different anaesthetic methods.

The present study is the first to compare the effects of 3 anesthesia methods on perioperative outcomes during THA. Our results revealed that SEA and CEA were more appropriate than GA for patients undergoing THA. This research may provide clinicians with useful information when choosing the best anesthesia technique for patients undergoing THA.

Material and Methods

Patients

We enrolled a total of 198 patients (106 females and 92 males, with an average age of 67 years) preparing to undergo THA. Using a computer-generated permutation digits method, patients were randomly allocated into 3 groups: general anesthesia group (GA group, n=66), caudal epidural anesthesia group (CEA group, n=66), and spinal-epidural anesthesia (SEA group, n=66). All study procedures were agreed upon and approved by the Institutional Ethics Committee of Huadong Hospital Affiliated to Fudan University. Informed consent was obtained from patients prior to inclusion.

Inclusion and exclusion criteria

As recommended by the guidelines of the American Society of Anesthesiologists (ASA), patients with ASA I-III preparing to undergo arthroplasty between March 2013 and March 2015 were included. The enrolled patients had no history of nervous system or cardiac surgery, no history of mental disorder, no severely defective vision, and no neurological disorders.

We excluded all patients who refused to participate, as well as those with Mini-Mental State Examination (MMSE) score less than 23, with neurological disease or mental disorder, with long-term use of sedatives or anti-depressant, with history of alcohol consumption, with preoperative hypovolemia, with puncture site infection, with delirium or agitation, and those who could not be successfully anaesthetized within 15 min of drug injection.

Anesthesia and monitoring

Electrocardiogram (ECG), non-invasive arterial blood pressure, heart rate, and peripheral blood oxygen saturation (SpO_2) levels were all monitored while patients were in the operating theater.

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GA was induced by administration of Midazolam (0.1 mg/kg), propofol (1–1.5 mg/kg), fentanyl (2–4 µg/kg), and vecuronium bromide (0.1–0.15 mg/kg). The tidal volume was 8–10 mg/kg, and respiratory frequency was 10–12 times/min. The end-tidal CO_2 partial pressure was also maintained within the range of 32 and 38 mmHg. Maintenance of anesthesia was performed with 6–8 mg/kg propofol infusion.

The sacral hiatus of patients in the CEA group was inspected when the operation position was changed to lateral decubitus position. A 22-gauge needle (Terumo, Japan) was used to continuously inject the anaesthetic (0.5% plain bupivacaine) into the epidural space. Negative aspiration technique was used to prevent intravascular insertion and accidental intrathecal injection.

In a seated position, SEA was performed using a needle-through-needle technique at L1–2 or L3–4 intervertebral disc space using an 18-gauge Tuohy needle (Perifix, Germany). Skin infiltration was achieved with 1% lidocaine. The dural puncturing was performed using a 27-gauge pencil point spinal needle. Once the cerebrospinal fluid aspiration was achieved, 2 ml 0.5% hyperbaric bupivacaine was injected. We then performed epidural injection of 10 ml 0.25% plain bupivacaine, 1 ml clonidine (2 µg/kg), and 1 ml fentanyl (25 µg).

Determination of sensory and motor blockade

Sensory blockade was assessed every 2 min within 30 min of epidural injection using a pinprick test. When the sensory blockade reached the dermatome of T10, the patients were considered ready for surgery.

Motor blockade was assessed every 5 min within 30 min after epidural injection, using the modified Bromage score (BS) [27]. BS0 is defined as full hip flexion; BS1 is defined as impaired hip flexion; BS2 is impaired hip; BS3 is unable to flex hip, and so on to complete motor block. Recovery from motor block was defined as time from epidural injection to BS0.

Hypotension is a fall of mean arterial blood pressure from the pre-surgery level or a systolic blood pressure lower than 100 mmHg. Once hypotension occurred, patients were treated with 5 mg *inj*. ephedrine. Bradycardia is the decline of heart rate below 50 beats/min, and if this occurred, patients were treated with 0.5 mg *inj*. atropine.

Pain assessment and management

Intraoperative and postoperative pain was assessed using the Visual Analog Scale (VAS). VAS score ranges from 0 (no pain) to 10 (worst pain possible). VAS was measured every 15 min intraoperatively and every 3 h postoperatively for the first 12 h, then 12 h afterwards by an anesthesiologist who was unaware of the patient grouping. All patients received injected acetaminophen (15 mg/kg) before the completion of surgery and every 6 h afterwards. After surgery, to patients with VAS >4, fentanyl was administered at 50 µg increments, whereas those with VAS <4 were given acetaminophen infusion [28,29].

Postoperative complication and cognition assessment

Postoperative adverse effects were recorded, including pulmonary embolism, pneumonia, cardiac infarction, hypertension, renal failure, blood transfusion, and mechanical ventilation.

POCD was estimated by Mini-Mental State Examination (MMSE) score. MMSE incorporates 30 questions equalling 30 points. POCD was diagnosed if the MMSE score was lower than 23.

β-amyloid (Aβ) expression

Aβ expression was detected using enzyme-linked immunosorbent assay (ELISA). We collected 5 ml fasting venous blood samples from patients at 1 day before surgery (T1), 1 day after surgery (T2), and 5 days after surgery (T3).

Statistical analysis

All statistical analyses were performed using SPSS 18.0 software (Chicago, IL, USA). Data are presented in the form of mean ± standard deviation (SD). One-way analysis of variance (ANOVA) or Kruskal-Wallis test was used to analyze between-group comparisons, whereas the chi-square test was used for assessing the differences of categorical variables between groups. $P<0.05$ was set as the threshold for statistical significance.

Results

Clinical characteristics

The clinical characteristics of all patients were compared among the 3 anesthesia groups. No significant difference in clinical characteristics, including sex, age, weight, height, body mass index (BMI), ASA physical status, preexisting diseases, preoperative diagnosis, and contralateral hip limitation, was identified among the 3 groups (Table 1).

Perioperative outcomes

Intraoperative outcomes, including duration of surgery and anesthesia, time until maximal sensory blockade (S max), and motor blockade as well as the analgesic requirement after surgery, were compared among the 3 groups to determine their efficiency and efficacy in pain management (Table 2). CEA and

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Table 1. Characteristics of the study population.

Variable	GA (n=66)	CEA (n=66)	SEA (n=66)	*P*-value
Gender (F/M)	37/29	34/32	35/31	0.868
Age (years)	68±11	67±12	66±10	0.582
Weight (kg)	70±11	69±9	70±11	0.815
Height (cm)	163±8	165±9	166±9	0.132
BMI (kg/m^2)	23.2±3.3	23.4±3.9	23.0±2.7	0.800
ASA physical status				
ASA I	11	15	12	0.878
ASA II	53	49	51	
ASA III	2	2	1	
Preexisting diseases				
Hypertension	31	33	34	0.995
Coronary heart disease	11	12	10	
Diabetes mellitus	39	42	41	
Hyperlipidemia	32	34	29	
Cardiopathy	0	2	1	
Cerebrovascular disease	9	11	6	
Renal failure	0	0	0	
Liver failure	1	1	1	
Preoperative diagnosis				
Arthrosis	43	45	49	0.745
Rheumatoid arthritis	11	4	7	
Ankylosing spondylitis	9	10	6	
Avascular necrosis	3	7	4	
Limitation of the contralateral hip				
Yes	42	43	40	0.860
No	24	23	26	

Data are n or mean ±SD. GA – general anaesthesia; CEA – caudal epidural anaesthesia; SEA – spinal-epidural anaesthesia; F – female; M – male; BMI – body mass index; ASA – American Society of Anesthesiologists.

SEA both demonstrated significantly shorter duration of surgery, faster motor blockade, and shorter duration of anesthesia than in the GA group. CEA patients showed significantly shorter time to S max than GA. Although the SEA group showed significantly longer surgery and anesthesia duration than in the CEA, the 2 groups did not differ in time to motor blockade or analgesic requirement. Patients in the GA group exhibited significantly higher analgesic consumption than those in the CEA or SEA groups, while patients in the CEA group consumed significantly less analgesic than those in the SEA group.

Postoperative complication assessments

Postoperative adverse effects, including pulmonary embolism, pneumonia, cardiac infarction, hypertension, renal failure, blood transfusion, and mechanical ventilation, were identified and compared among treatment groups (Table 3). No significant differences were observed among the 3 groups.

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Table 2. Perioperative outcomes statistics.

Variable	GA (n=66)	CEA (n=66)	SEA (n=66)
Duration of surgery (min)	120.5±26.5	86.4±18.5*	100.5±22.5*#
Time to S max (min)	18.2±2.6	12.5±1.8*	15.4±2.2
Time to motor blockade (min)	23.3±6.4	14.0±3.2*	14.4±3.6*
Total duration of anesthesia (min)	207.5±16.2	56.3±13.3*	48.3±11.8*#
Analgesics requirement within 48 h after surgery (g)	5.2±2.2	2.6±0.9	3.5±1.2

Data are n or mean ±SD. GA – general anaesthesia; CEA – caudal epidural anaesthesia; SEA – spinal-epidural anaesthesia; S max – maximal sensory blockade. * $P<0.05$ versus GA group, # $P<0.05$ versus CEA group.

Table 3. Postoperative adverse effects statistics.

Complications	GA% (n)	CEA% (n)	SEA% (n)	*P* value
Pulmonary embolism	3.0 (2)	0.0 (0)	1.5 (1)	0.9257
Pneumonia	1.5 (1)	0.0 (0)	1.5 (1)	
Renal failure	1.5 (1)	0.0 (0)	0.0 (0)	
Cardiac infarction	3.0 (2)	1.5 (1)	3.0 (2)	
Blood transfusion	6.0 (4)	3.0 (2)	6.1 (4)	
Mechanical ventilation	3.0 (2)	1.5 (1)	0.0 (0)	

Data were presented as % (n). GA – general anaesthesia; CEA – caudal epidural anaesthesia; SEA – spinal-epidural anaesthesia.

Table 4. VAS scores of patients within 24 h after surgery.

Variable	GA (n=66)	CEA (n=66)	SEA (n=66)
3 h	5.13±1.67	1.92±0.78*	2.95±0.89*#
6 h	5.12±1.65	1.20±0.46*	2.75±0.88*#
9 h	4.91±1.28	1.13±0.21*	1.49±0.50*
12 h	3.86±1.32	1.16±0.28*	1.34±0.48*
24 h	4.38±1.40	1.69±0.56*	2.75±0.96*#

Data are n or mean ±SD. GA – general anaesthesia; CEA – caudal epidural anaesthesia; SEA – spinal-epidural anaesthesia; VAS – Visual Analog Scale. * $P<0.05$ versus GA group; # $P<0.05$ versus CEA group.

VAS score

VAS scores were calculated within 24 h after surgery to evaluate pain intensity experienced by patients. Patients in the GA group had significantly higher VAS scores than those in the CEA or SEA groups, while those in the SEA group exhibited remarkably higher VAS scores than those in the CEA group at 3 h, 6 h and 24 h after surgery (Table 4).

MMSE score

We calculated the MMSE scores at different time points (T1, T2, and T3). The MMSE score generally decreased from T1 to T2 and increased from T2 to T3. GA group patients had remarkably lower MMSE scores than in group CEA at T2 and T3. The MMSE score of the CEA group was significantly higher than that of the SEA group at T2 and T3, especially at T2 (Table 5).

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Table 5. MMSE scores of patients in three groups at three time points.

Variable	GA (n=66)	CEA (n=66)	SEA (n=66)
T1 (1 d before surgery)	26.72±1.62	26.84±1.98	26.55±1.89
T2 (1 d after surgery)	22.45±2.32	24.46±1.43*	22.48±1.84#
T3 (5 d after surgery)	24.19±2.25	25.69±2.01*	24.69±1.98#

Data are presented as n or mean ±SD. GA – general anaesthesia; CEA – caudal epidural anaesthesia; SEA – spinal-epidural anaesthesia; * *P*<0.05 versus GA group, # *P*<0.05 versus CEA group.

Table 6. Aβ expression levels in three groups at each indicating time point.

Variable	GA (n=66)	CEA (n=66)	SEA (n=66)
T1 (1 d before surgery)	51.16±15.76	50.90±15.50	51.94±12.92
T2 (1 d after surgery)	79.85±13.44	53.49±11.11*	54.52±12.92*
T3 (5 d after surgery)	54.26±13.70	52.45±17.57	52.97±15.25

Data are presented as n or mean ±SD. GA – general anaesthesia; CEA – caudal epidural anaesthesia; SEA – spinal-epidural anaesthesia; * *P*<0.05 versus GA group.

Aβ expression

To further determine whether patients experienced cognitive deterioration after anesthesia, Aβ expression at different time points (T1, T2, and T3) was detected. Aβ expression peaked at T2. The GA group exhibited significantly higher Aβ expression compared with CEA and SEA groups at T2. No significant difference in the expression of Aβ was observed between the CEA and SEA groups at any time point (Table 6).

Discussion

This study aimed to compare the efficacy, efficiency, and safety of 3 anesthesia techniques during THA. VAS score, MMSE score, and Aβ expression were compared among patients treated with different forms of anesthesia. Our results demonstrated that neuraxial anesthesia (CEA and SEA) performed better than GA and that CEA worked better than SEA.

Recently, researchers have become concerned about the safety of using anesthesia in surgeries because patients may encounter significant blood loss during total joint arthroplasty and this is associated with worse surgical rehabilitation and complications [30]. CEA is considered an effective technique for reducing the amount of blood loss, which further reduces the cost of blood transfusion [31]. Although in this study the duration of surgery did not differ significantly among the 3 groups, both CEA and SEA were linked with a decrease in the amount of blood transfusion and analgesics required, and the duration of anesthesia. Wakamatsu et al, on the other hand, found that higher perioperative blood loss amount and operative blood loss rate were observed in the SEA group compared with the GA group [32]. Barnett et al. reported that postoperative complications, including cardiac arrhythmias, DVT, genitourinary, myocardial infarction, and hematological and pulmonary signs, may significantly affect surgical outcomes [33,34]. A meta-analysis conducted by Mauermann et al. revealed that patients under neuraxial block had lower rates of postoperative nausea and vomiting complications resulting from THA [23]. Peripheral nerve blocks have also been proven effective in reducing complications from joint arthroplasties [35]. In our study, patients in the SEA and CEA groups had significantly fewer complications than the GA group. We also discovered that GA group patients were more prone to experience pulmonary infection, myocardial ischemia, and postoperative cognitive dysfunction (POCD), and SEA group patients were more prone to have postoperative complications than were CEA group patients. POCD is one of the most severe potential complications, including perception disorders, and it can be triggered by inappropriate anesthesia techniques, especially among the elderly [24]. POCD may affect short-term memory as well as other cognitive functions, including visual and verbal memory, attention, language comprehension, and concentration [36]. In our experiments, patients in the GA group had significantly lower MMSE scores at T2 and T3 than those in the CEA and SEA groups. SEA patients demonstrated significantly lower MMSE scores than CEA patients at every time point. Our results suggest that CEA has the least effect on postoperative cognition recovery from anesthesia. Consistent with our results, Wulf et al. showed that patients who underwent hip replacement surgery receiving CEA had stronger

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mental identification and coordination than those who received GA [37]. Shi et al. also found that patients undergoing hip replacement surgery receiving GA had lower MMSE scores than those receiving CEA [38].

Aβ is derived from amyloid precursor protein (APP), and elevated Aβ production is central in cognitive disorder diseases such as Alzheimer disease [39,40]. Nonetheless, POCD is a more subtle symptom after anesthesia and has also been proven to be closely associated with Aβ expression [38,41]. Its expression level in patients receiving GA was significantly higher at T2 than those receiving CEA or SEA, indicating that GA stimulated the Aβ production process, leading to higher risk of POCD occurrence. Similar results also have been found in a study conducted by Shi et al., in which the Aβ level increased in patients who experienced POCD after GA [38]. Anwer et al. discovered that GA presented a significantly higher risk for POCD occurrence than did epidural anesthesia in elderly patients. All the evidence suggests that GA, rather than CEA or SEA, induces the production of Aβ, which then stimulates POCD. However, Wiliams-Russo et al. found that GA and epidural anesthesia did not present significant differences in terms of POCD magnitude [26,39]. These discrepancies among studies may be due to differences in sample sizes, which can affect statistical and clinical significance. Therefore, larger study populations are needed to fully illustrate the significance.

In addition, effective pain management using analgesics is crucial in facilitating early mobilization, reducing hospital stay, and lowering medical costs associated with THA [42,43]. We demonstrated that patients in the GA group had significantly higher analgesics consumption than in the CEA and SEA groups, whereas patients in the CEA group consumed less analgesic than those in the SEA group. In addition, a significantly higher VAS score was found in the GA group than in the CEA group and SEA groups. Therefore, we suspect that CEA and SEA are more appropriate for postoperative analgesia. As suggested by Horlocker et al, peripheral neuraxial anesthesia, together with analgesia with the combination of opioid and non-opioid analgesic agents, can efficiently reduce pain intensity [7]. The corresponding reduction in pain intensity accompanied by a reduced morphine dose has been verified in a randomized controlled trial (RCT) [33]. Studies on the postoperative effects of anesthesia are contradictory. For instance, Harsten et al. recommended that GA be used in conjunction with THA since it had some role in reducing hospital stay and alleviating pain intensity [32].

Conclusions

This is the first published study comparing the effects of 3 anesthesia methods on perioperative outcomes during THA. Our results reveal that SEA and CEA were more appropriate than GA for patients undergoing THA. However, we only analyzed the Aβ level in blood samples, and there may be other molecules that influence POCD. Therefore, we recommend carrying out further research to discover how GA affects Aβ and its relationship with certain postoperative cognitive disorders. In conclusion, CEA and SEA led to superior post-surgery recovery, both physically and mentally, compared to GA, and CEA appears to be a better anesthesia technique than SEA.

Availability of data and materials

Patient data were collected in Huadong Hospital Affiliated to Fudan University.

Competing interests

We confirm that we have read BioMed Central's guidance on competing interests. The authors declare that no competing interests exist.

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