Peripheral Nerve Block Combined with Low-Dose General Anaesthesia in Elderly Patients Receiving Hip Arthroplasty

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ABSTRACT

The study assessed the effectiveness and safety of nerve block combined with low-dose general anaesthesia in elderly hip arthroplasty patients, conducted by a meta-analysis of RCTs. Six trials involving 403 patients were identified from databases such as Cochrane, MEDLINE, and PubMed. The results demonstrated a statistically significant difference in pain scores at postoperative 12hours (95% CI, -2.39 to -0.35, p = 0.008) and 24hours (95% CI, -1.86 to -0.50, p = 0.0007). Nerve block in combination with general anaesthesia holds a significant advantage over conventional general anaesthesia regarding perioperative opioid consumption (95% CI, -38.32 to -7.48, p = 0.004). This combined approach was superior in reducing the incidence of complications (95% CI, 0.11 to 0.55, p = 0.0007). However, between the two groups, there was no statistically significant difference in the 48hour pain score (95% CI, -2.58 to 0.62, p = 0.23). Essentially, this approach effectively reduces early post-surgical pain and it minimises anaesthetic use, whilst simultaneously lowering the risk of complications.

Key Words: *Nerve block, Elderly patients, Hip arthroplasty, Pain, Postoperative complication.*

How to cite this article: Liu Y, Zhu Y, Fu H. Peripheral Nerve Block Combined with Low-Dose General Anaesthesia in Elderly Patients Receiving Hip Arthroplasty. *J Coll Physicians Surg Pak* 2025; **35(01)**:76-82.

INTRODUCTION

Hip fracture is a significant cause of disability and death in the elderly. With the intensification of ageing, the incidence of what is known as the life's last fracture in the elderly, or hip fracture, is increasing year by year. It has been estimated that worldwide hip fractures will double between 1990 and 2025, and then double again by 2050, ranging from 7.3 million to 21.3 million.[1] Hip fractures commonly occur in the osteoporosis-affected elderly population; early surgery is usually the preferable treatment, as these patients often have declining organ function and multiple chronic medical conditions. These individuals are therefore at high risk for complications and mortality during the perioperative period.[2,3]

Hip arthroplasty presents substantial physical trauma with considerable blood loss and postoperative complications. The predominance of concomitant conditions such as hypertension, coronary heart disease, chronic lung disease, and diabetes among these elderly patients means that their tolerance to surgery and anaesthesia is low, consequently increasing perioperative risk.[4]

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Received: August 24, 2023; Revised: May 15, 2024; Accepted: August 17, 2024
DOI: https://doi.org/10.29271/jcpsp.2025.01.76

Selecting an appropriate anaesthesia method hence becomes vital for the perioperative safety of elderly patients undergoing hip arthroplasty.[5,6] Anaesthesia for hip arthroplasty may take the form of general anaesthesia, nerve block anaesthesia, or combined anaesthesia.[7] General anaesthesia provides a simple, safe, and effective option, particularly for cases where intraspinal anaesthesia puncture proves difficult. However, postoperative respiratory obstruction, hypoventilation, atelectasis, and delayed recovery are potential risks.[8-10] A peripheral nerve block can reduce these risks but it requires superior equipment and expertise, hence it has not yet gained widespread adoption in most hospitals.[11] A combination of general anaesthesia and peripheral nerve block represents a common choice for combined anaesthesia. This approach reduces the required dosage of general anaesthesia medicines, thus minimising the associated adverse reactions, however, it does increase anaesthesia time and procedural-related complications.[12,13] Currently, both general anaesthesia and combined anaesthesia are frequently utilised in surgical procedures on elderly patients, yet the influence of these two methods on perioperative complications and patient rehabilitation has not been uniformly determined, and no systematic evaluation has been conducted.

This study aimed to compare the results of using a nerve block in combination with a low-dose general anaesthesia *versus* just general anaesthesia in elderly patients undergoing hip arthroplasty; the findings offered valuable insights for further refinement of clinical anaesthesia application.

METHODOLOGY

The Cochrane Library, The Cochrane Anaesthesia Group database, MEDLINE, EMbase, PubMed, Ovid, Springer, CBM, CNKI, VIP, and Wanfang databases were searched electronically. Randomised controlled trials (RCTS) comparing nerve block combined with general anaesthesia *versus* conventional general anaesthesia in elderly patients undergoing hip arthroplasty were sought from the inception of these databases until February 2022.

The literature search results were independently reviewed by two investigators. Studies met inclusion criteria if they involved patients undergoing hip arthroplasty, allocated one group to receive general anaesthesia, assigned another group to receive combined nerve block and general anaesthesia, selected one or more of the following outcomes; dosage of anaesthetic medicine, postoperative pain score, and complications, and were randomised controlled trials. Exclusion criteria encompassed studies where data could not be extracted and lack of consensus among independent reviewers on selected studies, furthermore, case reports, letters, and reviews were excluded.

Authors were contacted for additional required details. Data related to the primary authors' name, publication date, intervention used, basic information, number of patients, and management of adverse outcomes were extracted. Additional necessary data were also retrieved from individual articles.

RevMan5.3 software was utilised for the analysis. Heterogeneity across the included studies was initially assessed. If there was no heterogeneity in outcomes ($p > 0.1$), a fixed-effect model was engaged for meta-analysis. Where heterogeneity existed among study results ($p > 0.1$), causes were analysed, and potential sources of heterogeneity underwent subgroup analysis. If statistical heterogeneity without clinical heterogeneity was detected between the study groups, a random-effects model was employed. Sensitivity analysis was performed when heterogeneity resulted from low-quality studies.

RESULTS

In the search strategy, a total of 113 studies were retrieved. Of these, 41 studies were excluded by Endnote software and 34 were eliminated after reviewing the title and abstract. Consequently, six RCTs were included in this meta-analysis (Figure 1).[5-7,12,22,27] The fundamental characteristics are summarised in Table I.[14-18] The methodological quality of each randomised controlled trial was appraised using the Jadad Scale, scoring between 0 and 5 points. A Jadad score of 2 suggests low quality, while a score of ≥3 indicates high quality (Table I).

The Cochrane Collaboration's Risk-of-Bias tool was engaged to evaluate the included articles on research in randomness methods, blinding of participants and staff, data integrity, and selective result reporting. Each domain was further classified into low risk, high risk, or unclear risk. Any disagreements were resolved through discussion (Table II).

Five studies comprising 374 patients reported VAS scores 12 hours post-surgery.[5-7,22,27] Notable disparities were identified between the experimental and control groups (MD = -1.37; 95% CI, -2.39 to -0.35, $p = 0.008$; Figure 2). Considerable heterogeneity was detected in the VAS for the initial 12 hours post-surgery ($Chi^2 = 204.90$; $df = 4$, $p < 0.001$, $I^2 = 98\%$; Figure 2). Consequently, a random-effects model was employed.

Three studies which involved a total of 162 patients, reported visual analogue scale (VAS) scores for the first 24 hours following surgery.[6,7,27] Notable differences were detected between the two groups (MD = -1.18; 95% CI, -1.86 to -0.50, $p = 0.0007$; Figure 3). In addition, significant heterogeneity was identified in the VAS scores for the postoperative 24-hour period ($Chi^2 = 29.05$; $df = 2$, $p < 0.001$; $I^2 = 93\%$; Figure 3).

Table I: The Characteristics of included studies.

Author (year)	Experimental group / Control group						
	Patients	Age (years)	Female gender (%)	BMI	ASA (I/II/III/IV)	Reference type	Jadad scale
Shi *et al*. 2018[12]	15/15	74.6/76.8	60/46	NA	7/14/9/0	RCT	4
Li *et al*. 2018[14]	30/30	71.6/68.3	50/46	22.9/23.8	0/36/24/0	RCT	4
Mei *et al*. 2017[15]	66/66	77/74	67/44	24.6/24.3	NA	RCT	4
Bang *et al*. 2016[16]	11/10	81.6/82.0	54/80	20.6/22.2	0/18/3/0	RCT	4
Kratz *et al.* 2015[17]	40/40	66.9/65.8	65/42	28.1/28.5	NA	RCT	4
Wiesmann *et al.* 2014[18]	40/40	67/66	62/45	NA	NA	RCT	4

Table II: Quality evaluation of included studies.

Study	Random sequence generation	Blinding of participants and personal	Incomplete outcome data	Selective reporting	Other bias
Shi *et al*. 2018[12]	low risk	unclear risk	low risk	unclear risk	unclear risk
Li *et al*. 2018[14]	low risk	low risk	low risk	unclear risk	unclear risk
Mei *et al*. 2017[15]	low risk	unclear risk	low risk	unclear risk	unclear risk
Bang *et al*. 2016[16]	low risk	low risk	low risk	unclear risk	unclear risk
Kratz *et al.* 2015[17]	low risk	low risk	low risk	unclear risk	unclear risk
Wiesmann *et al.* 2014[18]	unclear risk	low risk	low risk	unclear risk	unclear risk

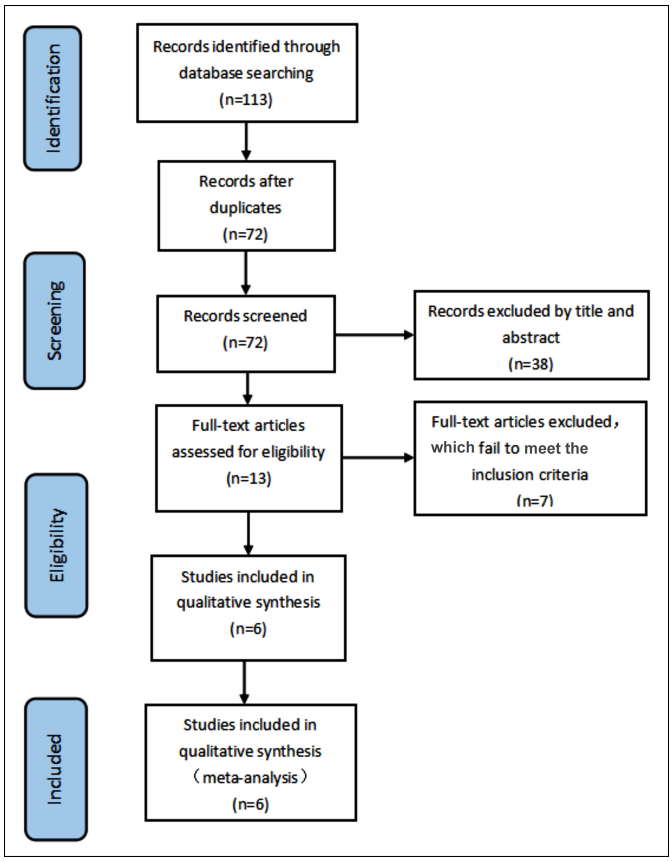

Figure 1: Search results.

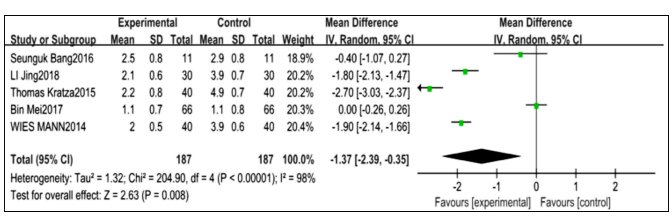

Figure 2: VAS scores at 12 hours postoperative.

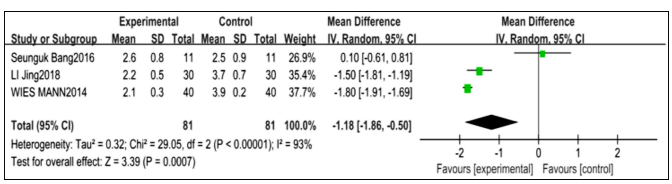

Figure 3: VAS scores at 24 hours postoperative.

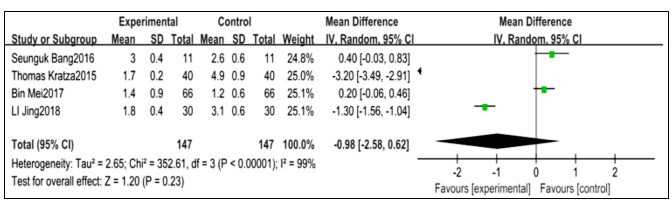

Figure 4: VAS scores at 48 hours postoperative.

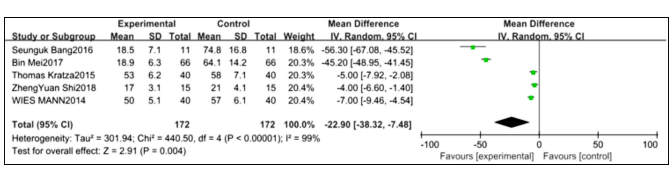

Figure 5: Total sufentanil consumption.

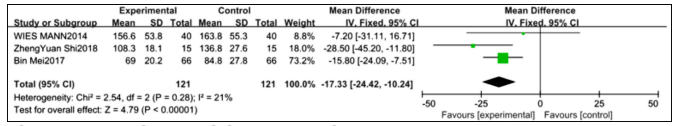

Figure 6: Total propofol consumption.

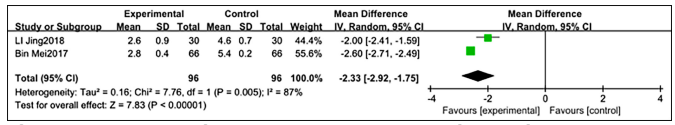

Figure 7: Postoperative MMSE score *versus* perioperative score.

Data from four studies,[5-7,22] assessing a total of 294 patients, reported the visual analogue scale (VAS) scores for postoperative pain at 48 hours. The results indicated that the experimental group reported comparable pain scores to those of the control group (MD = -0.98; 95% CI, -2.58 to 0.62, p = 0.23; Figure 4). However, significant heterogeneity was found in VAS scores at postoperative 48 hours (Chi^2 = 352.61; df = 3, p <0.001; I^2 = 99%; Figure 4).

Total sufentanil consumption was reported in five studies comprising 344 patients.[5,7,12,22,27] The pooled data signified that there were significant differences between the two groups (MD = -22.90; 95% CI, -38.32 to -7.48, p = 0.004; Figure 5).

Due to the heterogeneity between the studies, a random-effects model was utilised (Chi^2 = 440.50; df = 4; p <0.001; I^2 = 99%).

Total propofol consumption was documented in three studies including 242 patients.[5,12,27] Significant differences were noted between the two groups (MD = -17.33; 95% CI, -24.42 to -10.24, p <0.001; Figure 6).

A fixed-effect model was adopted due to the low heterogeneity (Chi^2 = 2.54; df = 2, p = 0.28; I^2 = 21%).

Data drawn from three studies covering 214 patients were used to compare the incidence of complications during the hospital stay.[5-7] There were significant differences detected between the two groups (MD = 0.24; 95% CI, 0.11 to 0.55, p = 0.0007). A fixed-effect model was applied.

The mini-mental state examination (MMSE score) was reported in two studies involving 192 patients.[5,6] Statistically significant divergence was observed between the two groups (MD = -2.33; 95% CI, -2.92 to -1.75, p = <0.00001; Figure 7).

Due to evident heterogeneity, a random-effects model was enacted (Chi^2 = 7.76; df = 1, p = 0.005; I^2 = 87%).

DISCUSSION

Perfect perioperative analgesia can alleviate severe pain caused by hip arthroplasty, enhance satisfaction in relation to the surgery, and lower the opium dosage.[19-21] However, which pain management method is most efficacious continues to be

a subject of contention. Opium has been extensively used for pain relief following hip arthroplasty but opioid-related adverse medicine reactions are acknowledged, particularly among elderly patients.[22-24] Mei *et al*. in their study involving conventional general anaesthesia, found that high sedation levels and more opioids were associated with increased vasoactive drug intake during surgery.[15] In contrast, patients who received regional nerve block along with mild intraoperative sedation showed reduced postoperative delirium rates and were discharged earlier from the hospital.[25-27] Recently, several published studies have indicated that adding a supplemental nerve block to hip arthroplasty surgery enhances the lung function six hours post-surgery and provides superior pain control within 24 hours of surgery.[28,29] Nerve block, as an adjunct to general anaesthesia, has been developed in clinical anaesthesia practice, and studies have pointed to its advantages in hip arthroplasty. Yet, data that assess the perks of nerve blocks administered to elderly patients undergoing hip arthroplasty—specifically regarding perioperative analgaesia effect, cognitive dysfunction, and postoperative complications—are scant. Hence, the authors conducted a related meta-analysis of RCTs to compare nerve block combined with low-dose general anaesthesia and general anaesthesia in hip arthroplasty.

This systematic review included six studies, consisting of 403 patients. Each record index was both extensive and detailed. Three studies outlined the implementation of specific randomisation methods. Two studies utilised a digital table randomisation, while another study employed computer randomisation. The remaining three studies mentioned randomisation, but did not clarify the specific randomisation method, leading to a moderate risk of selection bias.

Three studies elaborated on the application of double-blinding of anaesthesiologists and data collectors. The rest of the studies failed to discuss in detail the specific blinding practises they adopted. Pain score, cognitive dysfunction, and postoperative complications were consistently assessed using standardised metrics based on the objective data, removing any potential subjective influence, and reducing the measuring bias to low bias. Considering the inherent peculiarities of surgical anaesthetic treatment, it is noteworthy that achieving complete double-blind procedures is challenging, hence there may be a likelihood of implementation and measurement bias in actual clinical practice. All the studies had less than 15% loss to follow-up and exclusions after randomisation for each group, indicating a low likelihood of incomplete data bias. Every study examined, did not explicitly describe the completeness of their findings, thus indicative of a moderate bias towards selective result reporting. Most of the studies detailed applicable inclusion and exclusion criteria, and the homogeneous age and gender of the two patient groups excluded any likely non-comparability, reducing other sources of bias to low risk.

The research findings indicate that there are statistically significant differences in the VAS score- 24 hours post-surgery, amount of general anaesthetics used, incidence of complications, and postoperative cognitive dysfunction between the elderly patients who underwent hip arthroplasty under conventional general anaesthesia *versus* nerve block compounded with a low dose of general anaesthesia. However, no noticeable difference was seen between both groups' postoperative VAS scores at the 48-hour mark.

Six RCTs, involving a total of 374 patients, provided pain score data. After hip arthroplasty, the VAS method was used to evaluate pain (0 ~ 10 cm). Meta-analysis results suggested that nerve block coupled with general anaesthesia significantly reduces the VAS score within the first 24 postoperative hours after hip arthroplasty. Findings from the literature reports have shown that the peripheral nerve blocks effectively alleviate hip pain within 24 hours post--surgery, corroborating the conclusions of this meta-analysis.[30] Peripheral nerve block obstructs the ascending conduction pathway of surgical incision pain, thus extending the postoperative analgaesia duration. This study revealed that the combined use of nerve block and anaesthesia offers superior analgaesic effects in the initial 24 postoperative hours. However, there were also research reports indicating that there was no remarkable difference between both groups' analgaesic effects 48 hours after the operation, which may be explained by the local anaesthetics' metabolism and the nerve block analgaesia gradually failing to develop.

Opioids are usually effective in relieving pain but often come with side effects that delay hospital discharge.[31] Sufentanil, a type of mu - opioid agonist, interacts with and triggers the corresponding receptors of the central and peripheral nervous systems to relieve pain. As an extensively used analgaesic anaesthetic during the perioperative period, sufentanil has been associated with high incidents of adverse reactions such as nausea, vomiting, headache, and urinary retention, seriously impairing postoperative rehabilitation.[32] Moreover, propofol, the most commonly used general anaesthetic, particularly among elderly patients undergoing hip arthroplasty, has a low tolerance level. These patients are frequently frail when they enter the operating room (OR) and have lower physiological function reserves due to pre-existing diseases. This makes them more susceptible to the haemodynamic changes triggered by the medicine such as propofol, leading to hypotension and low perfusion. Severe intraoperative hypotension is linked to adverse events in older adults. Research has shown that using propofol exceeding the induction dosage limit imposed by the U.S. Food and Drug Administration (FDA) is positively correlated with severe hypotension incidences. This outcome was confirmed in over 20% of patients monitored non-invasively and approximately a third of those monitored invasively.[33]

At present, there is insufficient dependable evidence regarding the opioid-sparing attribute of nerve block during hip replacement. In the analysis, five RCTs provided outcomes of opioid consumption, and this meta-analysis concluded that nerve block is linked with a notable reduction in perioperative opioid usage in hip replacement. Moreover, three RCTs provided outcomes data of propofol consumption and the result indicated that the combined nerve block group had a significant decrease in the dosage of propofol during surgery.

In total, there are three RCTs that have shown complications after hip arthroplasty. Complication rates were 8/107 in the nerve block group, compared to 28/107 in the control group. The research suggests that the application of nerve block can significantly lower postoperative complication risks. At present, only these three RCTs were included, and no dose-related studies were conducted, so further investigation is warranted.

These three RCTs compared the impact on postoperative cognitive dysfunction. For the purposes of this systematic review, the authors did not segregate short-term from long-term postoperative cognitive dysfunction. The findings suggest that composite nerve block anaesthesia significantly decreases the incidents of short-term postoperative cognitive dysfunction compared to general anaesthesia. However, the incidence rate of long-term postoperative cognitive dysfunction requires additional study. The conventional general anaesthesia group exhibited slower selective response times (psychomotor) in the weeks following surgery, mirroring results from the International Postoperative Cognitive Impairment Study Collaboration (ISPOCD) amongst other studies. It is thought that the incidence rate for short-term postoperative cognitive decline is higher amongst the conventional general anaesthesia group. Many theories suggest that this short-term cognitive impairment may be due to the incomplete metabolism of high-dose anaesthetic medicines, and with the elimination of residual medicines from the body, it does not affect the patient's long-term cognitive function adversely.[34] Some postulate that general anaesthetics in high doses can induce apoptosis in some brain neurons and alter their protein expression by acting on the central neurotransmitter and receptor systems.[35] Propofol primarily affects its anaesthetic action by enhancing the function of γ-aminobutyric acid (GABA) receptors, and the enhancement of GABA receptor activity can inhibit long-term potentiation (LTP) expression in the hippocampal CA1 region - the foundation of learning and memory.[36] It is also believed that cerebral oxygen metabolism imbalance and the release of pro-inflammatory cytokines due to different stress factors during operations may also contribute.[37]

This study has certain limitations. Firstly, postoperative hip joint function score, among other key results, was not included in the analysis. Secondly, because heterogeneity was found in some of the findings, this can affect the research outcome. Thirdly, as this analysis consists of only six studies, the sample size and statistical testing might not be robust enough. Lastly, detected languages were limited to English and Chinese, which introduces potential bias in the findings.

CONCLUSION

In the immediate aftermath of hip arthroplasty, a combination of nerve block and low-dose general anaesthesia can effectively alleviate postoperative pain. Simultaneously, it may reduce the cumulative consumption of general anaesthesia and the risk of postoperative complications.

FUNDING:
Chongqing Municipal Health Commission Medical Research Project (2024WSJK010); Chongqing Municipal Health Commission Medical Research Project (2021MSXM060); Norman Bethune Charitable Foundation, Enze Pain Management Medical Research Project (ezmr2022-024); Chongqing Municipal Studios for Young and Middle-Aged Top Medical Talents, Chongqing Municipal Health Commission Project [ZQNYXGDRCGZS2019006].

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
YL: Research, data collection, data analysis, and interpretation, drafting of the initial manuscript, and revision.
YZ: Literature review, data extraction, and methodological validity assessment of the included studies, and assistance in data interpretation.
HF: Conceptualisation of the research study, guiding the research process, data analysis, and critical revision of the manuscript for the important intellectual content.
All authors approved the final version of the manuscript to be published.

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