Analgesic effect of perioperative ketamine for total hip arthroplasties and total knee arthroplasties
A PRISMA-compliant meta-analysis
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Abstract
Background: Total hip arthroplasties (THA) and total knee arthroplasties (TKA) are always associated with a frequent incidence of postoperative pain. Effective pain management after surgery is quite essential for surgeons and patients. The purpose of the present meta-analysis is to evaluate the analgesic effect of perioperative ketamine after THA and TKA.

Methods: Seven online databases, Embase, Cochrane Library, Pubmed, Web of Science, China National Knowledge Infrastructure (CNKI), China Biomedical Literature Database (CBM), and Wanfang Data were searched for the related randomized controlled trials (RCT) by August 15, 2019. The qualities of the included studies were assessed based on the Cochrane Handbook for Systematic Reviews of Interventions 5.0. The visual analog scale (VAS), morphine equivalent consumption, and the side effects were used to evaluate the postoperative analgesic effect of ketamine by meta-analysis, which was performed by Review Manager version 5.3 software.

Results: The VAS scores at 6 hours, 12 hours, 24 hours, and 48 hours after surgery were statistically lower in the ketamine group. The morphine equivalent consumptions in 24 hours and 48 hours after surgery were also significantly lower in the ketamine group. For the side effects, no statistical differences in odds ratio (OR) of sedation, dizziness, hallucination, sweating, pruritus, urinary retention, constipation, version trouble, nightmares, and delirium were observed between the ketamine group and the control group. But postoperative nausea and vomiting (PONV) showed lower OR in the ketamine group.

Conclusion: The present meta-analysis demonstrated perioperative ketamine could be used as a safe and effective analgesic agent for THA and TKA.

Abbreviations: CBM = China Biomedical Literature Database, CI = confidence interval, CNKI = China National Knowledge Infrastructure, COX = cyclooxygenase, NMDA = N-methyl D-aspartate, NSAIDs = nonsteroidal anti-inflammatory drugs, OR = odds ratio, PCIA = patient-controlled intravenous analgesia, PONV = postoperative nausea and vomiting, RCT = randomized controlled trials, THA = total hip arthroplasties, TKA = total knee arthroplasties, VAS = visual analog scale, WMD = weighted mean difference.

Keywords: analgesia, ketamine, meta-analysis, total hip arthroplasties, total knee arthroplasties

1. Introduction
Given the aging society and the obesity epidemic, total hip and knee arthroplasties (THA/TKA), as highly effective surgery procedures, have been widely performed since 1970s.\textsuperscript{1,2} In the United States, more than 700 thousand TKAs and 330 thousand THAs have been performed.\textsuperscript{3} The number of THA and TKA performed in the US has been steadily increasing and is expected to exceed 4 million by 2030.\textsuperscript{4} Both THA and TKA are painful processes, and effective pain management after surgery is critical to the evaluation of the outcome of the procedure.\textsuperscript{5} Effective
pain management has been shown to improve outcomes, including faster recovery, lower complication rates, lower care costs, and higher patient satisfaction.\(^6\)–\(^8\) Therefore, perioperative analgesia is extremely important for THA and TKA. Several analgesia protocols have been used in THA and TKA, including traditional oral opioids, femoral nerve block, intra-articular injection, and epidural analgesia.\(^9\)–\(^11\) However, each analgesic option has some limitations.\(^12\) Currently, multimodal analgesia is demonstrated by many studies to be effective for pain control after THA and TKA.\(^3\)–\(^5\),\(^7\) The multimodal analgesia addresses multiple pain mechanisms and improves postoperative pain by combining pharmacologic and other modalities while reducing adverse effects using lower doses of individual modalities.\(^12\)–\(^14\) There is no immutable and standard protocol for multimodal analgesia. Multiple pathways and mediators are involved in nociception, and targeting several mechanisms can increase analgesic efficacy, using combinations of systemic and regional anesthesia. Various medications have been used in multimodal therapy, including nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase (COX)-2 inhibitors, acetaminophen, or paracetamol, neumodulatory medications (gabapentin and pregabalin), opioid agonists, steroids, and N-methyl D-aspartate (NMDA) antagonists.\(^14\)

Ketamine is a non-specific competitive NMDA receptor antagonist that produces anesthetic effects in large doses and anti-allergic, anti-allodynic, and opioid tolerance in small doses.\(^15\) Because ketamine is highly lipid soluble, it allows for very rapid onset of its effect and is useful in general induction of anesthesia along with perioperative pain management.\(^16\)\(^16\) The addition of ketamine in the multimodal analgesia regimen has been applied to many analgesic studies after THA and TKA. Many studies have been conducted to investigate ketamine as a modality in the multimodal approach to perioperative pain control and demonstrated that ketamine can provide superior pain relief, and reduced opioid dependence and opioid-related side effects, improving patient satisfaction, safety, and timely return to function.\(^17\)–\(^19\)

However, no previous study meta-analyzed the analgesic effect of perioperative ketamine for total hip and knee arthroplasties. So, the purpose of the present meta-analysis is to evaluate the analgesic effect of perioperative ketamine after THA and TKA.

## 2. Material and methods

### 2.1. Literature searching strategy

Two independent investigators (Wang and Yang) thoroughly searched seven online databases, Embase, Cochrane Library, PubMed, Web of Science, China National Knowledge Infrastructure (CNKI), China Biomedical Literature Database (CBM), and Wanfang Data by August 13, 2019. A combination of medical subject headings (MeSH) word and its corresponding entry word were utilized in the searching strategy. For example, the following refined PubMed/MeSH search words were: ("Arthroplasty, Replacement, Hip" [MeSH Terms] OR "Arthroplasty, Replacement, Knee" [Mesh Terms]) AND ("Ketamine" [MeSH Terms]) AND ("Analgesia" [MeSH Terms] AND "Randomized controlled trial" [Publication Type]); Then, the unrelated or improper studies were excluded by scanning abstracts, and the data was extracted from included studies by reading full texts carefully.

### 2.2. Inclusion and exclusion criteria

Studies with all of the following criteria were included into the systematic review and meta-analysis:

1. randomized controlled trial and categorical sample contents;
2. study on the analgesic effect of ketamine in THA or TKA;
3. Visual analog scale (VAS), morphine equivalent consumption, or the side effects was used to evaluate the postoperative analgesia;
4. sufficient data was provided to get weighted mean difference (WMD) and the corresponding 95% confidence interval (CI) or p values for diagnosis outcomes.

Studies were excluded with any of the following:

1. repeated published data or studies;
2. non-controlled studies;
3. poor-quality or illogical statistically studies;
4. not involved in the analgesic effect of ketamine in THA or TKA;
5. provided data was not enough to get WMD or 95% CIs.

### 2.3. Data extraction and assessment of methodological quality

Literature screening, data extraction, and quality assessment were conducted according to inclusion and exclusion criteria by 2 independent investigators. The first author name, published year, surgery process, sample size, age, intervention mode, the anesthesia mode, and outcome data were extracted. VAS and morphine equivalent consumption were regarded as the primary outcome, and the side effect was considered to be the secondary outcome. The qualities of the included studies were assessed based on the Cochrane Handbook for Systematic Reviews of Interventions 5.0 by 2 independent investigators (Wang and Yang). A table of “Risk of Bias” was conducted with the following parameters: random sequence generation, allocation concealment, blinding, incomplete outcome data, free of selective reporting, and other bias. Each parameter was recorded by “Yes”, “No”, and “Unclear”. A third investigator was needed with the occurrence of discrepancy after cross-checking. Each risk of bias item was presented as a percentage, which indicated the proportion of different levels of each risk of bias item, across all the included studies.

### 2.4. Statistical analysis

Meta-analysis was performed by Review Manager version 5.3 software, and the result was carried out by WMD due to the different units and 95% CI among the included literature. Cochran’s Q test and Higgens I² were used to evaluating the heterogeneity of the articles. If $P<.05$ and/or $I^2 > 50\%$, which represented the heterogeneity were significant, the random-effect module would be used; if not, the fixed-effect module would be used.

## 3. Results

### 3.1. Included studies

A total of 266 literature were collected independently by two investigators (Wang and Yang) in seven online databases after comprehensively searching based on the searching strategy: 10 in...
PubMed, 34 in Embase, 31 in Cochrane Library, 105 in Web of Science, 36 in Wanfang Data, 31 in CBM, 19 in CNKI. A final decision was determined by a third independent investigator (Cao) when different opinions appeared. Of all the articles, 83 were excluded due to duplication, and another 160 were excluded on account of insufficient data, data duplication, and no full text. Finally, two records were removed because of repeatedly published data. In general, 21 studies were included in the present meta-analysis, the literature search process is shown in Figure 1.

3.2. Characteristics of the included studies

The sample size ranged from 12 to 154, and totally 1145 patients were included in the present meta-analysis. Patients in the experimental groups received ketamine treatment. The intravenous injection was performed in 10 of the included studies. The intra-articular injection was performed in 2 of the included studies. The epidural puncture injection was performed in 5 of the included studies. Patients in the control groups received the placebo or normal saline with the same mode of corresponding experimental groups. All the included studies showed statistically similar baseline characteristics, which are showed in Table 1.

3.3. Risk of bias

We assessed the risk of bias of all the RCTs according to the Cochrane Handbook for Systematic Review of Interventions. Of all the included articles, one study (4.76%) did not report its randomization methodology which was considered as a high risk of bias. Twelve studies (57.14%) described their utilization of computer-generated randomization. Twelve studies (57.14%) reported their allocation concealment by using a closed envelope or label. Sixteen studies (76.19%) reported double blinding in the RCTs, and the blind investigators were also showed in outcome assessment. Eight studies (38.10%) did not report their
Table 1

Characteristics of the included studies.

| Studies               | Surgical procedure | Patient numbers (Female) | Intervention |
|-----------------------|--------------------|--------------------------|--------------|
| Himmlsieber, 2007[35] | TKA                | 18 (12) 19 (13) 65±13    | Patients in ketamine group received 0.25 mg/kg epidural ketamine 10 min before surgery, immediately followed by 3 ug/kg/h during surgery. |
| Laurenti, 2005[36]    | TKA                | 14 (6) 13 (5) 48±17      | Patients in ketamine group received 0.1 mg/kg epidural ketamine postoperatively. |
| Adam, 2009[27]        | TKA                | 20 (14) 20 (13) 69±7     | Patients in ketamine group received an initial bolus of 0.5 mg/kg ketamine intravenously followed by a continuous infusion of 3 ug/kg/min during surgery and 1.5 ug/kg/min for 48 h after surgery. |
| Ma, 2005[34]          | TKA                | 15 (7) 15 (9) 46±14.9    | Patients in ketamine group received 0.5 mg/kg epidural ketamine postoperatively. |
| Wang, 2007[21]        | TKA                | 20 (14) 20 (13) 20–75    | Patients in ketamine group received an initial bolus of 0.05 mg/kg ketamine intravenously followed by a continuous infusion of 3 ug/kg/min during surgery and 1.5 ug/kg/min for 48 h after surgery. |
| Liu, 2008[22]         | THA                | 10 (4) 10 (5) 68.6±10.49 | Patients in ketamine group received 0.6 mg/kg epidural ketamine postoperatively. |
| Perrin, 2009[24]      | TKA                | 5 (2) 7 (3) 62.5±11.1    | 0.5 mg/kg of bolus intravenous ketamine was injected preoperatively followed by 4 ug/kg/min infusion during the surgery. |
| Remérand, 2009[23]    | THA                | 79 (42) 75 (34) 64.5±13.5| Patients in ketamine group received an initial bolus of 0.5 mg/kg ketamine intravenously followed by a continuous infusion of 2 ug/kg/min for 48 h after surgery. |
| Akkurt, 2009[25]      | TKA                | 20 (9) 20 (10) 16–65     | Patients in ketamine group received 0.15 mg/kg intravenous ketamine postoperatively. |
| Aveline, 2009[26]     | TKA                | 25 (15) 24 (15) 71±8     | Patients in ketamine group received an initial bolus of 0.2 mg/kg ketamine intravenously followed by a continuous infusion of 120 ug/kg/h during surgery and 60 ug/kg/h for 48 h after surgery. |
| Zhai, 2010[30]        | THA                | 30 (8) 30 (11) 70.5±11.9 | Patients in ketamine group received 30 mg epidural ketamine postoperatively. |
| Wang, 2011[41]        | THA                | 60 (32) 30 (13) 76.6±5.8 | 1 mg/ml or 2 mg/ml ketamine was injected postoperatively by patient-controlled intravenous analgesia with a bolus dose of 0.5 ml and a 15-min lockout. |
| Guári Sobrinho, 2012[31] | TKA | 19 (16) 20 (17) | Patients in ketamine group received 0.25 mg/kg intra-articular ketamine postoperatively. |
| Zhao, 2012[29]        | TKA                | 20 (14) 20 (12) 63.13±8.62 | Patients in ketamine group received an initial bolus of 1 mg/kg ketamine 10 min intravenously before surgery followed by a continuous infusion of 1 mg/kg/h during surgery and 1.5 ug/kg/min for 48 h after surgery. |
| Chen, 2013[37]        | TKA                | 30 30 70.9±4.0 0.4 mg/ml ketamine was injected postoperatively by patient-controlled intravenous analgesia with a bolus dose of 2 ml and a 6-min lockout. |
| Martinez, 2014[28]    | THA                | 34 (23) 38 (13) 18–80    | Patients in ketamine group received intravenous ketamine with 0.5 mg/kg bolus at the time of anesthesia induction immediately followed by 3 ug/kg/h infusion stopped at skin closure. |
| Cengiz, 2014[47]      | TKA                | 30 (25) 30 (19) 18–65    | Patients in ketamine group received intravenous 6 ug/kg/min ketamine during the surgery until would closure. |
| Ji, 2015[38]          | TKA                | 25 (17) 25 (14) 50–70    | 2 mg/kg ketamine was injected postoperatively by patient-controlled intravenous analgesia with a bolus dose of 0.5 ml and a 15-min lockout. |
| Liu, 2015[39]         | TKA                | 60 (50) 30 (26) 66.7±5.5 | 1 mg/ml ketamine was injected postoperatively by patient-controlled intravenous analgesia with a bolus dose of 2 ml and a 60-min lockout. |
| Zhang, 2018[41]       | TKA                | 21 (15) 23 (16) 42–74    | Patients in ketamine group received 2 mg/kg intra-articular ketamine postoperatively. |
| Tan, 2019[29]         | TKA                | 48 (28) 43 (25) 18–85    | Patients in ketamine group received 60 mg intravenous ketamine at a rate of 6 mcg/kg/min once situated on the table and was discontinued at skin closure. |

incomplete outcome data. Low risk of bias of all the included studies due to selective outcome reporting was detected. The methodological quality assessment and the percentage of the risk of bias were shown in Figure 2 and Figure 3.

3.4. Meta-analysis of outcomes

3.4.1. Pain scores. Five studies, including 259 patients, reported VAS at 6 hours after surgery. Meta-analysis was performed through a fixed-effect model due to the insignificant heterogeneity ($I^2=42\%$, $P=.14$). The pooled results revealed that the VAS at 6 hours was statistically lower in the ketamine group than that in the control group (WMD $=-1.45$, 95% CI: $-1.71$ to $-1.18$, $P<.00001$; Fig. 4A).

Six studies, including 299 patients, reported VAS at 12 hours after surgery. Meta-analysis was performed through a random-effect model due to the significant heterogeneity ($I^2=91\%$, $P<.00001$). The pooled results revealed that the VAS at 12 hours was statistically lower in the ketamine group than that in the control group (WMD $=-1.55$, 95% CI: $-2.28$ to $-0.82$, $P<.00001$; Fig. 4B).
Thirteen studies, including 732 patients, reported VAS at 24 hours after surgery. Meta-analysis was performed through a random-effect model due to the significant heterogeneity ($I^2 = 90\%, P < .00001$). The pooled results revealed that the VAS at 24 hours was statistically lower in the ketamine group than that in the control group (WMD $= -0.78$, 95% CI: $-1.25$ to $-0.31$, $P = .001$; Fig. 4C).

Seven studies, including 534 patients, reported VAS at 48 hours after surgery. Meta-analysis was performed through a random-effect model due to the significant heterogeneity ($I^2 = 92\%, P < .00001$). The pooled results revealed that the VAS at 48 hours was statistically lower in the ketamine group than that in the control group (WMD $= -0.74$, 95% CI: $-1.26$ to $-0.22$, $P = .006$; Fig. 4D).

3.4.2. Morphine equivalent consumption. The morphine equivalent consumptions at 24 hours after surgery were reported in five studies, including 315 patients. Meta-analysis was performed through a random-effect model due to the significant heterogeneity ($I^2 = 96\%, P < .00001$). The pooled results revealed that the morphine equivalent consumption at 24 hours was significantly lower in the ketamine group than that in the control group (WMD $= -17.58$, 95% CI: $-29.07$ to $-6.10$, $P = .003$; Fig. 5A).

The morphine equivalent consumptions at 48 hours after surgery were reported in 5 studies, including 299 patients. Meta-analysis was performed through a random-effect model due to the significant heterogeneity ($I^2 = 94\%, P < .00001$). The pooled results revealed that the morphine equivalent consumption at 48 hours was significantly lower in the ketamine group than that in the control group (WMD $= -16.82$, 95% CI: $-27.75$ to $-5.89$, $P = .003$; Fig. 5B).

3.4.3. Side effects. The meta-analysis of the odds ratio (OR) for sedation, dizziness, hallucination, PONV, sweating, pruritus, urinary retention, constipation, version trouble, nightmares, delirium were performed. Because different studies reported different side effects, the meta-analysis of each side effect included various amounts of studies.

Thirteen studies, including 721 patients, reported PONV after surgery. Meta-analysis was performed through a fixed-effect model due to the insignificant heterogeneity ($I^2 = 0\%, P = .48$). Statistically lower OR was observed in the ketamine group than that in the control group after the pooled analysis (OR $= 0.54$, 95% CI: $0.37$ to $0.77$, $P = .0008$). The meta-analysis of the other side effects showed no differences between the two groups. The details are shown in Table 2.

4. Discussion

The present meta-analysis evaluated the analgesic effect of perioperative ketamine after THA and TKA. The VAS scores at 6 hours, 12 hours, 24 hours, and 48 hours after surgery were statistically lower in the ketamine group than those in the control group. The morphine equivalent consumptions in 24 hours and
48 hours after surgery were also significantly lower in the ketamine group. For the side effects, no statistical differences in OR of sedation, dizziness, hallucination, sweating, pruritus, urinary retention, constipation, version trouble, nightmares, and delirium were observed between the ketamine group and the control group. But PONV showed lower OR in the ketamine group. THA and TKA are always associated with a frequent incidence of postoperative pain.[32,41] Uncontrolled pain increases the risk of complications, morbidity, and some other adverse effects such as sleep disorder and anxiety, thereby hindering physical therapy, rehabilitation, and increasing length of hospital stay.[41] Wall first proposed the term multimodal pain management in 1988.[42] In recent years, various analgesic patterns have been suggested for minimizing the pain after arthroplasty, including the utilization of ketamine, which has been discussed in a large number of studies as supplemental analgesia for perioperative pain control.[43,44] However, whether the analgesic effect of ketamine for THA and TKA holds true is
still a question. To the best of our knowledge, this is the first meta-analysis to investigate the analgesia effect of perioperative and postoperative ketamine for THA and TKA. Our results confirmed that the perioperative application of ketamine could reduce postoperative pain in patients.

Ketamine, a classical antagonist of NMDA excitatory glutamate receptor, mainly exerts analgesia by selectively acting on the brain contact pathway and the new cortical system of the thalamus. It plays the biological roles by inhibiting the transmission of the spinal cord to the reticular structure to the central nervous system, exciting the medulla and marginal system, and inhibiting the non-specific nuclei of the midbrain and thalamus.\[45–48\] Therefore, ketamine has been increasingly used in a range of diseases as well as treatment-induced pain.\[43\]

VAS score and morphine equivalent consumption are always used as regular and objective indicators to evaluate the postoperative pain control in most of the analgesia studies, and they are considered as the primary outcome to evaluate the postoperative pain in the present meta-analysis. We meta-analyzed VAS scores at 6 hours, 12 hours, 24 hours, and 48 hours after surgery. The pooled results in all the comparison groups showed statistically lower scores in the ketamine groups than that in the control groups. The morphine equivalent consumption was also meta-analyzed in 24 hours and 48 hours after surgery. The pooled results in both groups revealed significantly less morphine equivalent consumption in the ketamine groups than those in the control groups. All the evidence demonstrated perioperative ketamine could be used as a supplementary analgesic agent in multimodal pain management strategy. Interestingly, as the time after surgery increased, the WMD of the VAS scores and morphine equivalent consumption at each time point gradually decreased. The decreasing trend may be related to the short half-life of ketamine and indicated that the analgesic effect of ketamine might be more effective in the early postoperative period.\[29\]

In addition, although the present meta-analysis showed the lower VAS scores and the less morphine equivalent consumption of patients in the ketamine groups, we have to note that ketamine is an addictive drug that may cause psychedelic experiences such as delusions, hallucinations, confusion, cognitive dysfunction, delirium, and mystical experiences.\[49–51\] The psychological effect is related to the dose of ketamine.\[49,52\] However, a large number of clinical studies have shown that the subanesthetic dose

![Figure 5. Forest plot of morphine equivalent consumption in the ketamine group and the control group after surgery. A, morphine equivalent consumption at 24 hours after surgery; B, morphine equivalent consumption at 48 hours after surgery.](image)

| Side Effect         | Included studies | Included patients | Odds Ratio (OR) [95% CI] | \(P\) | \(I^2\) | \(P\) value of Heterogeneity |
|---------------------|------------------|-------------------|--------------------------|------|-------|---------------------------|
| Sedation            | 2 [28, 31]       | 111               | 0.94 [0.29, 3.09]         | .92  | 0%    | .39                        |
| Dizziness           | 7 [26, 28, 30, 31, 35, 36, 39] | 321               | 1.15 [0.43, 3.06]         | .79  | 0%    | .59                        |
| Hallucination       | 5 [25–28, 30]    | 365               | 0.73 [0.30, 1.78]         | .49  | 0%    | .95                        |
| PONV                | 13 [20, 22, 25–28, 30–32, 35–37, 39] | 721               | 0.54 [0.37, 0.77]         | .0008| 0%    | .48                        |
| Sweating            | 2 [22, 31]       | 89                | 1.15 [0.15, 8.53]         | .89  | 0%    | .86                        |
| Pruritus            | 5 [25, 26, 28, 35, 37] | 346               | 1.20 [0.57, 2.50]         | .63  | 0%    | .55                        |
| Urinary retention   | 6 [22, 25, 28, 31, 32, 35] | 372               | 1.12 [0.58, 2.16]         | .73  | 0%    | .94                        |
| Constipation        | 2 [28, 31]       | 129               | 1.29 [0.41, 4.03]         | .71  | 73%   | .06                        |
| Version trouble     | 4 [25–27, 35]    | 274               | 1.13 [0.34, 3.69]         | .84  | 44%   | .17                        |
| Nightmares          | 2 [25, 30]       | 193               | 1.19 [0.54, 2.64]         | .66  | 0%    | .53                        |
| Delirium            | 2 [30, 37]       | 29                | 5.86 [0.26, 130.26]       | -    | -     | .26                        |
of ketamine has a central nervous analgesic effect with minimal impact on consciousness and cognition. None of the included study reported the side effect of post-operative cognitive dysfunction. It was demonstrated infrequent or recreational ketamine use does not appear to be associated with long-term cognitive impairment. Therefore, it can be used as a safe analgesic agent, especially for acute pain in the perioperative period, which is currently determined by the World Health Organization as a crucial drug for the administration of many other anesthetics. Further, the toxicity of ketamine can cause a variety of neurological, cardiovascular, psychiatric, genitourinary, and abdominal symptoms, which are dose-dependent. In the present study, we meta-analyzed the side effects of the included study. The ketamine group showed a lower pooled OR of PONV than the control group. The meta-analysis of the other side effects showed no differences between the 2 groups, which might be due to the small dose of ketamine applied in most included studies. Our results further confirmed the safety of small-dose ketamine for analgesia.

There are some limitations to the present meta-analysis. First, due to the different doses of ketamine used in each included study, we did not investigate the impact of the dose of ketamine. At present, there is no research report on the most suitable ketamine dose for perioperative evaluation of efficacy and safety. In addition, different anesthetic methods may affect postoperative pain control. These might be the cause of high heterogeneity. Second, only short-term outcomes (<48 hours) were investigated in the present study. Therefore, further studies about the analgesic effect of ketamine are still required in the future to determine the ideal patients and conditions for ketamine treatment and the ideal dose for analgesia.

5. Conclusion

The present study meta-analyzed the analgesia effect of perioperative ketamine for THA and TKA. The statistically lower VAS scores at 6 hours, 12 hours, 24 hours, and 48 hours after surgery and lower morphine equivalent consumptions in 24 hours and 48 hours after surgery were observed. These findings demonstrated the analgesic effect of perioperative ketamine for THA and TKA. The analysis of side effects further confirmed the safety of ketamine for analgesia. All the evidence indicated that perioperative ketamine could be used as a safe and effective analgesic agent for THA and TKA.

Author contributions

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