Systematic Review and Meta-Analysis

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The efficacy of celecoxib for pain management of arthroscopy

A meta-analysis of randomized controlled trials

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Abstract

Background: The efficacy of celecoxib for pain management of arthroscopy remains controversial. We conduct a systematic review and meta-analysis to assess if celecoxib before the surgery decreases postoperative pain intensity of arthroscopy.

Methods: We search PubMed, Embase, Web of science, EBSCO, and Cochrane library databases for randomized controlled trials (RCTs) assessing the effect of celecoxib versus placebo on pain control of arthroscopy.

Results: Five RCTs are included in the meta-analysis. Celecoxib is administered at 200 mg or 400 mg dosage before the surgery. Overall, compared with control group for arthroscopy, preemptive celecoxib has remarkably positive impact on pain scores at 2 to 6 hours (standard mean difference (SMD) = −0.66; 95% confidence interval (CI) = −0.95 to −0.36; $P < .0001$) and 24 hours after the surgery (SMD = −1.26; 95% CI = −1.83 to −0.70; $P < 0.0001$), analgesic consumption (SMD = −2.73; 95% CI = −5.17 to −0.28; $P = .03$), as well as the decrease in adverse events (risk ratio (RR) = 0.56; 95% CI = 0.39 to 0.79; $P = .001$), but shows no obvious effect on first time for analgesic requirement (SMD = 0.02; 95% CI = −0.22 to 0.26; $P = .87$), nausea, or vomiting (RR = 0.70; 95% CI = 0.42 to 1.17; $P = .18$).

Conclusion: Celecoxib administered at 200 mg or 400 mg dosage before the surgery decreases postoperative pain intensity of arthroscopy.

Abbreviations: CI = confidence interval, RCTs = randomized controlled trials, SMD = standard mean difference.

Keywords: arthroscopy, celecoxib, meta-analysis, pain management, randomized controlled trials

1. Introduction

Arthroscopy has been widely used for the treatment of knee and hip diseases.[1–3] Many patients still encounter moderate to severe pain, although arthroscopic surgery has less morbidity compared with open procedures.[4–6] This pain is caused by the insertion of arthroscopic instruments into the joint, soft tissue dissection, and distention caused by the irrigation of joint.[7,8] Inadequate management of perioperative pain can lead to prolonged hospital stays, delayed recovery, poor outcomes, and greater consumption of health care resources.[9–11]

Celecoxib is known as the selective cyclooxygenase (COX)-2 inhibitor, and has the properties of rapid absorption, high oral bioavailability, and preferential distribution into inflamed tissue.[12,13] Celecoxib may have the ability to prevent heterotopic bone formation for arthroscopy.[14] In one recent study, celecoxib administered 1 hour before arthroscopic surgery of hip benefits to pain control at 12 and 24 hours postoperatively and leads to the increase in physical composite scores.[15]

However, the efficacy of celecoxib versus placebo for pain management of arthroscopy has not been well established. Recently, several studies on the topic have been published, and the results have been conflicting.[15–18] With accumulating evidence, we therefore perform a systematic review and meta-analysis of randomized controlled trials (RCTs) to assess if celecoxib before the surgery decreases postoperative pain intensity of arthroscopy.

2. Materials and methods

Ethical approval and patient consent are not required because this is a systematic review and meta-analysis of previously published studies. The systematic review and meta-analysis are conducted and reported in adherence to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[19]

2.1. Search strategy and study selection

Two investigators have independently searched the following databases (inception to November 2018): PubMed, Embase, Web of science, EBSCO, and Cochrane library databases. The

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electronic search strategy is conducted using the following keywords: celecoxib and arthroscopy. We also checked the reference lists of the screened full-text studies to identify other potentially eligible trials.

The inclusive selection criteria are as follows:

(1) population: patients undergo arthroscopy;
(2) intervention treatments are celecoxib versus placebo;
(3) study design is RCT.

2.2. Data extraction and outcome measures

We have extracted the following information: author, number of patients, age, female, body mass index, duration of surgery, detail methods in each group, and so on. Data have been extracted independently by two investigators, and discrepancies are resolved by consensus. We also contact the corresponding author to obtain the data when necessary.

The primary outcomes are pain scores at 2–6 hours and 24 hours after the surgery. Visual analogue scale (VAS) is used to evaluate the pain intensity (VAS 0, no pain and 10, the worst unbearable pain). Secondary outcomes include analgesic consumption, first time for analgesic requirement, adverse events, nausea, and vomiting.

2.3. Quality assessment in individual studies

Methodological quality of the included studies is independently evaluated using the modified Jadad scale.[20] There are 3 items for Jadad scale: randomization (0–2 points), blinding (0–2 points), and dropouts and withdrawals (0–1 points). The score of Jadad scale varies from 0 to 5 points. An article with Jadad score ≤ 2 is considered to be of low quality. If the Jadad score ≥ 3, the study is thought to be of high quality.[21]

2.4. Statistical analysis

We estimate the standard mean difference (SMD) with 95% confidence interval (CI) for continuous outcomes (pain scores at 2–6 hours and 24 hours after the surgery, analgesic consumption, and first time for analgesic requirement) and risk ratios (RRs) with 95% CIs for dichotomous outcomes (adverse events, nausea, and vomiting). The random-effects model is used regardless of heterogeneity. Heterogeneity is reported using the I^2 statistic, and $I^2 > 50\%$ indicates significant heterogeneity.[22] Whenever significant heterogeneity is present, we search for potential sources of heterogeneity via omitting one study in turn for the meta-analysis or performing subgroup analysis. All statistical analyses are performed using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

3. Results

3.1. Literature search, study characteristics, and quality assessment

A detailed flowchart of the search and selection results is shown in Fig. 1. About 443 potentially relevant articles are identified initially. Finally, five RCTs are included in the meta-analysis.[15–18,23]

The baseline characteristics of five eligible RCTs in the meta-analysis are summarized in Table 1. The five studies are published between 2006 and 2017, and the total sample size is 548. There are knee and hip arthroscopies in the included RCTs. Mardani-Kivi 2013 (1) represented the study conducted by Mardani-Kivi et al for knee arthroscopic surgery of meniscectomy, while Mardani-Kivi 2013 (2) represented the same study for knee arthroscopic surgery of anterior cruciate ligament reconstruction.[17] Celecoxib is administered at 200 mg or 400 mg dosage before the surgery.

Among the five studies included here, two studies report pain scores at 2 to 6 hours after the surgery,[16,17] one study reports pain scores at 24 hours after the surgery,[17] two studies report analgesic consumption,[17,18] two studies report first time for analgesic requirement,[18,23] two studies report adverse events,[17,23] as well as two studies report nausea and vomiting.[17,23] Jadad scores of the five included studies vary from 3 to 5, and all five studies are considered to be high-quality ones according to quality assessment.

3.2. Primary outcomes: pain scores at 2–6 hours and 24 hours after the surgery

These outcome data are analyzed with the random-effects model, and compared to control group for arthroscopy, preemptive celecoxib results in significantly lower pain scores at 2 to 6 hours after the surgery (SMD = −0.66; 95% CI = −0.95 to −0.36; $P < .0001$) with low heterogeneity among the studies ($I^2 = 13\%$, heterogeneity $P = .32$) (Fig. 2A), and pain scores at 24 hours after the surgery (SMD = −1.26; 95% CI = −1.83 to −0.70; $P < .0001$) with significant heterogeneity among the studies ($I^2 = 50\%$, heterogeneity $P = .16$) (Fig. 2B).

3.3. Sensitivity analysis

Significant heterogeneity is observed among the included studies for pain scores at 24 hours after the surgery, but there is just one RCT reporting knee arthroscopic surgery of meniscectomy and anterior cruciate ligament reconstruction. It is not available to perform sensitivity analysis via omitting one study in turn.

3.4. Secondary outcomes

In comparison with control group for arthroscopy, preemptive celecoxib is associated with substantially reduced analgesic consumption (SMD = −2.73; 95% CI = −5.17 to −0.28; $P = .03$; Fig. 2C), but exhibits no obvious effect on first time for analgesic requirement (SMD = 0.02; 95% CI = −0.22 to 0.26; $P = .87$; Fig. 2D). In addition, preemptive celecoxib leads to the decrease in adverse events (RR = 0.56; 95% CI = 0.39 to 0.79; $P = .001$; Fig. 2E), but shows no significant impact on nausea or vomiting (RR = 0.70; 95% CI = 0.42 to 1.17; $P = .18$; Fig. 2F).

4. Discussion

Celecoxib is a novel selective COX-2 inhibitor, and has the property of preferential distribution into inflamed tissue.[24,25] Previous studies show that celecoxib is comparable with or superior to rofecoxib for the treatment of moderate pain.[26] Celecoxib is reported to be superior to lumiracoxib, and has become the first-choice analgesic agent for osteoarthritis pain.[27] Celecoxib has proved to be beneficial for pain control in various orthopedic surgeries. Patients receiving 400 mg of celecoxib 1 hour before knee arthroscopy have reduced consumption of opioid medication and incidence of opioid-related adverse events

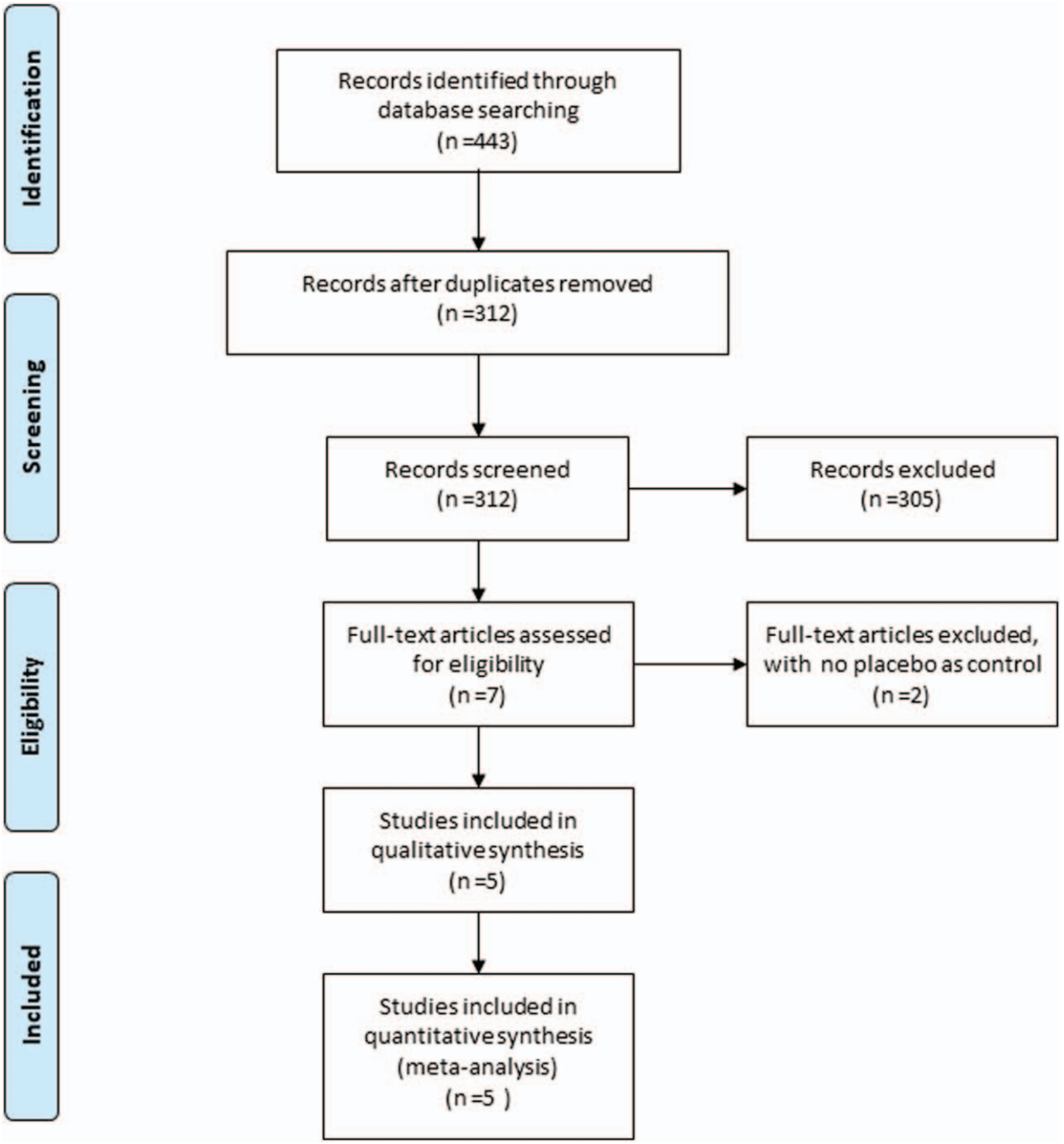

Figure 1. Flow diagram of study searching and selection process.

in the early postoperative period.[23] In another study, the decrease in pain intensity and opioid consumptions, as well as the increase in knee range of motion are observed after celecoxib use for knee arthroplasty.[28]

In addition, celecoxib before the surgery is proved to be more effective for pain control than that given postoperatively.[29] Our meta-analysis suggests that compared to control group for arthroscopy, preemptive celecoxib shows favorable influence on pain control at 2–6 hours and 24 hours after the surgery, as well as postoperative analgesic consumption, but reveals no obvious impact on first time for analgesic requirement. However, there is significant heterogeneity when performing sensitivity analysis and this heterogeneity may be caused by different procedures of arthroscopy, various doses of celecoxib, and the time of drug use.

Traditional pain management after orthopedic surgery mainly requires the use of narcotic medications,[30] but narcotic medications may have severe side effects on the gastrointestinal, respiratory, integumentary, genitourinary, and neurologic systems.[31] In order to reduce these side effects, multimodal pain management has been extensively developed for pain control.[16] Multimodal pain management aims to target multiple pathways in the pain signaling cascade to minimize pain intensity and side effects.[32–34] Celecoxib has emerged as an increasing important drug for multimodal pain management. The results of our

Table 1

Characteristics of included studies.

		Celecoxib group						Control group						
No.	Author	Number	Age (yrs)	Female (n)	Body mass index (kg/m^2)	Duration of surgery (min)	Methods	Number	Age (yrs)	Female (n)	Body mass index (kg/m^2)	Duration of surgery (min)	Methods	Jada scores
1	Kahlenberg 2017	50	34.2±11.9	26	–	95.4±20.2	400 mg celecoxib administered 1 h before hip arthroscopy	48	35.8±11.6	29	–	95.8±17.3	Matched placebo	4
2	Zhang 2014	27	41.0±4.9	13	33±5.1	67±7	200 mg celecoxib administered 1 h preoperatively for arthroscopic hip surgery	26	43.5±5.1	15	35±4.9	90±3	Matched placebo	5
3	Mardani-Kivi 2013 (1)	31	32.7±8	22	24±2.7	30.3±7	400 mg celecoxib administered 2 h before knee arthroscopic surgery of meniscectomy	32	32.2±9.8	20	23±2.6	31.7±4	Matched placebo	4
	Mardani-Kivi 2013 (2)	34	25.8±7.7	28	24±2.6	40±7	400 mg celecoxib administered 2 h before knee arthroscopic surgery of anterior cruciate ligament reconstruction	33	26.7±4.9	25	23.6±3.5	36.7±7	Matched placebo	4
4	Boonriong 2010	35	30	4	–	60.73±14.20	400 mg celecoxib administered 1 h before arthroscopic anterior cruciate ligament reconstruction	32	30	4	–	60.45±20.30	Matched placebo	3
5	Ekman 2006	99	45.5±11.1	46	–	–	400 mg celecoxib administered 1 h before arthroscopic knee meniscectomy	101	45.0±10.9	39	–	–	Matched placebo	4

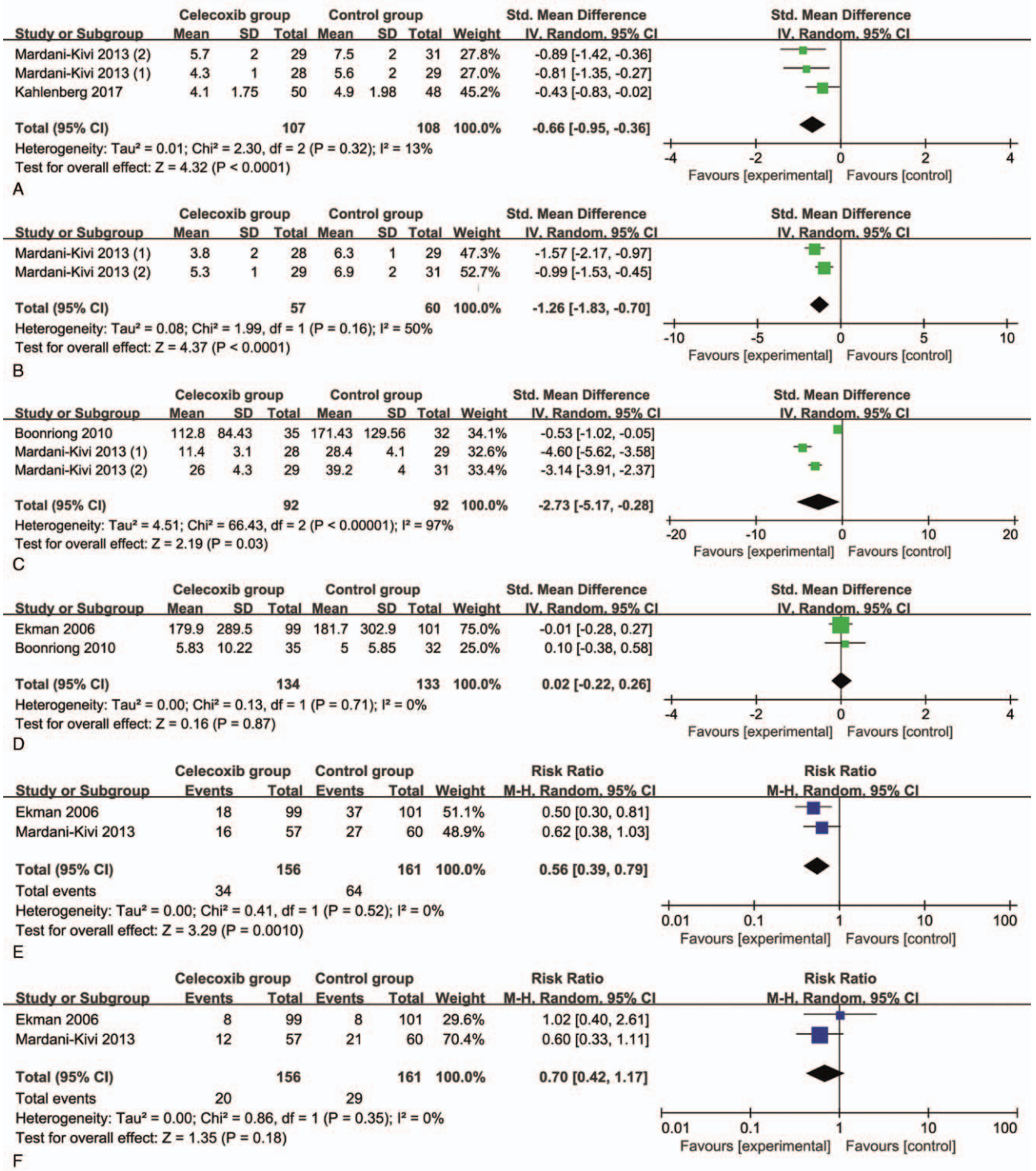

Figure 2. Forest plot for the meta-analysis of (A) pain scores at 2 to 6 hours postoperatively, (B) pain scores at 24 hours postoperatively, (C) analgesic consumption, (D) first time for analgesic requirement, (E) adverse events, and (F) nausea and vomiting.

meta-analysis show significant decrease in adverse events after using preemptive celecoxib for arthroscopy.

This meta-analysis has several potential limitations. First, our analysis is based on five RCTs, and three of them have a relatively small sample size ($n < 100$). Overestimation of the treatment effect is more likely in smaller trials compared with larger samples. Second, there is significant heterogeneity which may result from different procedures of arthroscopy, various doses of celecoxib, and the time of drug use. Finally, it is feasible to perform the meta-analysis of some important outcomes such as pain scores in longer time of follow-up and discharge time based on current RCTs.

5. Conclusions

In conclusion, celecoxib administered at 200 mg or 400 mg dosage before the surgery decreases postoperative pain intensity of arthroscopy.

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Author contributions

Conceptualization: Ruijie Wan.
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Funding acquisition: Pin Li.
Methodology: Ruijie Wan, Pin Li.
Project administration: Pin Li.
Supervision: Heng Jiang.
Writing – original draft: Heng Jiang.
Writing – review & editing: Heng Jiang.

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