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The Effect of Preoperative Tamsulosin on Ureteral Navigation, Operation, and Safety: A Systematic Review and Meta-Analysis

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Keywords
Preoperative tamsulosin · Ureteral navigation · Ureteroscopy · Meta-analysis

Abstract

Introduction: Urolithiasis is one of the most common diseases in the world, and at present, ureteroscopy (URS) is the first choice for its treatment. Although the effect is good, there is a risk of insertion failure of ureteroscope. Tamsulosin, as an α-receptor blocker, has the function of relaxing ureteral muscles, and can help stones to be discharged from ureteral orifice. In this study, we aimed to determine the effect of preoperative tamsulosin on ureteral navigation, operation, and safety. ***Methods:*** This study was conducted and reported according to the meta-analysis extension of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The PubMed and Embase databases were searched for studies. Data were extracted according to the PRISMA principles. We collected and combined randomized controlled trial and researches in reviews of preoperative tamsulosin to explore the effect of preoperative tamsulosin on ureteral navigation, operation, and safety. A data synthesis was performed using RevMan 5.4.1 software (Cochrane). Heterogeneity was mainly evaluated with I2 tests. Key metrics include: success rate of ureteral navigation, time of URS, stone-free rate, and postoperative symptoms. ***Result:*** We summarized and analyzed 6 studies. We noted a statistically significant improvement in the success rate of ureteral navigation (Mantel-Haenszel [M-H], odds ratio [OR]: 3.78, 95% confidence interval [CI]: [2.34, 6.12], $p < 0.01$) and stone-free rate (M-H, OR: 2.25, 95% CI: [1.16, 4.36], $p = 0.02$) with tamsulosin preoperatively. At the same time, we also observed that postoperative fever (M-H, OR: 0.37, 95% CI: [0.16, 0.89], $p = 0.03$) and postoperative analgesia (M-H, OR: 0.21, 95% CI: [0.05, 0.92], $p = 0.04$) were also reduced because of preoperative tamsulosin. ***Conclusion:*** Preoperative tamsulosin can not only increase the one-time success rate of ureteral navigation and the stone-free rate of URS but also reduce the incidence of postoperative adverse symptoms such as postoperative fever and postoperative pain.

Introduction

Urolithiasis is one of the most common urological diseases in the world. After several years of research and development, the currently recognized preferred treatment worldwide is ureteroscopy (URS) [1]. Ureteral calculi account for about 20% of urolithiasis cases, 70% of which are lower ureteral calculi, with most having obvious

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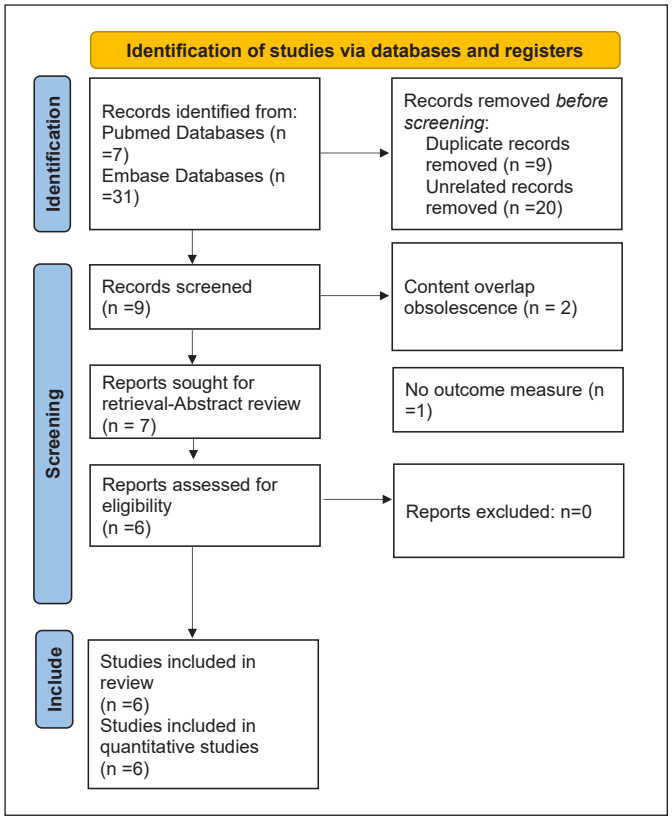

Fig. 1. Flowchart of selection of included studies.

symptoms [2]. As a possible culprit of worsening kidney function, ureteral stones should be treated as quickly as possible [3]. Although URS has been regarded as the best choice for treating urolithiasis in adults and children, the treatment method still has complications [4–6]. The failure of the first attempt to insert a ureteroscope is one of the greatest risks of complication. When access is difficult, ureteric balloon dilatation is a possible strategy for therapy. However, tissue ischemia means that ureteral balloon dilation is also associated with the risk of ureteral perforation and stricture [7]. Therefore, the success rate of ureteral orifice navigation for the first time largely determines the success of the treatment process.

The constriction of the ureteral orifice and the ureteral wall also determines the success of ureteral navigation. Three kinds of alpha-1 adrenoceptors are distributed in the wall of the ureter: alpha-1A, alpha-1B, and alpha-1D. The adrenoceptors distributed in the ureteral orifice are mainly alpha-1D and alpha-1A [8]. After alpha-blockers are administered, the receptors of the ureteral smooth muscle are inhibited, resulting in the relaxation of the ureteral orifice [9, 10]. The main targets of tamsulosin are alpha-1A and alpha-1D, which significantly relax the muscles of the ureteral orifice and help increase the discharge of stones [11]. Extracorporeal shock wave therapy has also been reported to heighten the stone clearance rate [12]. Some papers suggest that preoperative use of tamsulosin can reduce the occurrence of secondary treatment, such as ureteral balloon dilatation, and that it can raise the probability of a successful 1-time ureteral orifice navigation [8, 11, 13, 14]. Nonetheless, the specific effects of alpha-blockers, such as tamsulosin, on URS have not been fully studied. The aim of this study was to investigate the effect of the preoperative use of tamsulosin on URS surgery, the success rate of ureteral navigation, and postoperative symptoms.

Methods

This meta-analysis evaluated the effect of preoperative tamsulosin on ureteral navigation success and followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines [15].

Study Search

The medical databases PubMed, web of science, and Embase were our main search databases. We searched and screened the titles and abstracts of the articles. We searched for the terms "tamsulosin," "ureteroscopy," and "preoperative" and combined them using the Boolean operator (And).

Screening Process and PICOS Principle

We used the population, intervention, comparison, outcomes, and study (PICOS) principle during the screening process to select the literature [16]. The principle was applied as follows: population (P) – the patients who need to be cured by URS; intervention (I) – preoperative tamsulosin; comparison (C) – the patients without preoperative tamsulosin; outcomes (O) – the success rate of 1-time ureteral orifice navigation; study designs (S) – comparative studies.

Articles were excluded if they were (a) not related to preoperative tamsulosin or URS; (b) had no comparative data or relevant outcomes; or (c) were in the form of conference proceedings, letters or comments. The specific screening flow chart is shown in Figure 1.

Quality Assessment

The basic information of the literature we included can be viewed in Table 1. The Jadad scale was our tool to evaluate the quality of randomized controlled trials (RCTs) that were included. See online supplementary Table 1 for details (for all online suppl. material, see www.karger.com/doi/10.1159/000528889). The New Castle-Ottawa Scale (NOS) was used to evaluate the quality of non-RCTs. See online supplementary Table 2 for details. The evaluation process was completed by 2 authors (CC and YC). Any differences were settled through discussion, and a third person, one of random co-authors, was invited to judge if necessary.

Data Acquisition

The success rate of 1-time ureteral orifice navigation in URS was used as the main outcome index. In order to explore other advantages of the preoperative use of tamsulosin, the second outcome index included operation time, stone clearance rate, postoperative fever, and analgesia. Regarding the definition of the stone clearance rate, since we included both adult and children's studies, our definition of complete clearance changed depending on the participant. In adult studies, the patient was considered stone free if they had a stone less than 3 mm in size, while children were not considered stone free if only any stone residue remained.

Indicator Selection

Since we needed to compare the effects of preoperative tamsulosin on ureteral orifice navigation and ureteroscopic surgery, we chose the 1-time success rate of ureteral orifice navigation as the main indicator. The operation time, stone-free rate, and postoperative symptoms were secondary indicators. Regarding the 1-time success rate of ureteral navigation, different definitions of indicators are reported in the literature. We also considered the 1-time success rate of no ureteral stent, 16-French ureteral sheath, and reaching the stone as the 1-time success rate of ureteral navigation.

Data Consolidation and Analysis

We completed the complicated data synthesis operation process using RevMan 5.4.1 software (Cochrane). As in other literature studies, a p value <0.05 was considered statistically significant, and a 95% confidence interval (CI) of the synthesized data was also provided. Our final evaluation index and analysis sources were the odds ratio (OR) and the mean difference of our synthesized data. The I^2 value was used as the index to assess heterogeneity. If the index was more than 50%, it indicated that heterogeneity was significant. Heterogeneity was also evaluated with a random-effects model.

Result

We ultimately screened 6 studies [17–22], including 2 RCTs and 4 researches in review. For the success rate of ureteral navigation, we merged the data of these 6 studies. We merged the data of 3 studies [17, 19, 22] to assess the URS operation time. To assess the stone clearance rate and postoperative symptoms, we also merged 2 studies correspondingly.

The Success Rate of Ureteral Navigation

After synthesizing the data from 576 patients, we found that preoperative tamsulosin increased the success rate of ureteral navigation, and the difference was statistically significant (Mantel-Haenszel (M-H), OR: 3.78; 95% CI: 2.34–6.12; $p < 0.01$; Fig. 2a). We concluded that there was no significant heterogeneity in these results by observing the I^2 value ($I^2 = 22\%$; $p = 0.27$). Further subgroup

Table 1. Basic information of included studies

Study	Year	Country	Study design	Mean age	Sample size	Treatment involved	Intervention	Control	Efficiency outcome assessment
Tawfeek et al. [17]	2020	Egypt	RCT	38	120	Stone disease	Preoperative tamsulosin	No tamsulosin	1. Operation time 2. First placement success rate 3. Postoperative symptom
Morley et al. [18]	2020	America	RIR	12	76	Stone disease	Preoperative tamsulosin	No tamsulosin	1. First placement success rate
McGee et al. [19]	2021	America	RIR	13	49	Stone disease	Preoperative tamsulosin	No tamsulosin	1. Operation time 2. First placement success rate
Kaler et al. [20]	2018	Germany	RIR	59	77	Stone disease	Preoperative tamsulosin	No tamsulosin	1. First placement success rate
Kaler et al. [21]	2017	Germany	RIR	58	84	Stone disease	Preoperative tamsulosin	No tamsulosin	1. First placement success rate
Demir et al. [22]	2022	Turkey	RCT	46	137	Stone disease	Preoperative tamsulosin	No tamsulosin	1. Operation time 2. First placement success rate 3. Postoperative symptom

RIR, research in review.

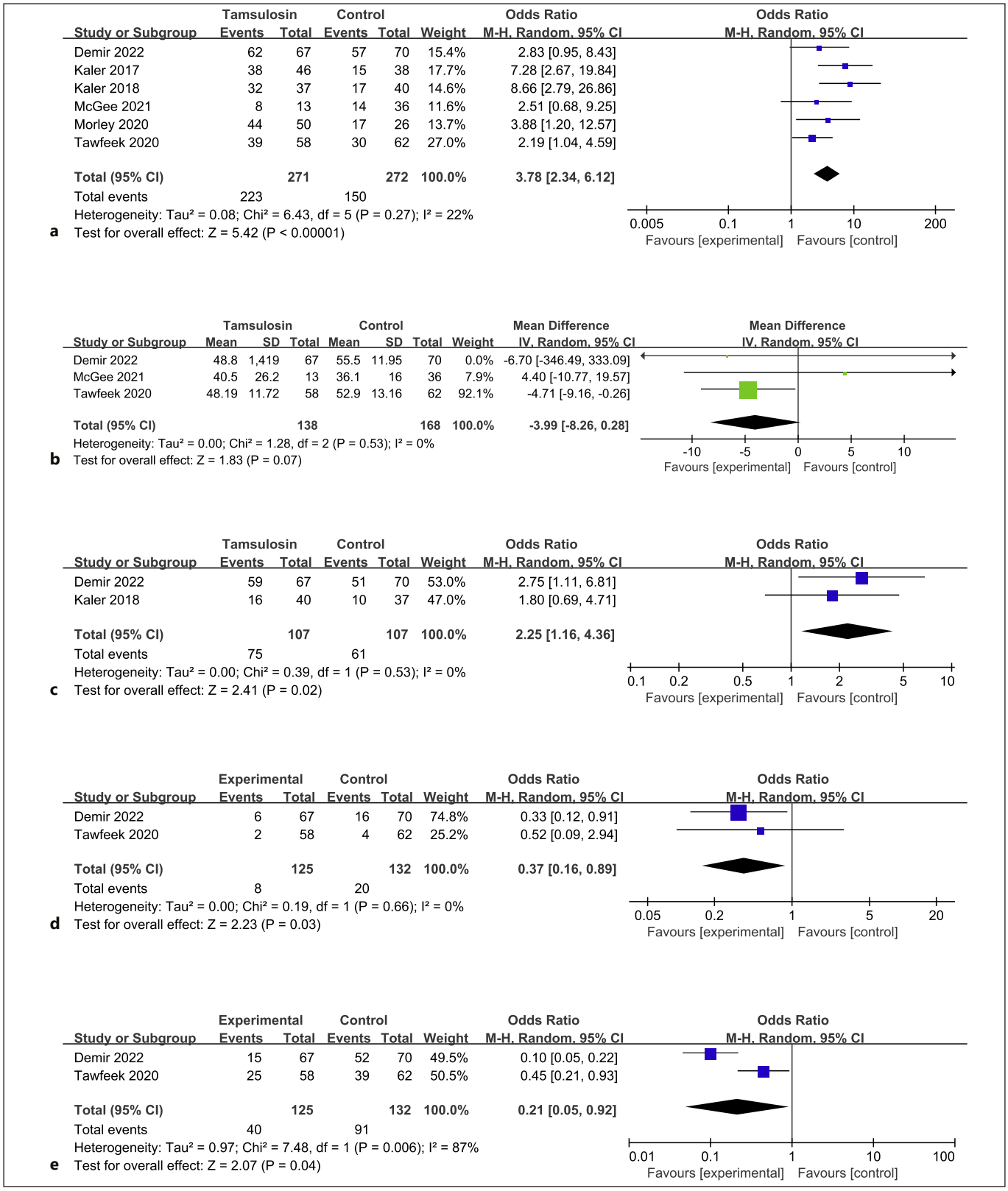

Fig. 2. Forest plots. **a** Success rate of ureteral navigation. **b** Time of ureteroscopy. **c** Stone-free rate. **d**, **e** Postoperative symptoms. MD, mean difference; IV, inverse variatiance.

Table 2. Subgroup analysis of efficiency data synthesis

Category of variables	Heterogeneity				*p* value for difference
	studies, *n*	I^2, %	*p* value	OR (95% CI)	
Efficiency	6				
Study design					
Randomized	2	0	0.70	2.37 [1.29, 4.38]	0.006
Non-randomized	4	0	0.45	5.36 [3.03, 9.47]	<0.00001
Geographic area					
America	2	0	0.63	3.20 [1.34, 7.65]	0.009
Europe	3	14	0.31	5.66 [2.90, 11.04]	<0.00001
Africa	1	–	–	2.19 [1.04, 4.59]	0.04
Patient age					
Adult (>18)	4	51	0.11	4.18 [2.09, 8.36]	<0.00001
Child (<18)	2	0	0.63	3.20 [1.34, 7.65]	0.009
Publication year					
2020–2022	4	0	0.88	2.62 [1.59, 4.32]	0.0002
Earlier than 2020	2	0	0.82	7.86 [3.71, 16.64]	<0.00001

analyses were performed, and no significant associations were found, suggesting that homogeneity between patients was relatively stable (Table 2).

Time of URS

After synthesizing the data from 306 patients, we found that preoperative tamsulosin did not reduce the duration of URS since the difference was not statistically significant (inverse variance, mean difference: −3.99, 95% CI: −8.26 to 0.28; $p = 0.07$; Fig. 2b). We concluded that there was no significant heterogeneity in these results by observing the I^2 value ($I^2 = 0\%$; $p = 0.53$).

Stone-Free Rate

After synthesizing the data from 214 patients, we found that preoperative tamsulosin increased the stone-free rate of URS and the difference was statistically significant (M-H, OR: 2.25; 95% CI: 1.16–4.36; $p = 0.02$; Fig. 2c). We concluded that there was no significant heterogeneity in these results by observing the I^2 value ($I^2 = 0\%$; $p = 0.53$).

Postoperative Symptoms

After synthesizing the data from 257 patients, we found that preoperative tamsulosin decreased the incidence of postoperative fever (M-H, OR: 0.37; 95% CI: 0.16–0.89; $p = 0.03$; Fig. 2d) and postoperative application of analgesic drugs (M-H, OR: 0.21; 95% CI: 0.05–0.92; $p = 0.04$; Fig. 2e). We concluded that there was no significant heterogeneity in postoperative fever by observing the I^2 value ($I^2 = 0\%$, $p = 0.66$). However, the postoperative application of analgesic drugs had notable heterogeneity ($I^2 = 87\%$, $p = 0.006$).

Discussion

After a clear diagnosis, the treatment of stones should be urgent. However, the primary treatment plan is formulated according to the size of the stone. The clinical symptoms are not obvious for stones smaller than 3 mm, and we usually choose conservative observation and treatment. For stones with a size of 7–10 mm, it is clinically believed that the stones will not be discharged on their own, and medical expulsion therapy (MET) is used for treatment [23]. The so-called MET involves the use of alpha-blockers to loosen the smooth muscle of the ureter, in order to facilitate the stone discharging. After treatment by MET, about 65% of stones can pass through and are discharged [24, 25]. Multiple studies recommended the application of URS on stones larger than 10 mm or after the failure of MET. Since its invention by Hopkins in 1956, URS has been widely recognized and regarded as the best practice in the treating ureteral stones [26].

Tamsulosin acts as an alpha-blocker that blocks alpha-1A and alpha-1D receptors on the ureter, slacking the muscles of the ureter and reducing its pressure. It also affects nerves and neurotransmitters, which can reduce the contraction of the bladder to reduce pain [27].

In our study, there was a statistically significant difference in the success rate of ureteral navigation with or without preoperative tamsulosin. One of the criteria for excluding patients in our included studies was that patients had ureteral stents before URS treatment because some investigators found that the placement of ureteral

stents before URS might also cause dilatation of the ureteral orifice and affect our observation and judgment of the effect of tamsulosin [28]. The results showed that preoperative tamsulosin increased the 1-time success rate of ureteral navigation, which might be related to the relaxation effect of alpha-blockers such as tamsulosin on ureteral smooth muscle. Results also showed that preoperative tamsulosin could increase the 1-time success rate of ureteral navigation, which might be related to the slack effect of alpha-blockers such as tamsulosin on ureteral smooth muscle. Surprisingly, preoperative tamsulosin did not make a significant difference in the URS operation time compared to when it was not used. The reason for this might be that there were too many factors affecting the operation time.

Regarding URS surgery, we observed the stone-free rate of URS surgery, which might be a concern for patients. The overall URS procedure was smoother due to the increased success rate of ureteral navigation, which might explain the results we obtained with regard to the stone-free rate: preoperative tamsulosin can increase the stone-free rate of the URS surgery. However, we could not just focus on the procedure of URS. We should also pay attention to postoperative symptoms. The occurrence of postoperative fever and the application of postoperative analgesic drugs are topics of common concern for surgeons and patients, and the appearance of these symptoms is also an indicator for judging the success of the surgery. Fortunately, the incidence of postoperative fever and the application of postoperative analgesic drugs decreased after treatment with preoperative tamsulosin, which once again confirmed the benefits of preoperative tamsulosin for URS surgery.

From a clinical perspective, the success of ureteral navigation could lower the use of ureteral stent dilation, which would benefit patients in terms of fewer surgical procedures and postoperative complications, and lower surgical costs. Preoperative tamsulosin can help ureteral navigation and improve the success rate of ureteral navigation, producing a series of advantages over pure URS.

Our study also has some limitations. First, with regard to the characteristics of stones, only a few of the included studies described the nature of the stones in the patients, while the rest did not, which made it difficult for us to analyze whether there were differences in the treatment for different types of stones. Second, the included literature had slightly different definitions of the outcome index of the 1-time ureteral oral navigation success rate. We could only understand and combine relevant data based on our experience, inevitably leading to bias. Third, from the perspective of drug dosage and time, the duration of drug use in a few reports was shorter than that in other studies, and some reports did not indicate the specific measurement of drug intake, which might have biased the final results. Eventually, the main limitation was that the sample size was too small, and the reliability of the final data still needs to be improved with an increase in sample size.

Conclusion

Preoperative tamsulosin can increase the 1-time success rate of ureteral navigation and the stone-free rate of URS and reduce the incidence of postoperative adverse symptoms, such as postoperative fever and postoperative pain.

Statement of Ethics

An ethics statement is not applicable because this study is based exclusively on published data.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Chao Cheng and Yucheng Ma have contributed equally to this work, including searching and screening literature, collecting data, and writing articles. Jun Wen, Liyuan Xiang, and Xi Jin provided guidance, revision, and contact for publication and other contributions.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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