Efficacy and Safety of Microsurgical Subinguinal Varicocelectomy with and without Testicular Delivery for Varicocele Patients: A Systematic Review and Meta-Analysis

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Purpose: This study reviewed the efficacy and safety of the microsurgical subinguinal varicocelectomy (MSV) with and without testicular delivery (TD) for varicocele patients.

Materials and Methods: A systematic literature search was conducted in EMBASE, PubMed, MEDLINE, Cochrane databases, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), and Google Scholar databases to identify relevant studies that reported MSV with and without TD for varicocele patients published in English or Chinese up to October 2018. The Newcastle-Ottawa Scale (NOS) and the Jadad scores were used to evaluate the methodological quality of all the included studies. We also used the Cochrane Collaboration's tool for assessing risk of bias for each study. The Review Manager Software version 5.3 was used to conduct data analysis.

Results: Four RCTs and three retrospective studies consisting of 993 patients were included. Meta-analysis results indicated that both of the two treatments were effective and safe. MSV with TD had a lower recurrence rate (OR = 0.20, 95% CI: 0.06 - 0.65, *P* = .007, I2 = 0%) and postoperative serum testosterone level (MD = -39.07, 95% CI: -51.95 - -26.18, P = .00001, I2 = 0%) compared with MSV without TD but was associated with higher postoperative complications rate (OR=7.35, 95% CI: 2.92-18.53, *P* < .0001, I2 = 0%). We found no significant differences in operation time (MD = 12.46, 95% CI:0.11-24.81,P= .05, I2 = 87%), sperm concentration (MD = 3.73, 95% CI: -2.88 - 10.35, *P* = .27, I2 = 81%), sperm motility (MD = 10.96, 95% CI: -11.93 - 33.86, *P* = .35, I2 = 99%), and pregnancy rate(OR = 0.65, 95% CI: 0.37- 1.16, *P* = .15, I2 = 0%).

Conclusion: This meta-analysis compared efficacy and safety of MSV with and without TD for varicocele patients. MSV with TD was associated with a higher postoperative complication rate but lower recurrence rate and postoperative serum testosterone level than MSV without TD. In terms of preoperative serum testosterone level, operation time, sperm concentration, sperm motility, and pregnancy rate, we found no significant differences.

Keywords: varicocele; microsurgical subinguinal varicocelectomy; testicular delivery

INTRODUCTION

Varicocele is defined as dilatation and tortuousness of pampiniform plexus of scrotal veins. The awful impact of varicocele upon spermatogenesis has been recognized for a long time, and the prevalence of varicocele in the normal male population is estimated to be 15 to 20%, and 21% to 41% of men with primary infertility, and 75% to 81% of men with secondary infertility[1-3]. Surgical repair is generally recognized as an effective method to treat varicocele[4], and it can improve sperm parameters, serum testosterone level, and pregnancy rates[5-7]. There were several common surgical options for varicoceles, including open techniques, microsurgical subinguinal varicocelectomy (MSV), and laparoscopic ligation. Some findings reported that among the kinds of approaches of surgical repair, MSV seems to have better outcomes such as higher pregnancy rate, shorter hospital stays, less cost, little effect of anesthesia, lower complication rates and postoperative recurrence[6,8-11]. However, there is still a huge controversy about the efficacy and safety of MSV with and without delivery of the testis and ligation of gubernacular veins in the treatment of varicocele. Some studies have pointed out that the main factor of recurrence after the operation of varicocele is the existence of the gubernacular vein, so MSV with delivery of the testis and ligation of gubernacular veins should be adequately carried out[12,13]. Investigators such as Kim and his colleagues held the opposite view; they thought that the dilatation of gubernacular vein maybe is caused by compensation of the body and MSV without testicular delivery (TD) was not responsible for the significant increase of recurrence rate, and it could shorten operation time and decrease the risk of side-injury during surgery[10,14].

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Table 1. Characteristics and quality assessment of the included studies.

Studies	Country	Study period (year)	Study design	Treatment	age,years	Varicocele grade (I/II/III)	Varicocele side (left/bilateral)	follow-up time (month)	LE	Study quality
Ramasamy et al.2006	America	-	Retrospective case control	TD	-	14/18/14	-	3,6,9,24	3b	7*
				NTD	-	13/34/27	-			
Hou et al.2015	China	2011-2012	RCT	TD	27.94 ± 3.46	6/13/31	36/14	3,6,12	2b	3#
				NTD	28.32 ± 3.89	7/10/33	35/15			
Spinelli et al.2016	Italy	2008-2013	RCT	TD	7-17	-	-	6,12	2b	3#
				NTD	-	-				
Choi et al.2017	Korea	2003-2013	RCT	TD	12.8 ± 3.08	0/4/21	25/0	12	2b	3#
				NTD	13.2 ± 3.19	0/5/28	33/0			
Nie et al.2017	China	2011-2014	Retrospective case control	TD	26/7	-	-	6	3b	7*
				NTD	-	-				
Allameh et al.2018	Iran	2014-2016	RCT	TD	27.3 ± 6.1	0/0/197	-	6	2b	3#
				NTD	25.9 ± 4.6	0/0/200	-			
Yang et al.2018	China	2015-2017	Retrospective case control	TD	24.7 ± 5.9	0/8/32	36/4	3	3b	7*
				NTD	27.6 ± 8.2	11/50/62	113/10			

TD = Microsurgical subinguinal varicocelectomy with testicular delivery ; NTD=Microsurgical subinguinal varicocelectomy without testicular delivery; RCT= randomized controlled trial; #Jadad scale (score from 0 to 5); *Using Newcastle-Ottawa scale (score from 0 to 9);- No specific figures but without significant difference.

So far, no meta-analysis has been conducted to compare the efficacy and safety of MSV with and without TD for varicocele patients. Therefore, the aim of this study was to systemically search and analyze the available literature to conduct a comprehensive meta-analysis of existing studies to compare efficacy and safety of MSV with and without TD for varicocele patients.

MATERIALS AND METHODS

This meta-analysis was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement[15].

Data sources and searches

A systematic literature search was conducted in the EMBASE, PubMed, MEDLINE, Cochrane, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBMdisc), and Google Scholar databases to identify relevant studies that reported microsurgical subinguinal varicocelectomy with and without testicular delivery for varicocele patients published in English or Chinese up to October 2018. The Medical Subject Heading (MeSH) terms and/or key words and/or free words used were (microsurgical subinguinal varicocelectomy OR MSV) AND (testicular delivery OR TD) AND varicocele. Then we used the reference lists from key studies to make additional manual searches to retrieve other papers relevant to our topic. Some missing data from selected studies were obtained by contacting corresponding authors.

Study selection

Two reviewers (B. L. and J. L.) reviewed all the full texts of the identified studies. Our meta-analysis included the studies which met the following inclusion criteria: 1. the study must be a retrospective case control study or randomized controlled trial; 2. subjects were varicocele patients treated by microsurgical subinguinal varicocelectomy (MSV) with and without testicular delivery (TD); 3. The study evaluated the efficacy of MSV with and without TD in management of varicocele patients in regards to these outcomes: operation time, sperm concentration, sperm motility, pregnancy rate, postoperative complications rate, recurrence rate, and serum testosterone level (at least two aspects must

Table 2. Summary of baseline patient characteristics and the operative effect of included studies.

Author, year	Treatment	Sample size (n)	Operation time (min)	Sperm concentration (× 10^6 /mL)		Motile Sperm		Pregnancy rate	Postoperative complications rate	The recurrence rate	Serum testosterone level	
				preoperatively	postoperatively	preoperatively	postoperatively				preoperatively	postoperatively
Ramasamy et al.2006	TD	55	-	-	-	63 ± 9×10^6/ejaculate	93 ± 5×10^6/ejaculate	40.5%(15/37)	0% (0/55)	0% (0/55)	406 + 23(ng/L) (n = 42)	432 ± 22(ng/L) (n = 42)
	NTD	110	-	-	-	30 ± 6	65 ± 11	56% (32/57)	0% (0/110)	0% (0/110)	323 ± 41(ng/L) (n=86)	471 ± 53(ng/L) (n=86)
Hou et al.2015	TD	50	90.50 ± 15.60	20.46 ± 5.79	27.99 ± 8.90	25.14 ± 10.38(%)	39.34 ± 14.23(%)	42%(21/50)	-	0%(0/50)	6.24 ± 2.25(ng/mL)	-
	NTD	50	84.30 ± 15.58	21.36±6.48	29.54±10.99	24.20±9.91(%)	40.59±13.05(%)	48%(24/50)	-	0%(0/50)	6.74 ± 2.17(ng/mL)	-
Spinelli et al. 2016	TD	35	-	-	-	-	-	-	0%(0/35)	0%(0/35)	-	-
	NTD	35	-	-	-	-	-	-	0%(0/35)	12%(3/35)	-	-
Choi et al. 2017	TD	25	-	-	-	-	-	-	60% (15/25)	20%(5/25)	-	-
	NTD	33	-	-	-	-	-	-	15%(5/33)	6%(2/33)	-	-
Nie et al.2017	TD	20	-	63. 10 ± 21. 10	168. 97 ± 43. 65	34. 80 ± 9. 95(%)	55. 96 ± 9. 90(%)	-	10% (2/20)	0%(0/20)	886. 5 ± 148(ng/L)	876. 5 ± 154(ng/L)
	NTD	20	-	71. 30 ± 22. 46	176. 38 ± 37. 49	26. 41 ± 13. 69(%)	60. 66 ± 10. 92(%)	-	0%(0/20)	0%(0/20)	903. 1 ± 159(ng/L)	918. 5 ± 124(ng/L)
Allameh et al. 2018	TD	197	-	40.3 ± 7.1	58.7 ± 6.4	32.5 ± 5.5(%)	78.8 ± 7.3(%)	-	0.5%(1/197)	1.5%(3/197)	-	-
	NTD	200	-	36.9 ± 7.1	54±5.3	28.1 ± 6.6(%)	43.3 ± 6.1 (%)	-	0%(0/200)	6.5%(13/200)	-	-
Yang et al. 2018	TD	40	81.1 ± 20.0	50.3 ± 54.6	88.4±39.1	31.3 ± 18. 7(%)	52. 5 ± 15. 2	-	12.5%(5/40)	0%(0/40)	14.5 ± 3.6(nmol /L)	-
	NTD	123	62.3 ± 9.6	42.9 ± 39.8	62.3±76.4	27.7 ± 15.7(%)	38.6 ± 20.1(%)	-	1.6%(2/123)	0%(0/123)	16.0 ± 5. 4(nmol /L)	-

TD = Microsurgical subinguinal varicocelectomy with testicular delivery ; NTD=Microsurgical subinguinal varicocelectomy without testicular delivery

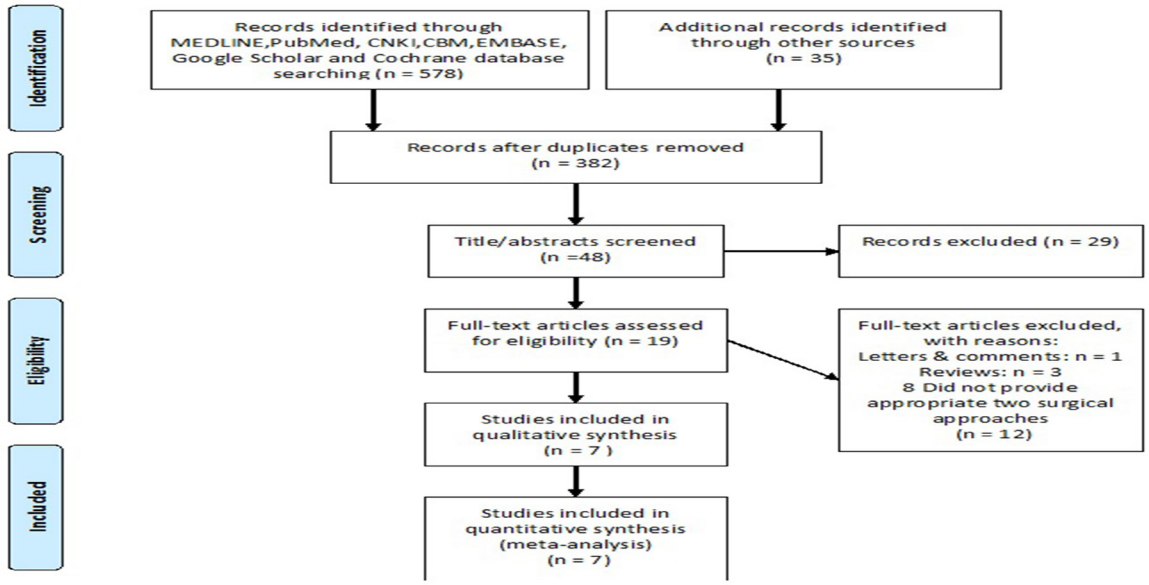

Figure 1. Flowchart for records selection process of the meta-analysis

have been studied); 4. The studies must have been published in Chinese or English language. If one of the above criteria was not met, the study would have been excluded.

Data extraction and quality assessment

A standardized data extraction form collecting information on the year of the study period, country, type of study design, treatment, the level of evidence (LE), sample size, patients' mean age, varicocele grade (I/II/III), side of varicocele, follow-up time, study quality, operation time, sperm concentration, sperm motility, pregnancy rate, postoperative complications rate, recurrence rate, and serum testosterone level was used to extract data. In order to ensure that the baseline data did not affect the results of our meta-analysis, we compared the preoperative status of sperm concentration, motile sperm and serum testosterone level. Two reviewers (B L. and J L.) independently estimated LE for all included studies in the meta-analysis according to the criteria provided by the Oxford Centre for Evidence Based Medicine[16]. The methodological quality of all the included studies was also appraised and determined by two independent reviewers (B L. and J L.). The Newcastle-Ottawa Scale (NOS)[17] was used to evaluate non-randomized controlled trials, and the Jadad Scale [18] was used to evaluate randomized controlled trials (RCTs). A NOS[17] score of 6-9 was identified as high methodological quality, 4-5 medium quality, and < 4 was considered low quality. We defined the Jadad[18] scores as > 2 being high methodological quality and ≤ 2 being low quality. The quality scores of NOS[17] and Jadad were used only as part of descriptive summaries for each study and they did not influence our decision to pool studies in meta-analysis. We also used the Cochrane Collaboration's tool for assessing risk of bias for each study. The results were presented by using "Low bias," "Uncertain" or "High bias" for each study. When two reviewers had different opinions about the same study, the conflict would be resolved by inviting the third researcher to assist in decision-making.

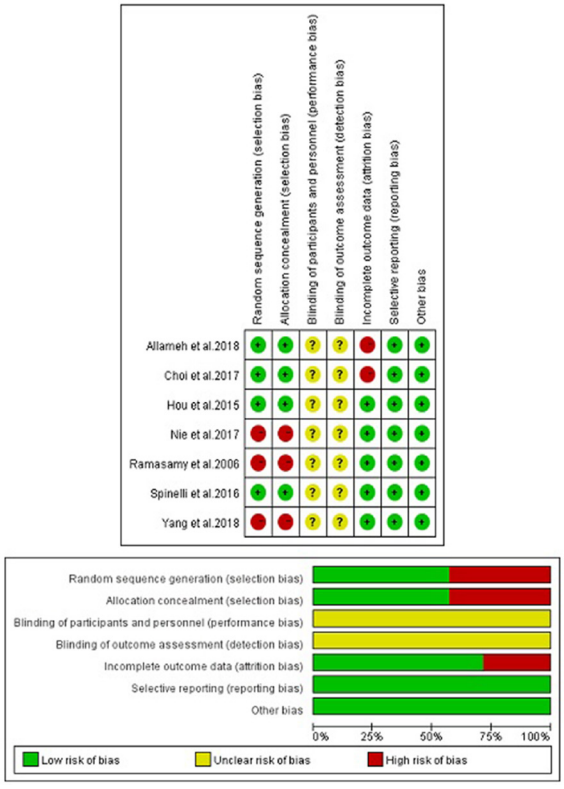

Figure 2. Summary of risk of bias graph.

Data synthesis and meta-analysis

Forest plots were used to present the results of our data analysis. Heterogeneity was defined as $p < .10$ or I2 > 50%. When homogeneity was adequate ($p \geq .10$ or I2 ≤ 50%), data were meta-analyzed using a fixed-effect model (19). Otherwise, data were meta-analyzed using a random-effect model. Heterogeneity was classified as

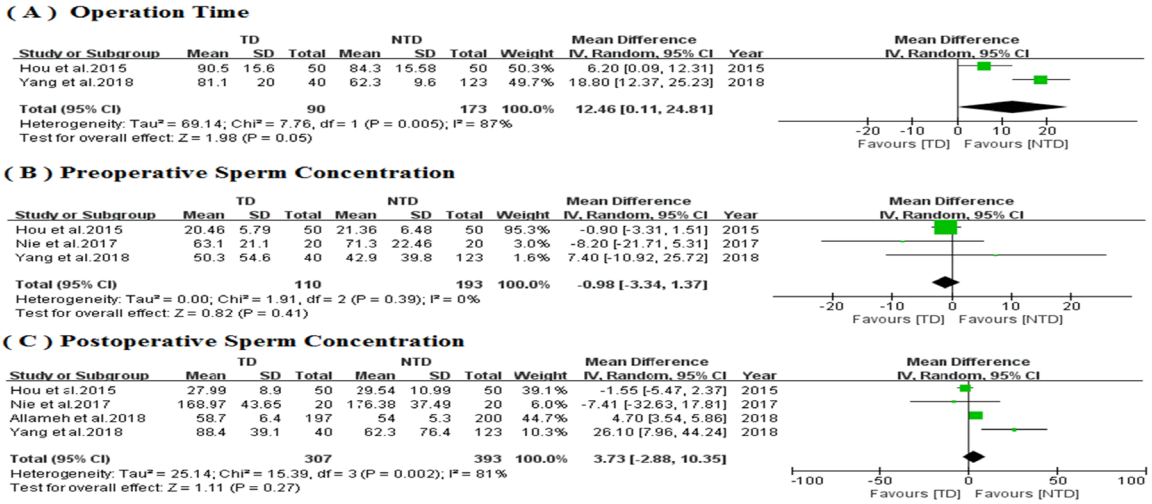

Figure 3 (A). Comparison of the operation time between TD and NTD. **(B & C)**. Comparison of pre and post-operative sperm concentration
TD= microsurgical subinguinal varicocelectomy with testicular delivery; NTD= microsurgical subinguinal varicocelectomy without testicular delivery

low (I2 ≤ 50%) and high (I 2 > 50%). If high heterogeneity still existed, then subgroup analysis or sensitivity analysis would be conducted. We calculated the odd ratio (OR) and mean difference (MD) with its 95% confidence interval (CI) using fixed or random-effect model to estimate operation time, sperm concentration, sperm motility, pregnancy rate, postoperative complications rate, recurrence rate and serum testosterone level of MSV with and without TD for varicocele patients. We used funnel plot to estimate publication bias. *P* values of less than 0.05 were considered statistically significant for all statistical analyses. The Review Manager Software (RevMan v.5.3, Cochrane Collaboration, Oxford, UK) was used to conduct data analysis.

RESULTS

Literature search and study election

A PRISMA[15] flow chart of screening and selection results is presented in **Figure 1**. 578 extracts and 35 additional citations from other sources were obtained after the systematic literature search was conducted. From 48 studies initially identified, 19 were considered potentially suitable. After a full-text review, there were 7 studies [10,12,20-24] in the final analysis, including four RCTs[21-24] and three retrospective case controls[10,12,20] comprising 993 varicocele patients treated by microsurgical subinguinal varicocelectomy with and without testicular delivery. NOS quality scores of the three retrospective case-control studies was seven being consid-

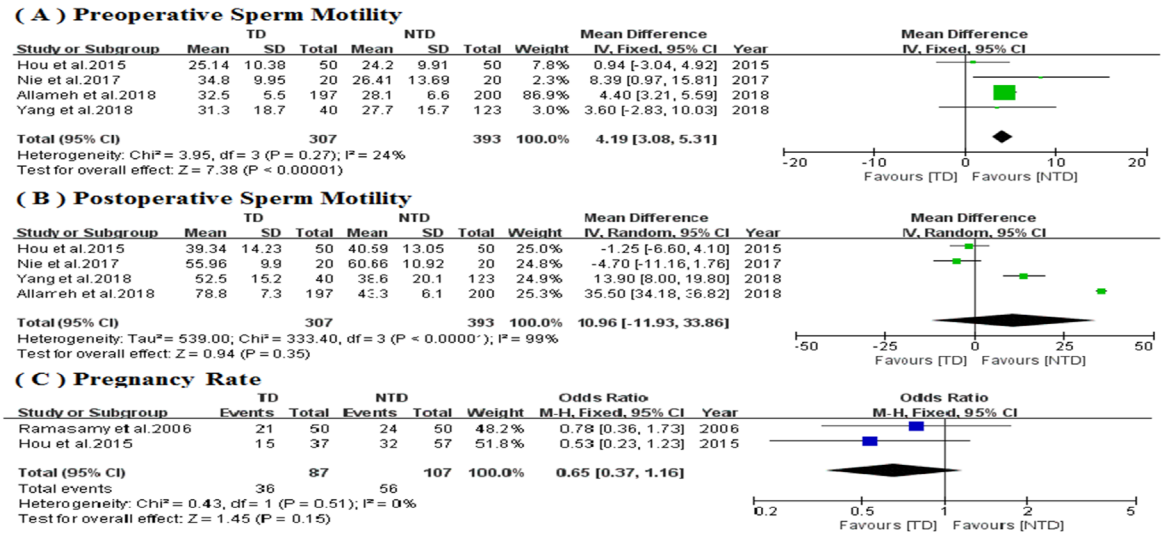

Figure 4. (A&B) Comparison of pre and post-operative sperm motility between TD and NTD.
TD= microsurgical subinguinal varicocelectomy with testicular delivery; NTD= microsurgical subinguinal varicocelectomy without testicular delivery

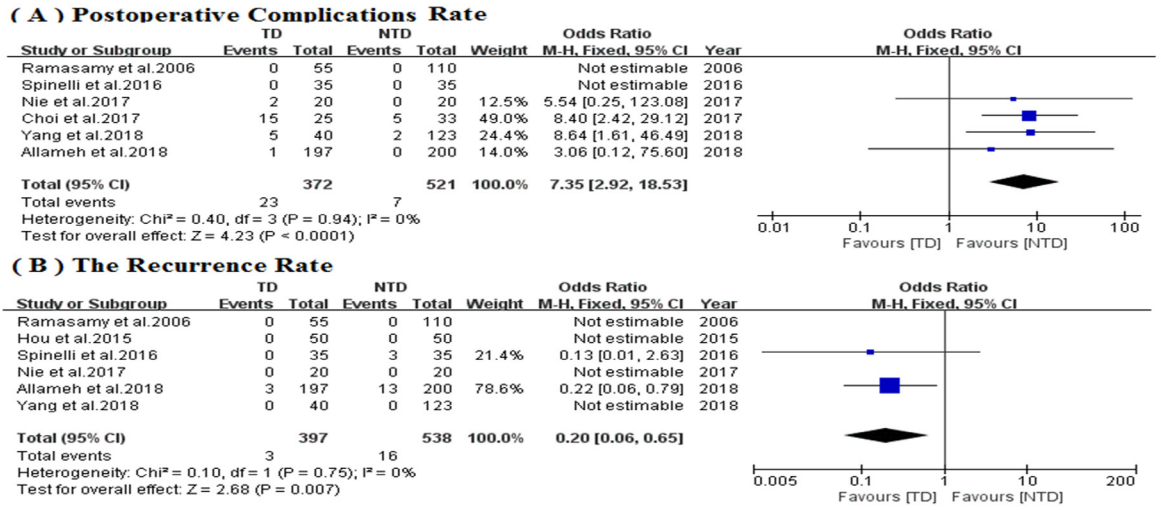

Figure 5(A). Comparison of postoperative complications rate between TD and NTD. **(B)** Comparison of the recurrence rate between TD and NTD.
TD= microsurgical subinguinal varicocelectomy with testicular delivery; NTD= microsurgical subinguinal varicocelectomy without testicular delivery

ered high quality. The Jadad score of all the RCTs was three with all of them being high quality. NOS [17] quality scores and Jadad [18] scores were presented in **Table 1**. The summary of baseline patient characteristics and the operative effect of included studies are shown in **Table 2**. The risk of bias for all the 7 studies assessed and summary results for the domains are shown in **Figure 2**.

Operation time

In terms of operation time, there were two studies comparing this point. Heterogeneity of the operation time displayed I2 > 50%. After using a random effects model analysis, the results showed no statistical significant difference of operative time between MSV with TD and MSV without TD (MD = 12.46, 95% CI: 0.11-24.81, *P* = .05, I2 = 87%) (**Figure 3**A).

Sperm concentration

As for sperm concentration, there were four studies comparing this outcome. We assessed both preoperative and postoperative sperm concentration. Based on heterogeneity analysis (I2 > 50 %) of preoperative sperm concentration, sensitivity analysis was conducted. After excluding one study, heterogeneity was significantly reduced and a fixed effects model revealed a non-significant statistical difference between preoperative sperm concentration of MSV with TD and MSV without TD (MD = -0.98, 95% CI: -3.34 - 1.37, *P* = .41 □I2 = 0%) (Figure 3B). Heterogeneity of postoperative sperm concentration displayed I2 > 50%. After using a random effects model analysis, the results showed that no statistical significant difference of postoperative sperm concentration exists between MSV with TD and MSV without TD (MD = 3.73, 95% CI: -2.88 - 10.35, *P* = .27, I^2 = 81%) (**Figure 3C**).

Sperm motility

Regarding sperm motility, there were four studies comparing this point. We evaluated preoperative and post-

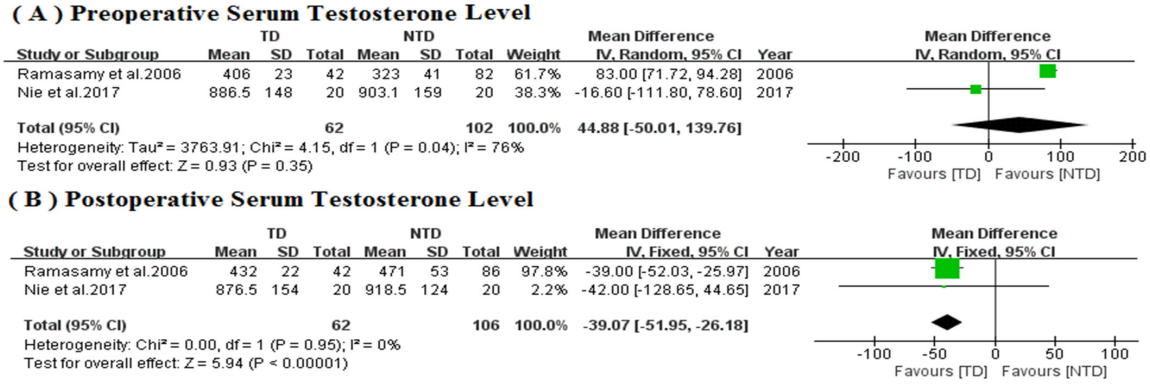

Figure 6 (A & B). Comparison of pre and post-operative serum testosterone level.
TD= microsurgical subinguinal varicocelectomy with testicular delivery; NTD= microsurgical subinguinal varicocelectomy without testicular delivery

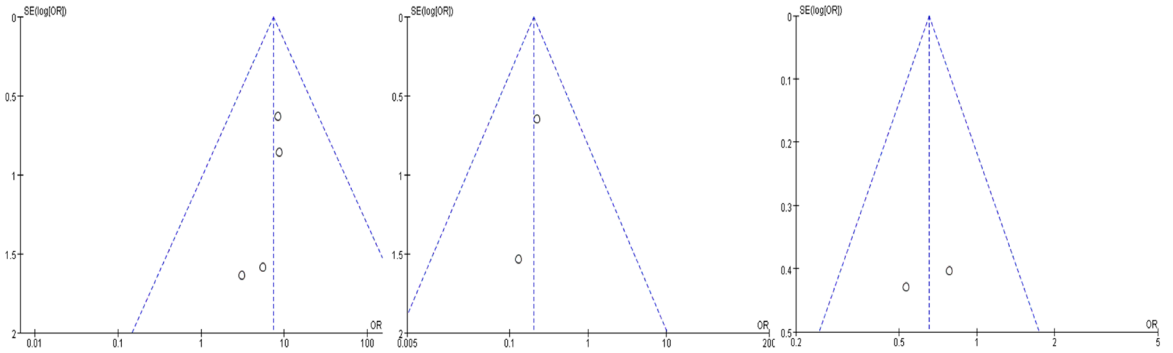

Figure 7. Funnel plot to detect publication bias.

operative sperm motility. Based on preoperative sperm motility heterogeneity analysis I2 ≤ 50%, a fixed effect model was employed. The results revealed that MSV with TD had a significantly higher preoperative sperm motility compared with MSV without TD (MD= 4.19, 95% CI: 3.08-5.31, *P* < .00001, I2 = 24%) (**Figure 4A**). Heterogeneity of postoperative sperm motility displayed I2 > 50%. After using a random effects model analysis, the results showed that there was no statistical significant difference of postoperative sperm motility between MSV with TD and MSV without TD (MD = 10.96, 95% CI: -11.93 - 33.86, *P* = .35, I2 = 99%) (Figure 4B).

Pregnancy rate

There were only two studies comparing pregnancy rate. Based on heterogeneity analysis I2 ≤ 50%, a fixed effects model was employed. The results indicated no statistical significant difference in pregnancy rate between MSV with TD and MSV without TD (OR = 0.65, 95% CI: 0.37 -1.16, *P* = .15, I2 = 0%) (**Figure 4C**).

Postoperative complications rate

For the postoperative complications rate, there were six studies comparing this point. Based on heterogeneity analysis I2 ≤ 50%, a fixed effects model was employed. The results demonstrated that MSV with TD offered a significantly higher postoperative complications rate compared to MSV without TD (OR=7.35, 95% CI: 2.92-18.53, *P* < .0001, I2 = 0%) (**Figure 5**A).

Recurrence rate

Speaking of the recurrence rate, there were seven studies comparing this point. Based on heterogeneity analysis I2 > 50 %, a sensitivity analysis was performed. After exclusion of one study, heterogeneity was significantly reduced, and a fixed effects model suggested that MSV with TD provided a significantly lower recurrence rate compared with MSV without TD (OR =0.20, 95% CI: 0.06-0.65, *P* = .007, I2 = 0%) (**Figure 5B**).

Serum testosterone level

For the serum testosterone level, there were only two studies comparing this point. We assessed preoperative and postoperative serum testosterone level. Heterogeneity of preoperative serum testosterone level displayed I2 > 50%. After using a random effects model analysis, the results demonstrated that there was no statistical significant difference of preoperative serum testosterone level between MSV with TD and MSV without TD (MD = 44.88, 95% CI: -50.01- 139.76, *P* = .35, I2 = 76%) (**Figure 6A**). Based on postoperative serum testosterone level heterogeneity analysis I2 ≤ 50%, a fixed effects model was employed. The results indicated that MSV with TD had a significantly lower postoperative serum testosterone level compared with MSV without TD (MD = -39.07, 95% CI: -51.95--26.18, *P* = .00001, I2 = 0%) (**Figure 6B**).

Sensitivity analysis and Publication Bias

When the pooled results were shown, there was still significant heterogeneity in regards to the operation time, sperm concentration, postoperative sperm motility, recurrence rate and preoperative serum testosterone level. For the operation time and preoperative serum testosterone level, because there were only two studies comparing the two outcome measures, the subgroup analysis or sensitivity analysis was not conducted. The random effects model (**Figure 3A & Figure 6A**) was conducted to estimate the two outcome measures but it did not completely abolish the heterogeneity. After analyzing the existing data, we finally attributed the high heterogeneity to the difference of surgical experience, the severity of illness, and too little included studies comparing the two outcome measures. For the preoperative sperm concentration and the recurrence rate, the sensitivity analysis was conducted. After exclusion of one study, heterogeneity was significantly reduced (**Figure 3B & Figure 5B**). For the postoperative sperm concentration and postoperative sperm motility, the sensitivity analysis was conducted, but the heterogeneity could not descend to the degree that we could accept. The random effects model (**Figure 3C & Figure 4B**) was conducted to estimate these two points. Depending on analyzing the existing data, we finally ascribed the high heterogeneity to the difference of surgical experience, the severity of illness, follow-up time and the instrument for analysis, and the small number of included studies comparing the two points was certainly a reason.

Publication bias

Publication bias would be reduced to the minimum according to our search strategy. There was no evidence of publication bias to be observed by visual inspection of the funnel plots (**Figure 7**). All data were strictly included into our review and the baseline data was analyzed to assess the preoperative and postoperative difference. Data extraction forms of our review from the seven selected studies are shown in **Table 1**.

DISCUSSION

To our knowledge, our study is the first meta-analysis carried out to represent the safety and efficacy of MSV with and without TD for varicocele and our meta-analysis of four RCTs and three retrospective studies including 993 patients comparing the efficacy and safety of MSV with and without TD showed that both of the two treatments were effective and safe. MSV with TD had high postoperative complications rate but lower recurrence rate and postoperative serum testosterone level than MSV without TD. In term of serum testosterone level, operation time, sperm concentration, sperm motility and pregnancy rate, we found no significant differences between two.

It is certain that varicocele has some adverse effects on the histologic, endocrine and testis function[25]. Some findings of the physiopathology of varicocele-related infertility also reported that some factors including blood stasis, spermatogenesis was impaired, accumulation of reactive oxygen species, nitric oxide, and some other toxins, would lead to dysfunction and morphological abnormalities of sperm, and they would eventually affect male fertility[26]. In the adolescent population, varicoceles were worrisome given the concern for progressive effects on testicular growth, ongoing spermatogenesis, and future fertility, therefore, the early diagnosis of varicocele in young people is important [27]. Less invasive surgery for varicocele correction was important, but it also had some potential side effects such as several trocar wounds, postlaparoscopic pain and so on[28]. Eliminating varicocele, reversing damage of venous stasis to spermatogenesis, minimizing recurrence rate and complications rate were the goal of varicocele treatment[29]. There were a variety of approaches for varicocele including laparoscopic varicocele ligation, open surgery, and MSV. Some evidence indicated that the laparoscopic varicocele ligation had more advantages in reducing postoperative complication rate, recurrence rate, and improving the pregnancy rate than the traditional open surgeries [30,31]. With the rapid development of microsurgery and the increase of aesthetic requirements, more and more studies comparing MSV and laparoscopic varicocele ligation had gradually been conducted. There were some conclusions of systematic review showing that MSV had higher spontaneous pregnancy rates, lower incidence of postoperative complications and recurrence than laparoscopic varicocele ligation [8,29]. In recent years, it was reported by several studies that MSV had been recommended as the standard treatment for varicocele in infertile men [32,33]. During the procedure of MSV, it was possible to additionally ligate the gubernacular, trans-scrotal, and collateral veins, which was considered to be a practice to reduce the incidence of varicocele recurrence. There seems to be confusion about whether MSV should involve testicular delivery or not, and this still remains a controversial issue[13,34]. It is not yet clear that whether MSV with testicular delivery is a more excellent technique than that without testicular delivery[21]. Therefore, we conducted a meta-analysis aiming to compare the efficacy and safety of MSV with and without TD, by means of evaluation of operation time, sperm concentration, sperm motility, pregnancy rate, postoperative complications rate, recurrence rate, and serum testosterone level for the purpose of providing evidence-based clinical treatment.

Both of the studies carried out by Hou et al[21]. and Yang et al[12]. reported that operation time of MSV with TD was longer than MSV without TD. But the conclusion of our study represented that no statistical significant difference of operative time was found between the two. Although multiple strategies were applied to identify studies, there were only two studies comparing operation time in our studies. Because of limited included studies comparing operation time in our meta-analysis, this could justify the difference. Future studies should be conducted to verify this conclusion.

Some animal studies reported ligation of the spermatic artery had detrimental effects upon ipsilateral testicular blood flow and morphology[35,36]. There was considerable evidence showing that varicocelectomy made an improvement in key sperm parameters including sperm concentration, sperm motility, and serum testosterone level, while reducing sperm DNA damage and seminal oxidative stress [6,37,38]. Hou et al. carried out a RCT indicated that MSV with TD conferred no additional benefit to the varicocele patients than the procedure carried out without TD and they insisted that excessive ligation of veins was not necessary [21]. Will et al also held a same point of view[39]. However, investigators such as Lee and his colleagues expressed in their paper that semen parameters (sperm concentration, sperm motility) improve significantly after MSV with TD[40], however, Ramasamy et al. proposed that the testosterone levels markedly rose after MSV without TD but did not change in men who had TD[20]. Our study compared the preoperative and postoperative semen parameters, the results showing that MSV with TD is associated with a lower postoperative serum testosterone level and we found no significant differences in terms of sperm concentration and sperm motility. As for infertility (pregnancy) rate, most literatures reported that there was no difference found between MSV with TD and without TD[20,21]. The result of our study was in line with this conclusion.

Both Yang et al.[12] and Hou et al.[21] showed their ideas that recurrence rate was not significantly different between MSV with TD and without TD. There were several studies involving MSV that have shown a very low recurrence rate (0-2%) in varicocele patients whereas the gubernacular vein thought to underlie recurrence was not ligated[41,42]. However, some studies pointed out that it was still theoretically possible to produce venous return from the testicle via the gubernacular veins following ligation of the internal and external spermatic veins, which may lead to varicocele recurrence[43]. Choi et al.[23] in their study also found that the recurrence rate of MSV without TD was slightly higher than MSV with TD (10%–13% versus 6.1%). Goldstein et al. reported gubernacular and scrotal veins as a major cause of recurrence. They also indicated that MSV with TD observably reduced the incidence of varicocele recurrence [44]. In our study, we also found that MSV with TD had a lower recurrence rate than that MSV without TD.

There were some findings that inflammatory changes in the scrotum were associated with the increased trauma and surgical time involving with TD, and they thought MSV with TD caused more complications than MSV without TD[20]. Yang et al. also showed the same idea that MSV with TD had a higher postoperative complications rate[12]. However, some people such as Goldstein et al. indicated that MSV with TD markedly reduced the

incidence of hydrocele[44]. Cho et al. also pointed out that the TD was a safe and useful way to easily ligate gubernacular veins and without any complication.[45]. We found that MSV with TD has a higher postoperative complication rate than MSV without TD.

Our systematic review had several limitations. First, there was great heterogeneity among studies for some parameters. Multiple strategies, strict inclusion criteria, sensitivity analyses was conducted to minimize the heterogeneity, but in terms of operative time, postoperative sperm concentration, postoperative sperm motility, and preoperative serum testosterone level, we could not reduce the heterogeneity to the degree that we could accept by these approaches. The reasons could be the difference of surgical experience, follow-up time, the instrument for analysis, the severity of illness, and limited included studies comparing these outcomes. Second, in spite of many efforts of contacting authors and obtaining original data, there were still some missing data in our meta-analysis, but the missing data did not influence our results. Third, it is difficult to compare semen analysis from different patients because post-op results are based on grade of varicocele, testicular volume, and semen quality before surgery. We did not analyze testicular volume and severity of varicocele, because there were few studies comparing testicular volume and severity of varicocele. Finally□due to the fact that fertility is not necessarily associated with the presence of varicocele, it is difficult to compare fertility rates because there is also the female factor. Further well-designed RCTs and retrospective case controls with sufficient power are needed to better compare the efficacy and safety of MSV with and without TD.

CONCLUSIONS

Our meta-analysis of four RCTs and three retrospective studies including 993 patients comparing the efficacy and safety of MSV with and without TD showed that both of the two treatments were effective and safe. MSV with TD had high postoperative complications rate but lower recurrence rate and postoperative serum testosterone level than MSV without TD. In term of preoperative serum testosterone level, operation time, sperm concentration, sperm motility, and pregnancy rate, we found no significant differences between two. More large-samples, multi-center, well-designed RCTs with complete follow-up data are required to verify and update our knowledge in this field in the future.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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