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Systematic Review

The efficacy and safety of thulium laser resection of bladder tumor versus standard transurethral resection in patients with non-muscle-invasive bladder cancer: a systematic review and meta-analysis

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Abstract

Purpose: This study was to analyze the efficacy and safety of thulium laser resection of bladder tumor (Tm-TURBT) versus TURBT for patients with non-muscle-invasive bladder cancer (NMIBC).

Materials and Methods: Randomized controlled trial data were retrieved using the MEDLINE, Embase, Web of Science, and the Cochrane Library. We also searched Chinese databases including Chinese National Knowledge Infrastructure (CNKI), Wanfang data and VIP data.

Results: A total of sixteen articles including 1662 participants were enrolled into our meta-analysis. We found no significant difference in terms of operation time, urethral stricture, 1-year recurrence rate, overall 1-year recurrence rate and overall 3-year recurrence rate between the two groups. Less intraoperative blood loss and a lower incidence of obturator nerve reflex (ONR), bladder perforation and bladder irritation were identified in Tm-TURBT group than in TURBT group in our analysis. The analysis also demonstrated faster postoperative recovery in terms of the catheterization, bladder irrigation and hospitalization time in Tm-TURBT group. The subgroup analysis was conducted based on different postoperative chemotherapy (epirubicin and non-epirubicin) concerning recurrence rate whereas no significant difference was noted.

Conclusion: Tm-TURBT is an efficient and safe treatment for NMIBC and it could be an alternative choice for TURBT. Given that some limitations are clearly identified, more large-scale and well-designed RCTs are needed to confirm our findings.

Keywords

Transurethral resection of bladder tumor; Bladder tumor; Thulium laser; Meta-analysis; Randomized controlled trials

1. Introduction

Bladder cancer is the tenth most common cancer worldwide. In the year 2018, there was approximately 549000 new cases and 200000 deaths reported [1]. Nearly three quarters of newly diagnosed cases are non-muscle-invasive bladder cancer (NMIBC), which is defined as the focal lesion barely confined to the mucosa (Ta or Tis) or submucosa (T1) [2]. However, with a rising prevalence of smoking habits, bladder cancer, as a smoking-related cancer, may increase as well [3].

For patients with NMIBC, the gold standard treatment is considered to be the transurethral resection of the bladder tumor (TURBT) combined with adjuvant intravesical chemotherapy or immunotherapy [4, 5]. However, there are some disadvantages of the widely accepted procedure discovered from exposure and practice. For instance, unforeseen obturator nerve reflex (ONR) may be stimulated due to the electric current passing through the tissue. Thus, it appears to be increasingly important to develop both effective and safe alternative procedures. Laser therapy, as a promising energy sources, has been widely applied in urologic surgery in recent years, especially in transurethral resection of prostate. However, thulium laser (thulium: yttrium alluminum garnet; Tm: YAG), or 2 μm continuous wave laser is gradually recognized in TURBT. Although many studies have been conducted to compare the efficacy and safety of thulium laser resection of bladder tumor (Tm-TURBT) and TURBT for the treatment of NMIBC, results from these studies differ widely. Therefore, we initiated a meta-analysis and systematic review of currently published studies aiming to evaluate the efficacy and safety between Tm-TURBT and TURBT in treating patients with NMIBC.

2. Patients and methods

2.1 Study design

Systematic review of randomized controlled trials (RCTs) was carried out following the principle of preferred reporting items for systematic review and meta-analysis protocols (PRISMA) [6].

2.2 Search strategy

A systematic search of the literature was undertaken using PubMed, Embase, Web of Science, and the Cochrane Library to retrieve published randomized controlled trials (RCTs) investigating Tm-TURBT versus TURBT in patients with NMIBC. We also searched available Chinese databases including Chinese National Knowledge Infrastructure (CNKI), Wanfang data and VIP data. The databases were respectively searched using the combinations of the terms "thulium", "2-micron", "bladder cancer" and "bladder tumor" up to January 2021. We applied no language restriction. In addition, all available relevant studies were further screened.

2.3 Inclusion criteria and selection of RCTs

The following criteria were used to select RCTs: (1) study type: only the literatures of randomized controlled trails were selected. (2) study design: studies comparing thulium laser resection of bladder tumor and standard transurethral resection were included. (3) study population: patients with primary bladder cancer grade of G1 to G3, confirmed by biopsy and non-muscle invasion (Ta, Tis, and T1) confirmed by computerized tomography and/or cystoscopy. (4) study outcome: at least one outcome of interest was available, such as operation time, intraoperative blood loss, postoperative bladder irrigation time, catheterization time, hospitalization time, obturator nerve reflex, bladder perforation, bladder irritation, urethral stricture and 1-year recurrence rate. (5) The full text of the study could be accessed. Studies would be excluded if they were discussing patients with other diseases, muscle invasive bladder cancer or distant metastasis. This procedure was independently operated by two reviewers and all disagreements were finally resolved by consensus of all authors.

2.4 Quality assessment

We evaluated the quality of included RCTs according to the guidelines published in the Cochrane Handbook for Systematic Reviews of Interventions (version 6.0) [7]. Each study was evaluated and classified based on quality assessment criteria: A, the study was considered to have a low risk of bias when satisfying all quality criteria; B, the study would have a moderate risk of bias if one or more quality criteria were partially met or were ambiguous; C, if one or more of the quality criteria were barely met, the study was deemed to have a high risk of bias. Differences were settled by discussion between the authors.

2.5 Data extraction

The following information was extracted from each included study as baseline characteristics: first author' name, published year, number of participants, mean age (yr.), the percentage of male patients (%), tumor multiplicity, tumor size (cm), the postoperative adjuvant intravesical chemotherapy drug, monopolar/bipolar and resection method. And the outcome data was collected including perioperative data such as operation time (min), intraoperative blood loss (mL), postoperative bladder irrigation time (h), catheterization time (d), hospitalization time (d), obturator nerve reflex, bladder perforation, bladder irritation, urethral stricture, 1-year recurrence rate, overall 1-year recurrence rate and overall 3-year recurrence rate. The follow-up period varies from studies, so we adopted 1-year recurrence rate to record the recurrence data of included studies with 1-year follow-up period and overall 1-year recurrence rate with follow-up period less than or equal to 1-year. Similarly, the overall 3-year recurrence rate contained the recurrence data with follow-up period within 3-year.

2.6 Statistical analyses and meta-analysis

The meta-analysis was conducted using RevMan version 5.3.0 (Cochrane Collaboration, Oxford, UK). The mean difference (MD) was used to assess the continuous outcomes and dichotomous outcomes were evaluated by RR (Risk Ratio) using 95% confidence interval (CI) [8]. In addition, we analyzed inconsistency using I^2 value which illustrated the proportion of heterogeneity in the study. A random-effect model would be applied for the result if I^2 value is $>$ 50%. If *P* value was less than 0.05, the result was then considered to have statistical significance. No ethical approval was required for this study.

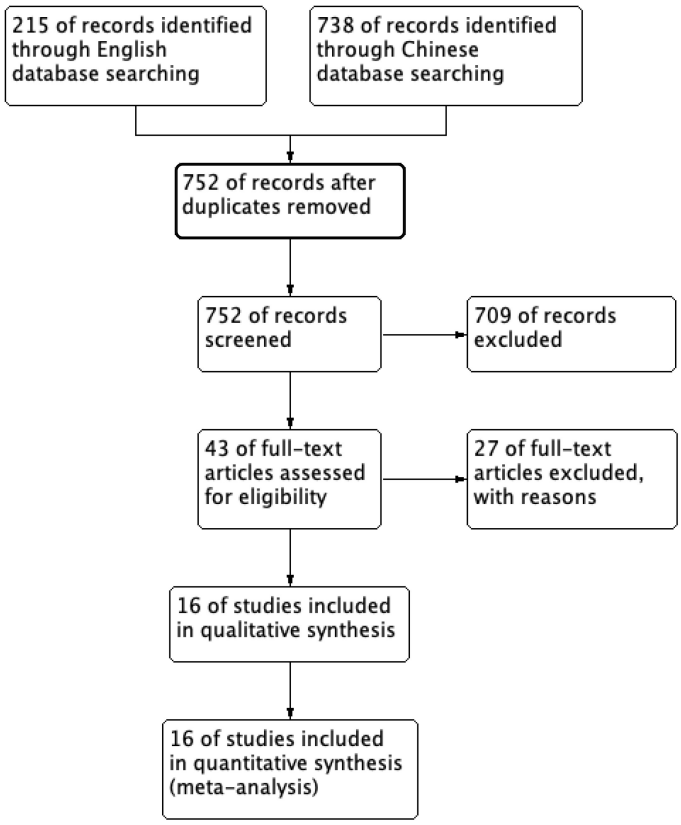

FIG. 1. A flow diagram of the study selection process.

3. Results

3.1 Studies selection and characteristics

Our search initially found 215 articles by retrieving English databases in which 72 duplicated studies existed and we acquired 738 articles by retrieving Chinese databases in which 129 duplicated studies existed. Screening abstracts and titles, we excluded 709 articles. For remaining 43 articles, we accessed the full text. Finally, 16 articles [9–24] containing 16 RCTs were involved to evaluate the efficacy and safety of Tm-TURBT versus TURBT in patients with NMIBC (details in Fig. 1). The baseline characteristics of the 16 included studies are listed in Table 1.

3.2 Quality of individual studies

The results of quality assessment of the selected studies were listed in Table 2. All studies included in the analysis were randomized controlled studies. But, some of the trials tended to be of low quality, and were ambiguous about the description of the surgical procedure.

3.3 Operation time (min)

Sixteen RCTs with a total of 1662 patients (847 in the Tm-TURBT group and 815 in the TURBT group) included data on operation time. The data suggested no significant difference was observed in terms of operation time in the Tm-TURBT group compared to TURBT group (95% CI: -9.96 to 0.74, MD = -4.61, $P = 0.09$) (Fig. 2A).

3.4 Intraoperative blood loss (mL)

Ten RCTs with an amount of 912 patients (464 in the Tm-TURBT group and 448 in the TURBT group) included data on intraoperative blood loss, which indicated that intraoperative blood loss was notably less in Tm-TURBT group than in TURBT group (95% CI: -29.90 to -16.18, MD = -23.04, $P < 0.00001$) (Fig. 2B).

3.5 Bladder irrigation time (h)

Seven RCTs including 620 patients (315 in the Tm-TURBT group and 305 in the TURBT group) were analyzed, which demonstrated significantly less time in bladder irrigation in the Tm-TURBT group when comparing to TURBT group (95% CI: -33.93 to -20.02, MD = -26.97, $P < 0.00001$) (Fig. 2C).

3.6 Catheterization time (d)

Eleven RCTs including 1076 patients (550 in the Tm-TURBT group and 526 in the TURBT group) were pooled. The data showed that the catheterization time was less in the Tm-TURBT group (95% CI: -3.14 to -1.50, MD = -2.32, $P < 0.00001$) (Fig. 2D).

3.7 Hospitalization time (d)

Thirteen RCTs evaluated the hospitalization time with a sample of 1224 patients (625 in the Tm-TURBT group and 599 in the TURBT group). The forest plots revealed a shorter hospitalization time for Tm-TURBT group compared with TURBT group (95% CI: -3.12 to -1.49, MD = -2.31, $P < 0.00001$) (Fig. 2E).

3.8 Obturator nerve reflex

Fourteen RCTs reported obturator nerve reflex. Pooled analysis revealed significantly lower rate of occurrence in the Tm-TURBT group (95% CI: 0.03 to -0.15, RR = 0.07, $P < 0.00001$) (Fig. 3A).

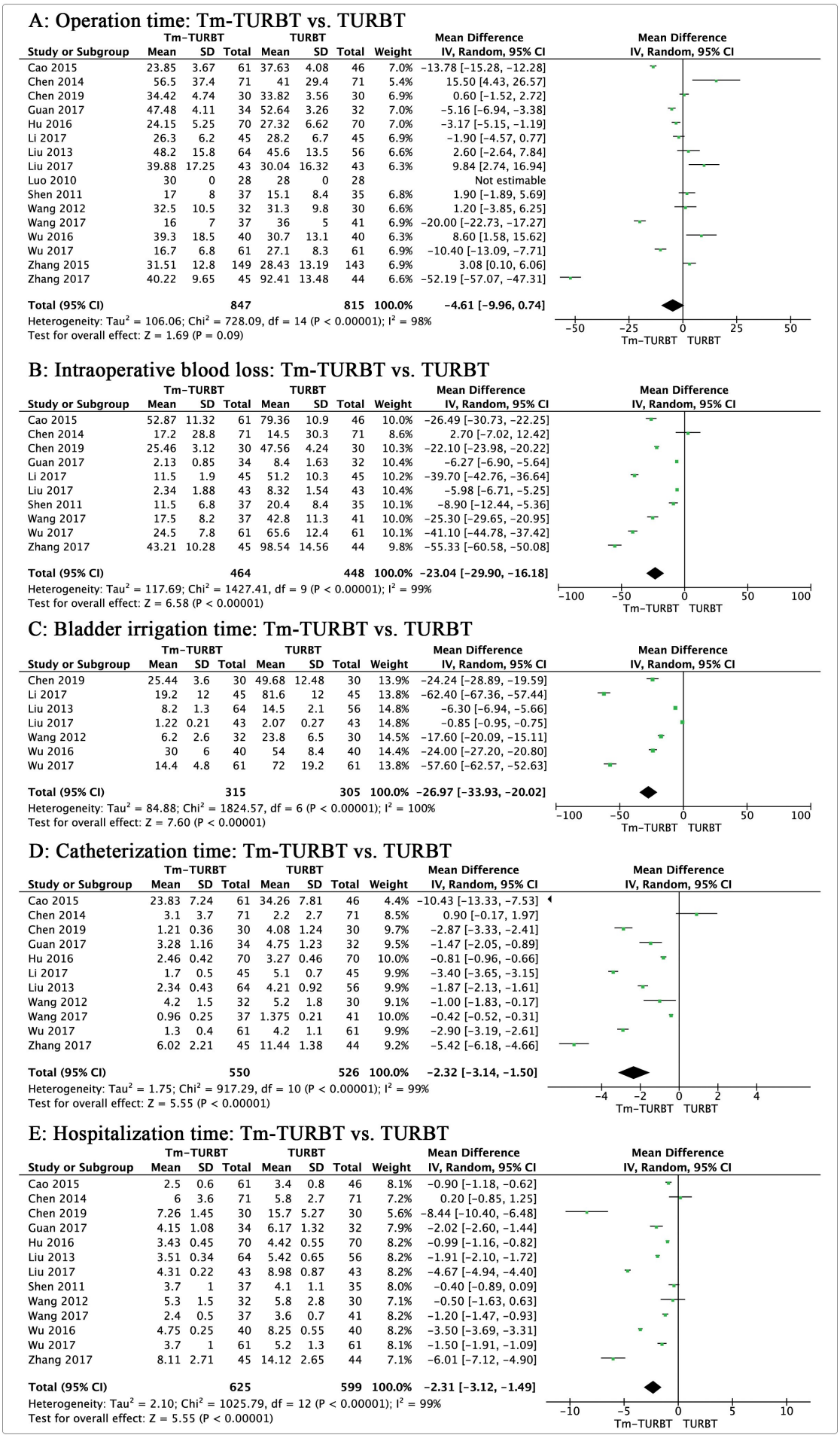

FIG. 2. Forest plots and meta-analysis of perioperative data. (A) Operation time. (B) Intraoperative blood loss. (C) Bladder irrigation time. (D) Catheterization time. (E) Hospitalization time. CI, confidence interval; SD, standard deviation; IV, inverse variance.

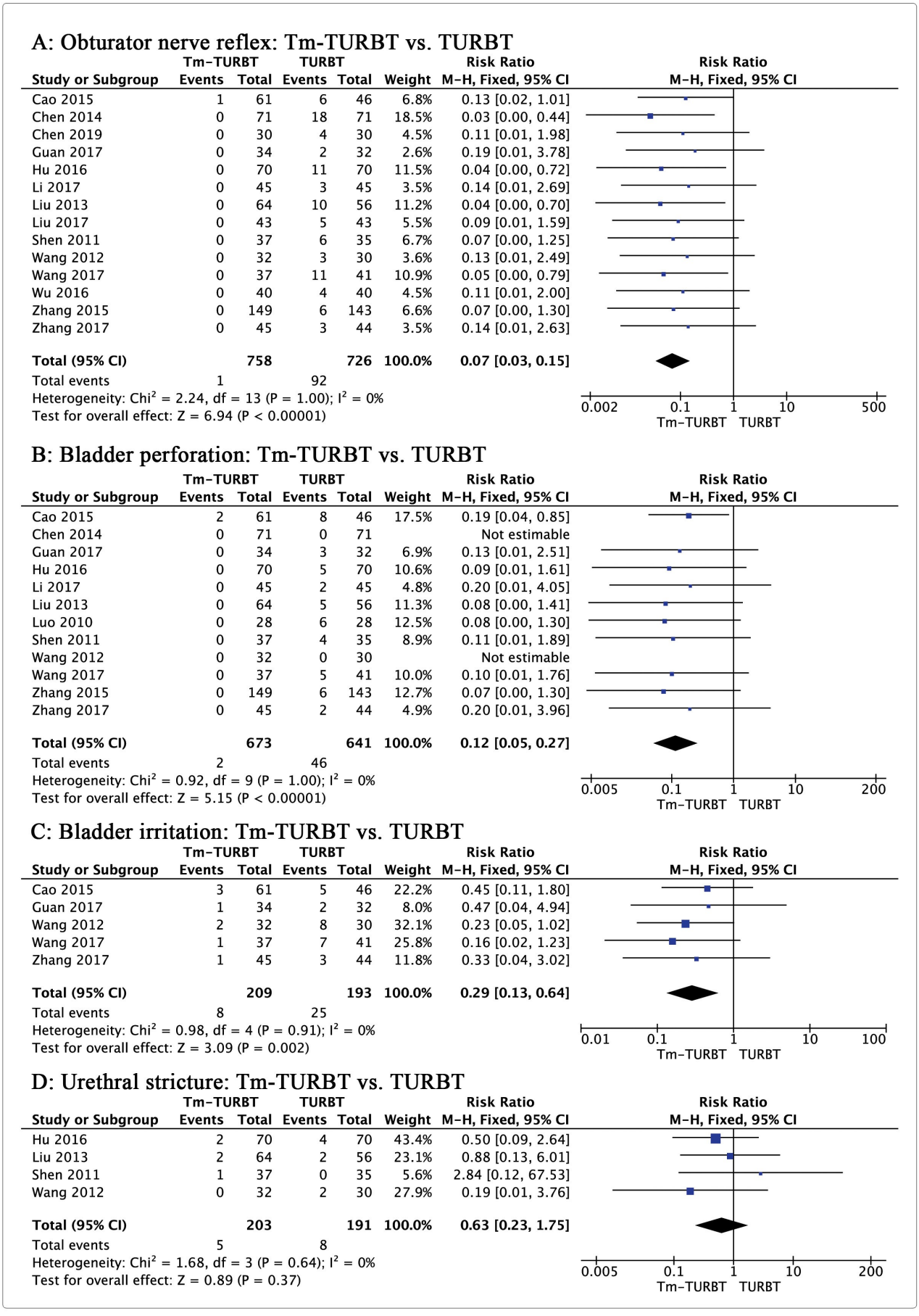

FIG. 3. Forest plots and meta-analysis of complications. (A) Obturator nerve reflex. (B) Bladder perforation. (C) Bladder irritation. (D) Urethral stricture. CI, confidence interval; SD, standard deviation; IV, inverse variance.

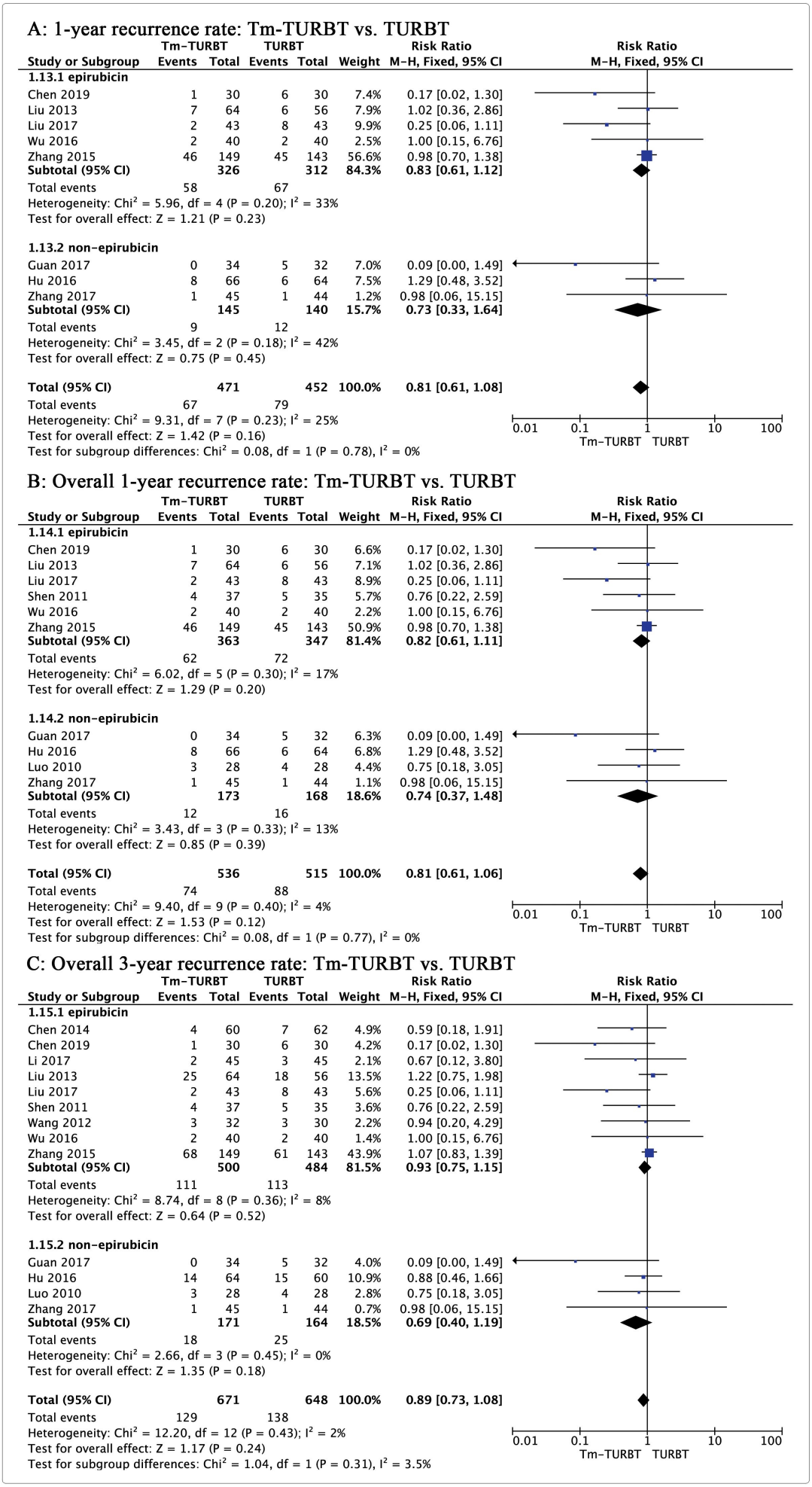

FIG. 4. Forest plots and meta-analysis of recurrence rate. (A) 1-year recurrence rate. (B) Overall 1-year recurrence rate. (C) Overall 3-year recurrence rate. CI, confidence interval; SD, standard deviation; IV, inverse variance.

TABLE 1. Characteristics of RCTs included in the present meta-analysis

Trials/yr.	Treatment	GRADE	NO. of patients	Age (yr.)	Male (%)	Tumor Multiplicity	Single Tumor (%)	Tumor Size (cm)	perfusate	Monopolar/Bipolar	Resection Method
Cao 2015 [9]	Tm	B	61	61.5	0.72	NA	0.66	NA	NA		AR
	TURBT		46	63.2	0.76	NA	0.67	NA	NA	Bipolar	NA
Chen 2014 [10]	Tm	B	71	63	0.76	1.8	NA	2.6	epirubicin		AR
	TURBT		71	62.1	0.72	1.7	NA	2.3	epirubicin	Monopolar	NA
Chen 2019 [11]	Tm	B	30	63.5	0.53	2.9	NA	NA	epirubicin		ERBT
	TURBT		30	62.1	0.57	2.7	NA	NA	epirubicin	Bipolar	NA
Guan 2017 [12]	Tm	C	34	62.29	0.79	NA	NA	NA	Gemcitabine		ERBT
	TURBT		32	62.35	0.81	NA	NA	NA	Gemcitabine	NA	NA
Hu 2016 [13]	Tm	B	70	58.32	0.71	NA	NA	1.62	epirubicin		AR
	TURBT		70	56.25	0.69	NA	NA	1.53	epirubicin	Monopolar	standard
Li 2017 [14]	Tm	C	45	51.7	0.62	NA	0.71	NA	epirubicin		ERBT
	TURBT		45	48.3		NA	0.67	NA	epirubicin	Bipolar	standard
Liu 2013 [15]	Tm	B	64	67.1	0.72	2.8	NA	NA	epirubicin		ERBT
	TURBT		56	66.3	0.71	2.7	NA	NA	epirubicin	Monopolar	NA
Liu 2017 [16]	Tm	C	43	66.8	0.51	2.8	NA	NA	epirubicin		AR
	TURBT		43	67.4	0.49	2.9	NA	NA	epirubicin	Monopolar	NA
Luo 2010 [17]	Tm	C	28	66	0.79	NA	0.64	NA	Hydroxycamptothecin		ERBT
	TURBT		28			NA		NA	Hydroxycamptothecin	Bipolar	standard
Shen 2011 [18]	Tm	C	37	51.3	0.57	NA	0.93	1.42	epirubicin		NA
	TURBT		35	48.6	0.57	NA		1.33	epirubicin	Monopolar	NA
Wang 2012 [19]	Tm	B	32	NA	0.74	NA	0.69	NA	epirubicin		AR
	TURBT		30	NA		NA		NA	epirubicin	Monopolar	standard
Wang 2017 [20]	Tm	C	37	64	NA	NA	0.78	NA	NA		ERBT
	TURBT		41	63	NA	NA	0.8	NA	NA	NA	standard
Wu 2016 [21]	Tm	C	40	64.8	0.5	1.9	NA	NA	epirubicin		AR
	TURBT		40	65.6	0.55	1.8			epirubicin	Bipolar	AR
Wu 2017 [22]	Tm	C	61	52.7	0.6	NA	0.84	2.6	epirubicin		NA
	TURBT		61	53.2	0.57	NA	0.80	2.4	epirubicin	Bipolar	NA
Zhang 2015 [23]	Tm	B	149	NA	0.47	NA	0.52	NA	epirubicin		AR
	TURBT		143	NA	0.55	NA	0.55	NA	epirubicin	NA	AR
Zhang 2017 [24]	Tm	B	45	66.24	0.71	NA	NA	NA	NA		ERBT
	TURBT		44	66.38	0.68	NA	NA	NA	NA	Bipolar	standard

TABLE 2. ROB for included randomized controlled trials

Study	Sequence generation	Allocation concealment	Blinding	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias
Cao 2015 [9]	+	+	+	?	+	+
Chen 2014 [10]	+	+	+	+	+	+
Chen 2019 [11]	+	+	?	+	+	?
Guan 2017 [12]	?	?	?	?	+	?
Hu 2016 [13]	+	?	?	+	+	+
Li 2017 [14]	?	?	?	+	+	?
Liu 2013 [15]	+	+	+	+	+	+
Liu 2017 [16]	+	+	+	-	?	+
Luo 2010 [17]	+	+	+	?	-	+
Shen 2011 [18]	+	+	+	?	-	+
Wang 2012 [19]	+	+	+	?	+	+
Wang 2017 [20]	+	+	+	-	+	+
Wu 2016 [21]	+	?	?	?	-	?
Wu 2017 [22]	?	?	?	+	+	?
Zhang 2015 [23]	+	+	+	-	-	+
Zhang 2017 [24]	?	?	?	+	+	?

ROB, risk of bias; +, indicates low risk of bias; ?, unclear risk of bias; -, high risk of bias.

3.9 Bladder perforation

Twelve RCTs reported bladder perforation, which indicated that the Tm-TURBT group was significantly less than the TURBT group in terms of bladder perforation (95% CI: 0.05 to 0.27, RR = 0.12, $P < 0.00001$) (Fig. 3B).

3.10 Bladder irritation

Five RCTs evaluated the incidence of bladder irritation, which demonstrated significantly lower rate of occurrence in the Tm-TURBT group (95% CI: 0.13 to 0.64, RR = 0.29, $P = 0.002$) (Fig. 3C).

3.11 Urethral stricture

Four RCTs reported urethral stricture. There is no significant difference between the Tm-TURBT group and the TURBT group (95% CI: 0.23 to 1.75, RR = 0.63, $P = 0.37$) (Fig. 3D).

3.12 1-year recurrence rate

Eight RCTs described the rate of 1-year recurrence rate from 8 studies of 923 patients. The data indicated no significant difference between the two groups (95% CI: 0.61-1.06, RR = 0.81, $P = 0.16$). Due to the underlying impact on recurrence by different chemotherapy strategy, we carried out a subgroup analysis, which indicated no significant difference in epirubicin and non-epirubicin (epirubicin, 95% CI: 0.61 to 1.11, RR = 0.82, $P = 0.23$; non-epirubicin, RR = 0.74, 95% CI: 0.37 to 1.48, $P = 0.45$) (Fig. 4A).

3.13 Overall 1-year recurrence rate

Ten RCTs with a sample of 1061 patients analyzed the overall 1-year recurrence rate. The data demonstrated no statistical significance between the Tm-TURBT and TURBT groups (95% CI: 0.62-1.06, RR = 0.81, $P = 0.12$). The subgroup analysis was conducted and no statistical difference was found (epirubicin, 95% CI: 0.61 to 1.11, RR = 0.82, $P = 0.20$; non-epirubicin, 95% CI: 0.37 to 1.51, RR = 0.75, $P = 0.39$) (Fig. 4B).

3.14 Overall 3-year recurrence rate

Thirteen RCTs including 1355 patients were pooled to analyze the overall 3-year recurrence rate, which indicated no significant difference between the two groups. (95% CI: 0.73 to 1.08, RR = 0.89, $P = 0.24$). There was no significant difference in the subgroup analysis (epirubicin, 95% CI: 0.75 to 1.15, RR = 0.93, $P = 0.52$; non-epirubicin, 95% CI: 0.42 to 1.24, RR = 0.69, $P = 0.18$) (Fig. 4C).

4. Discussion

Bladder cancer needs high lifetime treatment costs as a result of the long-term monitoring and a high recurrence and progression rate [25].TURBT has been widely acknowledged as the currently gold standard to treat patients with NMIBC [4]. However, TURBT has several disadvantages. The electric current passing through the tissue during surgery gives a high possibility of arousing the obturator nerve causing unforeseeable bladder perforation, especially for lesions located in the lateral bladder wall [26]. Although obturator nerve block has shown its efficiency in avoid the ONR, it is still difficult to work well in every case [27]. Mis-staging and residual tumour may result from insufficient cutting depth in a bid to avoid ONR [28]. Consequently, it is significant to improve the performance of TURBT and explore the new, efficient and safe energy source.

Fortunately, the applications of laser therapy techniques have provided an alternative method in terms of NMIBC treatment. Recently, a meta-analysis published by Xu *et al.* [29] reported a lower incidence of complications, less probability of recurrence and faster postoperative recovery in laser operation group for patients with NMIBC when comparing to TURBT. However, different type of laser has

distinct characteristic and may result in diverse outcome. Thus, we tended to mainly focus on thulium laser, which is a new energy source for laser therapy and is also widely applied in the surgery of benign prostatic hyperplasia (BPH) [30]. It is a diode pumped solid-state laser with approximately 2 μm wavelength with only a 0.2 mm depth of thermal damage [31, 32], which performs better than other types of laser energies. The absence of the electric field effect decreases the incidence of ONR and therefore reduces the risk of bladder perforation. It is also safe for use in patients with cardiac pacemakers [33]. Furthermore, the power setting can be adjusted freely based on the different tumor size so that the continuous wave of energy achieves a higher cutting efficiency [34]. High-quality specimens are obtained to determine the optimal further treatment and reduce the infield recurrence [35, 36]. Several meta-analysis have been carried out to discuss the efficacy and safety between TURBT and laser therapy. This is the first meta-analysis to discuss the comparison of Tm-TURBT and TURBT for NMIBC.

Perioperative bleeding is the most common complication during TURBT [37]. Our results showed that intraoperative blood loss was less in the Tm-TURBT group than in the TURBT group. The reason for this result may be the excellent hemostasis, shallow penetration and reduced thermal damage of tissue when using thulium laser [38]. Under these circumstances, the duration of bladder irrigation, catheterization as well as hospitalization was notably shorter in the Tm-TURBT group. However, no significant difference was identified in the comparison of operation time. The basic procedure of transurethral operation is similar when inserting the surgical equipment, which may explain the reason of nonsignificant difference in both operation time and urethral stricture. With the accumulation of experience, surgeons may become more proficient at the tumor resection when using the laser technique. Nonetheless, it may have an influence on our results due to the lack of standard on recording the clinical data.

Among all the possible complications, bladder perforation is the most significant and lead to prolonged catheterization time, application of antibiotics and even a laparotomy in the case of intraperitoneal perforation [4]. It may even seed tumor cells into the peritoneum or retroperitoneum and also disable the immediate postoperative intravesical chemotherapy instillation, resulting in a high risk of tumor recurrence [39]. Our study revealed that perioperative complications involving ONR, bladder perforation as well as bladder irritation were less common in the Tm-TURBT group. The incidences of ONR, bladder perforation and bladder irritation were respectively calculated to be 0.1%, 0.2% and 3.8% in Tm-TURBT group and 12.7%, 7.2% and 13.0% in the TURBT group. Although the difference in urethral stricture as a complication was not significant, the rate was 2.5% in Tm-TURBT group which was slightly lower than that in the TURBT group with 4.2%. In summary, Tm-TURBT may be a better choice for patients to treat NMIBC with less complications. Nevertheless, none of the selected studies conducted a systematic assessment concerning the rate of complications, such as Clavien scoring system or any other systematic classification system [40, 41]. Thus, the analysis was of limited quality.

In our meta-analysis, the 1-year recurrence rate was not statistically different between Tm-TURBT group and TURBT group. We further analyzed the overall 1-year recurrence rate which was referred to the follow-up time less than or equal to 1 year, and we also studied the overall 3-year recurrence rate with the follow-up time less than or equal to 3 years. However, neither of them reported statistical significance. There was no consensus on standard follow-up management, and the application of different chemotherapy might have an influence on the final results. Therefore, we conducted a subgroup analysis based on postoperative adjuvant intravesical chemotherapy (epirubicin and non-epirubicin group), and we identified no significant difference between Tm-TURBT and TURBT in the recurrence rate among different follow-up period in both of the subgroups.

Despite of the theoretical advantages of the thulium laser technique over the conventional treatment, the Tm-TURBT group did not statistically lower the 1-year recurrence rate statistically in our analysis. Based on the EAU guidelines, stage and grade are important prognostic factors that influence recurrence and progression. Zhang *et al.* demonstrated that the overall recurrence rate in low risk, intermediate-low risk, and intermediate-high risk subgroups was 14.7%, 42.1%, and 62.5% respectively [23]. However, none of the included studies recorded the respective recurrence rates of different grades and tumor sites. Many factors can affect the treatment of NMIBC such as potential bladder cancer stem cells (CSC) and immunological factors [42, 43]. More studies need to be conducted to confirm the comparison of the recurrence rate in the two different operations.

According to the international collaborative consensus statement on en bloc resection of bladder tumor (ERBT), the efficacy of ERBT is still under debate and more studies following the consensus statement are required to explore the issue [44]. It also remains debatable whether bipolar TURBT performs better in efficacy and safety in NMIBC treatment than monopolar TURBT [45, 46]. Thus, we don't distinguish different resection method and energy sources of TURBT, which leaves one source of the major heterogeneity.

Heterogeneity was identified in our pooled analysis. Therefore, we performed a sensitivity analysis and reached the same conclusion. We considered that the heterogeneity may be related to the nonuniform standard of catheter extraction, postoperative treatment and hospital discharge [47]. Longer catheterization and hospitalization time can increase the risk of postoperative complications, such as pneumonia, urinary tract infection and embolism [48]. Hence, it is important to carry out the studies based on the similar standards.

Despite these findings, we also acknowledged several limitations of our analysis. Firstly, although all the included studies were RCTs, it must be recognized that the analysis was of limited quality. Most of the studies concerning laser

techniques were carried out in Asia and some were poorly documented. Secondly, our included studies did not assess the outcome data based on the same standard. A uniform standard of perioperative treatment and a consensus assessment method of complications is required to make the studies more comparable. Lastly, it was not sufficient to assess the individual outcome based on distinct tumor grade and stage, so it was unclear whether it would make a difference in different disease condition and more detailed researches were required. Given the limitations identified, further large-scale and well-designed RCTs are required to investigate the procedures.

5. Conclusions

According to the results of our meta-analysis, transurethral resection of bladder tumor using thulium laser technique, as compared with TURBT, was associated with less intraoperative blood loss and a lower incidence of ONR, bladder perforation and bladder irritation. It also showed faster postoperative recovery regarding the catheterization, bladder irrigation and hospitalization time. There was no significant difference in operation time, urethral stricture, 1-year recurrence rate, overall 1-year recurrence rate and overall 3-year recurrence rate. To conclude, Tm-TURBT was a favorable alternative to traditional TURBT for patients with NMIBC.

Author contributions

Yong Zhang designed the research, interpreted the data. Yumeng Chai, Yuanshan Cui, Huantao Zong and Zhongbao Zhou performed the data extraction and did Meta-analysis. Yumeng Chai drafted the paper. Xiaoyi Zhang helped revise the paper. All of the authors approved the submitted and final versions.

Ethics approval and consent to participate

All analyses were based on previous published studies, therefore no ethical approval and patient consent are required.

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Conflict of interest

The authors report no conflict of interest.

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