ORIGINAL ARTICLE



Radical prostatectomy after previous transurethral resection of the prostate: oncological, surgical and functional outcomes—a meta-analysis

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Received: 28 May 2019 / Accepted: 13 October 2019 / Published online: 2 November 2019 © Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Background The current study aimed to carry out a comprehensive meta-analysis on the existing evidence to quantify and compare the oncological, surgical and functional outcomes following radical prostatectomy between TURP group and Non-TURP group.

Methods A systematic literature search was conducted using EMBASE, PubMed and Cochrane databases to identify relevant studies published in English up to March 2019. A meta-analysis was conducted using Review Manager.

Results There were 13 studies included in the present study. Our results suggest that TURP group demonstrates a significantly higher positive surgical margin rate, bladder neck reconstruction rate and overall complication rate compared with Non-TURP group (OR = 1.31, 95% CI 1.09–1.58, P = 0.004, $I^2 = 0\%$; OR = 14.36, 95% CI 2.93–70.45, P = 0.001, $I^2 = 81\%$; OR = 2.63, 95% CI 1.87–3.71, P < 0.00001, $I^2 = 0\%$); whereas TURP group demonstrates a significantly lower nerve sparing rate compared with Non-TURP group (OR = 0.30, 95% CI 0.22–0.43, P < 0.00001, $I^2 = 40\%$); the operation time, blood loss and 1-year urinary continence rate are same between TURP group and Non-TURP group (MD = 4.25, 95% CI – 0.13 to 8.63, P = 0.06, $I^2 = 34\%$; MD = 27.29, 95% CI – 10.31 to 64.90, P = 0.15, $I^2 = 39\%$; OR = 0.68, 95% CI 0.43–1.06, P = 0.09, $I^2 = 0\%$). **Conclusion** This meta-analysis demonstrates that Non-TURP group may have a great advantage over TURP group in terms of positive surgical margin rate, bladder neck reconstruction rate, overall complication rate and sparing rate. The operation time, blood loss and 1-year urinary continence rate are comparable between TURP group and Non-TURP group. Therefore, important information should be given to those patients at risk of prostate cancer that TURP procedure may increase perioperative complications in case of a following radical prostatectomy. In the meantime, our meta-analysis found that each of these four subgroups (RARP, LRP, ORP and RARP/ORP) has its own advantages or disadvantages in every pool results. So when radical prostatectomy is performed on patients with TURP history, the appropriate operation method should be selected as per the conditions of patients, doctors and hospitals.

Keywords Radical prostatectomy · Prostate cancer · Transurethral resection of the prostate · Meta-analysis

Hai Liao and Xi Duan contribuxted equally.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00345-019-02986-2) contains supplementary material, which is available to authorized users.

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Introduction

Benign prostatic hyperplasia and prostate cancer are common causes of lower urinary tract symptoms in elderly men. Therefore, it is common for men to be diagnosed with prostate cancer on transurethral resection of prostate (TURP) chips or to develop prostate cancer after having undergone TURP for benign prostatic hyperplasia [1]. Prostate cancer is found in 3-16% of specimens from TURP [2, 3]. Radical prostatectomy is an effective treatment for prostate cancer. The presence of peripheral venous fibrosis, scar tissue and inflammation following previous TURP may contribute to poor outcomes in radical prostatectomy [4]. In order to minimize the impact of TURP on radical prostatectomy, the interval between TURP and radical prostatectomy is of paramount importance, but no consensus has been reached with regards to the specific interval up until now. Radical prostatectomy was recommended in the first month after TURP or until 4 months after TURP [5]. However, some studies recommend waiting at least 3 months between TURP and radical prostatectomy [6, 7]. In the past few decades, robot-assisted radical prostatectomy (RARP), laparoscopic radical prostatectomy (LRP) and open radical prostatectomy (ORP) have been used for radical prostatectomy. However, these operative methods showed different oncological, surgical and functional outcomes on radical prostatectomy compared with patients who had not TURP. To our knowledge, there is no meta-analysis to compare the effects of a history of TURP on radical prostatectomy. Therefore, we conduct a meta-analysis to compare the oncological, surgical and functional outcomes of patients who had previous TURP prior to radical prostatectomy and patients who had no TURP prior to radical prostatectomy.

Methods

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and metaanalysis (PRISMA) statement [8].

Data sources and searches

Then, we performed additional manual searches of references in key studies to retrieve additional papers relevant to our topic.

Study selection

Two reviewers (X.D and XX.M) independently reviewed all the full texts of the included studies. If the following inclusion criteria were met, the studies were included in the metaanalysis: (1) patients were diagnosed with prostate cancer based on their pathological data; (2) patients in experimental group had a history of TURP, while those in control group had no history of TURP; (3) the outcome indicators included at least one or more of the following, positive surgical margin, nerve sparing, operation time, blood loss, bladder neck reconstruction, overall complications and 1-year urinary continence; (4) study that had a prospective cohort design or a retrospective case–control design; (5) studies that were published in English. Any study that did not meet the above criteria was excluded.

Data extraction and quality assessment

A standardized data extraction form collecting information on the year of publication, country, study design, prostate specific antigen (PSA), prostate volume, Gleason Score, operative method, number of TURP group and Non-TURP group, positive surgical margin (PSM) rate, nerve sparing (NS) rate, operation time (OT), blood loss (BL), bladder neck reconstruction (BNR) rate, overall complication (OC) and 1-year urinary continence (1 year UC). Each included article was appraised by two independent reviewers (X.D. and XX.M). According to the different methods of radical prostatectomy, we divided them into four subgroups (RARP, LRP, ORP and RARP/ORP). Two reviewers (X.D. and XX.M) independently assessed the methodological quality of the included studies based on the risk of bias in nonrandomized studies of interventions (ROBINS-I). Seven domains were assessed based on signaling questions tailored to either cohort or case-control study designs: bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes and bias in selection of the reported result. Risk of bias was assigned as low, moderate, serious or critical in each domain.

Data synthesis and meta-analysis

We used Review RevMan 5.3 Software (The Cochrane Collaboration, Oxford, UK) and Stata v.12.0 Software (StataCorp, College Station, TX, USA) to conduct our data analysis. Four subgroups (RARP, LRP, ORP and RARP/

ORP) were set in this meta-analysis, and the results were presented in the forest plots. For continuous variables, mean difference (MD) and 95% confidence interval (95% CI) were used. The odds ratio (OR) and its 95% confidence interval (95% CI) were used to represent the dichotomous variables. The heterogeneity was classified as low ($I^2 < 50\%$) and high $(I^2 > 50\%)$. According to whether the homogeneity was low or high, we used the fixed or the random effect model in our meta-analysis [9]. If high heterogeneity $(I^2 > 50)$ was still found, subgroup analysis or sensitivity analysis was used to find the sources of heterogeneity and exhaust them. If heterogeneity still exists, we used the random effect model (REM) in our meta-analysis. Subgroup analysis was carried out by the operative method in the meta-analysis. For all statistical analyses, a two-sided P < 0.05 was considered statistically significant. Publication bias was tested by Begg's tests.

Results

Literature search and study election

A PRISMA [8] flowchart of screening and selection results is shown in Fig. 1. Using our pre-specified search strategy, we retrieved 505 extracts and obtained 12 additional citations by other sources. From 43 studies initially identified, 34 were considered potentially suitable. After a full-text review, 13 studies [4, 6, 7, 10–19] with 1163 patients with TURP history and 5587 patients without TURP history met inclusion criteria and were included in the final analysis. Among all 13 studies, three studies were prospective case series studies, ten studies were retrospective case–control studies. Table 1 provides the basic information. Table 2 provides the oncological, surgical and functional outcomes of included studies. Supplemental Figure 1 provides the quality assessment results based on ROBINS-I.

Results of meta-analyses

Oncological outcomes

Positive surgical margin rate Positive surgical margin rate was reported in 12 studies. TURP group provided a significantly higher positive surgical margin rate compared with Non-TURP group (OR = 1.31, 95% CI 1.09–1.58, P = 0.004, I^2 = 0%). Subgroup analysis stratified based on the operation method was also carried out, and the RARP subgroup analysis showed a higher positive surgical margin rate in TURP group (OR = 1.71, 95% CI 1.16–2.52, P = 0.006, I^2 = 0%), whereas both groups shared the same positive surgical margin rate as demonstrated by LRP, ORP and RARP/ORP subgroup analysis (OR = 1.62, 95% CI 0.98–2.69, P = 0.06,

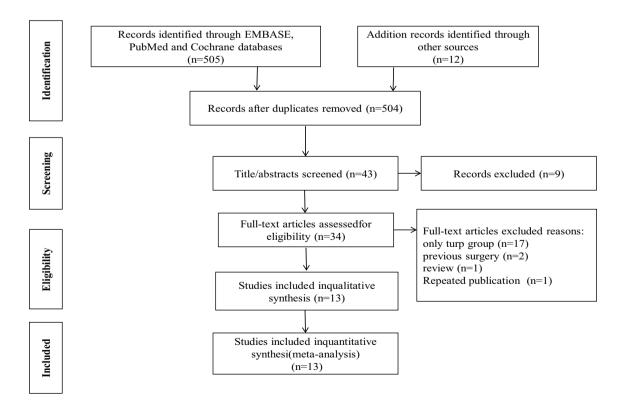


Fig. 1 Flow diagram of selection of eligible studies

Table 1 Char	acteristics	Characteristics of the included studies								
Study	Country	Mean age (year) (TURP/	Study	PSA (ng/ml) (TURP/	Prostate volume (ml)	Gleason score	Operative	Number		Propensity
		Non-TURP group)	design	Non-FURP group)	(TURP/Non-TURP group)	(TURP/Non-TURP group)	method	TURP group	Non- TURP group	scoring analysis
Colombo et al. (2006) [7]	Italy	$62.9 \pm 6.2/62.29 \pm 5.7$	Retrospec- tive	$6.5 \pm 3/6.0 \pm 2.9$	1	I	ORP	109	120	Yes
Gupta et al. (2011) [10]	India	66.6/63.4	Retrospec- tive	13.2/19.6	39/44	6.36/6.1	RARP	26	132	No
Hampton et al. (2008) [11]	America	1	Prospective	I	I	I	RALP	51	102	Yes
Hung et al. (2014) [12]	China	67.5±7.4/64.8±6.9	Retrospec- tive	26.4±29.6/17.9±20.3	I	$6.6 \pm 1.0/6.59 \pm 1.0$	RARP	16	184	No
Jaffe et al. (2007) [15]	France	$66.2 \pm 5.6/60.7 \pm 7.0$	Retrospec- tive	8.2±4/8.1±4.7	I	$6 \pm 1.1/6 \pm 1.0$	LRP	119	119	Yes
Menard et al. (2008) [4]	France	$66.7 \pm 4.9/62.8 \pm 6.7$	Prospective	7.8±5.2/10.3±8.8	I	$5.8 \pm 0.9/6.1 \pm 1.1$	LRP	46	594	No
Palisaar et al. (2009) [18]	Germany	Germany 67±4.3/63±6.4	Prospective	5.8±6.8/9.9±11.8	25.5±15.8/36.7±17.1	I	ORP	62	62	Yes
Pompe et al. (2018) [13]		Germany $67.9 \pm 0.2/67.4 \pm 0.3$	Retrospec- tive	$7.0 \pm 0.377.2 \pm 0.2$	$31.1 \pm 0.9/32.4 \pm 0.5$	I	ORP or RARP	470	1410	Yes
Su et al. (2015) [14]	America	63.65/59.77	Retrospec- tive	6.91/5.91	I	6.49/6.56	RARP	49	2644	Yes
Teber et al. (2009) [16]	Turkey	66/65.6	Retrospec- tive	I	25/46	LLL	LRP	55	55	Yes
Yang et al. (2015) [17]	China	63.9/68.9	Retrospec- tive	9.21/10.49	$19.2 \pm 5.6/34.4 \pm 15.5$	6.5/6.6	LRP	35	35	Yes
Yazici et al. (2009) [18]	Turkey	$60.97 \pm 6.57/61.04 \pm 7.77$	Retrospec- tive	6.4±5.2/7.2±2.9	1	1	ORP	45	50	Yes

 $I^2 = 0\%$; OR = 1.30, 95% CI 0.82–2.07, P=0.26, $I^2 = 0\%$; OR = 1.09, 95% CI 0.83 - 1.4, P = 0.53 (Fig. 2).

Nerve sparing rate As for the nerve sparing rate, TURP group provided a significantly lower nerve sparing rate compared with Non-TURP group (OR=0.30, 95% CI 0.16–0.54, P < 0.0001, $I^2 = 83\%$). Furthermore, analysis of RARP, LRP and ORP subgroups showed that the nerve sparing rate in TURP group was low (OR = 0.39, 95% CI 0.20-0.76, P=0.006; OR=0.35, 95% CI 0.22-0.54, P < 0.00001, $I^2 = 0\%$; OR = 0.12, 95% CI 0.07-0.20, $P < 0.00001, I^2 = 0\%$). However, RARP/ORP subgroup analysis suggested no statistically significant difference in the nerve sparing rate between TURP group and Non-TURP group (OR=0.77, 95% CI 0.55-1.10, P=0.15) (Fig. 3). Due to high heterogeneity ($I^2 = 83\%$), sensitivity analysis was performed by Stata. After removing the studies by Pompe [13] and Colombo [7] as the sample that was "left out", the pooled results did not change substantially and the heterogeneity was significantly reduced (OR = 0.30, 95% CI 0.22–0.43, P < 0.00001, $I^2 = 40\%$). In addition, no change was observed in the pooled results of RARP, LRP and ORP subgroup analysis (OR = 0.39, 95% CI 0.20-0.76, P=0.006; OR=0.35, 95% CI 0.22-0.54, P<0.00001, $I^2 = 0\%$; OR = 0.11, 95% CI 0.04–0.28, P < 0.00001) (Supplemental Figure 1).

Surgical outcomes

Operation time Referring to the operation time, TURP group offered a significantly longer operation time compared with Non-TURP group (MD=11.40, 95% CI 2.25–20.55, P=0.01, $I^2=67\%$) (Fig. 4). Sensitivity analysis was also carried out owing to the high heterogeneity $(I^2 = 67\%)$. After removing the study by Yazici [19] as the sample that was "left out", the heterogeneity was significantly reduced. The meta-analysis showed the same operation time in both groups (MD=4.25, 95% CI -0.13 to 8.63, P = 0.06, $I^2 = 34\%$). Furthermore, the two groups also shared the operation time as demonstrated by the RARP. ORP and RARP/ORP subgroup analysis (MD = 12.60, 95% CI - 39.00 to 64.20, P = 0.63; MD = 3.17, 95% CI - 6.34 to 12.67, P = 0.51, $I^2 = 0\%$; MD = 1.50, 95% CI - 4.33 to 7.33, P=0.61). However, TURP group offered a significantly longer operation time compared with Non-TURP group in LRP subgroup analysis (MD=12.26, 95% CI 2.83-21.69, $P=0.01, I^2=71\%$) (Supplemental Figure 2).

Blood loss The blood loss was the same in both TURP group and Non-TURP group (MD = 90.06, 95% CI - 7.09 to $187.21, P = 0.07, I^2 = 81\%$ (Fig. 5). Sensitivity analysis was employed due to the high heterogeneity $(I^2 = 81\%)$. When study of Colombo [7] was removed from our meta-analysis,

Table 1 (continued)

IND I-IION	Non-TURP group)	design	Non-TURP group)	Non-TURP group) (TURP/Non-TURP (TURP/Non-TURP method	(TURP/Non-TURP	method	DDD	Mon	scoring
				group)	group)		group	TURP group	analysis
Zugor et al. Germany 67.5/66.1 (2012) [6]		Retrospec- tive	9.5/9.2	30.9/30.1	I	RARP	80	80 Yes	Yes

Study	No. of PSM	М	No. of NS		0T (min)		BL (ml)		No. of BNR	٨R	No. of OC		No. of 1-	No. of 1-year UC
	TURP group	Non- TURP group	TURP group	Non- TURP group	TURP group	Non-TURP group	TURP group	Non-TURP group	TURP group	Non- TURP group	TURP group	Non- TURP group	TURP group	Non- TURP group
Colombo et al. (2006) [7]	28	27	40	86	135 ± 105	125 ± 85	820 ± 625	480±110	I	I	1	1	I	I
Gupta et al. (2011) [10]	S,	17	I	I	I	I	I	I	L	13	I	I	I	I
Hampton et al. (2008)	18	18	I	I	I	I	I	I	I	I	1	I	I	I
Hung et al. (2014) [12]	Γ.	74	1	I	189.6±104.4	177.0±46.8	189.6 ± 104.4 177.0 ± 46.8 145.0 ± 161.4 183.2 ± 18.06	183.2±18.06	15	28	Clavien I– II: 1 Clavien III–IV: 3	Clavien I– II: 18 Clavien III–IV: 2	15	180
Jaffe et al. (2007) [15]	26	15	I	I	179±44	171 ± 38	458 ±443	439 ±386	I	I	64	ξ	I	I
Menard et al. (2008) [4]	I	I	26	469	250 ±73	219±74	884±565	756±572	I	I	6	56	34	497
Palisaar et al. (2009) [18]	12	×	I	I	161 ± 32.5	159 ± 25.5	790±425	820±500	I	I	I	I	50	51
Pompe et al. (2018) [13]	87	243	420	1291	184.8±56.4	183.3±45.1	710.1±494.3	665.9±494.3	1	I	96	267	I	I
Su et al. (2015) [14]	15	555	I	I	I	1	1	I	I	I	I	I	I	I
Teber et al. (2009) [16]	∞.	6	30	40	I	I	I	I	51	40	Clavien I– II: 3 Clavien	Clavien I– II: 4 Clavien	49	50

Table 2 (continued)	ntinued)													
Study	No. of PSM	4	No. of NS		0T (min)		BL (ml)		No. of BNR	Ж	No. of OC		No. of 1-year UC	ear UC
	TURP group	Non- TURP group	TURP group	Non- TURP group	TURP group Non-TURP group	Non-TURP group	TURP group Non-TURP group	Non-TURP group	TURP group	Non- TURP group	TURP group	Non- TURP group	TURP group	Non- TURP group
Yang et al. 12 (2015) [17]	12	L	6	21	1	. 1	. 1	. 1	1	1	Clavien I– Clavien I– II: 9 II: 2 Clavien Clavien III–IV: 4 III–IV: 2	Llavien I– Clavien I– II: 9 II: 2 Llavien Clavien III–IV: 4 III–IV: 2	1	1
Yazici et al. (2009) [1 <mark>9</mark>]	6	×	6	35	173 ± 40	143±33	1374±679	1103±611	I	I	1	I	I	I
Zugor et al. (2012) [6]	S	4	42	59	I	I	I	I	47	0	22	6	70	73
PSM positi	ve surgical n	ıargin, NS r	terve sparing	, OT operat	PSM positive surgical margin, NS nerve sparing, OT operation time, BL blood loss, BNR bladder neck reconstruction, OC overall complication, UC urinary continence	od loss, BNR b	ladder neck reco	nstruction, OC	overall com	plication, <i>U</i>	'C urinary co	ntinence		

the heterogeneity was lower. The meta-analysis showed the same blood loss in both groups (MD=27.29, 95% CI -10.31 to 64.90, P=0.15, $I^2=39\%$). It was also the same in both groups after subgroup analysis (MD=-38.20, 95% CI -117.33 to 40.93, P=0.34; MD=49.43, 95% CI - 40.20 to 139.06, P=0.44, $I^2=73\%$; MD=44.20, 95% CI - 7.73 to 96.13, P=0.10) (Supplemental Figure 3).

Bladder neck reconstruction rate As for the bladder neck reconstruction rate, TURP group provided a significantly higher bladder neck reconstruction rate compared with Non-TURP group (OR = 14.36, 95% CI 2.93–70.45, P=0.001, I^2 =81%). In addition, RARP and LRP subgroup analysis came to the same results between TURP group and Non-TURP group (OR = 22.68, 95% CI 2.26–228.05, P=0.008, I^2 =86%; OR = 4.78, 95% CI 1.47–15.53, P=0.009) (Fig. 6).

Overall complication rate With regard to the overall complication rate, TURP group had a markedly increased overall complication rate relative to that in Non-TURP group (OR=2.09, 95% CI 1.26–3.46, P=0.004, $l^2=70\%$) (Fig. 7). Sensitivity analysis was carried out to account for high heterogeneity ($l^2=70\%$). We found that the heterogeneity was significantly reduced after study of Pompe [13] was removed. Our meta-analysis suggested higher overall complication rate in TURP group (OR=2.63, 95% CI 1.87–3.71, P < 0.00001, $l^2=0\%$), and that was the same between the two groups in the RARP and LRP subgroup analysis (OR=2.92, 95% CI 1.45–5.90, P=0.003, $l^2=0\%$; OR=2.55, 95% CI 1.72–3.77, P < 0.00001, $l^2=30\%$) (Supplemental Figure 4).

Functional outcomes

One-year urinary continence rate As for the 1-year urinary continence rate, TURP group provided no significantly higher or lower 1-year urinary continence rate compared with Non-TURP group (OR=0.68, 95% CI 0.43–1.06, P=0.09, $I^2=0\%$). Furthermore, there was no statistically significant difference in the 1-year urinary continence rate between the two groups upon RARP, LRP and ORP subgroup analysis (OR=0.62, 95% CI 0.24–1.58, P=0.31, $I^2=0\%$; OR=0.61, 95% CI 0.33–1.13, P=0.12, $I^2=0\%$; OR=0.90, 95% CI 0.36–2.22, P=0.82) (Fig. 8).

Sensitivity analysis and publication bias

The nerve sparing rate, operation time, blood loss, bladder neck reconstruction rate and overall complication rate had high heterogeneity ($l^2 > 50\%$) in our meta-analysis. Sensitivity analysis was performed for high heterogeneity. When one or two studies were removed from our metaanalysis, lowered heterogeneity was observed in the nerve

	TURP q	roup	Non TURP	group		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
1.1.1 RARP							
Gupta N P et al.2011	5	26	17	132	2.4%	1.61 [0.54, 4.84]	
Hampton L et al.2008	18	51	18	102	4.1%	2.55 [1.18, 5.48]	
Hung C et al.2014	7	16	74	184	3.5%	1.16 [0.41, 3.24]	
Su Y et al.2015	15	49	555	2644	7.3%	1.66 [0.90, 3.07]	
Zugor V et al.2012	5	80	4	80	2.0%	1.27 [0.33, 4.90]	
Subtotal (95% CI)		222		3142	19.2%	1.71 [1.16, 2.52]	◆
Total events	50		668				
Heterogeneity: Chi ² = 1.80	0, df = 4 (F)	= 0.77); I ² = 0%				
Test for overall effect: Z =							
1.1.2 LRP							
Jaffe J et al.2007	26	119	15	119	6.1%	1.94 [0.97, 3.88]	
Teber D et al.2009	8	55	9	55	4.0%	0.87 [0.31, 2.45]	
Yang Y et al.2015	12	35	7	35	2.4%	2.09 [0.71, 6.16]	
Subtotal (95% CI)		209		209	12.5%	1.62 [0.98, 2.69]	◆
Total events	46		31			. , .	
Heterogeneity: Chi ² = 1.85		P = 0.40	$ ^2 = 0\%$				
Test for overall effect: Z =			,,				
		,					
1.1.3 ORP							
Colombo R et al.2006	28	109	27	120		1.19 [0.65, 2.18]	
Palisaar J R et al.2009	12	62	8	62	3.4%	1.62 [0.61, 4.29]	
Yazici S et al.2009	9	45	8	50	3.2%	1.31 [0.46, 3.76]	
Subtotal (95% CI)		216		232	16.5%	1.30 [0.82, 2.07]	-
Total events	49		43				
Heterogeneity: Chi ² = 0.28); I² = 0%				
Test for overall effect: Z =	1.12 (P =	0.26)					
1.1.4 RARP /ORP							
Pompe R S et al.2018	87	470	243	1410	51.7%	1.09 [0.83, 1.43]	_
Subtotal (95% CI)	07	470	243	1410		1.09 [0.83, 1.43]	
Total events	87	470	243	1410	51.770	1.09 [0.05, 1.45]	T
Heterogeneity: Not applic			243				
Test for overall effect: Z =		0.50					
Test for overall effect. Z =	0.63 (F =	0.53)					
Total (95% CI)		1117		4993	100.0%	1.31 [1.09, 1.58]	◆
Total events	232		985			1225 42 6.2	
Heterogeneity: Chi ² = 8.21	1, df = 11	(P = 0.6	9); I ² = 0%				
Test for overall effect: Z =							0.01 0.1 1 10 100
Test for subaroup differer			df = 3 (P = 1	0.23). I ² =	30.0%		Favours [TURP group] Favours [Non TURP group]

Fig. 2 Forest plot of the positive surgical margin rate

sparing rate, operation time, blood loss and overall complication rate. For the sensitivity analysis of bladder neck reconstruction rate, we found that the heterogeneity was significantly reduced after removing studies of Zugor [6] and Hung [12]. However, when these two studies were excluded, only two studies were included in this metaanalysis. Finally, these two articles were not eliminated considering the small scope of studies included; we did not delete these two articles. Publication bias was tested by Begg's tests. Begg's funnel plot showed no substantial asymmetry and the regression tests indicated no significant publication bias for PSM (pBegg = 0.837, Supplemental Figure 5a), NS (pBegg=0.806, Fig. 5b), OT (pBegg = 0.452, Fig. 5c), BL (pBegg = 0.260, Fig. 5d),BNR (pBegg = 1.000, Fig. 5e), OC (pBegg = 0.452, Fig. 5f) and 1-year UC (pBegg = 1.000, Fig. 5g).

Discussion

This meta-analysis reviewed and analyzed 13 published studies to investigate and compare the oncological, surgical and functional outcomes of prostate cancer patients undergoing radical prostatectomy between TURP group and Non-TURP group. Ten published studies used a match-paired analysis. The results revealed that TURP group had higher the positive surgical margin rate, overall complication rate and bladder neck reconstruction rate, and lower nerve sparing rate.

Positive surgical margin is commonly accepted that the most affected sites are the prostatic apex and posterolateral location [20]. However, radical prostatectomy in patients undergoing TURP accounts for a difficulty in precisely

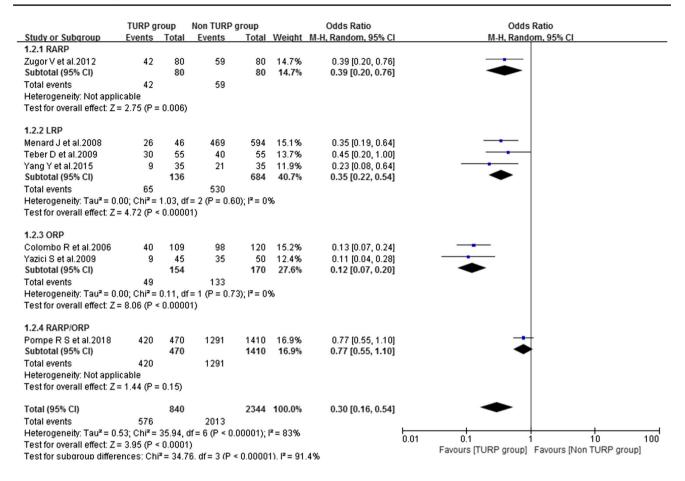


Fig. 3 Forest plot of the nerve sparing rate

identifying the prostatic apex and prostatic margins [21]; due to peripheral venous fibrosis, the anatomy of patients after TURP is technically difficult [22]; capsular perforation and fluid absorption during TURP can lead to fibrotic post-inflammatory reaction, this eventually leads to more difficult bladder neck dissection, which negatively affects the surgical margins in this area [7]; TURP can lead to surgical plane distortion [23]. Taken together, these reasons may increase the positive surgical margin rate and bladder neck reconstruction rate, whereas decreasing the nerve sparing rate in patients undergoing TURP after radical prostatectomy. These results are consistent with the results of this meta-analysis. However, the results of some subgroup analyses were inconsistent with the overall results, which may be due to the lack of adequate included studies in subgroups.

As suggested in most studies, TURP will add to the difficulty in radical prostatectomy. However, no consensus is reached about whether radical prostatectomy increases the operation time and blood loss in patients with previous TURP history. To be specific, some studies [4, 7, 12, 15, 19] suggested that radical prostatectomy might prolong the operation time in patients with previous TURP history. However, some studies [13, 18] had the opposite results, the result was the same as this meta-analysis. Three [12, 13, 15] of the six studies [4, 12, 13, 15, 18, 19] indicated that the blood loss in the two groups has statistical significance. However, this meta-analysis produced the opposite results. The results of meta-analysis may be attributed to the improvement of surgical techniques, the greater maturity of surgical methods and the more experienced operators, which may offset the negative effects of TURP. The need for bladder neck reconstruction is increased because preservation of the bladder neck after TURP was difficult.

Our meta-analysis on the overall complications in both groups showed that TURP group had a markedly higher overall complication rate than that in Non-TURP group. Such finding may be explained as follows: scar and fibrosis of bladder neck after TURP can make the healing of anastomosis more difficult; posterior dissection is difficult, leading to an increase risk of rectal injury; bladder neck thickening, fibrosis and stiffness after transurethral resection of prostate can increase anastomotic leakage; patients with tumors discovered on TURP chips may increase seminal vesiculitis, because tumors in the transition zone may be more easily transmitted through the ejaculatory duct; during

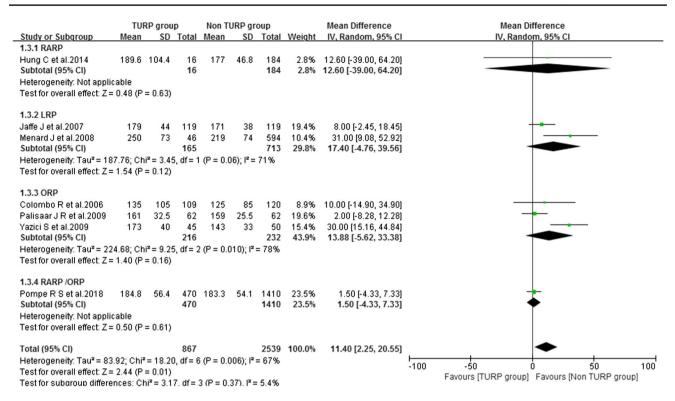


Fig. 4 Forest plot of the operation time

	TU	RP grou	р	Non T	URP gr	oup		Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI
1.4.1 RARP										
Hung C et al.2014	145	161.4	16	183.2	18.06	184	17.4%	-38.20 [-117.33, 40.93]		
Subtotal (95% CI)			16			184	17.4%	-38.20 [-117.33, 40.93]		-
Heterogeneity: Not appli	cable									
Test for overall effect: Z =	= 0.95 (P	= 0.34)								
1.4.2 LRP										
Jaffe J et al.2007	458	443	119	439	386	119	15.9%	19.00 [-86.57, 124.57]		
Menard J et al.2008	884	565	46	756	572	594	12.3%	128.00 [-41.63, 297.63]		
Subtotal (95% CI)			165			713	28.2%	52.45 [-46.08, 150.98]		
Heterogeneity: Tau ² = 74	4.65; Ch	ni ² = 1.14	4, df = 1	(P = 0.	28); I ² =	13%				
Test for overall effect: Z =	= 1.04 (P	= 0.30)								
1.4.3 ORP										
Colombo R et al.2006	820	625	109	480	110	120	15.2%	340.00 [221.03, 458.97]		
Palisaar J R et al.2009	790	425	62	820	500	62		-30.00 [-193.34, 133.34]		
Yazici S et al.2009	1,374	679	45	1,103	611	50	8.1%			
Subtotal (95% CI)			216			232	35.9%	192.46 [-61.81, 446.72]		
Heterogeneity: Tau ² = 41	703.20:	Chi ² = 1	3.05. d	f=2(P	= 0.001); I ² = 85	5%			
Test for overall effect: Z =						/				
1.4.4 RARP/ORP										
Pompe R S et al.2018	710.1	494.3	470	665.9	506.9	1410	18.6%	44.20 [-7.73, 96.13]		+ -
Subtotal (95% CI)			470			1410	18.6%	44.20 [-7.73, 96.13]		◆
Heterogeneity: Not appli	cable							-		
Test for overall effect: Z =		= 0.10)								
Total (95% CI)			867			2539	100.0%	90.06 [-7.09, 187.21]		
Heterogeneity: Tau ² = 12	2530.68;	Chi ² = 3	2.37, d	f=6(P	< 0.000	1); l ² = 1	31%		+	-250 0 250 500
Test for overall effect: Z =									-500	
Test for subaroup differe	ences: Cl	hi² = 4.9	0. df = 3	3 (P = 0	.18). I ² =	: 38.8%				Favours [TURP group] Favours [Non TURP group]

Fig. 5 Forest plot of the blood loss

	TURP gr	roup	Non TURP g	roup		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% Cl
1.5.1 RARP								
Gupta N P et al.2011	7	26	13	132	27.8%	3.37 [1.19, 9.53]		
Hung C et al.2014	15	16	28	184	20.6%	83.57 [10.61, 658.21]		_
Zugor V et al.2012	47	80	2	80	24.8%	55.55 [12.74, 242.17]		
Subtotal (95% CI)		122		396	73.1%	22.68 [2.26, 228.05]		
Total events	69		43					
Heterogeneity: Tau ² = 3	.54: Chi ² =	= 14.62	. df = 2 (P = 0	.0007):	I² = 86%			
Test for overall effect: Z	-							
1.5.2 LRP								
Teber D et al.2009	51	55	40	55	26.9%	4.78 [1.47, 15.53]		
Subtotal (95% CI)		55		55	26.9%	4.78 [1.47, 15.53]		
Total events	51		40					
Heterogeneity: Not appl	icable							
Test for overall effect: Z		= 0.009	3)					
Total (95% CI)		177		451	100.0%	14.36 [2.93, 70.45]		
Total events	120		83					
Heterogeneity: Tau ² = 2	.09; Chi ² =	= 16.17	df = 3 (P = 0	.001); I ^z	= 81%			
Test for overall effect: Z	•						0.001	0.1 1 10 1000
Test for subaroup differ	ences: Cl	hi ² = 1.3	9. df = 1 (P =	0.24), P	² = 27.9%			Favours [TURP group] Favours [Non TURP group]

Fig. 6 Forest plot of the bladder neck reconstruction rate

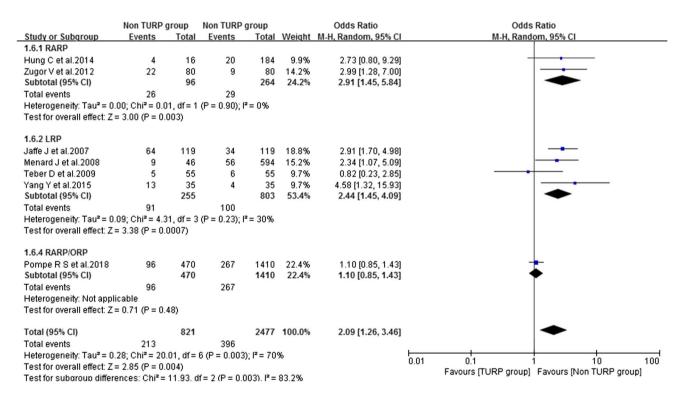


Fig. 7 Forest plot of the overall complication rate

TURP, there is an increased risk of stricture due to urethral manipulation and catheterization, which may lead to anterior urethral stricture.

Maintaining the quality of life is an important secondary goal after radical prostatectomy [24]. According to numerous studies, urinary incontinence is one of the most common factors affecting the quality of life following radical prostatectomy [25, 26]. The cause of urinary incontinence after radical prostatectomy remains unknown. A higher body mass index (BMI) is considered as an independent predictor of urinary incontinence following radical prostatectomy [27]. Besides, surgical technique and surgeon experience are also associated with postoperative urinary incontinence [28–30]. Preservation of the membranous urethral length,

	TURP g	roup	Non TURP	group		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.7.1 RARP							
Hung C et al.2014	15	16	180	184	4.0%	0.33 [0.04, 3.17]	
Zugor V et al.2012	70	80	73	80	20.3%	0.67 [0.24, 1.86]	
Subtotal (95% CI)		96		264	24.3%	0.62 [0.24, 1.58]	
Total events	85		253				
Heterogeneity: Chi ² = 0.3	31, df = 1 (F	P = 0.58); I ² = 0%				
Test for overall effect: Z =	= 1.01 (P =	0.31)					
1.7.2 LRP							
Menard J et al.2008	34	46	497	594	41.5%	0.55 [0.28, 1.11]	
Teber D et al.2009	49	55	50	55	12.2%	0.82 [0.23, 2.85]	
Subtotal (95% CI)		101		649	53.7%	0.61 [0.33, 1.13]	
Total events	83		547				
Heterogeneity: Chi ² = 0.2	29, df = 1 (F	P = 0.59); I ² = 0%				
Test for overall effect: Z =	= 1.57 (P =	0.12)					
1.7.3 ORP							
Palisaar J R et al.2009	50	62	51	62	22.0%	0.90 [0.36, 2.22]	
Subtotal (95% CI)		62		62	22.0%	0.90 [0.36, 2.22]	
Total events	50		51				
Heterogeneity: Not appli	cable						
Test for overall effect: Z =	= 0.23 (P =	0.82)					
Total (95% CI)		259		975	100.0%	0.68 [0.43, 1.06]	◆
Total events	218		851				
Heterogeneity: Chi ² = 1.1	17, df = 4 (F	^o = 0.88); I ² = 0%				
Test for overall effect: Z =	= 1.71 (P =	0.09)					
Test for subaroup differe	ences: Chi ^a	²= 0.52.	df = 2 (P = ().77). I ² =	0%		Favours [TURP group] Favours [Non TURP group]

Fig. 8 Forest plot of the 1-year urinary continence rate

preservation of the neurovascular supply, reconstruction of urethral and urethrovesical support were beneficial to urinary continence [31]. In our meta-analysis, the 1-year urinary continence rate was the same in both TURP group and Non-TURP group. Such results indicated that radical prostatectomy after TURP might have no significant effect on patients' functional results. However, we found that the urinary continence rate of TURP group was worsened in our clinical center, which contradicted our meta-analysis results. It might be ascribed to the fact that only five studies were included in this meta-analysis to analyze the urinary continence rate, and the sample size in TURP group was small. On the other hand, although there was no statistical significance in the urinary continence rate in this meta-analysis, the Non-TURP group was better than the TURP group in terms of the inclusion of the studies. It can be considered that the urinary continence rate in the two groups had clinical significance. Therefore, more well designed and randomized high-quality studies with large sample size should be carried out in the future to explore the effect of TURP on the urinary continence rate after radical prostatectomy.

According to our meta-analysis, prostate cancer patients with a history of TURP had poorer oncological outcomes, as well as higher bladder neck reconstruction rate and overall complication rate after radical prostatectomy. Through our clinical observation, it could be due to the fact that the age and prostate volume of patients in the TURP group may be larger. However, this might not be the case for the 13 studies included in this present study. Because there were only three studies showing different ages in the two groups, among which two studies showed significant differences in the prostate volume between the two groups. We should exclude the possibility of prostate cancer before operating on patients with TURP in clinical work, to avoid the diagnosis of prostate cancer after TURP as much as possible. Currently, surgery has become the primary approach to effectively relieve the lower urinary tract symptoms in patients with benign prostatic hyperplasia. However, currently TURP, vaporization of the prostate and endoscopic enucleation of the prostate can be selected as the current surgical methods [32], and each of above-mentioned methods has its own advantages and disadvantages. In the future, a better surgical method should be explored to reduce peripheral venous fibrosis, scar tissue and inflammation. As also shown in this metaanalysis, there was no difference in the operation time, blood loss and 1-year urinary continence rate between the two groups. Therefore, radical prostatectomy is still a good choice for prostate cancer patients with a history of TURP. In order to reduce the influence of TURP on radical prostatectomy, the interval time between TURP and radical prostatectomy is an important factor. However, currently no consensus has been reached in this regard. Consequently, more relevant studies are warranted to identify the optional interval, so that prostate cancer patients with a TURP history can have a better recovery after radical prostatectomy.

Several limitations of the meta-analysis should be noted. Firstly, the samples size in the TURP group was relatively small in some studies; secondly, the differences in surgical equipment and techniques might affect the outcomes since the studies were conducted in different countries and hospitals. Thirdly, the meta-analysis in terms of the nerve sparing rate, operation time, blood loss, bladder neck reconstruction rate and overall complication rate had high heterogeneity. After sensitivity analysis, the heterogeneities of this metaanalysis in terms of the nerve sparing rate, operation time, blood loss bladder neck reconstruction and overall complication rate were significantly reduced. At last, patients with a history of TURP might be older or have a late stage of prostate cancer, leading to poorer oncological and functional outcomes, which might lead to inherent biases. In the future, studies with well-designed retrospective or prospective case controls are needed.

Conclusions

This meta-analysis demonstrates that the TURP group provides a significantly higher positive surgical margin rate, overall complication rate, bladder neck reconstruction rate and lower nerve sparing rate compared with Non-TURP group. The operation time, blood loss and 1-year urinary continence rate are same between TURP group and Non-TURP group.

Acknowledgements This work was supported by the Natural Science Foundation of Sichuan Provincial Department of Education (16ZB0227), Scientific Research Foundation of Health and Family Planning Commission of Sichuan Province (17PJ155) and City of Nanchong Strategic Cooperation with Local Universities Foundation of technology (NSMC20170421, NSMC20170111, 18SXHZ0581, 18SXHZ0128).

Authors' contributions SC, TW: project development, public funding. XD, XXM, THH, TC, JBL: data collection. HL, XD: data analysis, manuscript writing/editing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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