REVIEW

Does previous transurethral resection of the prostate negatively influence subsequent robotic-assisted radical prostatectomy in men diagnosed with prostate cancer? A systematic review and meta-analysis

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Abstract

It is not uncommon to incidentally discover prostate cancer during the transurethral resection of the prostate (TURP) for the treatment of benign prostatic hyperplasia and necessitate a subsequent robotic-assisted radical prostatectomy (RARP). The study aims to evaluate whether TURP have negative influence on subsequent RARP. Through a literature search using MEDLINE, EMBASE and the Cochrane Library, 10 studies with 683 patients who underwent RARP after previous TURP and 4039 patients who underwent RARP only were identified for the purposes of the meta-analysis. Compared to standard RARP, RARP after TURP was related to longer operative time (WMD: 29.1 min, 95% CI: 13.3–44.8, $P < 0.001$), more blood loss (WMD: 49.3 ml, 95% CI: 8.8–89.7, $P = 0.02$), longer time to catheter removal (WMD: 0.93 days, 95% CI: 0.41–1.44, $P < 0.001$), higher rates of overall (RR: 1.45, 95% CI: 1.08–1.95, $P = 0.01$) and major complications (RR: 3.67, 95% CI: 1.63–8.24, $P = 0.002$), frequently demand for bladder neck reconstruction (RR: 5.46, 95% CI: 3.15–9.47, $P < 0.001$) and lower succeed in nerve sparing (RR: 0.73, 95% CI: 0.62–0.87, $P < 0.001$). In terms of quality of life, there are worse recovery of urinary continence (RR of incontinence rate: RR: 1.24, 95% CI: 1.02–1.52, $P = 0.03$) and potency (RR: 0.8, 95% CI: 0.73–0.89, $P < 0.001$) at 1 year in RARP with previous TURP. In addition, the RARP with previous TURP had greater percentage positive margins (RR: 1.24, 95% CI: 1.02–1.52, $P = 0.03$), while there is no difference in length of stay and biochemical recurrence rate at 1 year. RARP is feasible but challenging after TURP. It significantly increases the difficulty of operation and compromises surgical, functional and oncological outcomes. It is important for urologists and patients to be aware of the negative impact of TURP on subsequent RARP and establish treatment strategies to lessen the adverse effects.

Keywords Prostate cancer · Robotic-assisted radical prostatectomy · Transurethral resection of the prostate · Quality of life · Prognosis · Safety

Introduction

Prostate cancer (PCa) is the most frequent cancer, and as the second leading cause of cancer-related mortality in men in western countries, is a global public health problem [1]. Radical prostatectomy is recommended as the standard treatment for localized prostate cancer. With the advances in robotic-assisted technique, robotic-assisted radical prostatectomy (RARP) has become the dominant prostatectomy approach [2].

Generally, prostate cancer is diagnosed by prostate biopsy on the basis of elevated prostate-specific antigen (PSA) or abnormal digital rectal examination. However, age is a risk factor for both benign prostatic hyperplasia (BPH) and prostate cancer, hence it is not uncommon for older men to be incidentally identified with prostate cancer during a transurethral resection of the prostate (TURP) performed to treat their BPH. This accounts for between 2 and 12% of all new cases of prostate cancer [3–5]. Patients incidentally discovered of prostate cancer during TURP are recommended to

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receive a consecutive radical prostatectomy after 3 months. It is anticipated that periprostatic inflammation, fibrosis, and adhesion of the surgical planes caused by perforation of the prostatic capsule and extravasation of blood and irrigation fluid during TURP would make future RARP more challenging. As a consequence, several studies have been published to evaluate the impact of prior TURP on RARP, however, showed controversial findings [4, 6–9].

In order to benefit the men who underwent RARP with a history of TURP, the internal association between TURP and RARP is of paramount importance. Hence, we performed a meta-analysis of the available literature to evaluate the surgical, functional or oncological outcomes between RARP with or not previous TURP. Moreover, we hypothesized that RARP with previous TURP offers undesirable outcomes, therefore, a literature review would be made to find out some strategies to mitigate the adverse effect of TURP on RARP.

Methods

Search strategy and study selection

Following the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a comprehensive review was conducted [10]. This study is registered at the INPLASY register (INPLASY202310062). For this purpose, we searched MEDLINE, EMBASE, and the Cochrane Library from 1998 to November 2022 that met our criteria for inclusion. The search terms were (''TURP'' OR ''transurethral resection'' OR "enucleation") AND (''robotic OR ''robot'' OR ''robot assisted'') AND ("radical prostatectomy"). There were no linguistic constraints imposed. The references of retrieved articles were also searched for additional studies. The following requirements should be satisfied by the chosen studies: (1) randomized controlled trials, prospective or retrospective cohort study; (2) compared robot-assisted radical prostatectomy patients with previous TURP (TURP Group) to patients without TURP (no-TURP Group); (3) reported at least one surgical, functional or oncological outcomes of interest; (4) studies relied on a mixed surgical cohort (robot-assisted, laparoscopic, open) were excluded; (5) letters to the editor, reviews, case-series and case reports were not considered, and (6) in the event when studies focusing on the same population, the more informative of the information was included.

Data extraction and quality assessment

Two authors meticulously and independently retrieved data from relevant research, which may include demographics, surgical results, functional, or oncological outcomes.

Statistical techniques were used to determine standard deviations (SDs) for research that provided continuous data as means and ranges [11]. The quality of individual included studies was assessed based on the Downs and Black tool [12] by two authors independently. All disagreements were resolved through discussions with another author. When necessary information was missing from the available studies, we contacted the study's corresponding author for more details.

Outcomes of interest

The surgical outcomes of interest were operative time, estimated blood loss (EBL), time to catheter removal, length of hospital stay (LOS), overall complications, major complications, bladder neck construction and neurovascular bundle (NVB) sparing rate. The functional outcomes included urinary incontinence and potency at 1 year. Either incontinence or potency reported within 1 year or at the last follow-up were not extracted for analysis. The oncological outcomes were positive margin and biochemical recurrence rates (BCR).

Statistical analysis

Comparisons of continuous and dichotomous variables were performed using weighted mean difference (WMD) and risk ratio (RR), respectively, along with 95% confidence interval (95% CI). A P value < 0.05 was considered statistically significant. The presence of heterogeneity between studies were calculated by the χ^2 based Q test and I^2. An I^2 value $> 50\%$ accompanied with P value < 0.05 was considered to indicate substantial heterogeneity, in which case, the pooled effect was calculated by a random-effects model (the DerSimonian and Laird method). Otherwise, the fixed effects model (Mantel–Haenszel method) was used for the meta-analysis [13]. For pooled outcomes with significant heterogeneity, sensitivity analyses were performed to explore the potential effect of heterogeneity by eliminating studies that did not use propensity scoring matching. Begg's funnel plot and Egger's test were used to evaluate the possibility of publication bias. All the statistical analyses were performed using Review Manager Version 5.4 (The Cochrane Collaboration, Oxford, London, United Kingdom) and STATA software (version 15.0; Stata Corporation, College Station, TX).

Results

Study selection and characteristics of studies

Figure 1 is a flowchart depicting the processes used to choose relevant literature. Our search of the literature yielded a total

Fig. 1 Flow diagram of selection of eligible studies
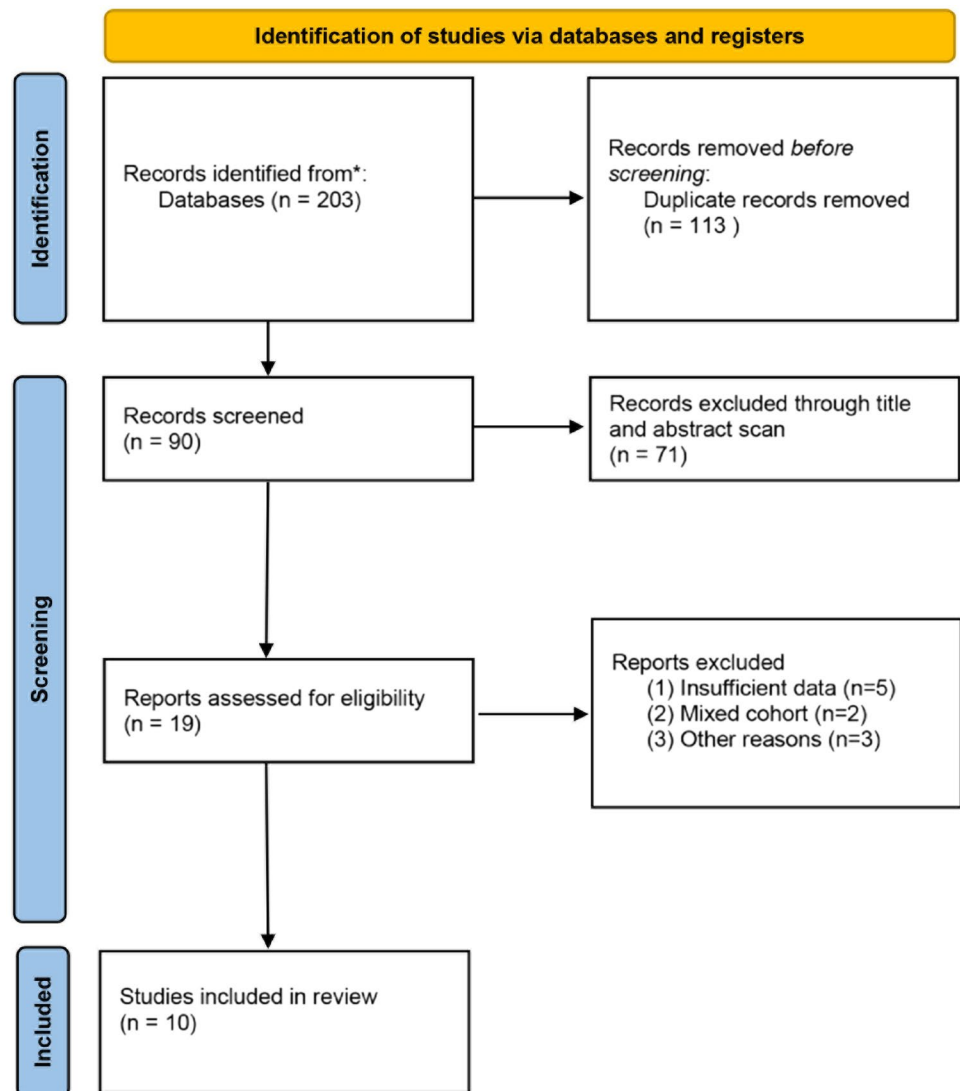
of 203 articles. After excluding the duplicates and articles not met the inclusion criteria based on the title, abstract scan and subsequent full-text scan, 10 articles with 683 and 4039 patients in TURP and no-TURP group were included in our meta-analysis [3–9, 14–16]. The characteristics and quality assessment of included studies are shown in Table 1. Both ten articles were retrospective cohort design and 3b in level of evidence. Among them, seven articles performed a propensity scoring matching (PSM) [6–9, 14–16], in which age, prostate-specific antigen (PSA) and Gleason score were the most frequent matching factors. According to the quality ratings, the majority of the articles were considered to be of a moderate standard (mean 17, SD 1.49).

Surgical outcomes

Results are summarized in Table 2 and Fig. 2. Compared to the No-TURP group, the operative time (seven articles extracted) of TURP Group is significant longer (WMD: 29.1 min, 95% CI: 13.3–44.8, $P < 0.001$; $I^2 = 81\%$, $P < 0.001$). In terms of the EBL (eight articles extracted), the TURP Group offered unfavorable outcomes than the No-TURP group (WMD: 49.3 ml, 95% CI: 8.8–89.7, $P = 0.02$; $I^2 = 93\%$, $P < 0.001$). Patients in TURP Group demonstrated longer time to catheter removal (WMD: 0.93 days, 95% CI: 0.41–1.44, $P < 0.001$; $I^2 = 39\%$, $P = 0.16$) and similar LOS (WMD: 0.03 days, 95% CI: − 0.31–0.37, $P = 0.85$; $I^2 = 0\%$, $P = 0.71$), as reported in five and three article, respectively. The overall (RR: 1.45, 95% CI: 1.08–1.95, $P = 0.01$; $I^2 = 27\%$, $P = 0.24$) and major complication rates (RR: 3.67, 95% CI: 1.63–8.24, $P = 0.002$; $I^2 = 19\%$, $P = 0.3$) was significantly higher in TURP group than no-TURP group. Regarding to rates of bladder neck reconstruction, 64.7% patients in TURP group received bladder neck reconstruction, which is much higher than that in no-TURP group (9.9%, RR: 5.46, 95%

Table 1 Characteristic and quality of retrieved studies

References	Year	Patient number		Design, LOE	PSM	Matching factors	Quality score	TURP technique
		TURP	no-TURP					
Hampton [14]	2008	51	102	R,3b	Yes	1, 7	16	Standard
Abedali [15]	2010	27	27	R,3b	Yes	1,3, 4	17	HoLEP
Gupta [3]	2011	18	132	R,3b	No	No	15	NR
Zugor [9]	2012	80	80	R,3b	Yes	1,2,3,4,5, 6	19	NR
Hung [4]	2014	16	184	R,3b	No	No	16	NR
Gellhaus [8]	2015	11	22	R,3b	Yes	3,4	17	HoLEP
Su [5]	2015	49	2644	R,3b	No	No	15	NR
Tugcu [7]	2015	25	36	R,3b	Yes	1, 2, 3, 4,5,6	18	Mixed*
Bannurah [16]	2021	368	736	R,3b	Yes	1,3,4,5, 6, 7	19	Mixed**
Garg [6]	2022	38	76	R,3b	Yes	1, 3, 4	18	NR

PSM Propensity scoring matching. *LOE* level of evidence. *R* retrospective. 1 = age, 2 = body mass index (BMI), 3 = prostate-specific antigen (PSA), 4 = Gleason score, 5 = prostate volume, 6 = pathological staging, 7 = nerve-sparing status. *NR* none reported

*Standard resection and open surgery

**Standard resection and HoLEP

Table 2 Overall meta-analysis of and outcomes of interest

Outcomes of interest	No. of studies	No of patients		WMD/RR (95% CI)	P value	Heterogeneity	
		TURP	No-TURP			I^2	P value
Surgical outcomes							
Operating time, min	7	565	1161	**29.1 (13.3, 44.8)**	**0.001**	**81%**	**0.001**
EBL, ml	8	607	3901	**49.3 (8.8, 89.7)**	**0.02**	**93%**	**0.001**
Time to catheter removal, day	5	172	389	**0.93 (0.41, 1.44)**	**0.001**	39%	0.16
LOS, day	3	103	2904	0.03 (− 0.31, 0.37)	0.85	0%	0.71
Overall complications	6	554	1139	**1.45 (1.08,1.95)**	**0.01**	27%	0.24
Major complications	4	159	376	**3.67 (1.63, 8.24)**	**0.002**	19%	0.3
Bladder neck reconstruction	7	215	557	**5.46 (3.15, 9.47)**	**0.001**	**53%**	**0.05**
NVB sparing	5	159	349	**0.73 (0.62, 0.87)**	**0.001**	49%	0.1
Functional outcomes							
Incontinence at 1 year	6	535	1197	**1.54 (1.19, 2)**	**0.001**	21%	0.28
Potency at 1 year	5	496	959	**0.8 (0.73, 0.89)**	**0.001**	16%	0.31
Oncologic outcomes							
Positive margin	10	683	4039	**1.24 (1.02, 1.52)**	**0.03**	0%	0.79
BCR at 1 year	3	392	1005	1.41 (0.87, 2.29)	0.16	36%	0.21

Statistically significant values are highlighted in bold

WMD/RR weighted mean difference/risk ratio, *EBL* estimated blood loss, *LOS* length of hospital stay, *NVB* neurovascular bundle, *BCR* biochemical recurrence-free rates

CI: 3.15–9.47, $P < 0.001$; $I^2 = 53\%$, $P = 0.05$). Six articles reported NVB sparing rate, among which one article [16] propensity scoring matched with NVB sparing, thus five articles were extracted for pooled analysis, and the results showed less patients in TURP group successfully received NVB sparing than that in no-TURP group (RR: 0.73, 95% CI: 0.62–0.87, $P < 0.001$; $I^2 = 49\%$, $P = 0.1$). Since the heterogeneity exist in pooled outcomes of operative time,

EBL and bladder neck reconstruction, the sensitivity analyses were performed by excluding non-PSM studies. Both the operative time (WMD: 30.3 min, 95% CI: 13.6–47.1, $P < 0.001$) and bladder neck reconstruction rate (RR: 6.38, 95% CI: 2.6–15.6, $P < 0.001$) exhibited permanent significant differences. Though the TURP group had greater EBL (WMD: 44.2 ml, 95% CI: − 5.9–94.4, $P = 0.08$), the difference was not statistically significant (Supplemental Fig. 1).

Fig. 2 Forest plot of operative time (**A**), estimated blood loss (**B**), time to catheter removal (**C**), overall complications (**D**), major complications (**E**), bladder neck reconstruction (**F**), and nerve sparing (**G**)

Functional outcomes

Given the importance of long-term urinary and sexual function, only the data of incontinence or potency at 1 year were extracted for analysis. At 1-year follow-up, 16.4% patients in TURP group remained incontinence which was significantly higher than that in no-TURP group (9.6%) (RR: 1.54, 95% CI: 1.19–2, $P < 0.001$, Table 2 and Fig. 3). In addition, patients in the TURP group also reported lower sexual satisfaction (potency at 1 year: 49.4% vs. 59.1%, RR: 0.8, 95% CI: 0.73–0.89, $P < 0.001$, Table 2 and Fig. 3).

Oncologic outcomes

All ten articles reported positive margins, the pooled outcomes indicated a higher rate positive margin in TURP group compared with no-TURP group (RR: 1.24, 95% CI: 1.02–1.52, $P = 0.03$, Table 2 and Fig. 3). Only three articles [3, 4, 16] reported BCR at 1 year and one article [8] reported BCR at last follow-up, thus data of BCRs at 1 year were extracted for pooled analysis. There were no statistical differences in BCR at 1 year between groups (RR: 1.41, 95% CI: 0.87–2.29, $P = 0.16$, Table 2 and Fig. 3).

Publication bias

There was no discernible asymmetry in the Begg's funnel plot of the results (Supplemental Fig. 1). Moreover, Egger's test P values for each outcome were > 0.05, also indicating no substantial publication bias.

Discussion

Incidental cancer of the prostate is found in 3–16% of specimens from TURP [17] and these patients are recommended to receive radical prostatectomy after 3 months. The question of whether a previous TURP has an adverse impact on a future RARP stays debatable at now. To further elucidate these topics, we conducted a meta-analysis and systematic review of the relevant literature.
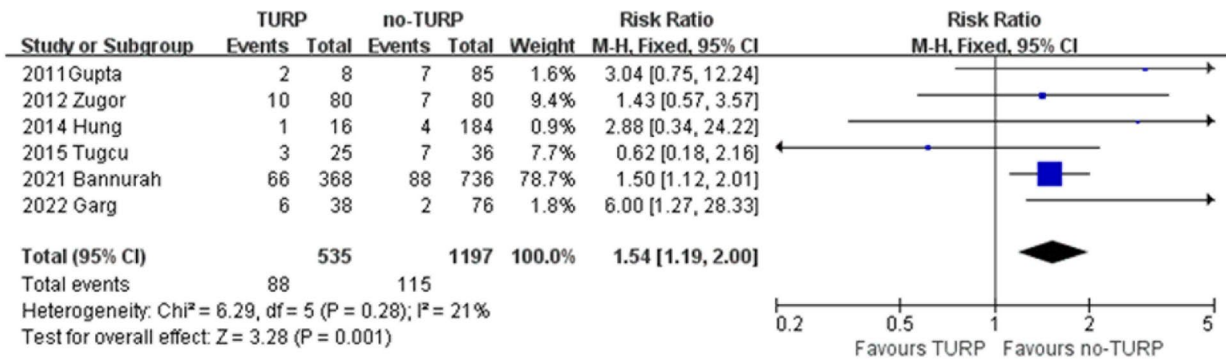
There are several concerns with respect to the post TURP scenario: (1) potential causes of periprostatic inflammation and fibrosis include infection of the prostate, capsular rupture, and extravasation of irrigation fluid after a TURP [18], (2) inflammation-induced increases in periprostatic adhesions following TURP recovery [19], (3) once the prostate is removed, the prostatovesical junction becomes lax and difficult to define [3], (4) an improper urethrovesical anastomosis is impeded by the surrounding fibrosis, which makes it difficult to identify and preserve appropriate residual urethral length [3], (5) identifying NVBs can be challenging because to periprostatic adhesions, which can make NVB

sparing problematic, (6) when a TURP is performed, the ureteric orifices are pulled closer to the bladder neck, making it more difficult to distinguish between the two [19]. Collectively, these factors may exacerbate the difficulties of RARP following TURP, which is consistent with our findings. Consistent with this, the pooled results of our meta-analysis revealed that TURP group had worse surgical outcomes int terms of longer operative time, more blood loss, longer time to catheter removal, higher rates of overall and major complications, frequently demand for bladder neck reconstruction and lower succeed in nerve sparing.
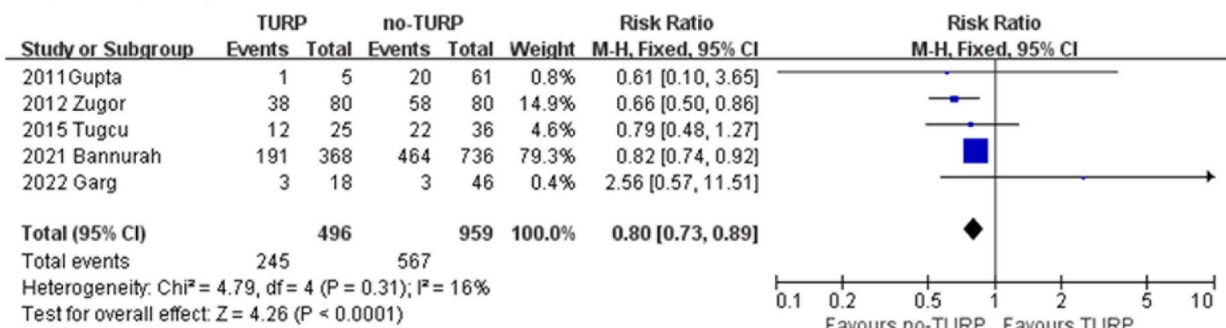
Maintaining the quality of life is an important secondary goal after radical prostatectomy. Urinary incontinence and sexual dysfunction are the most frequent and distressing factors affecting the quality of life for men after radical prostatectomy. The cause of urinary incontinence after radical prostatectomy remains unknown. Pre-prostatectomy physical activity and obesity are important factors in post-prostatectomy continence levels [20]. Besides, surgical technique and surgeon experience are associated with postoperative urinary incontinence [21, 22]. Our results indicated prior TURP also had malign effect on subsequent RARP regarding to long-term incontinence. According to literature reports, selective deep dorsal vein complex division, puboprostatic-sparing techniques, nerve-sparing technique, and restoration of the pelvis space as well as anterior and posterior musculofascial reconstruction were advocated as surgical aspects potentially able to lessen the likelihood of urinary incontinence after RARP [23, 24]. In addition, recovery of continence is enhanced in the short-, intermediate-, and long-term with pelvic floor muscle training administered both pre- and post-operatively [25]. Taken together, patients who have undergone RARP, particularly those who have undergone prior TURP, benefit from a mix of surgical methods and rehabilitation in order to regain continence. Despite the fact that radical prostatectomy is primarily performed on the elderly, still many patients are concerned about their sexual function recovery. Almost half patients remain impotency at 1 year in TURP group, which is more prevalent than no-TURP Group. Both urologists and patients should be aware of this important information.

The presence of a positive margin adversely affects biochemical recurrence and cause specific survival in men with Pca [26]. In our study, positive margins were found to be significantly greater in TURP group compared with the no-TURP group. However, higher positive margins did not increase the biochemical recurrence rate at 1 year in our results. Actually, the rate of biochemical recurrence in each extracted studies [3, 4, 4, 16] is higher in TURP group than that in no-TURP group, despite statistically insignificant. Considering the paucity number of included patients and the relatively low incidence of short-term biochemical recurrence, it is plausible to suppose that RARP following TURP
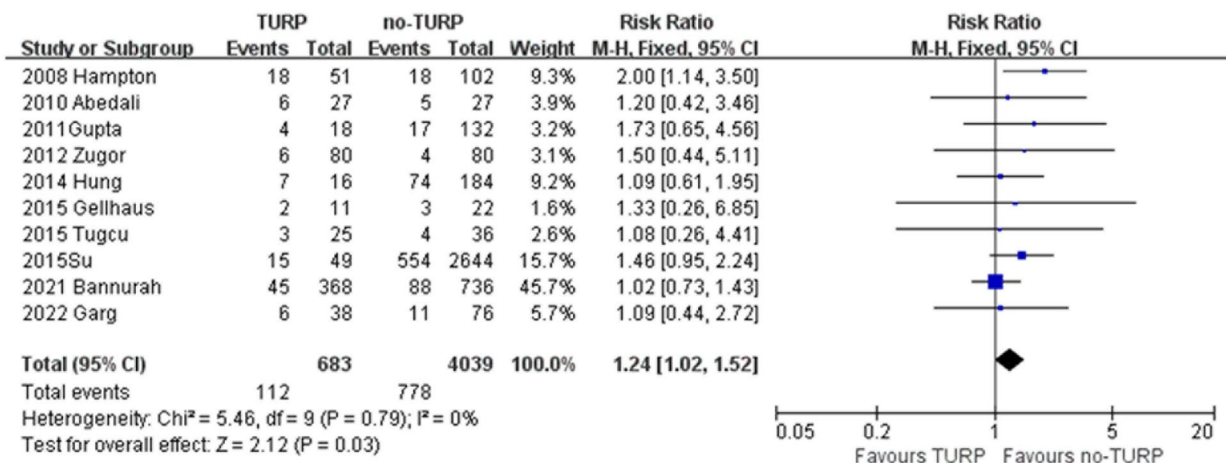
A. incontinence at 1 year

Study or Subgroup	TURP Events	Total	no-TURP Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2011 Gupta	2	8	7	85	1.6%	3.04 [0.75, 12.24]
2012 Zugor	10	80	7	80	9.4%	1.43 [0.57, 3.57]
2014 Hung	1	16	4	184	0.9%	2.88 [0.34, 24.22]
2015 Tugcu	3	25	7	36	7.7%	0.62 [0.18, 2.16]
2021 Bannurah	66	368	88	736	78.7%	1.50 [1.12, 2.01]
2022 Garg	6	38	2	76	1.8%	6.00 [1.27, 28.33]
Total (95% CI)		535		1197	100.0%	1.54 [1.19, 2.00]
Total events	88		115			

Heterogeneity: Chi² = 6.29, df = 5 (P = 0.28); I² = 21%
Test for overall effect: Z = 3.28 (P = 0.001)

B. potency at 1year

Study or Subgroup	TURP Events	Total	no-TURP Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2011 Gupta	1	5	20	61	0.8%	0.61 [0.10, 3.65]
2012 Zugor	38	80	58	80	14.9%	0.66 [0.50, 0.86]
2015 Tugcu	12	25	22	36	4.6%	0.79 [0.48, 1.27]
2021 Bannurah	191	368	464	736	79.3%	0.82 [0.74, 0.92]
2022 Garg	3	18	3	46	0.4%	2.56 [0.57, 11.51]
Total (95% CI)		496		959	100.0%	0.80 [0.73, 0.89]
Total events	245		567			

Heterogeneity: Chi² = 4.79, df = 4 (P = 0.31); I² = 16%
Test for overall effect: Z = 4.26 (P < 0.0001)

C. positive margin

Study or Subgroup	TURP Events	Total	no-TURP Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2008 Hampton	18	51	18	102	9.3%	2.00 [1.14, 3.50]
2010 Abedali	6	27	5	27	3.9%	1.20 [0.42, 3.46]
2011 Gupta	4	18	17	132	3.2%	1.73 [0.65, 4.56]
2012 Zugor	6	80	4	80	3.1%	1.50 [0.44, 5.11]
2014 Hung	7	16	74	184	9.2%	1.09 [0.61, 1.95]
2015 Gellhaus	2	11	3	22	1.6%	1.33 [0.26, 6.85]
2015 Tugcu	3	25	4	36	2.6%	1.08 [0.26, 4.41]
2015 Su	15	49	554	2644	15.7%	1.46 [0.95, 2.24]
2021 Bannurah	45	368	88	736	45.7%	1.02 [0.73, 1.43]
2022 Garg	6	38	11	76	5.7%	1.09 [0.44, 2.72]
Total (95% CI)		683		4039	100.0%	1.24 [1.02, 1.52]
Total events	112		778			

Heterogeneity: Chi² = 5.46, df = 9 (P = 0.79); I² = 0%
Test for overall effect: Z = 2.12 (P = 0.03)

D. biochemical recurrence-free rates at 1 year

Study or Subgroup	TURP Events	Total	no-TURP Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2011 Gupta	3	8	9	85	6.8%	3.54 [1.19, 10.50]
2014 Hung	3	16	21	184	14.7%	1.64 [0.55, 4.92]
2021 Bannurah	16	368	27	736	78.6%	1.19 [0.65, 2.17]
Total (95% CI)		392		1005	100.0%	1.41 [0.87, 2.29]
Total events	22		57			

Heterogeneity: Chi² = 3.14, df = 2 (P = 0.21); I² = 36%
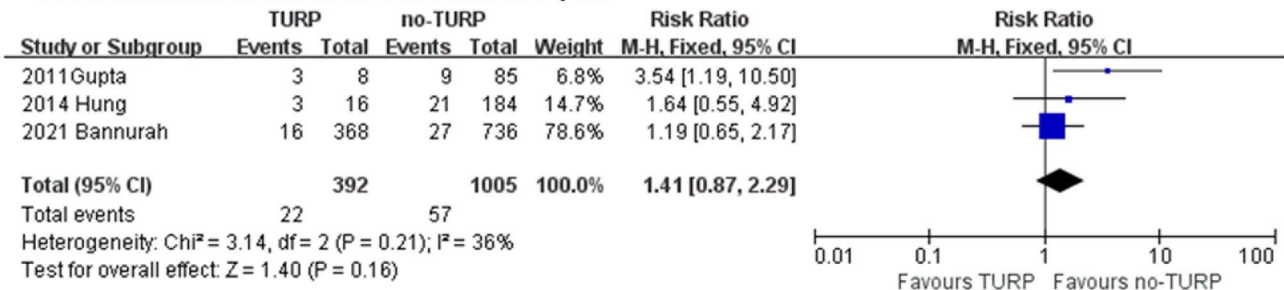Test for overall effect: Z = 1.40 (P = 0.16)

Fig. 3 Forest plot of incontinence at 1 year (**A**), potency at 1 year (**B**), positive margin (**C**), biochemical recurrence-free rates at 1 year (**D**)

offers worse long-term oncologic outcomes. Nevertheless, future research using well-designed, large samples and extensive follow-up is needed to corroborate these findings.

Considering prior TURP compromises surgical, functional and oncological outcomes of subsequent RARP, any attempt to prevent the incidentally discovery of Pca by TURP should be accomplished. PSA screening is routinely recommend for men aged older than 50 years and is associated with an increased early detection of PCa [27]. However, foley catheterization [28] and larger prostate volume in BPH patients are associated with elevated PSA level, which may confused the urologists. Patients with BPH who are at risk of Pca should have a digital rectal exam [27]. Meanwhile, multiparametric magnetic resonance imaging undoubtedly facilitates the detection of clinical Pca [29]. Combining the PI-RADS score with the PSAD, as described in the published work by Wang et al. [30], has been shown to increase diagnostic certainty for prostate cancer and decrease the number of needless prostate biopsies. Furthermore, PSMA PET/CT can discriminate clinically significant prostate cancer from benign prostate diseases in patients with suspected prostate cancer [31]. Taken together, detailed assessment for elderly individuals with BPH can help them avoid unneeded TURP surgery.

There are some limitations that had to be taken into account. First, all included studies were retrospective. Improper randomization and lack of blinding were major sources of bias. Nevertheless, benefits of patients and ethical considerations prevent a randomized controlled trial from being conducted. Second, differences in surgical equipment and techniques between TURP and RARP might have an impact on the outcomes. Third, there was identified variability in a number of continuous variables. Consequently, the random-effects model was used to lessen the influence of heterogeneity, although it was unable to eradicate it entirely. Fourth, possibly due to its non-normal distribution properties, continuous variables were sometimes given as median and range in research. Statistical techniques were used in our calculations of the mean and standard deviation, which may introduce some degree of error.

In conclusion, RARP is feasible but challenging after TURP. It significantly increases the difficulty of operation and compromises surgical, functional and oncological outcomes. It is important for urologists and patients to be aware of the negative impact of TURP on subsequent RARP and establish treatment strategies perioperatively and post-operatively to lessen the adverse effects.

Declarations

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