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Reprint – Bipolar vs. monopolar transurethral resection of the prostate for lower urinary tract symptoms secondary to benign prostatic obstruction: A Cochrane review

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Appendix available at cuaj.ca

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Abstract

Introduction: There remains uncertainty regarding the differences in patient outcomes between monopolar transurethral resection of the prostate (MTURP) and bipolar TURP (BTURP) in the management of lower urinary tract symptoms (LUTS) secondary to benign prostatic obstruction (BPO).

Methods: A systematic literature search was carried out up to March 19, 2019. Methods in the Cochrane Handbook were followed. Certainty of evidence (CoE) was assessed using the GRADE approach.

Results: A total of 59 randomized controlled trials (RCTs) with 8924 participants were included. BTURP probably results in little to no difference in International Prostate Symptom Score (IPSS) at 12 months (mean difference -0.24, 95% confidence internal [CI] -0.39--0.09; participants=2531; RCTs=16; moderate CoE) or health-related quality of life (HRQOL) at 12 months (mean difference -0.12, 95% CI -0.25-0.02; participants=2004, RCTs=11; moderate CoE), compared to MTURP. BTURP probably reduces TUR syndrome (relative risk [RR] 0.17, 95% CI 0.09-0.30; participants=6,745, RCTs=44; moderate CoE) and blood transfusions (RR 0.42, 95% CI 0.30-0.59; participants=5727, RCTs=38; moderate CoE), compared to MTURP. BTURP may carry similar risk of urinary incontinence at 12 months (RR 0.20, 95% CI 0.01-4.06; participants=751; RCTs=4; low CoE), re-TURP (RR 1.02, 95% CI 0.44-2.40; participants=652, RCTs=6, I²=0%; low CoE) and erectile dysfunction (International Index of Erectile Function [IIEF-5]) at 12 months (mean difference 0.88, 95% CI -0.56-2.32; RCTs=3; moderate CoE), compared to MTURP.

Conclusions: BTURP and MTURP probably improve urological symptoms to a similar degree. BTURP probably reduces TUR syndrome and blood transfusion slightly postoperatively. The moderate certainty of evidence available for primary outcomes suggests no need for further RCTs comparing BTURP and MTURP.

Introduction

Transurethral resection of the prostate (TURP) using a monopolar electrosurgery unit (ESU), also known as monopolar TURP (MTURP), is a well-established surgical management option for bladder outlet obstruction (BPO) due to benign prostate enlargement (BPE), but continues to be associated with significant patient morbidity.¹ In light of this, new technologies have been developed with the aim of reducing the risk of complications. In contrast to MTURP, bipolar transurethral resection of the prostate (BTURP) makes use of energy confined between an active electrode (resection loop) and a return electrode situated on the resectoscope tip or sheath, and as such has the advantages of allowing the use of physiological irrigation fluid and lower voltages, theoretically removing the risk of TUR syndrome and reducing thermal damage to surrounding tissues.²⁻⁴

Despite the accumulation of evidence comparing MTURP and BTURP over the last decade, there has been ongoing uncertainty regarding the differences between these two surgical methods in terms of surgical outcomes. Previous systematic reviews that have compared these surgical methods⁵⁻¹⁰ do not incorporate the significant number of recently published randomized controlled trials (RCTs), and have not consistently adhered to the methodological standards of Cochrane, including the publication of a review protocol,





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implementation of a rigorous search strategy, application of GRADE, and use of patient-focused outcomes. The objective of this review was to compare the effects of BTURP and MTURP.

Methods

Search strategy and selection criteria

This systematic review and meta-analysis were based on a published protocol.¹¹ We performed a comprehensive search using multiple databases, including Cochrane Central Register of Controlled Trials in the Cochrane Library, MEDLINE Ovid, and EMBASE Ovid. The search strategy was up to date as of March 19, 2019. To identify unpublished trials or trials in progress, we searched the following sources: ClinicalTrials.gov (http://clinicaltrials.gov), the World Health Organization International Clinical Trials Registry Platform (http://www.who.int/ictrp/en), and the abstract proceedings for the European Association of Urology (EAU) (https://urosource.uroweb.org/urosource?page=1&search =&types=abstract) and American Urological Association (AUA) (https://www.auanet.org/research/annual-meetingabstracts) conferences from 2009–2018. Two review authors (CEA, MS) independently screened all relevant records and classified studies in accordance with criteria for each provided in the Cochrane Handbook for Systematic Review for Interventions.¹² We only searched for RCTs because they are likely to provide the most reliable evidence.

Types of participants

We included participants aged >18 years with lower urinary tract symptoms (LUTS) secondary to BPO. BPO was defined as bladder outlet obstruction secondary to BPE.

Types of intervention

We compared BTURP with MTURP.

Types of outcome measures

The primary outcomes of the review were urological symptoms (as measured by the International Prostate Symptom Score [IPSS] questionnaire score at 12 months), bother (as measured by health-related quality of life [HRQOL] questionnaire score at 12 months) and TUR syndrome. The secondary outcomes were urinary incontinence at 12 months, postoperative blood transfusion, incidence of second TURP (i.e., re-do TURP), and erectile function (as measured by the International Index of Erectile Function questionnaire score [IIEF-5] at 12 months.

Assessment of the risk of bias in included studies

Two review authors (CEA, MS) independently assessed the risk of bias of each included study on a per-outcome basis. We resolved disagreements by discussion and consensus. We assessed risk of bias using the Cochrane "risk of bias" assessment tool. We judged the risk of bias domains as low-risk, high-risk, or unclear risk, and evaluated the individual bias items as described in the Cochrane Handbook for Systematic Reviews of Interventions.¹²

Data collection and data extraction

Data extraction was carried out independently by two authors (CA, MS) using data extraction forms created in Microsoft Word. We resolved any disagreements by discussion or, if required, by consultation with a third review author (MIO). We combined data from individual studies for meta-analysis where interventions were similar enough. We have expressed dichotomous data as a risk ratio (RR) with 95% confidence interval (CI). For continuous outcomes measured on the same scale we estimated the intervention effect using the mean difference (MD) with 95% CI. We summarized data using a random-effects model. Heterogeneity was analyzed using the Chi-squared test, with an alpha of 0.1 used for statistical significance, and the I² test. I² values of 25%, 50%, and 75% generally correspond to low, medium, and high levels of heterogeneity. Where we have encountered heterogeneity, we attempted to determine possible reasons for it by examining individual study and subgroup characteristics.

Subgroup and sensitivity analysis

We expected the following characteristics to introduce clinical heterogeneity and we planned to carry out subgroup analyses with investigation of interactions:

- Prostate volume (large vs. small prostate volume, with specific categories for these defined by primary authors)
- Patient age (older vs. younger patients, with specific categories for these defined by primary authors)

We undertook sensitivity analyses to explore the influence of the following factors on effect sizes by restricting analysis to the following:

- Taking into account risk of bias
- Very long or large trials to establish the extent to which they dominate the results

Summary of findings table

We presented the overall certainty of evidence for each outcome according to GRADE, which accounts for five criteria not only related to internal validity (study limitations, imprecision, publication bias), but also to external validity, such as directness of results.

Results

Search results

We identified 1249 records through an electronic database search. We identified 40 records through hand-searching of other sources. After removal of 432 duplicates, we screened the titles and abstracts of 857 records and excluded 647 records. We screened 210 full text records and excluded 81 records that did not meet the inclusion criteria. We included a total of 59 RCTs.^{4,13-70} We did not identify studies awaiting classification or ongoing RCTs. The flow of literature through the assessment process is shown in the PRISMA flowchart (Fig. 1).

Included studies

All studies were RCTs that compared BTURP to MTURP. Characteristics of the included studies are detailed in the Appendix (available at *cuaj.ca*). Four studies were multi-institutional,^{4,20,24,48} and all other studies were single-institution. The included studies were performed between 2002 and 2016. The followup duration varied from the immediate postoperative period only to 48 months²⁷ and 60 months⁶⁵ postoperatively.

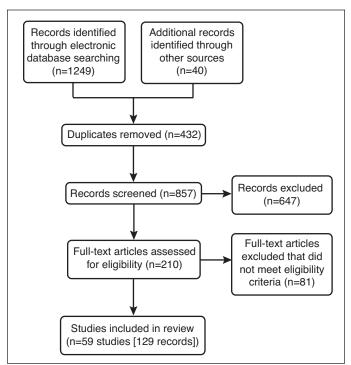


Fig. 1. PRISMA flow diagram.

Participants

We included 8924 randomized participants. Of these, 6745 contributed data to the primary and secondary outcomes. The mean age of the included participants ranged from 59.0 (BTURP) and 61.0 (MTURP)²⁷ to 74.1 (BTURP) and 73.8 (MTURP)⁶⁴. The mean prostate volume ranged from 39 cc (BTURP and MTURP)²⁹ to 82.4 cc (BTURP) and 82.6 cc (MTURP).²¹

Risk of bias in included studies

Assessments of risk of bias are summarized in Fig. 2. Further details on the assessment of risk of bias were stated in the review published in the Cochrane Library.

Summary of findings tables

We summarized the results in the summary of findings tables in accordance with GRADE methodology (Table 1).

Effect of the intervention

Primary outcomes

Urological symptoms as measured by IPSS at 12 months

We included 16 studies with 2531 participants. BTURP probably results in similar improvements in urological symptoms, as measured by IPSS at 12 months (MD -0.24, 95% CI -0.39–0.09, moderate certainty of evidence [CoE]) compared to MTURP.

Bother as measured by HRQOL score at 12 months

We included 11 studies with 2004 participants. BTURP probably results in similar improvements in bother, as measured by the HRQoL scores at 12 months (MD -0.12, 95% CI -0.25–0.02, moderate CoE) compared to MTURP.

TUR syndrome

We included 44 studies with 6745 participants. BTURP probably reduces TUR syndrome events slightly (RR 0.17, 95% CI 0.09–0.30, moderate CoE) compared to MTURP.

Secondary outcomes

Urinary incontinence at 12 months

We included 4 studies with 751 participants. BTURP may result in similar rates of urinary incontinence at 12 months (RR 0.20, 95% CI 0.01–4.06, low CoE) compared to MTURP.

Blood transfusion

We included 38 studies with 5727 participants. BTURP probably reduces blood transfusions slightly (RR 0.42, 95% CI 0.30–0.59, moderate CoE) compared to MTURP.

	Random sequence generation (selection bias): All outcomes	n bias): All outcomes	Blinding of participants and personnel (performance bias): All outcomes	Blinding of outcome assessment (detection bias): Subjective outcomes (IPSS, HRQoL, IIEF-5, TUR syndrome,	unitary incommence) Blinding of outcome assessment: Objective outcomes (blood transfusion, re-TURP)	incomplete outcome data (attrition bias): Immediate postoperative outcomes (TUR syndrome, blood transfusion)	Incomplete outcome data (attrition bias): Long-term outcomes (IPSS/HRQoL/IIEF-5/urinary incontinence at 12 months. and re-TURP)	s): All outcomes		Random sequence generation (selection bias): All outcomes	h bias): All outcomes	Blinding of participants and personnel (performance bias): All outcomes	Blinding of outcome assessment (detection bias): Subjective outcomes (IPSS, HRQoL, IIEF-5, TUR syndrome, urinary incontinence)	Blinding of outcome assessment: Objective outcomes (blood transfusion, re-TURP)	Incomplete outcome data (attrition bias): Immediate postoperative outcomes (TUR syndrome, blood transfusion)	Incomplete outcome data (attrition bias): Long-term outcomes (IPSS/HRQoL/IIEF-5/urinary incontinence at 12 months, and re-TURP)	s): All outcomes		Random sequence generation (selection bias): All outcomes	Allocation concealment (selection bias): All outcomes	Blinding of participants and personnel (performance bias): All outcomes Blinding of outcome assessment (detection bias): Subjective outcomes (IPSS, HRQoL, IIEF-5, TUR syndrome,	urinary incontinence) Distinguistics of sufferences comments of the second support support	bilinuing or outcome assessment. Objective outcomes (prood translusion), re-rour / Incomplete outcome data (attrition bias): Immediate postoperative outcomes (TUR syndrome, blood transfusion)	incomplete outcome data (attrition bias): Long-term outcomes (IPSS/HRQoL/IIEF-5/urinary incontinence at 12 months, and re-TURP)	s): All outcomes
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Chen 2010	۲	0			۲	3	3	0	Komura 2015	۲	0		۲	۲	۲	3	۲	Terrone 2006	0	0		8 0	0	0	•
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Fagerström 2011	۲	8		0	۲	Ø	0	0	Nuhoglu 2006	0	0		0	۲	۲	0	0								

Fig. 2A. Risk of bias summary: Review authors' judgements about each risk of bias item for each included study.

Low risk of bias	Unclear risk of bias	High risk of bias				
		0%	25%	50%	75%	
	Selective repo	ting (reporting bias): All outcomes				
Incomplete outcome data (attrition b	as): Long-term outcomes (IPSS/HRQoL/IIER-5/urinary incontin	ence at 12 months, and re-TURP)				
Incomplete out	come data (attrition bias): Immediate postoperative outcomes (UR syndrome, blood transfusion)				
	Blinding of outcome assessment: Objective outco	mes (blood transfusion, re-TURP)				
Blinding of outcome assessment (d	etection bias): Subjective outcomes (IPSS, HRQoL, IIEF-5, TU	R syndrome, urinary incontinence)				
	Blinding of participants and personne	(performance bias): All outcomes				
	Allocation concealr	nent (selection bias): All outcomes				
	Random sequence genera	tion (selection bias): All outcomes				

Fig. 2B. Risk of bias graph: Review authors' judgements about each risk of bias item presented as percentages across all included studies. HRQoI: health-related quality of life; IIEF: International Index of Erectile Function; IPSS: International Prostate Symptom Score; TURP: transurethral resection of the prostate.

Re-TURP

We included six studies with 652 participants. BTURP may result in similar rates of re-TURP (RR 1.02, 95% CI 0.44–2.40, low CoE) compared to MTURP.

Erectile function as measured by IIEF-5 score at 12 months

We included three studies with 321 participants. BTURP probably results in similar erectile function as measured by the IIEF-5 at 12 months (MD 0.88, 95% CI -0.56–2.32, moderate CoE) compared to MTURP.

Subgroup analyses

Of the included RCTs, Kumar 2013⁴⁵ was the only study to include specific subgroup analyses by prostate volume. They defined small prostates as >20 cc to <50 cc and large prostates as 50–80 cc. They observed no significant difference in effect for urological symptoms, bother, TUR syndrome, or erectile function. They did observe a significant difference in effect for blood transfusion in men with large prostates. The number of events of postoperative blood transfusion in men with large prostates was six who had undergone MTURP (n=31) compared to one blood transfusion for BTURP (n=27). We did not identify any analysis or data within the included RCTs that would allow for subgroup analysis by patient age.

Sensitivity analysis

In light of the judged high risk of attrition bias seen with Demirdag 2016,²⁶ with 37 patients excluded due to loss to followup or missing data and the significant differential loss to followup (23/59 participants lost to followup for BTURP vs. 14/59 for MTURP), we performed sensitivity analysis where this study was excluded from the meta-analysis for the outcomes it assessed. The exclusion of Demirdag 2016²⁶ from the meta-analyses did not result in any significant change in the effect size that would impact on the overall conclusions

of the analysis. In light of the size of the largest included RCT by Al-Rawashdah 2017,¹⁸ with 497 included participants, we performed sensitivity analysis where this study was excluded from the meta-analysis for the outcomes it assessed. The exclusion of Al-Rawashdah 2017¹⁸ from the meta-analyses did not result in any significant change in the effect size that would impact on the overall conclusions of the analysis.

Discussion

BTURP and MTURP probably result in similar improvements in urological symptoms and bother. BTURP probably reduces TUR syndrome and postoperative blood transfusion slightly compared to MTURP. BTURP and MTURP probably do not differ in terms of erectile function. The moderate CoE available for urological symptoms, bother, TUR syndrome, blood transfusion, and erectile function suggests there is no need for further RCTs comparing BTURP and MTURP for these outcomes. BTURP and MTURP may also have similar effects on postoperative urinary incontinence and the need for re-TURP, but the low CoE for these outcomes means that they deserve further study in the form of prospective RCTs which incorporate standardized and clinically meaningful definitions, as well as sufficient duration of followup.

There have been a number of previously published systematic reviews and meta-analyses comparing BTURP and MTURP.⁵⁻¹⁰ While the focus of this review has been limited to a smaller number of key primary and secondary outcomes, its findings are in keeping with the conclusions of previous reviews that no clinically relevant differences exist in the shortterm (up to 12 months) effectiveness (urological symptoms as measured by IPSS, bother as measured by HRQOL score) or in short-term incidence of adverse events (urinary incontinence, need for re-TURP, erectile function), but BTURP may be preferable due to a more favorable perioperative safety profile (lower incidence of TUR syndrome and blood transfusion rates).

The favorable perioperative safety profile of BTURP may have potential implications in reducing morbidity and mor-

Table 1. Summary of findings: BTURP compared to MTURP for lower urinary tract symptoms secondary to benign prostatic obstruction

Patient or population: Men with lower urinary tract symptoms secondary to benign prostatic obstruction Setting: Hospital

Intervention: BTURP

Comparison: MTURP

Outcomes	No of	Certainty of	Relative effect	Anticipated absolute effects* (95% CI)						
	participants (studies) followup	the evidence (GRADE)	(95% CI)	Risk with MTURP	Risk difference with BTURP					
Urological symptoms (IPSS ^a at 12 months ^a)	2531 (16 RCTs)	⊕⊕⊕⊝ Moderate ^ь	—	Mean urological symptoms (IPSS at 12 months) was 6.4 Weighted mean=6.4	MD 0.24 lower (0.39 lower to 0.09 lower)					
Bother (HRQoL° at 12 months)	2004 (11 RCTs)	⊕⊕⊕⊝ Moderate ^ь	—	Mean bother (HRQOL at 12 months) was 1.7 Weighted mean=1.7	MD 0.12 lower (0.25 lower to 0.02 highe					
TUR syndrome	6745	$\oplus \oplus \oplus \ominus$	RR 0.17	Study populati	ion					
	(44 RCTs)	Moderate ^b	(0.09 to 0.30)	24 per 1000 Weighed mean number of events=1.8	20 fewer per 1000 (22 fewer to 17 fewer)					
Urinary incontinence	751	$\oplus \oplus \ominus \ominus$	RR 0.20	Study population						
at 12 months	(4 RCTs)	Low ^{b,d}	(0.01 to 4.06)	5 per 1000 Weighted mean number of events=0.5	4 fewer per 1000 (5 fewer to 16 more)					
Blood transfusion	5727	$\oplus \oplus \oplus \ominus$	RR 0.42	Study populati	on					
	(38 RCTs)	Moderate ^b	(0.30 to 0.59)	48 per 1000 Weighted mean number of events=3.7	28 fewer per 1000 (34 fewer to 20 fewer)					
Re-TURP	652	$\oplus \oplus \ominus \ominus$	RR 1.02	Study population						
	(6 RCTs)	Low ^{b,d}	(0.44 to 2.40)	34 per 1000 Weighted mean number of events=1.8	1 more per 1000 (19 fewer to 48 more)					
Erectile function (IIEF- 5° score at 12 months)	321 (3 RCTs)	⊕⊕⊕⊝ Moderate ^ь	—	Mean erectile function (IIEF-5 score at 12 months) was 19.2 Weighted mean=19.2	MD 0.88 higher (0.56 lower to 2.32 higher)					

GRADE Working Group grades of evidence:

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% Cl). ^aIPSS questionnaire scores range from 0 to 35, with higher values signalling more severe lower urinary tract symptoms; the minimum clinically important difference was defined as 4. ^bDowngraded by one level for study limitations: blinding of operating surgeon considered unlikely in all trials; method of randomisation, allocation concealment, and blinding of outcome assessment unclear in > 50% of included trials. ^cHRQOL questionnaire scores range from 0 to 6, with higher values signalling poorer quality of life. ^dDowngraded by one level for imprecision: wide confidence intervals, very small numbers of events for urinary incontinence and re-TURP. ^eIIEF-5 questionnaire scores range from 5–25, with higher values signalling better erectile function; the minimum clinically important difference was defined as 4. BTURP: bipolar transurethral resection of the prostate; Cl: confidence interval; HRQOL: health-related quality of life; IIEF-5: International Index of Erectile Function; IPSS: International Prostate Symptoms Score; MD: mean difference; MTURP: monopolar transurethral resection of the prostate; OR: odds ratio; RCT: randomized controlled trial; RR: risk ratio; TUR: transurethral resection; TURP: transurethral resection of the prostate.

tality associated with the surgical treatment of BPO. BTURP may allow for longer resection times and resection of larger prostates without the risk of TUR syndrome. The allowance for longer resections may also permit further time to ensure sufficient coagulation time to secure hemostasis, thereby reducing the risks of bleeding. These features may be particularly beneficial for urologists in training.

Compared to all relevant previous meta-analyses, our present systematic review and meta-analysis represents the largest body of evidence by far, being based on 59 RCTs. The largest systematic review published prior to this was by Omar and colleagues⁹ and included 24 RCTs. One of

the major strengths of the present meta-analysis is that the strict methodology described in the Cochrane Handbook for Systematic Reviews of Interventions¹² was used and that GRADE was applied for evaluating the CoE.

However, this review has several limitations. A potential source of bias is the clinical heterogeneity across subgroups of interventions. For instance, BTURP represents a diverse range of interventions with differences in equipment, magnitude of energy, and techniques.³ The various bipolar systems represent distinct technological advancements based on different electrophysiological principles regarding current flow, and in this review, there was insufficient data to per-

form sensitivity or subgroup analysis on how the different types of BTURP compared to each other. There was also heterogeneity of outcome measurement and reporting, with some studies not reporting how outcomes were measured. In particular, the primary outcome of TUR syndrome was inconsistently defined, with some studies failing to provide a clear definition. Accordingly, the incidence of TUR syndrome varied across studies. Furthermore, despite our stringent inclusion criteria and comprehensive search strategy, it is possible that not all eligible RCTs were included in the databases that was searched. For some of the older reports of RCTs, there were limited usable data, and despite contacting trial authors for further information, we did not always receive a response.

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