Examining the 'gold standard': a comparative critical analysis of three consecutive decades of monopolar transurethral resection of the prostate (TURP) outcomes

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Accepted for publication 18 January 2012

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This study examined contemporary TURP for significant changes, specifically regarding prostate size, operative parameters, and outcomes, compared with two preceding decades. Electronic databases PubMed, EMBASE & Cochrane collaboration were searched for English literature on prospective randomized controlled trials, published between 1997 and 2007 using keywords "transurethral resection" and "prostate". Monopolar TURP (M-TURP) cohort data of each study were selectively pooled for analysis, weighting studies according to patient numbers. Where possible, pooled post-operative outcomes data were compared with two large cohort landmark studies of successive preceding decades. A total of 3470 patients from 67 studies were included. Mean patient age (67 years) was unchanged, while mean pre-operative prostate volume of 47.6 g was greater than previously reported. Mean resected prostate tissue (25.8 g) with a resection time of 38.5 minutes suggested improved resection efficiency. A statistically significantly reduced transfusion rate and increased urinary tract infection (UTI) rate were reported. Hospital stay (3.6 days) and initial catheterisation duration (2.5 days) were similar, but post-operative urinary retention rate was slightly higher (6.8%). Contemporary RCTs of M-TURP showed larger prostate volume, and reduced major morbidity, compared with large cohort studies from successive past eras. The higher reported failure to void rate, may possibly reflect worse detrusor function at time of TURP. Delaying surgery by prolonged medical monotherapy may compound this. Trials methodology in this area requires quality improvement and standardisation in future.

What's known on the subject? and What does the study add?

Transurethral resection of the prostate (TURP) remains the dominant and definitive treatment for lower urinary tract symptoms due to benign prostatic hyperplasia (LUTS-BPH), but the widespread use of medical therapies (particularly monotherapies) for rapid symptom improvement has meant that the most common indication for TURP has shifted to moderate–severe medical therapy refractory LUTS to, coupled with abnormal objective parameters, or when complications arise.

Patients undergoing TURP as part of contemporary randomised controlled trials are not older but have a larger preoperative prostate volume and reduced major morbidity compared with large cohort studies from successive past eras. Delayed surgery because of prolonged medical monotherapy may explain a higher reported failure to void rate, possibly because of negative impact on detrusor function from unrelieved obstruction.

KEYWORDS

lower urinary tract symptoms, benign prostatic hyperplasia, prostate, monopolar transurethral resection of prostate

INTRODUCTION

Monopolar TURP (M-TURP) has dominated surgical treatment of LUTS due to BPH (LUTS-BPH) for >70 years. The increasing LUTS-BPH prevalence in an ageing population and relatively high TURP associated morbidity [1] spurred the development of surgical alternatives including transurethral microwave thermotherapy (TUMT), transurethral needle ablation (TUNA), interstitial laser coagulation, visual laser ablation, KTP photoselective laser vaporization, Holmium laser ablation, Holmium laser enucleation and Thulium laser ablation, resection or enucleation. Through this technologically diverse era, M-TURP remained the enduring reference standard because of the availability of long-term outcome data in large patient numbers treated in academic and community settings. Recent improvements in anaesthetic techniques and surgical instrumentation also reduced immediate and long-term M-TURP complications, favouring its continued use [2,3].

The indications for surgical LUTS-BPH treatment have been transformed in modern practice with increasing use of medical therapies (α-adrenergic antagonists and 5α-reductase inhibitors), either in isolation or combined for larger prostates. LUTS-BPH are now commonly treated with medical monotherapy for rapid effective stabilization or symptom improvement [4], while only combined therapy can effect prostate size. The most common indication for TURP has shifted from LUTS-BPH (without formal subjective or objective quantification using validated instruments to assess domains of bother or quality of life impact), to moderate-severe LUTS-BPH refractory to medical therapy, coupled with abnormal objective parameters (impaired flow rate and/or increasing residual urine volume), or when BPH-BOO complications arise. A recent retrospective single institution experience review reported that although combined medical therapy (unreported duration) use had increased from 5% to 58%, failed 'medical therapy' as an indication for TURP also increased from 36% in 1998 to 87% in 2008, while a worrying increase was seen in hydronephrosis [5].

This dramatic recent shift to initial LUTS-BPH medical monotherapy, where prostate growth may have continued unchecked for many years longer than in previous decades, raised the issue as to whether there may be knock-on consequences to surgical outcomes. The primary aim of the present study was to determine the preoperative prostate volume (PV) and resected prostate weight reported in contemporary TURP series, comparing them with the large reference cohort studies of Borboroglu *et al.* [6] and Mebust *et al.* [7], 10 and 20 years ago respectively (i.e. had prostates 'grown' during the medical paradigm era), as large randomised controlled trials (RCTs) during this time were lacking. Secondary aims were to compare postoperative outcomes of contemporary M-TURP with those two studies. Where possible, data was compared with Madersbacher and Marberger [8] who, using similar methods, extracted data on 1480 patients who had undergone TURP as part of an RCT during the period 1986–1998. The objective of their review was to determine the current status of TURP, compared with previous observational studies, but with particular reference to less invasive techniques, e.g. TUMT and TUNA.

MATERIALS AND METHODS

Searches of electronic databases limited by the dates 1 January 1997 to 1 January 2007 were performed including: PubMed, EMBASE and Cochrane collaboration. English language published articles were selected using the keywords 'transurethral resection' and 'prostate'. Bibliographies of included articles were reviewed for additional relevant citations.

Studies were included if they met all of the following criteria:

- Article comparing M-TURP vs another technology as LUTS-BPH treatment
- Prospective randomised patient selection study design
- Assessing clinical outcomes as study endpoint

Different articles based on the same patient cohort with different follow-up duration and/or outcome measures were considered as one study, and all relevant data were extracted and aggregated for analysis.

DATA EXTRACTION

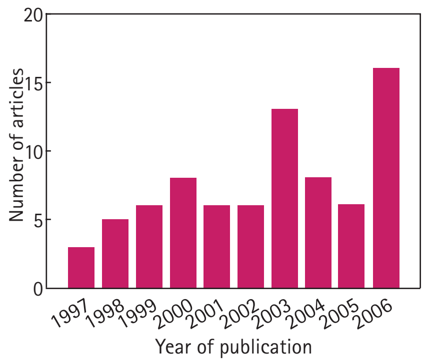
Two authors (S.K. and S.C.) independently assessed articles for inclusion/exclusion and extracted relevant data. All reported patient demographics, operative and postoperative parameters, were considered in extracted studies. Variation in outcome measures definition was present. Assessed variables are summarised in Table 1 ([6–8]; refer to online supplementary references [Appendix S1]).

Data for the M-TURP cohort of each study were pooled for analysis, weighting studies according to patient numbers in the M-TURP cohort. The mean values with ranges were calculated. Chi-square tests were used to compare outcomes from this study with the reference studies [6,7].

RESULTS

In all, 77 articles that matched the inclusion criteria were extracted. Of these, 16 studies reported on the same patient cohorts, leaving 67 studies incorporating 3470 patients after aggregation, for final analysis. The distribution of publication year for extracted articles is shown in Fig. 1. There was considerable variation in the number of studies reporting each operative variable and postoperative outcome of interest (Table 1).

FIG. 1. Summary of year of publication for the extracted articles.



The mean patient age was 67 years, with a weighted mean (WM) reported preoperative prostate volume of 47.6 g. Of the 56 RCTs in the present study that reported preoperative PV, 35 used PV inclusion/exclusion criteria (Table 2); 27 had an upper limit threshold, and 23 had a lower limit threshold. If the 23 studies that had a lower limit threshold (therefore potentially biasing toward only large prostates) were excluded, this value became 45.7 g. If we only excluded those eight studies that had a lower limit of >30 g, on the assumption that for men with small (<30 g) prostates transurethral incision of the prostate is an ideal therapeutic option [8], then the WM PV became 46 g.

The WM M-TURP resected prostate tissue weight was 25.8 g (54% gland volume). In all, 56 of the 67 studies reported mean preoperative PV, while only 25 studies (about one third) reported mean resected prostate tissue weight. The WM operative duration was 47.6 min (unweighted mean 46.5 min). The WM and unweighted mean resection times were 38.5 and 35.5 min, respectively. The mean pre- and postoperative residual urine volumes were 118 mL (WM 126 mL) and 26.8 mL (WM 27.4 mL), respectively. In all, 25 studies reported a pre- and postoperative residual

TABLE 1 Summation of the outcome measures from the present study compared with the single institution results of Borboroglu et al. *[6] and the multi-institutional experience reported by Mebust* et al. *[7] and Madersbacher and Marberger [8]. References 1–75 available in the Appendix S1 (online)*

Present study							
Variable	Number of RCTs	References	Mean unweighted	Mean weighted	Borboroglu *et al.* [6]	Mebust *et al.* [7]	Madersbacher and Marberger [8]
Age, years	61	[1–66]	66.8	67	67	69	n/r
Preoperative prostate volume, g	56	[1–5,7–15,17–19,21,23–29,31–36,38–40,42,44–53,55,56,58–71]	47.9	47.6	37.1	85% < 45 g	n/r
Resected prostate weight, g	25	[1,8,11,13,14,16,20,21,23–29,31–34,38,39,41,42,45,50,54,55,68,69,72,73]	24.3	25.8	18.8	22	n/r
Duration of catheterisation, days	43	[1,3,6,7,11–13,15,16,20–28,32–36,38–40,42,45,46,48–50,53–57,59–63,67–69,71,74,75]	2.5 (2.4)*	2.5	3.2	82% removed by day 3	n/r
Hospital stay, days	36	[1,3,6,10–13,15,16,21,23,25–28,31,33–36,38,39,41,42,47,48,50,53,54,56,58–61,64, 66–68,71,74,75]	3.4 (3.6)*	3.6	2.4	78% discharged by day 5	n/r
Operation time, min	38	[1,5,7,8,11,13–15,22,24–28,32–36,38,39,41,42,44,48,50,53,54,57–61,66,69,71–75]	46.5	47.6	n/r	77	n/r
Resection time, min	9	[3,16,20,21,29,31,54–56]	35.5	38.5	62.5	57	n/r
Transfusion rate, %	33	[1–3,8,11,12,14–16,21,23,24,26–28,31,33,34,38,39,41,43–46,56–61,64–66,69,71,74]	4.5	4.4	0.4	6.4	8.6/7.2
TUR syndrome, %	14	[1,3,8,11,15,26–28,33,38,39,42,46,66,69,71]	2.1	1.8	0.8	2	3.4/4.7/6.7
UTI, %	18	[2,3,12,14,20,21,23,26–28,33,40,43,46,54,56,62–65,68,69]	9.0	7.9	6.2	2.3	n/r
Clot retention, %	20	[3,8,11,13,15,20,26,28,33,41,43,46,55,59–61,72,74]	7.3	7.2	1.3	3.3	5.5
Postoperative urinary retention/ failure to void, %	16	[3,11,14,15,26–28,31,40,42,51,52,62,63,71]	5.4	6.8	7.1	6.5	n/r
Re-catheterisation, %	31	[2,3,13,21,24,25,34,38,39,56,57,64,65,75]	6.1	6.1	n/r	n/r	n/r
Re-intervention rate, %	18	[3,7,10,14,15,17,21,26–30,38,39,41,56,57,59–61,64,65,75]	5.4	5.2	n/r	n/r	2.6
Persisting haematuria, %	14	[8,14,20,33,35,36,40,44–46,51,52,62,63,67,71,72]	15.6	15.7	n/r	n/r	n/r
Bladder neck stenosis, %	18	[2,3,8–11,15,17,26–28,31,33,34,54,64,66,69,70,74,75]	3.8	3.2	2.1	n/r	4.7
Urethral stricture, %	34	[1–3,7,10,14,15,17,21,24–31,33,34,38,40,42,48,50–52,55–65,67,69–71,75]	4.7	4.1	1.0	n/r	3.8
Mortality, %	4	[14,15]	n/r	n/r	0	0.23	n/r
Total number of patients			3470		520	3885	1480

**Median value in parentheses; n/r, not reported.*

TABLE 2 Count of studies that used inclusion/exclusion criteria for PV

Prostate volume, g	Count of studies
Upper Limit	
200	2
120	1
100	10
85	1
80	3
75	1
70	4
65	1
60	2
50	1
25	1
Total	27
Lower Limit	
15	2
20	2
25	1
30	10
35	1
40	5
50	2
Total	23

volume (at 12 months) giving a calculated mean change of 90.7 mL.

A summary of postoperative outcomes for the pooled unweighted and weighted results according to patient numbers in the M-TURP cohort of each extracted study is given in Table 1. Only four studies explicitly reported mortality data. Compared with the past era reference studies [6,7], although mean patient age remained similar, both preoperative PV and resected tissue weight had seemingly increased (Fig. 2). The comparison for secondary outcomes (WMs where possible) to the reference studies [6,7] is shown in Table 1. Figure 3 summarises the secondary outcomes for the pooled analysis of RCTs. There were statistically significant differences across the three studies for rates of blood transfusion and UTI (Table 3) [6–8].

DISCUSSION

The present study suggests that surgically treated patients' age has remained constant in the last decade, but baseline PV at M-TURP included in RCTs seem to have increased compared with the past-era reference cohort studies. The relatively unchanged WM PV after having excluded studies with lower limit PV exclusion criteria suggests that the PV results were not significantly influenced by including RCTs that included only large prostates (>30 g) according to their protocol. Resected prostate weight was higher, but resection times shorter. For each of PV and resected weight, there was a single study with a relatively high value potentially causing an outlier effect (Fig. 2). Having removed these two studies, re-analysis of the data made little difference to the results (WM preoperative PV of 47.2 vs 47.6 g and resected prostate weight of 24.2 vs 25.8 g). These findings may validate our hypothesis that contemporary preoperative prostate size had increased during the era of medical therapy as a first-line method for surgical candidates with LUTS-BPH, suggesting low medical combined therapy utility in this group. It is difficult to explain why prostates were bigger in patients with the same age at this time beyond blaming selection bias, as well as unknown dietary and environmental factors. Currently, the main indication for elective TURP is bothersome LUTS refractory to medical therapy, suggesting that smaller prostates that may have been resected during earlier decades may now be treated initially with medical therapy. Moreover, where medical monotherapy was ineffective or intolerable, PV would most probably have increased over time. From the present analysis, only 10 studies specifically mentioned excluding patients on either an α-blocker or a 5α-reductase inhibitor; two further studies excluded patients on a 5α-reductase inhibitor, supporting our assumption that most patients undergoing M-TURP initially received medical therapy.

The finding that resected prostate weight had also increased could be a result of larger glands being resected in the contemporary era (with more adenoma for removal), or due to skill of surgeons participating in RCTs compared with those in large community cohorts, or both. Reich *et al.* [1], reported mean resected tissue weight of 28.4 g in a large community cohort, suggesting that resection of larger prostates in the contemporary era was most likely. Shin and Park [9] have also reported an increase in the PV of their contemporary TURP series. Despite this, resected prostate weight increased and resection time decreased suggesting improved resection efficiency (resection volume per minute of TURP).

Other factors that may have collectively improved resection weight and efficiency, included changes in video-resection capability, and improved anaesthetic

*FIG. 2. Scatter plot of each RCT sample size vs (**a**) preoperative PV and (**b**) resected weight. The three vertical lines indicate the weighted mean of all RCTs (present study) and the means reported by Borboroglu* et al. *[6]. The Mebust* et al. *[7] study result represents the reported value.*

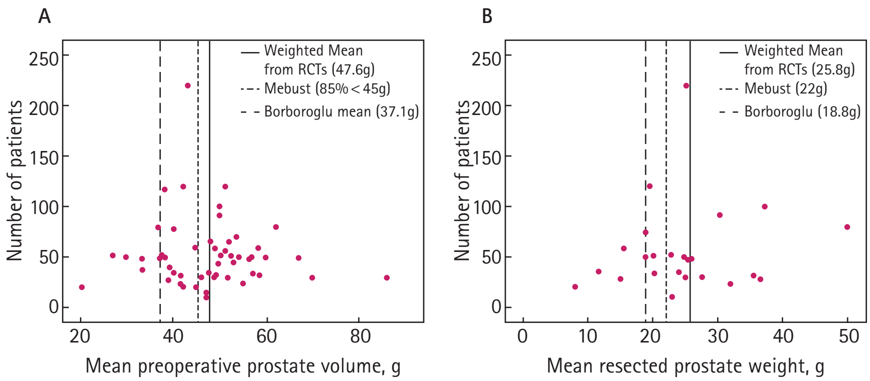


FIG. 3. Box and Whisker plot showing the weighted mean (horizontal white line) and ranges (interquartile and minimum and maximum) for the secondary outcomes (complications) after TURP.

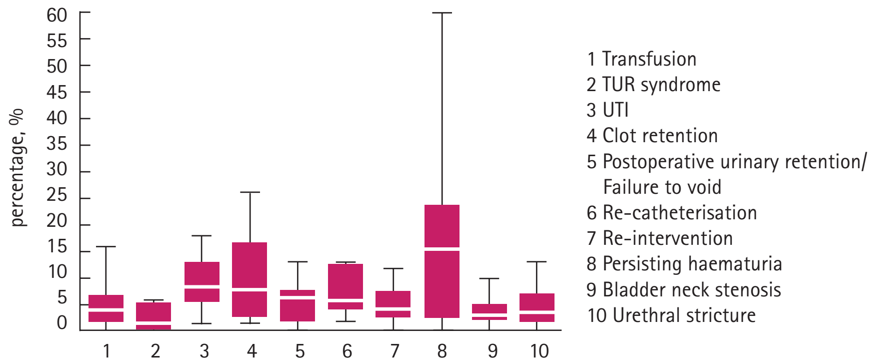


TABLE 3 Comparison of transfusion rate, TUR syndrome, UTI, postoperative urinary retention/failure to void, among the three studies [6–7]

	Present study Pooled data	Borboroglu *et al.* [6]	Mebust *et al.* [7]	
	Mean	Mean	Mean	*P*
Transfusion rate, %	4.4	0.4%	6.4	<0.01
Standardised residual	–1.8	–4.9	3.0	
TUR syndrome, %	1.8	0.8	2	0.14
Standardised residual	0.0	–1.8	0.7	
UTI rate, %	7.9	6.2	2.3	<0.01
Standardised residual	6.5	3.2	–4.1	
Postoperative urinary retention/failure to void, %	6.8	7.1	6.5	0.85
Standardised residual	0.2	0.4	–0.3	

n/r, not reported.

techniques or M-TURP technology (particularly electrosurgical generators, electrodes, and continuous flow resectoscopes). Preoperative prostate weight was partly determined by DRE in the past-era reference studies [6,7], while all modern RCTs described here used TRUS. As it has been shown that PV was overestimated by DRE in prostates of <50 mL, their data might be subject to measurement error [10]. Resected weight generally corresponded well to PV. As most prostates in the reference studies were <50 mL, this again suggested that PV was probably smaller previously. Although it is not possible to substantiate, the improved accuracy of preoperative PV measurement using TRUS as compared with DRE may have influenced the surgeon to resect more tissue to achieve an acceptable resected tissue weight. Resection time was much shorter in the contemporary era (WM 38.5 min) compared with an average of 57 and 62.5 min respectively, in the past cohort reference studies [6,7]. Larger prostates in the present pooled RCT analysis were apparently resected with greater efficiency (shorter resection times) without increasing TUR syndrome incidence. Bipolar-plasmakinetic resection and vaporization studies were excluded from the present analysis due to the confounding effect of saline irrigant. Since the work of Hahn [11], the increased awareness of TUR syndrome, particularly associated with extended resection times, by surgeons and anaesthetists may also have influenced the shorter resection times seen during the contemporary RCTs.

Comparing major morbidity outcomes between the present pooled RCT analysis and the reference studies [6,7], contemporary practice blood transfusion rates had apparently decreased compared with Mebust *et al.* [7]. Whereas higher resection weight has been previously associated with greater blood loss [12], the decreased transfusion requirement was also reported by Reich *et al.* [1] in their large contemporary population cohort. Other modern contributory factors may include improved preoperative patient optimization (giving less physiological need to transfuse early), shorter resection time and greater resection efficiency yielded by better technology. The impact of preoperative 5α-reductase inhibitor drug therapy, which can reduce vascularity even with short term use before any downsizing effect on PV [13], was difficult to quantify from the published data, as drug washout times before M-TURP were unfortunately not reported. Borboroglu *et al.* [6] reported an extremely low transfusion rate of 0.4%, which is inconsistent with the established M-TURP literature and differed considerably to the present pooled mean transfusion rate of 4.5% and the mean transfusion rate of 8.6% from the Madersbacher and Marberger [8] pooled RCTs during a similar period. This might be explained by the single centre, single-surgeon, cohort of Borboroglu *et al.*, where perioperative care pathways could be micromanaged to a greater degree than would be possible when aggregating multiple centre practices in different countries.

Surprisingly, UTI rates were significantly higher compared with the reference series [6,7] ($P < 0.01$). This finding was difficult to explain on a cause-and-effect basis, but may reflect improved documentation in RCTs and/or greater antibiotic resistance. Only 10 studies systematically described their antibiotic protocol in the modern era RCT studies, while a further 11 studies implied that perioperative antibiotics were given (without specific details).

Mebust *et al.* [7] reported that 2.4% of patients were discharged from hospital with a catheter, of which most (55%) were reported as due to a ‘hypotonic bladder’. Borboroglu *et al.* [6] reported that 7.1% of their patients were discharged from hospital with an indwelling catheter due to inability to void postoperatively (with 1.4% needing long-term bladder drainage for ‘hypocontractile bladder’). They related their high rate of patient discharge with catheter to a significant reduction in postoperative hospital stay, thereby not allowing patients ample opportunity to void successfully while hospitalised, presumably to save inpatient costs. The contemporary higher 6.8% failure to void rate was unexpected and may reflect detrusor hypo-contractility after prolonged BOO. This finding may be a possible negative impact of prolonged α-adrenergic antagonist medical monotherapy, where during periods of symptomatic relief, PV could increase concurrently with asymptomatic detrusor functional deterioration. Evidence supporting this hypothesis comes from several other sources. Logie *et al.* [14] reported that over the years the interval between medical therapy and TURP has increased. It has been shown that long-term symptomatic or urodynamic gains from TURP in men with detrusor under-activity are poor [15]. Long-term Veterans Affairs Co-operative Trial data suggested that early M-TURP gave better improvement in bladder function measures than long-term outcomes after initial watchful waiting with cross-over to TURP for men with moderate LUTS-BPH [16]. As the present mean study population age did not differ from older reference series, any age-related changes reduction in detrusor compliance or contractility was unlikely. Further explanation of the underlying causative mechanisms was impossible in the context of the present analysis, as detrusor function was not objectified in the reference studies, making it difficult to relate postoperative voiding failure directly to detrusor function.

Another challenge was the inability to accurately determine what percentage of all pooled RCT analysis patients underwent TURP with an indwelling catheter after ≥1 episodes of urinary retention. In all, 24 studies stated excluding patients if they had acute urinary retention or were catheterised before TURP and 19 excluded patients with chronic urinary retention, although the post-voiding residual urine volume threshold used varied, but never exceeded 400 mL. The exclusion of patients in urinary retention would tend to under-report pre-existing detrusor hypocontractility rates. From the Borboroglu *et al.* [6] and Mebust *et al.* [7] cohorts, 15% and 27% respectively had urinary retention as an indication for TURP, while 27.5% of the Reich *et al.* [1] cohort were catheterised for acute/chronic retention preoperatively. Because of the pooled analysis technique chosen, it was felt that heterogeneity of the ‘cohort’ of patients would better reflect the heterogeneity of the study populations as seen in the reference studies, thereby allowing a fairer comparison [6,7]. It was acknowledged that only 12 studies stated that they excluded patients on medication that could affect voiding function.

The past-era landmark reference studies [6,7] did not encompass a population included in RCTs, but were retrospective studies from one or multiple centres from a USA patient population and healthcare perspective. This makes true comparison of the data between different eras problematic due to possible confounding effects of verification or other unintended biases. One transparent difference that sets the Borboroglu *et al.* study apart from others is that it was a single centre study, where all 520 procedures were performed by one supervised resident. For the Mebust *et al.* study and the pooled cohort of RCTs, there were a number of surgeons across several institutions. An example of an unintended bias is the possibility that a surgeon taking part in an RCT comparing TURP with a 'newer intervention' might have had a vested interest in the success of the new intervention. This was similar for Madersbacher and Marberger [8] when they evaluated the status of TURP, but with particular reference to less invasive techniques, using data on patients who had undergone TURP as part of an RCT. The selection of the source data from published peer-reviewed RCTs does, however, potentially offer Level 1a evidence. When also considering that the data from a recent large European population-based study of Reich *et al.* [1] seemed to match the present contemporary RCT data, one may reasonably conclude that the data from the present analysis did reflect 'real world' practice and seemed to reduce the risk of, but not eliminate, methodological selection bias.

These analytical comparative discussion points with two historically important landmark reference series [6,7], highlight the continuing inadequacies in modern urological clinical trial design, methodology and reporting, and confirm the need for international consensus and standardisation on key reporting criteria in this and other areas of urological surgical practice in future [17]. The present pooled analysis has combined several RCTs to provide a relatively high total sample size and therefore improve statistical power. However, the mean (median, range) study size was only 53 (49, 11–220) patients. About two-thirds of studies had ≤50 patients raising important quality issues inherent in many of these small single-centre studies. For example, studies of 50 patients per group would only have at most 53% power to distinguish between complication rates of 8% and 0%. This applies to many of the complications occurring after TURP (Table 1). This re-emphasises previous reports that the quality of RCTs in urology is poor, thereby limiting the ability of surgical techniques to be critically assessed [18]. Future studies should also compare properly designed adequately powered prospective multicentre multinational RCTs encompassing standardised morbidity classifications that report data means, medians and standard deviations over different time spans, to allow meaningful analysis of time trends in key practice areas.

CONCLUSION

The present study provided evidence suggesting that PV in contemporary RCTs and population-based studies of M-TURP were larger than those reported in past eras for age-matched patients. Resected prostate weight was higher, but resection times shorter with modern M-TURP technology, despite declining TURP rates. The higher voiding failure rate after contemporary M-TURP raise a suspicion of poorer detrusor function, which may at least partly reflect the aftermath of long-term effects of primary medical monotherapy for uncomplicated LUTS-BPH. Trials methodology in this area requires standardisation and quality improvement in future.

CONFLICT OF INTEREST

None declared.

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Abbreviations: **M-TURP**, monopolar TURP; **LUTS-BPH**, LUTS due to BPH; **TUMT**, transurethral microwave thermotherapy; **TUNA**, transurethral needle ablation; **PV**, prostate volume; **RCT**, randomised controlled trial; **WM**, weighted mean.

SUPPORTING INFORMATION

Additional Supporting information may be found in the online version of this article:

Appendix S1. References of studies used in final analysis.