available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Benign Prostatic Obstruction

Editorial by Alexander Bachmann et al. on pp. 677–679 of this issue

Midterm Results from an International Multicentre Randomised Controlled Trial Comparing Bipolar with Monopolar Transurethral Resection of the Prostate

Charalampos Mamoulakis[a,b,*], *Michael Schulze*[c], *Andreas Skolarikos*[d], *Gerasimos Alivizatos*[d], *Roberto M. Scarpa*[e], *Jens J. Rassweiler*[c], *Jean J.M.C.H. de la Rosette*[a], *Cesare M. Scoffone*[e]

[a] *Department of Urology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands;* [b] *Department of Urology, University Hospital of Heraklion, University of Crete Medical School, Heraklion, Crete, Greece;* [c] *Department of Urology, SLK Kliniken Heilbronn, University of Heidelberg, Heilbronn, Germany;* [d] *Second Department of Urology, Sismanoglio Hospital, University of Athens Medical School, Athens, Greece;* [e] *Department of Urology, San Luigi Hospital, University of Turin, Orbassano, Turin, Italy*

Article info

Article history:
Accepted October 5, 2012
Published online ahead of print on October 12, 2012

Keywords:
Benign prostatic hyperplasia
Bipolar
Complications
Electrosurgery
Prostate
Randomised controlled trial
Transurethral resection of prostate
Treatment outcome

EU ACME
www.eu-acme.org/europeanurology

Please visit www.eu-acme.org/europeanurology to read and answer questions on-line. The EU-ACME credits will then be attributed automatically.

Abstract

Background: Pooled data from randomised controlled trials (RCTs) with short-term follow-up have shown a safety advantage for bipolar transurethral resection of the prostate (B-TURP) compared with monopolar TURP (M-TURP). However, RCTs with follow-up >12 mo are scarce.
Objective: To compare the midterm safety/efficacy of B-TURP versus M-TURP.
Design, setting, and participants: From July 2006 to June 2009, TURP candidates with benign prostatic obstruction were consecutively recruited in four centres, randomised 1:1 into the M-TURP or the B-TURP arm and regularly followed up to 36 mo postoperatively. A total of 295 patients were enrolled.
Intervention: M-TURP or B-TURP using the AUTOCON II 400 electrosurgical unit.
Outcome measurements and statistical analysis: Safety was estimated by complication rates with a special emphasis on urethral strictures (US) and bladder neck contractures (BNCs) recorded during the short-term (up to 12 mo) and midterm (up to 36 mo) follow-up. Efficacy quantified by changes in maximum urine flow rate, postvoid residual urine volume, and International Prostate Symptom Score was compared with baseline, and reintervention rates in each arm were also evaluated.
Results and limitations: A total of 279 patients received treatment after allocation. Mean follow-up was 28.8 mo. A total of 186 of 279 patients (66.7%) completed the 36-mo follow-up. Posttreatment withdrawal rates did not differ significantly between arms. Safety was assessed in 230 patients (82.4%) at a mean follow-up of 33.4 mo. Ten US cases were seen in each arm (M-TURP vs B-TURP: 9.3% vs 8.2%; $p = 0.959$); two versus eight BNC cases (M-TURP vs B-TURP: 1.9% vs 6.6%; $p = 0.108$) were collectively detected at the midterm follow-up. Resection type was not a significant predictor of the risk of US/BNC formation. Efficacy was similar between arms and durable. A total of 10 of 230 patients (4.3%) experienced failure to cure and needed reintervention without significant differences between arms. High overall reintervention rates, withdrawal rates, and sample size determination not based on US/BNC rates represent potential limitations.
Conclusions: The midterm safety and efficacy of B-TURP and M-TURP are comparable.
Trial registration: Netherlands Trial Register, NTR703 (http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=703).

* Corresponding author. Department of Urology, University Hospital of Heraklion, P.O. Box 1031, 71001 Heraklion, Crete, Greece. Tel. +30 6944 568862; Fax: +30 2810 542066.
E-mail address: c.mamoulakis@med.uoc.gr (C. Mamoulakis).

0302-2838/$ – see back matter
http://dx.doi.org/10.1016/j.eururo.2012.10.003

1. Introduction

For decades, transurethral resection of the prostate (TURP), traditionally carried out with monopolar circuitry, has been the reference standard for the surgical management of lower urinary tract symptoms secondary to benign prostatic obstruction (BPO), principally due to the well-documented long-term efficacy of the procedure [1]. Similar durability data for other instrumental treatments are limited, and high-quality evidence favouring newer surgical modalities including minimally invasive techniques is lacking [2–4]. Consequently, monopolar TURP (M-TURP) is regarded as both clinically and cost effective [5–7].

Nevertheless, the procedure is definitely associated with a number of challenges including the occurrence of potentially severe complications that may follow during and beyond the perioperative period, such as transurethral resection (TUR) syndrome, significant bleeding, and urethral strictures (US) or bladder neck contractures (BNC) [8]. Recent technical modifications and technological innovations have decreased the incidence of procedural negative outcomes, but morbidity, although reduced, remains considerable [8,9].

B-TURP has been one of the most significant advances to TURP addressing the fundamental flaw of M-TURP by allowing performance in normal saline irrigation. Based on evidence from several randomised controlled trials (RCTs), B-TURP is preferable to its predecessor due to a more favourable safety profile [10]. However, questions have arisen regarding the quality of many of these RCTs, the need for data derived from well-designed multicentre/international RCTs, and the paucity of data from RCTs with a follow-up >12 mo [10].

Data from RCTs with follow-up ≥24 mo are also scarce [11–14], failing to detect a difference in the safety/efficacy of B-TURP versus M-TURP. According to the European Association of Urology guidelines, lack of sufficient long-term data precludes definite conclusions on the duration of improvements or advantages of B-TURP over M-TURP [1].

We previously reported the perioperative results of the first international RCT showing no clinical advantage for B-TURP [15]. The 36-mo follow-up of this RCT, one of the longest to date, was recently completed. The objective was to compare the midterm safety and efficacy of B-TURP versus M-TURP.

2. Materials and methods

2.1. Study design, protocol, and participants

A description of the study design, joint registered protocol, and inclusion-exclusion criteria was previously reported in detail [15]. Briefly, from July 2006 to June 2009, patients with BPO were consecutively recruited in four academic centres (centre 1: Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands; centre 2: SLK Kliniken Heilbronn, University of Heidelberg, Heilbronn, Germany; centre 3: Sismanoglio Hospital, University of Athens Medical School, Athens, Greece; centre 4: San Luigi Hospital, University of Turin, Orbassano, Turin, Italy). An independent local medical ethics committee at each centre approved the protocol. A total of 295 patients were enrolled and randomised 1:1 into an M-TURP or B-TURP arm after signing written informed consent. Sample size determination was based on perioperative safety aspects (changes in sodium levels immediately postsurgery). Randomisation was performed blindly among centres through the trial Web-based central electronic system (http://www.turp.nl) using a stratified permuted computer algorithm. Surgeons were not blinded due to the nature of the interventions. However, outcome assessors were different from the surgeons and the data analyst, who was also not blinded. The outcome assessor at each centre and the patients were blinded for the intervention type. All procedures were performed by one senior urologic surgeon per centre using an AUTOCON II 400 electrosurgical unit, compatible resectoscopes, and disposables (Karl Storz Endoscope, Tuttlingen, Germany). Patients were evaluated at baseline and followed up at 6 wk, 6, 12, 24, and/or 36 mo.

The primary outcome of this international multicentre parallel group RCT was safety quantified by perioperative complication rates (up to 6 wk) and rates of complications typically occurring later, with a special emphasis on US/BNC. They were recorded and compared between arms in the short-term (up to 12 mo) and the midterm (up to 24–36 mo) follow-up period. Efficacy and reintervention rates were secondarily compared between arms in the short-term and the midterm follow-up periods. In patients with spontaneous voiding, efficacy was quantified by maximum flow rate (Q_{max}), postvoid residual urine volume (PVR), and International Prostate Symptom Score (IPSS) improvements compared with baseline. In patients on catheterisation, and thus without applicable baseline Q_{max}, PVR, and IPSS values, efficacy was quantified by the absolute respective postoperative values.

2.2. Statistical analysis

Continuous outcome variables of interest (Q_{max}, PVR, and IPSS) were tested for normality and equality of variances using the Shapiro-Wilk *W* test and Levene *F* test, respectively. They were subsequently tested in univariate or repeated-measure analysis of variance models adjusted for the centre of data origin. For patients present at both midterm follow-up visits (at 24 and 36 mo), the longest follow-up efficacy data were used. Safety outcomes were assessed by the occurrence of US or BNC and were compared by the Yates corrected Pearson chi-square test or the Fisher exact test at short- and midterm follow-up, and by Cox regression analysis adjusted for centres. Quality of life (QoL) score was analysed with the Mann-Whitney *U* test or Wilcoxon test. Descriptive statistics for continuous data were presented as mean (standard deviation [SD]), regardless of variable distributions for uniformity purposes. Rates were expressed as number of patients (%). Data were analysed using SPSS v.18.0 for Windows (Chicago, IL, USA). Two-tailed $p \leq 0.050$ was considered significant.

3. Results

Figure 1 presents the flow diagram showing the phases of the RCT. The mean follow-up of the 279 treated patients was 28.8 (11.7) mo. There was no difference between arms (M-TURP: 27.9 [12,9] mo vs B-TURP: 29.7 [10.2] mo; $p = 0.687$). A total of 186 patients (66.7%) completed the 36-mo follow-up. Baseline/perioperative characteristics remained robust throughout follow-up, and differences between arms were comparable (Table 1). Consequently, adjustments for potential confounders apart from the centre of data origin were not necessary.

Primary outcome (safety) assessment was based on 230 of 279 treated patients (82.4%) at 24–36 mo (mean follow-up: 33.4 [5.5] mo; 34.1 [4.6] mo vs 32.8 [6.2] mo for M-TURP vs B-TURP, respectively; $p = 0.077$). The only additional