VALUE IN HEALTH 18 (2015) 376–386

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/jval

The Continuing Story of the Cost-Effectiveness of Photoselective Vaporization of the Prostate versus Transuretheral Resection of the Prostate for the Treatment of Symptomatic Benign Prostatic Obstruction

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A B S T R A C T

Background: In 2008, a UK assessment of technologies for benign prostatic obstruction concluded negatively about photoselective vaporization of the prostate (PVP), and the 2010 National Institute for Health and Care Excellence guidance caused several UK institutions to abandon PVP. **Objective:** To reassess the costs and effects of PVP versus transurethral resection of the prostate (TURP) on the basis of most recent data. **Methods:** The same model was used as in 2008. Transition probabilities were estimated using a Bayesian approach updating the 2008 estimates with data from two meta-analyses and data from GOLIATH, the latest and largest trial comparing PVP with TURP. Utility estimates were from the 2008 assessment, and estimates of resource utilization and costs were updated. Effectiveness was measured in quality-adjusted life-years gained, and costs are in UK pounds. The balance between costs and effects was addressed by multivariate sensitivity analysis. **Results:** If the 2010 National Institute for Health and Care Excellence analysis would have updated the cost-effectiveness analysis with figures from its own meta-analysis, it would have estimated the change in quality-adjusted life-years at −0.01 (95% confidence interval [CI] −0.05 to 0.01) instead of at −0.11 (95% CI −0.31 to −0.01) as in the 2008 analysis. The GOLIATH estimate of −0.01 (95% CI −0.07 to 0.02) strengthens the conclusion of near equivalence. Estimates of additional costs vary from £491 (£21−£1286) in 2008 to £111 (−£315 to £595) for 2010 and to £109 (−£204 to £504) for GOLIATH. PVP becomes cost saving if more than 32% can be carried out as a day case in the United Kingdom. **Conclusions:** The available evidence indicates that PVP can be a cost-effective alternative for TURP in a potentially broad group of patients.

Keywords: benign prostatic obstruction, cost effectiveness analysis, NICE guidance, health care, United Kingdom.

Introduction

Benign prostatic obstruction (BPO) leading to bothersome lower urinary tract symptoms negatively affects quality of life in older men. Prevalence is more than 50% in men in their sixties, increasing to 90% for those older than 80 years [1,2]. Men aged 40 to 50 years who present with lower urinary tract symptoms have a 20% to 30% chance of ever undergoing a prostatectomy [3].

Typically, medical therapy is the first-line treatment offered. When this fails, standard treatment is transurethral resection of the prostate (TURP). TURP requires anesthesia and 2- to 4-day hospitalization and is associated with several potential complications including transurethral resection syndrome (<1.1%), blood transfusion (2.9%–8.4%), urethral stricture (3.8%), bladder neck contracture (4.7%), retrograde ejaculation (65.4%), impotence (6.5%), urinary incontinence (2.2%), and mortality (0.1%–0.25%) [4].

Consequently, alternative procedures were developed in an attempt to minimize invasiveness, reduce complications, and shorten recovery times. In 2008, the National Institute for Health Research commissioned a health technology assessment (HTA) comparing alternative therapies with TURP. The assessment concluded that "In the absence of strong evidence in favor of newer therapies, TURP remains both clinically effective and cost-effective. The use of minimally invasive technologies in the NHS is not appropriate until a more effective and/or less costly technology is available" [5]. Moreover, it recommended that "A well conducted head-to-head trial of treatment strategies …. would be most desirable to establish the gold standard. Such a

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1098-3015$36.00 – see front matter http://dx.doi.org/10.1016/j.jval.2015.04.002

trial should take prostate size into account and should include direct measures of utility" [5].

Laser vaporization of the prostate was one of the innovative therapies included in the 2008 assessment. The assessment pooled data from multiple laser systems, delivering energy from different light spectrums, resulting in different methods of vaporizing obstructing prostate tissue. A publication summarizing the cost-effectiveness analysis stated, "Potassium titanyl phosphate laser vaporisation was unlikely to be cost effective … which argues against its unrestricted use until further evidence of effectiveness and cost reduction is obtained" [6]. The National Institute for Health and Care Excellence (NICE) guidance that followed in 2010 recommended to "only consider offering laser vaporisation techniques …. as part of a randomised controlled trial that compares these techniques with TURP." Strangely, although NICE reevaluated the evidence base, eliminating a Dutch study [7] with an atypical rate of incontinence, it did not reevaluate the cost-effectiveness, thereby never noticing the consequences of deleting this Dutch study from the evidence. As a result, utilization of laser vaporization decreased dramatically in the United Kingdom.

Photoselective vaporization (PVP) was one of the systems adding to the evidence base by one study [8]. Since 2008, two significant technological improvements in PVP were introduced: increased laser power and an improved laser delivery system for rapid and hemostatic treatment of large prostate glands. In addition, the largest randomized controlled trial (RCT) comparing PVP with TURP, the GOLIATH trial—a noninferiority study of men with lower urinary tract symptoms due to BPO—was initiated [9]. The clinical manuscript summarizes the results by saying that

> The study demonstrated the non-inferiority of XPS to TURP for IPSS, Qmax (maximum flow rate) and complication-free proportion. PV and PVR were comparable between groups. Time until stable health status, length of catheterisation, and length of hospital stay were superior with XPS ($p < 0.001$). Early re-intervention rate within 30 d was three times higher after TURP ($p = 0.025$); however, the overall postoperative re-intervention rates were not significantly different between treatment arms. Conclusions: XPS was shown to be non-inferior (comparable) to TURP in terms of IPSS, Qmax, and proportion of patients free of complications. XPS results in a lower rate of early reinterventions but has a similar rate after 6 mo. [9]

However, it may be noted that the difference in the International Prostate Symptom Score is borderline, significantly in favor of TURP, and that the secondary end points—concerning symptoms—are also, albeit nonsignificantly, in favor of TURP. So, there may a trade-off between efficacy, safety, convenience, and costs and each aspect may be associated with its own "value." In 2008, the difficulty to bring together the various risks, disutilities, and costs was acknowledged by the use of a cost-effectiveness model that included all these in a structured and transparent way. The model, a Markov-type model, included parameters concerning baseline risks, probability of success, and incidence of transient and permanent adverse effects as well as estimates of costs and disutilities due to adverse effects. Estimates of efficacy and adverse effects were based on meta-analyses. Now, more RCTs are available, not only GOLIATH using the 180-W system but also four trials using the 120-W system and four that used the 80-W laser system, as included in a 2012 meta-analysis [10].

The emerging situation seems tailormade for a Bayesian approach. Bayesian statistics build on the idea of continuously updating the relevant estimates by combining prior information with new data [11]. The combination of priors with new data leads to posterior distributions in which means or medians can be used as point estimates and 95% credible intervals can be used to indicate the degree of remaining uncertainty. Within this, the posterior distributions of today become the prior distributions of tomorrow. The 2008 data can be used to formulate a "prior" distribution, and to combine this with the "data" from subsequent studies to estimate the current, most up-to-date "posterior" distributions of costs, effects, and the balance between costs and effects. The expectation may be that such stepwise Bayesian approach will iterate to less and less uncertainty. This applies, however, only to a rather stable situation. Medical technologies such as PVP and TURP continuously evolve, and as such prior distributions may reflect only outdated information. One might expect improvements, especially in the active treatment arm but also in the control arm. In addition, one might expect surgeons to broaden the indication, given the increased safety and efficacy. Expert elicitation might be used to capture such phenomena reflected by the inclusion of parameters indicating the improvements in technology and case mix. The analysis presented here does not go that far. The Bayesian case, building on former evidence is the one, rather conservative extreme, building the evidence in time, without acknowledging any progress by weighing newer data more heavily. The other extreme is to use separate chunks of evidence as used in previous analyses and to add the data from the GOLIATH study as another separate chunk. Both approaches will lead to updated estimates of costs and effects, and together they are a source of information for an updated decision of the position of laser therapy for benign prostatic hyperplasia (BPH).

Methods

The Model

The parameters and model used in the 2008 HTA form the basis of this analysis [5]. The model is a state transition Markov-type model with a lifelong time horizon in which patients, after initial treatment, are categorized in mutually exclusive states guided by their urinary symptoms and whether or not they have incontinence symptoms (Fig. 1). In line with the 2008 model, reoperations may be carried out in case of insufficient relief but not in case of persistent urinary incontinence. Also, the use of alpha-blockers and five alpha reductase inhibitors in case of failure is not included except after two treatment failures. Mortality is assumed not to be affected by treatment, and age-specific population mortality rates for English men are used.

The 2008 model was programmed in TreeAge. To gain insight and to optimize computer time, it was reprogrammed in Excel. The only estimates that were not taken from the original model, keeping the structure and most estimates identical, concerned procedural cost parameters, unit cost estimates, and estimates concerning efficacy and safety. The latter estimates were obtained by reading the efficacy and safety data—as reported in Appendix 1—into R and calling WinBugs from R. Multivariate sensitivity analysis was carried out on the basis of 1000 random draws using a macro in Excel.

In case of discrepancies between the publication and the TreeAge program, the TreeAge program was taken as reference. For example, the 2008 TreeAge model used a meta-analysis of all TURP data for the estimate of the incidence of adverse effects, leading to, among others, a baseline rate of urinary incontinence of 151/1935 (=7.8%). This is contrary to the estimate of 0.03 as published in Table 30. Similarly, with respect to the utilities, estimates from the TreeAge code were used (where the 95% confidence intervals are surrounding the point estimates, as one would expect.) Another change is that in the rare case of multiple adverse effects, utilities were estimated by multiplication.