

INVITED EDITORIAL

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Evaluation and results of treatments for prostatism

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Abstract Men with symptoms of prostatism form a heterogeneous group. The best treatment of proven obstruction or retention in fit men remains transurethral prostatectomy (TURP). Men presenting with symptoms of prostatism may have bladder outflow obstruction, detrusor instability or weak bladder contraction leading to low pressure/low flow voiding so it is perhaps not surprising that only 75% of men selected for TURP purely on the basis of symptoms have a good outcome. Pressure flow studies are the only precise method of diagnosing outflow obstruction. The problem of accurately diagnosing obstruction before treatment is started applies particularly to trials of new treatments such as lasers, high energy focused ultrasound and drugs. Laser treatment is producing short term results that are slightly inferior to TURP but may have less morbidity. The role of conservative treatment is important in selected men. Men who have severe intercurrent illness may be treated by means of intra-prostatic stents. In order to accurately assess a new treatment it is necessary to determine the short-term mortality, the morbidity, complication rate and outcome as well as the cost-effectiveness, long-term outcome and patient preference. These conditions have not yet been met for any of the new treatments for prostatism.

Key words Prostatism · Benign prostatic hyperplasia (BPH) · Outcome · Laser treatment · Drug treatment · Minimally invasive techniques

In this paper, the term bladder outflow obstruction (BOO) is reserved for urodynamically proven obstruction, prostatism refers to a symptom complex, benign prostatic hypertrophy (BPH) is a histological diagnosis. About 15% of men in their 40's will eventually undergo prostatec-

tomy; of these men 25% present with acute retention, 15% present with chronic retention and the remainder present with symptoms and undergo an elective operation. Transurethral prostatectomy (TURP) can be made a very safe operation and for most men with retention it remains the correct method of management. However, the majority of men in the UK undergoing elective prostatectomy do so on the basis of symptom severity and only 40% have a flow rate measured (Emberton and Neal, unpublished data from the National Prostatectomy Audit, 1993). The proportion of men experiencing a good outcome after elective TURP varies from 60 to 90% depending on the severity of pre-operative symptoms and on whether they were actually obstructed urodynamically.

It is true to say that most new treatments have presently been tested purely on the basis of changes in symptoms and flow rates. In very few studies has a urodynamic diagnosis of outflow obstruction been arrived at prior to treatment, thus rendering the definition of outcome difficult and a comparison of different studies and different treatments impossible. Assessment of the results of treatment for bladder outflow obstruction is not straightforward. Crude measures of safety such as peri-operative morbidity and mortality remain important, but these do not tell us anything regarding the cost effectiveness of treatments. To do this one needs to know the indication for treatment. Was it done for acute or chronic retention, complications such as stone formation and infection or for treatment of symptoms as an elective procedure? Other factors such as the patient's tolerance of the symptoms, the type of symptoms, whether the patient had urodynamically proven bladder outflow obstruction or had developed associated detrusor instability all affect the outcome in terms of health gain.

Benign prostatic hyperplasia, symptoms of prostatism and outflow obstruction

By the age of 60 years, 50% of men have nodules of BPH and up to 20% have areas of early prostate cancer. The

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relationship between histological BPH, symptoms of "prostatism" and urodynamically proven BOO is weak, for many men have symptoms owing to detrusor instability or weak detrusor contraction that are indistinguishable from those of proven BOO [20]. Urodynamic assessment of men selected for TURP purely on the basis of symptoms has shown that only 60% are obstructed, 20% are equivocally obstructed and 20% are non-obstructed [2, 20]. Prostatectomy is performed for acute retention (25% in the UK), chronic retention with or without dilatation of the upper urinary tract (10–15%) or as an elective procedure for symptoms (60%).

Symptoms and urodynamic findings

One study of the relationship between symptoms and urodynamic findings in elderly men who had never consulted a doctor for voiding symptoms [27] found a significant increase in hesitancy, weak stream, nocturia and urge incontinence, but no change in post-micturition dribbling in the 5th, 6th and 7th decade compared with younger men. Of this group 20% had symptoms of a similar severity to those undergoing TURP, suggesting that many men see these symptoms as part of normal ageing. Many ageing patients develop non-specific symptoms such as frequency and weak voiding which may be related to problems affecting the detrusor muscle rather than being related to BOO. This is reinforced by a report which showed that AUA (American Urological Association) symptom scores in elderly females with voiding dysfunction are similar to those seen in men with prostatism [11] showing incidentally that such symptom scores are certainly not specific for outflow obstruction.

Even in elderly men without symptoms, peak flow rates are decreased and voiding pressures are increased compared with younger men. However, flow rates are lower, residual urines are greater, instability is more common and voiding pressures are greater in men undergoing prostatectomy [13] than in asymptomatic elderly men. Satisfactory measurement of flow rates can be difficult in routine clinical practice; flow rates decrease if voided volumes are low and, because many men with obstruction have small capacities or detrusor instability, it follows that many will have low voided volumes. It is best for patients to attend a special flow rate clinic since flow low rates and residual volumes often are inconsistent over several voids and repeated measurements may be necessary before a clear impression of bladder emptying can be obtained.

The relationship between obstructive symptoms and urodynamic findings is weak [4, 20] and there is no evidence that any one type of symptom score is better than another. Abrams and Griffiths [2] found an association between low peak flow rates and high voiding pressures and it was suggested that a low measured flow rate was clinically useful. However, in men studied only before operation (the group in whom these measurements matter), no correlation was found between flow rates and voiding pressures [20] suggesting that it is not possible to

Table 1 Presence of symptoms before and after prostatectomy in 217 men (Neal et al. 1989)

Symptom	Before	After
Poor stream	82%	18%
Hesitancy	75%	12%
Post micturition dribble	78%	39%
Urgency	69%	32%
Nocturia	58%	19%
Urge incontinence	29%	10%
Stress incontinence	0%	0% ^a

After operation compared with before; $P < 0.001$ (except^a)

identify with precision men with high voiding pressures and obstruction by measurement of flow rates. A more consistent finding has been the relationship between detrusor instability and irritative symptoms of frequency, urgency and urge incontinence [1, 4, 20]. A third of men with clear symptoms of obstruction and low flow rates have normal or low voiding pressures [20], suggesting that some have "low pressure/low flow" bladders. An association has been found between a small prostatic size, weak voiding pressures and poor improvement after operation [21]. These findings suggest that certain men with severe symptoms, low flow rates, low voiding pressures and a small prostate have weak detrusor function as a cause of symptoms rather than obstruction. They may therefore experience little improvement after TURP.

Detrusor instability is found in half the men undergoing prostatectomy and in about a quarter afterwards. Persistent instability is a major cause of poor outcome, but a wide spectrum of severity is concealed by the term instability, usually defined as a phasic increase in pressure of more than 15 cm H₂O which the patient cannot inhibit. In some, detrusor instability is secondary to outflow obstruction, whereas in other unobstructed men idiopathic instability or neurological disease is the primary cause of frequency, urgency and incontinence with resultant low voided volumes and low measured flow rates.

Symptomatic outcome of prostatectomy

About 0.1%–0.5% of men die because of the operation and death is more common in very elderly men admitted with retention [17]. Major morbidity (bleeding, early re-operation and sepsis) is found in between 4% and 8% within 30 days of TURP. Within 3 months 15% of men reported occasional difficulty in voiding owing to clots, 9% needed catheterisation, 7% had infection lasting more than 2 weeks, 8% were readmitted to hospital and 24% had visited a doctor because of a prostate problem [10].

Measuring outcome after prostatectomy is not easy because the end point is ill-defined. Measuring outcome only by changes in symptoms – despite being the reason for the patient undergoing the procedure – is subjective and in the early stages will be influenced by a placebo effect. Few men are made worse or are no better, though about 4%

who claimed to be dry had varying degrees of incontinence after operation [10] and about 5% of sexually active men develop erectile impotence. Retrograde ejaculation occurs in over 60% of men after prostatectomy and may be a cause of litigation if patients are not counselled about this problem beforehand. Between 75 and 90% of men achieve a good outcome [3, 10, 21]. Fowler has reported that men with the most severe symptoms or retention do best after TURP [10]. In general, significant improvement is found in about 75% of men undergoing elective prostatectomy after one year [21] and this seems to continue in the long term [22]. The chance of individual symptoms improving varies. About a fifth of men continue with poor flow or hesitancy, about a third have urgency and no fewer than a tenth still have urge incontinence (Table 1).

After TURP, symptom scores decrease by over 80%. On average flow rates double after TURP (from about 9 ml/s to 18 ml/s), voiding pressures halve (from about 80 to 100 cm H₂O before to about 40 to 50 cm H₂O after operation), rates of detrusor instability decrease from 50–60% to 25%, bladder capacities increase and residual urine volumes decrease by 70% (from about 100 ml to 30 ml). These figures have not yet been matched by newer treatments. There is a need for high quality data on the measurement cost-effectiveness and of quality of life changes for men with prostatism treated by means of watchful waiting, TURP, drugs and newer modalities. Such data are not yet available.

Selection for operation and urodynamic findings associated with outcome

Men with low voiding pressures and stable detrusors have only a 60% chance of achieving a good result, whereas those with high voiding pressures and stable detrusors have about a 90% chance of doing well [21]. It is probably true that if only those men with symptoms, low flow rates and high voiding pressures were selected for prostatectomy, the outcome would be much better than if men were selected purely on the basis of symptoms and low flow rates because of the exclusion of men with low voiding pressures who do less well.

Re-operation after prostatectomy

The rate of re-operation is one, albeit crude, indicator of poor outcome and patient dissatisfaction. It may be a more important marker in the future when newer treatments are assessed as they may have a greater long term failure rate. One in eight men after TURP undergoes repeat prostatectomy after 8 years: a rate which is 3–5 times in excess of that found after open operation [22, 25, 26, 29]. It is often assumed that these men have undergone an incomplete TURP and might have been better served by open operation. Unfortunately, the issues are more complex than an initial inspection of the figures might suggest [19].

Newer treatments

Many of the newer treatments have been well evaluated in terms of short term morbidity, improvements in symptoms and urinary flow rates, but very few have undergone rigorous testing by means of urodynamic testing before and after operation. We do not yet know long term complication rates, whether short term improvements in symptoms and flow rates are durable in the long term and how they compare with TURP in terms of cost-effectiveness. We do not yet know how many men will subsequently require further treatment or TURP. Another problem is that many of the studies have relied on a single pre-treatment measure of flow rate in both placebo and active arms and it is known that flow rates will improve on repetition, partly owing to men being able to void larger volumes of urine. Nevertheless, many of these newer treatments are being offered to men with prostatism because they appear to be less invasive, may be safer and can be provided as day case treatment. It is also clear that microwave treatment, laser treatment and balloon dilatation are all presently more effective in men with minimal prostatic enlargement than in large prostates.

Conservative treatment (or watchful waiting)

Many urologists carry out flow rate and ultrasound residual urine measurements when they first see men with symptoms of prostatism. If the flow rate and symptoms are not too bad and prostate cancer can be excluded, then men are advised regarding the likely outcome and side effects of treatment. Many of them elect follow ups at 6 monthly intervals for a period of a year or more before a mutual decision is made regarding the need and likely outcome of TURP. This is undoubtedly a reasonable way of managing many men with mild symptoms of prostatism which appears to be safe in the long term [5]. If needed, it may be supplemented with advice regarding restriction of fluid intake in the evening, the use of anti-cholinergic agents or α -adrenergic blocking agents.

Drug treatments

Two main classes of drugs have been used in the treatment of men with prostatism. These include α -adrenergic blocking agents which inhibit the contraction of smooth muscle which is found in the prostate [15]. The other class of drug is the 5 α -reductase inhibitors which inhibit the conversion of testosterone (T) to di-hydro-testosterone (DHT) which is the androgen which is effective in the prostate and genital skin [28]. This drug when taken for a year results in a 25% shrinkage of the prostate gland [14]. On average, both drugs seem to be of similar effectiveness, although the 5 α -reductase inhibitors have fewer side effects than non-selective α -adrenergic blocking agents. They result in improvements in maximum flow rates by about 2 ml/s

greater than placebo and result in mild improvement in symptom scores by about 2 to 3 [12]. 5 α -reductase inhibitors are expensive amounting to about £ 500 for a year's course. The cost of a TURP is about £ 1,500. When one remembers that a significant proportion of men who try these drugs will subsequently undergo TURP and that the agents are significantly less effective than TURP it is questionable whether the agents should be used other than to supplement conservative treatment for a period. These drugs have little impact on urodynamic aspects of bladder outflow obstruction with voiding pressures changing very little after treatment in the majority, although a sub-set of men have been reported to respond better [14].

Stents

Several designs of stents are available for the treatment of men with bladder outflow obstruction and retention who are considered unfit for TURP. These range from wire spirals [24] and silicone stents [18] which can be relatively easily placed and removed to perforated titanium metal stents [30] which are not easily removed. At least 10% will require stent removal and encrustation is seen in 25% in the long term. There is little doubt that these devices are useful in very ill men with severe intercurrent disease and urinary retention who have a limited life expectancy in whom a TURP carries a high risk of death. There is little to recommend their use in fit men or in men without retention. Given the nature of the patient population, the outcome of these devices has been relatively good.

Balloon dilatation

These devices were originally recommended for the same category of men who are suitable for implantable stents, but some authors have reported their use in fit men or in men without retention. The published data on these men are not supportive of their use in fit men [7].

Microwave and laser treatments and other methods of tissue destruction

Microwave treatment aims at providing an external source of microwave energy which is then focused within the prostate gland. The energy source may be placed within the rectum or the urethra, although recent machines use the intra-urethral route. With the first generation machines, the prostate heats to between 40 and 45°C (hyperthermia). There is very minimal tissue destruction and there is no major rise in serum prostate specific antigen (PSA) confirming that little of the prostate is actually damaged. The patient usually undergoes several courses of treatment which involve the insertion of a transurethral energy source probe, although recent machines may be effective using only one course of transurethral treatment [6]. Usually, these treatments can be

given under local anaesthesia as a day case. There is no need for a post-treatment catheter. The results of several studies indicate overall results approximate those of drugs in terms of changes in flow rates and symptoms scores. The morbidity of these treatments is low [23, 31].

The next generation of microwave machines is able to provide an increased source of energy which destroys some of the prostate (thermo-therapy – temperature > 50°C). We do not yet know the detailed outcome of these newer machines, although it may be that they will provide better results than hyperthermia [9]. Machines producing even greater energy (thermo-ablation – temperatures > 70°C) are now becoming available.

Laser treatments can be of two types. In one a non-contact probe is used to vaporize prostatic tissue under direct vision. There is no bleeding and this treatment can be used to carry out bladder neck incisions in men with small prostate glands as day case treatment and a catheter may not be necessary. Hence this treatment would be potentially cost-effective in this setting. The cost of the probes at present however is £ 500 which would balance out any cost saving in terms of hospital stay. These probes are not useful in the treatment of men with large glands as the treatment would take too long. The other type of laser is a contact side-firing laser of lower energy but greater penetration. This energy results in necrosis of the prostate gland to a varying thickness. The energy can be applied transurethrally under direct vision or it can be applied transurethrally under the control of ultrasound. The potential advantage of the latter technique is that it means that greater energy can be applied to thicker areas of BPH ensuring a more complete treatment. A supra-pubic catheter is inserted for about 10–14 days whilst the necrotic prostate sloughs. There is little or no bleeding and the treatment can be given as a short stay procedure or day case procedure. Laser treatment however would usually require a general anaesthetic. The cost of the probes is about £ 500. The outcome of contact laser treatment appears to be better than microwave hyperthermia with improvements in flow rates from 9 ml/s to 14–16 ml/s and improvements in symptom score by about 50%. It is as yet unclear how effective it is in comparison to TURP in terms of cost-effectiveness, symptomatic and urodynamic outcome [8].

There are newer methods of treatment becoming available including focused high frequency ultrasound and direct treatment of the prostate with needles providing high energy electro-magnetic treatment. The outcome appears to be similar to those of laser treatment [16].

Conclusions

Men with symptoms of prostatism form a heterogeneous group. The best treatment of proven BOO remains TURP, but new methods of tissue destruction are producing short term results that are slightly inferior to TURP and may be safer in the short term. There is still a need for proper

controlled studies of these new treatments against TURP to evaluate the longer term results and to produce proper comparison of short term costs and effectiveness. The role of conservative treatment is important and may be supplemented by short term use of active drugs. Men who have severe intercurrent illness may be appropriately treated by means of intra-prostatic stents.

In terms of future studies of new methods of treatment for prostatism, there are lessons to be learnt. The use of symptom scores and flow rates as the only methods of assessment for new treatments of men with prostatism leaves much to be desired because it will be unclear how many men are obstructed, non-obstructed or equivocally obstructed. The results of such studies are therefore difficult to interpret. The best method of investigating men with symptoms remains urodynamic testing, for this allows proper categorization of the degree of obstruction.

New technologies will be introduced for treatment of men with prostatism and bladder outflow obstruction. However, it is not enough to show that new treatments can safely cause prostatic destruction and improve symptoms and flow rates. Proper careful assessment of cost-effectiveness, the durability of treatments, the effects of quality of life, symptoms and flow rates and pressure/flow studies is needed. These new treatments should be tested by random controlled trials against best standard treatments before they are adopted by urologists into clinical practice.

References

- Abrams PH, Feneley RCL (1978) The significance of the symptoms associated with bladder outflow obstruction. *Urol Int* 33:171-174
- Abrams PH, Griffiths DJ (1979) The assessment of prostatic obstruction from urodynamic measurements and from residual urine. *Br J Urol* 51:129-134
- Abrams PH, Farrar DJ, Turner Warwick RT, Whiteside CG, Feneley RCL (1979) The results of prostatectomy: a symptomatic and urodynamic analysis of 152 patients. *J Urol* 121:640-642
- Andersen JT, Nordling J, Walter S (1979) Prostatism I: The correlation between symptoms, cystometric and urodynamic findings. *Scand J Urol Nephrol* 13:229-236
- Ball AJ, Feneley RCL, Abrams PH (1981) The natural history of untreated "prostatism". *Br J Urol* 53:613-616
- Bdesha AS, Bunce CJ, Kelleher JP, Snell ME, Witherow R O'N (1993) Trans-urethral microwave treatment for benign prostatic hypertrophy: a randomised study. *Br Med J* 306:1293-1296
- Chiou YK, Chiou RK, Omaha NE, Lynch B, Binard JE, Horan JJ, Ebersole ME (1993) Randomized comparison of balloon dilatation and transurethral incision for symptomatic benign prostatic hyperplasia: long term follow up. *J Urol* 149:464A
- Costello AJ, Shaffer BS (1993) Laser ablation of benign prostatic hypertrophy (BPH): two and a half year experience with right angle delivery system. *J Urol* 149:214A
- Devonec M, Fendler JP, Nasser M, Joubert P, Perrin P, (1993) The clinical response to transurethral microwave thermotherapy is dose dependent: from thermo-coagulation to thermo-ablation. *J Urol* 149:249A
- Fowler FJ, Wennberg JE, Timothy RP, Barry MJ, Mulley AG, Hanley D (1988) Symptom status and quality of life following prostatectomy. *JAMA* 259:3018-3022
- Heritz D, Radomski S, Herschon S, Adanja G (1993) AUA BPH symptom score: can it be used to assess female voiding dysfunction. *J Urol* 149:367A
- Jardin A, Bensadoun H, Delauche-Cavallier MC, Attali P (1991) Alfuzosin for treatment of benign prostatic hypertrophy. *The Lancet* 337:1457-1461
- Jensen KME, Bruskewitz RC, Madsen PO (1984) Urodynamic findings in elderly males without prostatic complaints. *Urology* 24:211-213
- Kirby RS, Bryan J, Eardley I, Christmas T, Liu S, Holmes SAV, Vale JA, Shanmugnathan K, Webb JA (1992) Finasteride in the treatment of benign prostatic hyperplasia: a urodynamic study. *Br J Urol* 70:65-72
- Lepor H (1989) Non-operative management of benign prostatic hyperplasia. *J Urol* 141:1283-1288
- Marberger M, Madersbacher S, Kratzik C (1993) Treatment of BPH with transrectal high intensity focused ultrasound (HIFU). *J Urol* 149:217A
- Mebust WK, Holtgrewe HL, Cockett ATK, Peters PC (1989) Transurethral prostatectomy: immediate and post-operative complications. *J Urol* 141:243-247
- Miller PD, Gillatt D, Abrams P (1993) Selection of patients suitable for treatment with the ASI prostatic stent. *J Urol* 149:216A
- Neal DE (1990) Prostatectomy - an open or closed case. *Br J Urol* 66:449-454
- Neal DE, Styles RA, Ng T, Powell PH, Thong J, Ramsden PD (1987) The relationship between voiding pressures, symptoms and urodynamic findings in 253 men undergoing prostatectomy. *Br J Urol* 60:554-559
- Neal DE, Ramsden PD, Sharples L, Smith A, Powell PH, Styles RA, Webb RJ (1989) Outcome of elective prostatectomy. *Br Med J* 299:762-767
- Nielsen KT, Christensen MM, Madsen PO, Bruskewitz RC (1989) Symptom analysis and uroflowmetry 7 years after transurethral resection of the prostate. *J Urol* 142:1251-1253
- Ogden CW, Reddy P, Johnson H, Ramsay JWA, Carter SSC (1993) Sham versus transurethral microwave thermotherapy in patients with symptoms of benign bladder outflow obstruction. *The Lancet* 341:14-17
- Poulsen AL, Schou J, Oveseb H, Nordling J (1993) Memokath: a second generation of intra-prostatic spirals. *Br J Urol* 72:331-334
- Roos NP, Ramsay EW (1987) A population-based study of prostatectomy: outcomes associated with differing surgical approaches. *J Urol* 137:1184-1188
- Roos NP, Wennberg JE, Malenka DJ, Fisher ES, McPherson K, Anderson TE, Cohen MM, Ramsay E (1989) Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. *N Engl J Med* 320:1120-1124
- Sommer P, Nielsen KK, Bauer T, Kristensen ES, Hermann GG, Steven K, Nordling J (1990) Voiding patterns in men evaluated by a questionnaire survey. *Br J Urol* 65:155-160
- Stoner E (1992) The clinical effects of a 5 α -reductase inhibitor, Finasteride, on benign prostatic hyperplasia. *J Urol* 147:1298-1302
- Wennberg JE, Mulley AG, Hanley D, Timothy RP, Fowler FJ, Roos NP, Barry MJ, McPherson K, Greenberg ER, Soule D, Bubolz T, Fisher E, Malenka D (1988) An assessment of prostatectomy for benign urinary tract obstruction. *JAMA* 259:3027-3030
- Williams G, Coulange C, Milroy EJG, Sarraon JP, Rubben H (1993) The Urolume, a permanently implanted prostatic stent for patients at high risk of surgery. *Br J Urol* 72:335-340
- Yerushalmi A, Singer D, Katsnelson R, Levy E, Shani A (1992) Localised deep microwave hyperthermia in the treatment of benign prostatic hyperplasia: long-term assessment. *Br J Urol* 70:178-182

Editorial Comments

If it is still a general agreement that a TUR is the ("gold-")standard therapy for this heterogenous disease entity, would not an open prostatectomy in some cases be a better option? Not very long ago, one would have been killed for this type of question by "TUR-monomans", and now official studies are on the way with issue to answer this once more open question. What will be – ten years from now – the indication for the alternative treatments discussed in this review? There are reasons to believe that TUR will have lost some of its "gold". Just a better flow pattern will most probably no longer be a sufficient argument for surgical treatment – especially if the irritative symptoms of the patient remain uninfluenced. We will surely have a much more "case-adapted" indication for our different forms of therapy, and this on the basis of an extended diagnostic work-up which includes not only an improved and more easily understood symptom score, but also a much more detailed and situation-adapted (and eventually repeated) urodynamic evaluation. For today one is tempted to speculate in how many of the roughly 300000 prostatectomies per year in Europe the indication has a more solid basis than a superficial interview, a rectal examination and a residual urine estimation. In any case there is again a lot of work to do in BPH evaluation and treatment, a domain where only a few years ago all pertinent problems seemed to be solved.

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