A little more than 10 years has passed since Clayman and Kavoussi performed the first laparoscopic nephrectomy [1]. Although techniques have flourished in the few units dedicated to laparoscopic endeavour, the problem of training a generation of urologists in laparoscopy, a technique that is rapidly becoming the standard of care, remains.

The wide use of laparoscopy in many other surgical specialties means the junior trainee has often had considerable previous exposure to laparoscopy with associated development of spatial awareness and appropriate motor skills. Nevertheless an integrated programme designed to improve laparoscopic competency is essential. To this end BAUS and the Specialist Advisory Committee in urology have supported the development of a pathway to facilitate the acquisition of aptitude and knowledge in urological laparoscopy, although this training programme stops short of recognizing competence as an endpoint. The programme consists of a basic skills course, complemented by assisting and observing at various laparoscopic urological procedures, and independent practice on bench models, followed by an advanced skills course that includes operative experience on animal or cadaver models. Mentored operating follows until independent practice appears to be safe.

However, the number of cases required to achieve satisfactory performance varies and depends on numerous factors that are independent of mentor or apprentice, and most controlling bodies have avoided assigning a minimum number for certification. However, the Endourological Society, among other criteria, requires at least 40 laparoscopic procedures to be undertaken or assisted in a 1-year period for a fellowship to be recognized. The European Society of Urotechnology, a full participant in the European Association of Urology, which has espoused the British model, also wishes to see a minimum number of procedures specified.

The pathway described above is more suited to specialty registrars, who are able to incorporate the programme into their period of training. Mentoring trained urologists requires the cooperation of the mentor and trainee, as well as their respective hospital managers and patients [2]. At least 50 laparoscopic cases within 2 years is thought to be adequate for someone to perform as mentor. The acquisition of laparoscopic skills, like most endo-urological techniques, is uniquely appropriate for modular training and mentoring. Once the minimum of skills have been acquired for safe tissue handling, the trainee can be guided by a mentor and video feedback used to facilitate confidence and competency, which can be achieved safely and quickly by most. Videotape recording can be a double-edged sword, for the scrutiny under which the laparoscopic surgeon is placed is intense and far exceeds that of conventional ‘scapel’ surgery.

The development of other endourological techniques should not be under-emphasized as a method of improving laparoscopic skills, although it is recognized that laparoscopy is a technique that applies across the breadth of urology rather than to a subspeciality. Wide experience with endoscopic surgery facilitates the development of spatial awareness and the specific motor skills required by the laparoscopist.

There is as yet no recognized way to select those suitable for laparoscopic training. A conspicuous omission from the pathway to achieving operative competence is the use of simulators or tools to select applicants, based on aptitude. At present, those who train further in laparoscopy are those who have chosen to do so. Tools such as the Advanced Dundee Endoscopic Psychomotor Tester [3] and Minimally Invasive Surgical Trainer – Virtual Reality [4] have not yet been adequately validated to justify their expense [5]. The testing of airline pilots, often used as a model for surgical training, has used simulators for selection and training for decades. There is little doubt that similar tests will play a role for laparoscopists of the future if they can be validated.

Consideration of future service provision also needs to be considered in selecting urologists for further training in laparoscopy. The number of urologists offering laparoscopy in a geographical area should be limited to maintain the highest technical standards. This might otherwise be compromised by dilution of cases.

The laparoscopic approach is of proven benefit in laparoscopic nephrectomy and nephroureterectomy, in terms of blood loss and recovery [6,7], without adversely affecting oncological control [Bariol SV, Stewart G, MacNeil SA, Tolley DA, Oncological control following laparoscopic nephroureterectomy: 7-year outcome, unpublished], but its role in radical pelvic surgery has yet to be firmly established. However, as laparoscopy in urology increases the challenge will be to establish and maintain a system for training in laparoscopic skills and mentoring urologists during their early experience with new techniques. This can easily be incorporated into current
Three drug therapy is best for symptomatic prostate enlargement: could a combination of doxazosin and finasteride change clinical practice? J.M. FITZPATRICK and R.S. KIRBY* – Department of Surgery, Mater Hospital, Eire, and “St George’s Hospital, London, UK

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Over 200 years have passed since John Hunter noted that prostate enlargement was related to the normal ageing process and depended on testicular function. In 1895 bilateral orchidectomy was proposed as a treatment for BPH, and although completely effective it is not surprising that castration never became a popular treatment.

BPH is currently a common condition amongst older men, and which fundamentally causes morbidity through the associated urinary symptoms. While a small proportion of men will have a prostatectomy for absolute indications, e.g. acute urinary retention (AUR) or UTI, most have traditionally had surgery to relieve the bothersome urinary symptoms and improve their quality of life [1]; TURP has long been considered the standard surgical treatment for symptomatic BPH.

More recently, as understanding of the disease has improved so too has the number of medical treatments increased. The use of α-blockers and 5α-reductase inhibitors in patients with BPH is commonplace, and their value has been well documented. Short-to-moderate duration trials showed the effectiveness of α-blockers for relieving symptoms and improving urinary flow rate [2–5]. Until recently, trials combining the two classes of drugs showed little superiority in alleviating symptoms and improving urinary flow rate. The Veterans Affairs Cooperative Studies Benign Prostatic Hyperplasia Study compared terazosin, finasteride and combination therapy with placebo [6], whereas the Prospective European Doxazosin and Combination Therapy Trial compared doxazosin, finasteride and combination therapy with placebo [7]. Results from both trials (each at 1-year) showed no benefit in the use of combined therapy over monotherapy. However, these trials assessed changes in AUA symptom score and maximum urinary flow rate at 1 year, rather than the effect of medical therapy on the clinical progression of BPH and the long-term reduction in the risk of associated complications.

The recently published Medical Therapy of Prostatic Symptom (MTOPS) trial [8] at 5 years has the longest follow-up of any study investigating the usefulness of α-blockers, and investigated >3000 men. MTOPS was designed to determine whether monotherapy with either doxazosin or finasteride, or as combination, would delay or prevent the clinical progression of BPH (defined primarily as either a significant worsening of symptoms, recurring UTI, AUR, incontinence, or invasive therapy such as surgery). The trial had the same four treatment arms as the PREDICT study and its aim was to evaluate BPH progression. Analysis of the results at 1 year showed similarities to both the Veterans Affairs and the PREDICT study. However, by 5 years the risks of AUR and the need for invasive surgery were significantly lower with combined therapy.

Over a mean follow-up of 4.5 years the rate of overall clinical progression (the primary endpoint) among men in the placebo group was 4.5 per 100 person years. Compared with placebo, doxazosin significantly reduced the risk of progression by 39% (P = 0.001) and finasteride reduced it by 34% (P = 0.002). Therefore the reduction in risk between the drugs, used as a single agent, did not differ significantly. For combined therapy the risk of overall clinical progression was reduced by 66% (P = 0.001), a significantly greater reduction than was induced by either drug alone. Equally, MTOPS showed that combined therapy and finasteride alone reduced the need for invasive therapy, with the magnitude of the reduction similar to that in previous trials with 5α-reductase inhibitors [9,10].

In contrast, treatment with doxazosin monotherapy delayed the time to AUR slightly, but over the duration of the trial...
failed to reduce the risk of AUR and invasive surgery, suggesting that the continued growth of the prostate eventually overcame the reduction in the urethral obstruction achieved by relaxing the smooth muscle in the prostate.

MTOPS shows that combined therapy provides long-lasting relief from symptoms and fewer episodes of AUR. To date, both doxazosin and finasteride have been widely used singly, but the increased benefits of combined therapy show for the first time that there is almost certainly a medical alternative to surgery for patients with BPH.

Consequently, the advent of effective medical therapies has offered the possibilities for GPs to manage patients with bothersome LUTS caused by BPH as an alternative to immediate urological referral. Treatment guidelines for urologists are available but they are not aimed at GPs [11]. The BAUS revisited its guideline of 1997 for the primary management of male LUTS to reflect this change and the manuscript is published in this issue of the BJU International [12]. The new guideline places GPs firmly in the front rank for the initial therapy of BPH.

The new guideline is for both GPs and patients, and reflects the high degree of team-working required for their implementation. This guideline will hopefully offer real practical advice to both doctors and other healthcare professionals, and the many patients suffering from symptomatic BPH.

While TURP remains the mainstay of surgical treatment for BPH, putting the findings of MTOPS into practice at a primary-care level with the BAUS guidelines may reduce the number of patients requiring surgery.

REFERENCES


COGNITIVE EFFECTS OF HORMONAL TREATMENT FOR PROSTATE CANCER

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Hormonal manipulation is a well established treatment for prostate cancer, but long-term treatment can be associated with troublesome side-effects. Recently, interest has turned to the possible adverse effects hormonal therapy may have on cognitive function.

Manipulating androgen levels is an established treatment for many gynaecological conditions. As a result the cognitive effects of LHRRH agonists in women have been well documented. There are detrimental effects on verbal memory and the capacity for new learning [1]. Although these changes were not profound enough to cause serious impairment of daily activities they were statistically significant, and in many cases were subjectively apparent to individuals. Fortunately, these adverse effects appear to be reversible with oestrogen-replacement therapy.

It would be reasonable to assume that LHRH agonists have similar effects in men. Substantial declines in testosterone levels and neuropsychological function are well acknowledged in the ageing male population [2]. Interestingly, in addition to the adverse effects on verbal memory seen in female populations, falling androgen levels have been shown to have a negative effect on visual memory and visual-spatial performance in men. Once again, treatment with exogenous androgens can reverse these changes, and has therefore been advocated in certain situations.
Although hormone manipulation for prostate cancer has been shown to cause adverse cognitive effects, a consensus on which cognitive functions are selectively affected remains outstanding. Cherrier et al. [3] reported minor effects arising from combined androgen blockade. Although testosterone levels were lower in all patients than at baseline, only a decline in spatial ability was detected. Surprisingly, they found that verbal memory scores actually improved with treatment.

In the light of findings in women, Green et al. [4] postulated that men receiving LHRH agonists would have a greater deterioration in their cognitive function than controls or those receiving cyproterone acetate. Furthermore, they suggested that memory performance would be affected more than other cognitive functions. Testosterone suppression was achieved in all patients, and this was associated with a wide range of effects on cognitive function. There were impairments of memory, attention and executive functions on patients receiving LHRH agonists. In addition to these effects, patients receiving cyproterone acetate also had an impairment in performance functions. The authors suggested that this could be related to differences in pharmacology between the drugs.

Several possibilities exist for the differences between male and female study populations. The duration of androgen suppression was shorter in patients with prostate cancer than in women, particularly in those after bilateral salpingo-oophorectomy. The possibility arises that the degree and type of cognitive effects are related to the period of treatment.

There are inherent differences in neuropsychological function between men and women; the latter excel in verbal abilities and men tend to excel in visual-spatial abilities [5]. This observation seems to be related to the influences that different androgen levels in the sexes have on brain organization during prenatal development. Oestrogen and testosterone continue to be important in adults, where they enhance areas of the brain which subserve verbal and visual-spatial functions, respectively. Therefore, their suppression during hormonal manipulation could result in the selective cognitive effects observed between the genders.

Sample sizes in many of the studies to date have been small and may contribute to some of the inconsistencies reported. Furthermore, the role of learning bias, which is inherent to such cognitive tests, cannot be ignored.

In conclusion, the adverse effects of hormonal manipulation for prostate cancer need to be appreciated. Because of their age, comorbidities and polypharmacy this group of patients is particularly susceptible to cognitive impairment. This has implications both for patients’ quality of life and treatment compliance. By acknowledging the effects which may be caused by androgen suppression we can provide patients with more information about hormone treatment. As a result they will be able to make informed decisions when faced with the prospect of long-term therapy. Further studies in this field are obviously required, both to formulate a standardized and reproducible assessment of cognitive function, and to investigate the role of other hormonal therapies. Studies in progress at our centre are examining the possible cognitive effects of bicalutamide. The results will be of interest, as bicalutamide competes with testosterone at a receptor level rather than affecting its production.

REFERENCES


EARLY REHABILITATION OF ERECTILE FUNCTION AFTER NERVE-SPARING RADICAL PROSTATECTOMY: WHAT IS THE EVIDENCE? P. GONTERO and R. KIRBY – St George’s Hospital, London, UK

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HOW MUCH DO PATIENTS WORRY ABOUT SEXUAL FUNCTION AFTER NSRP?

Comparing sexual function after normal (no nerve sparing) and NSRP, Grahnke et al. [3] reported that the latter had significantly better quality-of-life scores for both sexual and physical function. The negative effect of sexual bother on quality of life may become even more marked with a longer time after the procedure. In the study by Penson et al. [4] sexual dysfunction was an independent determinant of worse general health-related quality of life at 2 years from primary treatment for prostate cancer. However,
current reports show a closer linkage between sexual dysfunction and quality of life in patients after NSRP, making the recovery of sexual function an important issue for patients surgically treated for prostate cancer.

HAS ERECTILE REHABILITATION IMPROVED OVERALL POTENCY RATES OF NSRP SO FAR?

The proportion of men who have a complete recovery of erectile function after bilateral anatomical preservation of neurovascular bundles during NSRP remains a matter of debate, but probably is less than half overall. Differences in surgical technique, patient selection, outcome measurements and follow-up duration have been proposed to explain these discrepancies, but in almost all the reported studies there is no mention of whether the patients had undergone specific erectile rehabilitation treatment during the follow-up. However, the only series of radical RP where patients were counselled to start a pharmacological erectile treatment as early as the second month after surgery gave the best results of potency recovery at 2 years [5]. By contrast, in the study of Katz et al. [6] patients were deliberately asked not to use any erectile rehabilitation after laparoscopic RP, and despite that there was a high potency preservation rate.

As yet data on the efficacy of early postoperative erectile treatment rely on few randomized trials. In the study of Montorsi et al. [7] recovery of spontaneous erection occurred at 6 months in eight of 12 patients who self-injected with prostaglandin-E vs three of 15 who did not. More recently, 27% of 51 patients taking sildenafil at bedtime for 9 months regained potency 1 year after surgery, compared with only 4% in the control group [8]. Because the natural recovery of erectile function has been reported to take as long as 2 years [9] it is possible that the erectile rehabilitation may simply bring forward the natural ‘healing’ time of potency rather than saving patients from permanent erectile failure. Larger randomized trials with at least 2 years of follow-up are required before a definite conclusion can be drawn on the true efficacy of rehabilitative sexual therapy in this context.

IS THERE SCIENTIFIC EVIDENCE TO SUPPORT EARLY REHABILITATION OF ERECTILE FUNCTION?

Spontaneous erectile function is absent for most patients soon after NSRP, but there is a progressive return over 2 years in a variable proportion of them. This observation led to the hypothesis of the so-called ‘neuropraxia’ phenomenon, a temporary deficit of the cavernosal nerves which would abolish any form of erection. The low oxygen tensions in a constantly flaccid penis may initiate severe fibrotic changes in the cavernosal tissue. In a recent experimental model, penile tissue from rats which had undergone bilateral incision of cavernosal nerves 3 months earlier showed a significant overexpression of hypoxia-related substances like TGF-β and collagen I and III compared with the same tissue from a control group [10]. Histomorphometric studies showed that when a high proportion of trabecular smooth muscles is replaced by collagen, the caverno-occlusive mechanism is lost, with subsequent venogenic erectile dysfunction.

A penile haemodynamic study on patients after NSRP who had no pharmacological support in the initial year after surgery revealed a progressive incidence of venous leakage, varying from 14% at 4 months to 50% at >12 months [11]. Similarly, in the study of Montorsi et al. [7], eight of 15 patients who did not self-inject with alprostadil in the first 4 months after surgery had a colour Doppler diagnosis of venous leakage, compared with only two of 12 of the treatment group. These findings corroborate the hypothesis that erectile rehabilitation prevents the occurrence of vasculogenic erectile dysfunction during the process of nerve healing after NSRP.

WHAT IS CURRENTLY THE MOST EFFECTIVE REHABILITATIVE THERAPY?

The ideal treatment designed to promote the restoration of erectile function after NSRP should combine proven efficacy with acceptable tolerability. Nocturnal penile tumescence is still severely impaired 8 months after NSRP [12]. The early intake of the phosphodiesterase type 5 (PDE-5) inhibitor sildenafil at bedtime has been advocated with the aim to potentiate nocturnal erections. In the preliminary study from Padma-Nathan et al. [8] patients who regained sexual function after 9 months of treatment (27%) also had better nocturnal erections recorded a year after surgery.

Unfortunately that study did not address the prevalence of nocturnal erections over the 9 months for all the patients in the treatment arm compared with those in the placebo arm. It is possible that sildenafil and the other currently available PDE-5 inhibitors, e.g. vardenafil and tadalafil, may not be so effective in the early phase of nerve healing, as documented by the lack of clinical efficacy of sildenafil in the first 9 months after NSRP [13]. Conversely, withdrawal rates for pharmacological side-effects have been reported to be up to 20% for patients under daily sildenafil prophylaxis.

Three-monthly intracavernosal injections with prostaglandin E1 starting in the first month after surgery significantly enhanced the subsequent response to sildenafil compared with sildenafil alone started after 4 months. At the 6-month follow-up, 82% of patients in the combination arm responded to subsequent sildenafil, vs only 52% in the sildenafil-only arm [14]. Intracavernosal therapy produces a high erectile response in patients after standard (not nerve-sparing) RP and therefore it may be the treatment of choice in soon after NSRP. Similarly, the use of the vacuum constrictor device may facilitate early sexual intercourse and potentially an early return of natural erections, although no controlled study has been carried out to test this hypothesis.

CONCLUSIONS

Erectile dysfunction may significantly affect the quality of life of patients who have had NSRP, and every effort should be made to improve sexual outcomes of these procedures. The current scientific evidence supporting the early postoperative use of erectile aids is at present based mainly on indirect proof of cavernosal damage that may follow the temporary postoperative ‘erectile silence’.

Based on the few data available, either intracavernosal injections or a vacuum device should be offered as a first-line option for the first few months after the procedure, as their mechanism of action does not require intact neural tissue for erection. Thereafter sildenafil, or equivalent PDE-inhibitor therapy, may be a reasonable choice for those patients who can achieve at least a partial erection. A PDE-5 inhibitor may not be effective when
spontaneous erections are absent. Possibly, as the rehabilitation of sexual function aims to prevent cavernosal tissue damage by providing oxygenation to the erectile tissue, the choice of a potentially ineffective treatment may jeopardize the longer term results of a successful NSRP. Ultimately, while a rehabilitative treatment should probably be offered to all patients undergoing NSRP, patient counselling should reflect honestly the current level of knowledge about the potential efficacy of rehabilitative protocols.

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