Invited review

The problem of obstruction in prostate cancer

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The exact incidence of bladder outlet obstruction secondary to locally advanced prostate cancer is difficult to define, since benign prostatic hyperplasia is often concomitant in these patients. Therefore, it is not surprising that the reported incidence ranges from 18% to 72% [5, 19]. On the other hand, of all the patients presenting with bladder outlet obstruction and clinically benign prostates, depending on age and sectioning technique, 14% have tumours in the transurethral resection (TUR) specimens [17, 18].

Transurethral resection

So far the standard treatment for patients with obstructive prostate cancer has been either hormonal treatment or a channel TUR or a combination of both methods. However, there is growing concern about the possible role of TUR in the dissemination of cancer.

In 1961 Jonasson et al. [8] demonstrated the presence of tumour cells in blood samples collected from patients with incurable prostate cancer during TUR. Cancer cells were found in samples from 6 out of a total of 9 patients. However, metastasis is a complex sequence of events and it has not yet been shown that release of cancer cells into the bloodstream during any manipulation results in metastatic disease.

In 1980 McGowan [13] was the first to demonstrate a difference in survival and intervals free of disease between patients undergoing radiation therapy whose diagnosis was established by TUR and those in whom needle biopsy was performed. Patients with stage B2/C did significantly worse when diagnosed by TUR.

Hanks and coworkers [7] reported on a pattern of care study in 247 patients and found an adverse influence of TUR on distant recurrence and survival, but only in T3 and T4 tumours. Despite the fact that most of the cancers in the TUR group were poorly differentiated, while those in the needle biopsy group were mostly well differentiated, the adjusted data again showed an adverse effect of prior TUR. However, in this study the status of the pelvic lymph nodes was unknown and there was no account of obstructive voiding symptoms. Furthermore, local staging in prostate cancer is quite subjective and patients may have been understaged after the tumour was debulked by TUR.

In 1986 Forman and associates [5] studied the effect of TUR on tumour dissemination in 240 patients with localized prostate cancer who received external beam radiation therapy. Patients who had TUR had an almost two-fold higher relative risk of disease progression than those who had a needle biopsy. In the needle biopsy group, 56% of patients presented with obstructive symptoms compared with 97% of patients in the TUR group, indicating that the TUR group had more advanced disease.

Kuban et al. [10] in 1985 evaluated 169 patients who underwent either external beam radiation or interstitial iodine 125 implantation and pelvic lymphadenectomy with regard to the interval to bone metastases and found no difference between patients diagnosed by TUR and those diagnosed by needle biopsy.

Paulson and Cox [16] reported on 145 patients treated with radical prostatectomy, 33 of whom were diagnosed by TUR and 106 by needle biopsy. Both groups were similar in terms of Gleason grade and margin-positive disease. They found no significant difference between these two groups relative to time to first evidence of treatment failure.

In 1989 Mecham and colleagues [14] analysed a series of 379 patients treated with definitive radiotherapy, i.e. a combination of radioactive gold seed implantation and external beam irradiation, for localized prostate cancer. Of these patients, 71% were diagnosed by needle biopsy and 29% by TUR. All patients underwent a pelvic lymph node dissection. When the analysis was restricted either to patients with substantial obstructive voiding symptoms or to patients with negative pelvic lymph node dissection, in both cases there was no longer any significant difference between those who did or did not undergo TUR. The authors observed that patients with TUR were more likely to have positive lymph nodes than those diagnosed by

Table 1. Urinary incontinence versus pre- and/or post-radiation therapy TUR-P (1956–1984) (M. A. Bagshaw, unpublished work)

	No. of patients	No. with persistent incontinence
TUR-P	394	34* (8.6%)
No TUR-P	499	5* (1.0%)
Total	893	39 (4.4%)

TUR-P, Transurethral resection of prostate
*$P = <0.01$

needle biopsy within each clinical stage and grade. Therefore they concluded that the adverse effect of TUR on distant metastases as reported in previous studies [7, 13] resulted from the poor prognosis of tumours causing obstructive voiding symptoms rather than as a direct effect of the resection itself. Finally, the two most recent studies on this subject again showed no adverse impact of prior TUR on survival [12, 15].

Hormonal therapy

Since the early, 1940s, hormonal therapy has bee a well-established standard method for the local and systemic control of prostate cancer. In 1942 Chute et al. [3] reported on 13 patients with urinary retention from prostate cancer treated with orchiectomy and oestrogens and found that 9 (69%) improved and could void freely and thus did not require a prostatic operation. If this improvement did not occur within 2 weeks, they considered a TUR. Shrinkage of the prostate is common after endocrine treatment. In 1984 Carpentier and Schroeder [2] using transrectal ultrasound (TRUS) compared the changes in prostate size in 39 patients after orchiectomy with those in 27 patients after external beam radiotherapy. They found a statistically significant difference between the decrease of volume in the two groups at all intervals of their study. After castration approximately two-thirds of all patients had a significant decrease in prostate volume with most of the changes occurring within the first 3 months after the operation. Only 1 patients suffered local progression of the tumour. In the other group the decrease in volume was much less. Furthermore, 8 of the 27 patients treated with radiation therapy showed an early increase in prostate size due to transient oedema. In 1985 Varenhorst and Alund [19] noticed that of 749 patients with prostate cancer, 133 (18%) presented with total urinary retention at the time of diagnosis. Of this group, 122 patients received hormonal therapy either by orchiectomy, oestrogens, or anti-androgens. Eighty patients (66%) required no catheter within 6 months after the initiation of endocrine manipulation and remained so for at least another 6 months. Bladder outlet obstruction was relieved significantly faster by orchiectomy than by oestrogen therapy (mean time to relief from obstruction was 2.7 months after orchiectomy and 3.4 months after starting

oestrogen therapy), but the local response to oestrogens or anti-androgens noted after 6 months did not differ from the response to orchiectomy.

Similar results were also demonstrated by Fleischmann and Catalona [4]. They reported 35 patients with urinary retention as a result of prostate cancer. Twenty-four of these 35 patients (69%), all treated by orchiectomy alone, were relieved of bladder outlet obstruction. If a patient failed to void within 2 months, TUR was performed. Minimum follow-up was 4 months (median, 27 months). The authors also noticed that neither tumour stage nor grade correlated significantly with the response to orchiectomy.

Radiation therapy

There have only been a few reports on the topic of external beam radiation therapy as the primary mode of therapy for bladder outlet obstruction due to prostate cancer. Virtually all of these patients are first seen by urologists who perform a TUR and/or initiate some kind of hormonal therapy.

In 1979 Gibbons et al. [6] evaluated the local clinical control of 209 patients with stage C prostate cancer treated with definitive external radiation therapy. The diagnosis was established by transperineal needle biopsy in 129 patients and by open or transurethral prostatectomy in 80 patients. In the needle biopsy group obstructive symptoms improved in 90% of the patients and they did not require a subsequent TUR. However, the degree of bladder outlet obstruction before the initiation of radiotherapy was not defined and thus it is questionable how may patients would have faced severe voiding problems at all. If transurethral resection was necessary after radiation therapy it was technically more difficult, but the morbidity was not significantly increased. The authors found an 8% post-irradiation stricture rate, which was independent of the type of diagnosis, i.e. needle biopsy versus prostatectomy. In summary, 174 of the 209 patients (83%) did not have any urinary complaints after external beam radiation therapy. According to Bagshaw (M. A. Bagshaw, personal communication 1990), about 90% of patients with stage C disease and obstructive symptoms will benefit locally from external beam radiation therapy. Voiding function usually improves near the end of treatment or shortly afterwards. To avoid total urinary retention secondary to transient oedema after radiation therapy (2,000 cGy), the placement of a percutaneous suprapubic tube is preferable for those who need temporary diversion.

The best results with regard to local control after radiation therapy are achieved in patients with stage A cancer [1]. Ten years after irradiation, over 90% of the patients have no progression as determined by digital rectal examination and no local symptoms necessitating therapeutic intervention. However, in general there was a significantly higher incidence of urinary incontinence if a TUR was performed either prior to or after radiotherapy, as shown in Table 1 (M. A. Bagshaw, unpublished work).

Table 2. Summary

	Transurethral resection (TUR)	Hormonal therapy	Radiation therapy
Efficacy with regard to relief of bladder outlet obstruction	– very good	– 69% [3] – 66% within 6 months [19] – 69% within 2 months [4]	– 83% [6] – 90%[a] – 88% (after hormonal therapy ± TUR), 44% after 11 months [11]
Advantages	– Repeatable	– Applicable for non-surgical candidates – Medical or surgical treatment options – Better results than with radiation therapy [2]	– Applicable for non-surgical candidates
Disadvantages	– Incontinence in combination with radiation therapy 8.6%[b] – General complications of TUR (bleeding, strictures, anaesthesia) – Hospitalization	– Impotence in 50–100% – Other sideeffects (hot flushes, GI, rash, depression)	– Incontinence in combination with radiation therapy 8.6%[b] – Strictures 8% [6] – General side effects (cystitis, proctitis) – Impotence 50–70% – Transient oedema during radiation therapy
Comments	Dissemination of cancer by TUR? [5, 7, 13] Better studies reject this hypothesis [10, 12, 14–16]	Early hormonal therapy seems to be superior to late therapy in advanced disease [9] and thus will be first-line treatment anyway	If a subsequent TUR is necessary, it is techniqually more difficult

[a] M. A. Bagshaw, personal communication, 1990; [b] M. A. Bagshaw, unpublished work

In 1990 Kynaston and coworkers [11] reported on 26 patients who received local palliative radiotherapy for recurrent bledding and/or bladder outlet obstruction. All of the patients had previously been treated by hormonal manipulation and 65% of the patients had undergone TUR at least once. Of the 17 patients with voiding dysfunction, symptoms improved in 15 (88%) and remained so in 8 of them at 11 months.

Clinical recommendations

The issue as to whether hormonal therapy should be initiated early or late in patients with advanced prostate cancer has been controversial for a long time. However, recent data as well as a re-evaluation of the two VACURG studies are strongly supportive of early hormonal therapy [9]. This observation partly resolves the dilemma of how to treat patients with bladder outlet obstruction! It is now only logical to take endocrine therapy as a first-line treatment. About two-thirds of all patients presenting with obstruction will benefit (Table 2). Furthermore, an unknown number of patients will never experience obstruction at all. For those patients in whom endocrine treatment fails with regard to voiding problems and for those who refuse to undergo hormonal manipulation, e.g. because they wish to retain potency, we recommend transurethral resection. The majority of studies, in particular the more carefully designed ones, clearly reject the hypothesis of cancer dissemiantion (Table 2). Furthermore, TUR can be repeated. We are not infavour of
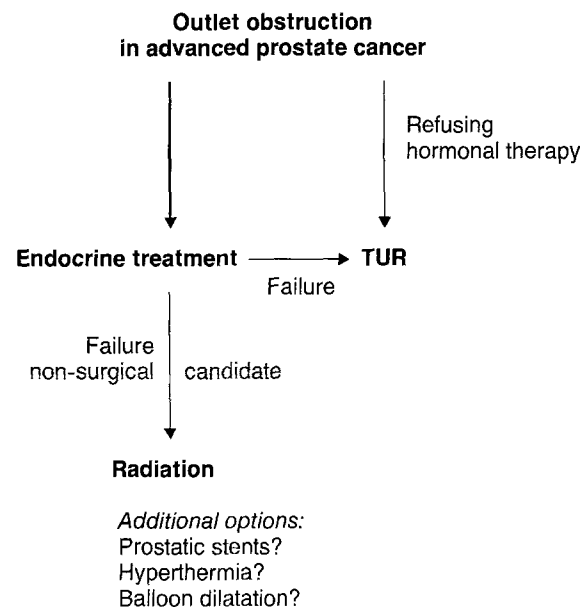
Outlet obstruction in advanced prostate cancer

Fig. 1. Algorithm for treatment

radiation therapy, mainly because of the many side-effects (Table 2).

New modalities for the treatment of benign prostatic hyperplasia have been described in the past few years (hyperthermia, prostatic stents, intraurethral balloon dilatation). However, no study to date has been undertaken on prostate cancer.

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