Advances in radiotherapy: Ensuring balance in the discussion

Gorayski, Pinkham and Lehman have written an excellent article on the advances in radiotherapy for prostate cancer (*AFP* September 2015).[1] Emphasising the relative equivalence of treatment in older men is important so that patients can be well informed. However, there were some issues that needed to be clarified because the side effects tend to be under-reported.[2]

Neo-adjuvant androgen deprivation therapy (ADT) is commonly given for about six months in patients with low-risk disease and up to two years in patients with high-risk disease.[3] This means that erectile dysfunction (ED) and other associated side effects of ADT can occur early. The original article perpetuates the idea that ED is a late side effect of external beam radiotherapy (EBRT), but this is not entirely correct. Patients and general practitioners (GPs) should be aware that the impact of ED and other associated side effects of ADT is significant. This is accepting that surgery also has a significant impact on ED, but without the additional side effects of ADT.

The incidence of urinary toxicity has reduced with improved techniques as outlined in the article, but remains a source of morbidity in up to 24% of patients.[4] This includes dysuria, frequency and haematuria. Late invasive bladder cancer can also occur years after EBRT, and the protocols for monitoring this are unclear.[5]

Anorectal dysfunction has a considerable impact on quality of life and continues to five years and beyond.[6] This issue may be positively impacted upon by using hydrogel (to distance the prostate from the rectal wall), an advance over the past two years that was not mentioned in the article.[7,8]

Surgery and EBRT both have a place in the management of prostate cancer with curative intent. Additionally, positive margin disease after surgery does benefit from lower dose adjuvant EBRT with fewer side effects than primary EBRT.[9] Conversely, undertaking surgery after EBRT is fraught with significant side effects.

GPs need to encourage patients to seek both a surgical and radiation oncology opinion. They should at least have their case discussed at a multidisciplinary uro-oncology meeting before deciding on the best option for them, on the basis of accurate and relevant information. It is accepted that making such a decision is easier for some and harder for others.

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Reply

We thank Rashid, Liu and Pirpiris for their comments regarding our publication on technological advances in radiotherapy for localised prostate cancer.

The potential side effects and impact on quality of life are understandably important considerations for any man evaluating treatment options. In our experience, moderate or severe urinary toxicity, or anorectal dysfunction, are rare complications following radiotherapy using modern techniques. Data quantifying these risks were stated in our paper[1] and corroborated by another recently reported modern Australian series.[2] The two studies cited by Rashid et al on this matter are both based on analyses of men predominantly treated using old-generation technology that is of limited relevance to men treated today.

We agree with the authors that hydrogel spacer insertion is a promising development that may enable additional reductions in late rectal radiotherapy-related toxicity in the future. We did not mention its use in our article because it does not currently represent the standard of care. Evidence of long-term benefits is lacking; thus, the risks and expense of an additional invasive procedure may not be justified in all men. Although such products can increase separation between the anterior rectal wall and prostate at the level of the gland, the seminal vesicles typically remain in close relation to the rectum above and are

included within the treatment volume in certain situations. Men who undergo hydrogel insertion prior to radiotherapy planning usually also require magnetic resonance imaging (MRI) of the pelvis to guide target delineation, which is not funded by Medicare for this indication.

Erectile dysfunction is a well-recognised, early onset side effect of androgen deprivation therapy (ADT). Contrary to what is stated by Rashid et al, ADT should not be given to all men prior to radiotherapy. Current Australian guidelines recommend that ADT be considered for men with unfavourable intermediate-risk and high-risk disease only.[3] These risk groups have been shown to benefit the most from ADT.[4] This was summarised in Table 1 of our article. As with all management approaches, the decision to use ADT should be individualised, having discussed the expected benefits and risks with the patient.

Radiotherapy is associated with an increased risk of bladder and rectal cancers manifesting many years later. The absolute risk is very small and patients should receive appropriate counselling so they understand this in an appropriate context. Given the older age of many men diagnosed with prostate cancer, this is not usually a source of significant clinical concern. In an analysis of a national cancer registry in the US of more than 500,000 men diagnosed with prostate cancer between 1973 and 2005, bladder cancer was subsequently diagnosed in 1.48% of men treated with radiotherapy and 1.09% of men treated surgically.[5] Given such low incidences, surveillance protocols are not warranted. Instead, we recommend that men presenting to their general practitioner (GP) with new red flag symptoms (eg haematuria or an altered bowel habit) undergo suitable investigations in the usual manner.

In general, we believe that appropriately selected individuals are best treated with a single modality (either surgery or radiotherapy, rather than both) when possible. This avoids unnecessary exposure to the potential risks and toxicities of multiple treatments. Although Rashid et al stated that surgery followed by adjuvant radiotherapy results in fewer side effects than definitive radiotherapy alone, this cannot be known because the two modalities have never been successfully compared in a randomised trial. The study they cited[6] was a secondary analysis of quality of life in men with high-risk histopathological features after surgery, comparing those randomised to adjuvant radiotherapy versus observation. An important message for GPs is that a meta-analysis of three randomised trials, including this one, demonstrated that adjuvant radiotherapy in this setting improves cancer-specific survival and overall survival at 10 years.[7]

Given that adjuvant radiotherapy can lead to additional side effects after surgery, whether it can be deferred or delayed in carefully monitored individuals is now the focus of a large Australian randomised trial (ClinicalTrials.gov identifier NCT00860652). The question of surgical salvage after radical radiotherapy for localised recurrence is an extremely rare clinical situation. If disease does recur, it is much more likely to be beyond the pelvis irrespective of the initial treatment modality employed.

Discussing treatment options between doctors within a multidisciplinary cancer service is important, but should not substitute for a one-on-one consultation between the patient and his specialists when clinical equipoise exists. The letter by Rashid et al illustrates some of the variability in information and opinions that men may receive about radiotherapy for prostate cancer from other sources. Men should have the opportunity to discuss treatment options with both a urologist and a radiation oncologist because they are the most appropriate experts to describe the relative benefits, risks, practicalities and costs of the treatment that they can provide. We recognise the important role that GPs also play in this decision-making process and their need for succinct, accurate and up-to-date information.

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Letters to the editor

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