Primary Radical Therapy Selection in High-risk Non-metastatic Prostate Cancer

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Abstract

As the incidence of prostate cancer rises, the detection and management of men with high-risk non-metastatic prostate cancer is becoming increasingly important. The benefits of radical treatment have been clearly shown in this group from a number of publications. The current mainstays of treatment are radical prostatectomy (with selective use of adjuvant radiation) and radical radiotherapy with concurrent androgen deprivation. The outcomes from these two approaches seem to be remarkably similar and are considered equally valid options for primary treatment. The choice of therapy is critically dependent on a number of factors, but ultimately left to the decision of the patients with advice from clinicians. Clinicians themselves, however, are known to be biased towards their particular skill set and experiences. Attempts at randomised comparisons between these two modalities have so far failed and are confounded by patient—clinician bias, the continual advances in therapy as well as the long natural history of the disease. In the lack of level 1 comparable evidence, this article explores the existing literature as to the key factors that should be considered in radical treatment selection for high-risk prostate cancer. These factors include disease aggressiveness, comorbidity and life expectancy, functional outcomes and the consequences of therapy failure with regards to salvage treatment. We propose that these factors may be useful in developing a decision guide for rationale radical therapy selection in the light of two apparently equally effective treatments. Ultimately, however, there is an urgent need for added clinical and biological markers that can provide a more precise approach to therapy selection.

Key words: Decision algorithm; high risk; prostate cancer; radical prostatectomy; radical radiotherapy; rational therapy selection

Statement of Search Strategies Used and Sources of Information

This overview was written based on a search of the literature pertaining to radical therapy for high-risk prostate cancer. The primary search was through PubMed and other articles were sourced from related papers or from primary research conducted by the authors.

Introduction

The management of high-risk non-metastatic prostate cancer (HR-PC) remains a major clinical conundrum for clinicians and patients. It does, however, have the best evidence base for survival benefit from radical therapy [1]. Using data from the Swedish Cancer Registry, Rider et al. [2] recently showed that in men with non-metastatic disease managed with non-curative intent, only those with high-risk disease had a greater risk of death from prostate cancer compared with other causes of death over a follow-up of 15 years.

There is an ongoing debate as to the best primary radical therapy for HR-PC. The main therapy options are between radical prostatectomy or radical radiotherapy [3]. It is also widely accepted that multimodality therapy is the standard...
Incidence

HR-PC, as defined by National Institute of Health and Care Excellence (NICE) and D’Amico criteria, covers a wide spectrum and most published studies do not distinguish between high-risk localised (organ confined) and high-risk locally advanced (≥T3) but non-metastatic disease [14,15]. Many surgical series have a majority of the former, whereas radical radiotherapy series have a majority of the latter in their published cohorts. Recent work has attempted to redefine the criteria and introduce further sub-stratifications of risk, but these have as yet not entered widespread clinical or guideline use. The principal differences are sub-stratification of low-risk disease and identifications of a high- and very high-risk group [16]. Based on the original D’Amico criteria, the incidence of HR-PC has been shown to be about a quarter of all new prostate cancer diagnoses. From US data, Meng et al. [17] reported a 26% incidence in the CAPSURE database and Abdullah et al. [10] reported a 33% incidence in the SEER registry. Data from the UK have shown that HR-PC accounts for about 39% of all presentations and 22% of men aged 50–69 years referred by general practitioners to tertiary clinics [18]. Analysis of trends over time has also shown significant increases in HR-PC in line with the increasing numbers of men diagnosed with prostate cancer [19]. In UK radical treatment series, HR-PC accounts for 17–19% of radical radiotherapy-treated men and 10–13% of surgically treated men [20,21]. HR-PC is thus a significant and growing demographic of men diagnosed with prostate cancer.

Outcomes from Radical Therapy

Data from radical prostatectomy and radical radiotherapy series are hard to compare because of the essentially different therapy types and outcome measures. Moreover, there will be inherent errors in grade and stage assignment, as radical radiotherapy can only rely on biopsy findings and pretherapy imaging for risk stratification. Radical radiotherapy outcomes can also only be properly assessed after the completion of long courses of concurrent ADT, which is the current gold standard in the treatment of HR-PC [4]. The earliest measurable end point is the incidence of biochemical relapse, but this is acknowledged as a poor surrogate of eventual disease progression and death from prostate cancer [22,23]. Prostate cancer mortality is arguably the most robust clinical end point and certainly the most important outcome for patients and clinicians. Available long-term data show very encouraging cancerspecific mortality (CSM) from either radical therapy. In high-risk surgical series, Hsu et al. [24] reported a 10 year cancer-specific survival (CSS) of 91%. In a multicentre European collaborative study of 712 men with presenting prostate-specific antigen (PSA) >20, the overall CSS was 89.8% at 5 years and 85% at 10 years [25]. In radical radiotherapy series, D’Amico et al. [26] have reported 88% overall survival in men with high-risk disease. Widmark et al. [27] reported a 10 year CSS of 88% and progression-free survival of 74%. Most recently, the NCIC CTG/MRC PR07 trial reported a 7 year CSS and progression-free survival rates of 90 and 84%, respectively [28].

There are no prospective randomised controlled trials that have compared radical radiotherapy and radical prostatectomy in high-risk men. Therefore, the only available data come from institutional- or population-based retrospective studies and these have been previously reviewed [29]. Inevitably there are inherent significant differences in patient selection, tumour characteristics and treatment regimens necessitating statistical corrections to make the groups more comparable [8,10,30,31]. In the paper by Zelefsky et al. [32], which reported better outcomes from surgery, the radical radiotherapy group had over twice as many high-risk cases and significantly higher numbers of men with locally advanced disease. Both the median presenting PSA and age were also higher in the radical radiotherapy group. In the recently published Prostate Cancer Outcome Study (PCOS) there were significant differences in age, comorbidity and distribution of high-risk cancers
favouring radical prostatectomy [33]. Radical prostatectomy still appeared to have a survival benefit after correcting for these, although the authors acknowledged the possibility of undocumented confounding factors. As a result of these cohort differences, many studies use propensity scoring to balance the groups and achieve comparability. However, propensity scoring does have limitations and cannot account for undocumented variables or inherent patient selection biases (e.g. suspected lymph node-positive disease precluding selection for surgery) [34,35]. Moreover, most published radical radiotherapy cohorts do not have all men treated with concurrent ADT, which is the current recommendation for high-risk disease [4,5]. Indeed this is a major limitation of almost all studies to date in that radical radiotherapy delivery and regimens are evolving rapidly over time and many men would have been previously undertreated by current radical radiotherapy standards. Within the context of these issues and limitations, published studies have reported mixed results. Sooriakumaran et al. [8] published one of the largest comparative studies using a Swedish cancer registry with up to a 15 year follow-up. In this study of 35 000 men, the most encouraging finding was an overall CSM rate of only 3% from radical therapy. In the high-risk non-metastatic group, the CSM from radical prostatectomy was 4.5% versus 8.3% from radical radiotherapy. Notably, in this study, men who had initial ADT were censured from inclusion in this study and this may possibly have excluded men who went on to have subsequent combination treatment with ADT and radical radiotherapy. Very few studies have focused exclusively on comparing outcomes in HR-PC. One exception is the paper by Boorjian et al. [9], which compared 1847 men with high-risk disease treated by radical prostatectomy or radical radiotherapy (half with combined ADT). This study found no difference in the 10 year CSS or progression-free survival between radical prostatectomy- or radical radiotherapy-treated men.

Factors that Influence Radical Therapy Choice and Outcome

Given the close parity in cancer-related mortality between treatments, other factors become very important in selecting therapy. A particularly important aspect is the relative risks of death from prostate cancer versus other-cause mortalities. Natural history studies by Albertson et al. [1] and Rider et al. [2] have shown that the benefits of treatment in reducing prostate cancer mortality are most apparent in men in whom the risk of death from malignancy exceeds that of other causes. This is also relevant when considering the differences in quality of life (QOL) from each therapy. Evidence from long-term studies has suggested more debilitating and prolonged side-effects from radical prostatectomy compared with radical radiotherapy [36]. Equally, the impact on QOL of prolonged courses of ADT can be considerable. A proportion of men treated by radical prostatectomy or radical radiotherapy will also fail treatment, in this context the effectiveness and toxicity of salvage options also need to be considered in the early primary treatment decision-making process. Thus, the choice of therapy for an individual (in addition to cancer outcomes) arguably needs to consider the life expectancy, other comorbidities, disease aggressiveness, functional outcomes and the consequences of radical treatment failure. Indeed the paradigm needs to move from the competitive comparison of radical prostatectomy and radical radiotherapy to a more rational discussion on personalised recommendations of treatment choice based on both patient and tumour characteristics. Below we consider the key factors that may influence the treatment decision process. For the purposes of this review, a broad PubMed search was conducted using the MeSH headings ‘prostate neoplasms, high risk, localised, locally advanced, radical radiotherapy, radical prostatectomy, outcome, comorbidity, salvage therapy, age and comorbidity’. The search was limited to papers in English and in humans from 1995 to July 2014. Abstracts were assessed for initial eligibility before full papers were extracted and re-reviewed for content and subject suitability. Any further papers of relevance were also identified from referenced work within extracted papers. Localised disease in this review refers to primary non-metastatic disease both organ confined and locally advanced.

Disease Aggressiveness

A key criticism of comparative studies between radical prostatectomy and radical radiotherapy is the differences in the cohorts with regards to the definition of high-risk disease. Current definitions of high-risk disease encompass any PSA ≥20, any grades ≥8 and any stage ≥ T2c [15]. The discrepancy between clinical, radiological and pathological assessment has made the comparison of disease stage between treatment cohorts particularly difficult. The true pathological stage is only ever known after radical prostatectomy, whereas conversely very obvious clinical and radiological advanced stage at presentation may reduce enthusiasm for surgery. Not surprisingly, therefore, radical radiotherapy series have typically included significant numbers of men with high volume tumours (T3b and T4) and high PSA values [27], whereas in radical prostatectomy series, most tumours will be defined as high-risk based mainly on grade (Gleason 8–10). As an example in the comparative study by Zelefsky et al. [32] the radical radiotherapy cohort had 41 T3b cases versus one in the radical prostatectomy group and over three times as many Gleason 8 patients. In the EMPACT collaborative study, which focused on radical prostatectomy-treated high-risk men, the median PSA was only 8 and there were no T4 cases [37]. In contrast, in a study by Bolla et al. [38] of radical radiotherapy, 9% of men had T4 disease and 50% had a PSA > 20. Modern preoperative imaging by multiparametric magnetic resonance imaging is becoming ever more sophisticated in defining disease stage [39,40]. However, its impact, together with better biopsy techniques, on treatment selection trends remains to be determined [41]. However, it is likely that in future it will allow a better comparison of outcomes
between cohorts because of a more balanced pretherapy assessment of disease stage and risk stratification. This might also reduce the incidence of disease up- and down-staging, which have been reported from radical prostatectomy series in men with apparent clinical T3 disease at presentation [42,43]. Of note, these studies (although not comparing with radical radiotherapy) have shown encouraging results from radical prostatectomy as a monomodality therapy for initial T3 disease [42,43]. Nevertheless, although in localised disease the evidence base for radical radiotherapy and radical prostatectomy may arguably show equivalence of outcomes, the same cannot currently be said of locally advanced disease because of the paucity of good-quality radical prostatectomy data that in the main have come from single institution case series.

Studies in both radical prostatectomy and radical radiotherapy cohorts have shown more adverse outcomes in the presence of more than one high-risk feature. Spahn et al. [25] examined outcomes from radical prostatectomy in men with a presenting PSA > 20 ng/ml. CSM was progressively increased in men who had combinations of a high PSA and/or high-grade and high-stage disease. These results were further validated in a larger cohort of radical prostatectomy-treated men [44]. Sundi et al. [45] recently published outcomes from radical prostatectomy in 753 men with HR-PC. Using sequential permutation modelling they identified the presence of multiple high-risk features as a key predictor of a worse outcome from surgery. Studies in external beam radiotherapy cohorts have similarly identified a strong adverse outcome association with combinations of high-risk features and outcome. Tsai et al. [46] looked at the effect of combinations of a PSA ≥ 10, Gleason sum of 8–10 or stage of T2b or T2c in a cohort of 3240 treated with radical radiotherapy. Men with all three factors fared the worse, with a nearly 10-fold greater risk of CSM compared with men with only one factor. These data suggest that the number of high-risk factors plays an important role in determining outcome from radical therapy. The effects, however, are not clearly additive and may have significant interactions with other variables, such as comorbidity. Nevertheless the population with more than one high-risk factor arguably benefits most from aggressive multimodal combination therapy.

### Life Expectancy

The natural history of prostate cancer is such that long follow-ups are needed to realise the true incidence of CSM and overall mortality. In low- and intermediate-risk disease, follow-ups in excess of 15 years are needed to establish benefit [1,2]. In high-risk disease, these timescales are shorter but still need to be at least a decade for reliable interpretation with sufficient events. It is thus reasonable to consider that radical therapy might be most beneficial in men with the longest life expectancy. This seems to be borne out in large cohort studies. The study by Rider et al. [2] of non-curatively treated men showed that it was only younger and fitter men (with longer life expectancy) with high-risk disease who had a risk of CSM that equalled or exceeded other causes of mortality. In the same observational population cohort, but focusing on radical therapy, Sooriakumaran et al. [8] found that the benefit of radical prostatectomy over radical radiotherapy was most apparent in younger men (<64 years) with more aggressive disease. Within the context of surgery, Briganti et al. [47] published life tables on the mortality outcomes of radical prostatectomy in high-risk disease. In this work, CSM again only exceeded other-cause mortality in younger men (<59 years).

A further consideration with regards to therapy choice is the theoretical possibility of a delayed second cancer from radical radiotherapy. The 2014 UK NICE guidelines have reviewed the risk of a secondary bowel cancer and found no robust evidence of an increase in colonic cancers, but an increased risk of rectal cancers (relative risk of 1.2) [14]. The estimated risk is that 1000 men needed to be treated and followed up for 10 years to detect an additional two cancers [14,48]. Thus, life expectancy after treatment is a key factor to consider in the context of radical radiotherapy delivery. Taken together it is reasonable to suggest that radical prostatectomy may be the preferred radical therapy option for younger men with high-risk disease. Indeed, this seems to be the opinion of both urologists and oncologists in a UK survey of practice [13]. Absolute age is probably not a good standalone surrogate marker for life expectancy. The UK Office of National Statistics estimates the life expectancy of a UK male at 79 years. However, if a man reaches the age of 65 years then he can expect to live for an average of 18 years depending on other comorbidities.

#### Comorbidity

Intimately linked to life expectancy is an individual’s general fitness. By the nature of the age group of men who present with prostate cancer, many will have other competing comorbidities. The issue of comorbidity and treatment has been widely covered in the literature. Elegant studies by Albertson et al. [1], among others, have shown that the risks of other-cause mortality is greater than CSM in all patient groups other than in high-risk and metastatic disease [1,2,49]. Therefore, comorbidity scoring may be an important tool in discriminating men who would benefit most from radical treatment. The most widely used scoring system is the Charlson Co-morbidity Index (CCI), which includes 19 health domains and weighted on their association with death [50]. In the population-based Swedish cohort study, CCI was a strong independent factor predicting all-cause mortality versus CSM in all age and risk groups, including the high-risk population [2]. In a study of 1482 men with non-metastatic disease, Daskivich et al. [49] reported a stepwise increase in all-cause mortality rates with a progressively higher CCI score ranging from 17 to 74%. In contrast, prostate CSM by risk only varied between 0.4 and 8.0%, suggesting that CCI was a stronger overall predictor of risk of death. These data and many other population-based studies strongly implicate comorbidity as a key factor to consider when deciding management and selecting treatment, even in high-risk disease. Evidence for
this is further reinforced by data from the EMPACT collaborators in Europe [47]. In this study, the 10 year CSM for a radical prostatectomy-treated cohort of 3828 high-risk men was only 5.9% at 10 years compared with an other-cause mortality rate of 14.3%. Indeed, CSM was only greater than other-cause mortality in men aged \( \leq 59 \) years and with a CCI of 0. This study did not assess the impact of CCI on radical radiotherapy-treated men and we have not been able to identify comparable studies looking specifically at the impact of comorbidity on radiotherapy outcomes. Notably though, many studies have shown that men having radical radiotherapy generally have much more comorbidity than in radical prostatectomy series [8,31,33,51].

**Functional Outcomes**

The anatomical position of the prostate inevitably means that radical treatment carries the risk of collateral damage to important structures involved in urinary, sexual and bowel function. This risk is one of the main drivers behind the concept of focal therapy [52]. Radical treatment of HR-PC will probably cause functional debility as treatment fields are wider; in radical prostatectomy a non-nerve-sparing approach and in radical radiotherapy wider radiation fields. The effects of radical radiotherapy are also increased if pelvic lymph nodes are in the treatment volume or higher local doses are used. The concurrent use of ADT in radical radiotherapy can further affect sexual function as well as general vitality during and for some time after the planned duration of therapy [27,53]. There are also cardiovascular risks associated with ADT use that must be taken into account, particularly if given over a prolonged period [54,55]. With very comparable oncological outcomes between the two treatments, the functional results of each are critically important factors to patients in decision making. A limitation in assessing outcomes between treatments is the variability in the assessment tools used [56]. A few long-term studies have used common measurement tools to assess the effect on QOL and function. Sanda et al. [57] reported QOL and functional outcomes in 1201 radical prostatectomy and radical radiotherapy-treated men. This study focused on T2 disease and only 7% of men had high-risk features. In this study, sexual and urinary function were more adversely affected by surgery, whereas bowel function was more affected by radical radiotherapy. These effects did improve over the 24 months of review, although only urinary symptoms in radical radiotherapy-treated men returned to baseline levels. Sexual function in radical radiotherapy-treated men was also only significantly affected in those who had concurrent ADT. Ferrer et al. [58] studied the functional impact in 614 men treated by radical prostatectomy, radical radiotherapy or brachytherapy. Using EPIC scores, they found that men who had radical prostatectomy had the worse sexual and urinary scores and this effect persisted for up to 2 years after treatment. The largest and longest study to look at functional outcomes is the PCOS, which ran from 1994 to 2010 [36]. This study again showed that men treated by radical prostatectomy had significantly greater and more prolonged deteriorations in urinary and sexual dysfunction scores. However, bowel dysfunction was more likely in the radical radiotherapy group. These effects were apparent for the whole cohort as well as in those with normal baseline functions before treatment. Men who had radical prostatectomy were five times more likely to have urinary incontinence and twice as likely to have erectile dysfunction compared with radical radiotherapy-treated men. The study also showed that after 5 years the differences between groups began to narrow, but they never returned to baseline and instead progressively deteriorated slowly with time. Given the age groups that were treated, age and general debility were probably the causes of this approximation. Analysis of the absolute functional scores sheds interesting light on the functional consequences over time. In the PCOS study, urinary and sexual function deteriorated by 50 and 70%, respectively, in the radical prostatectomy group in the first year. In contrast, these figures were 8 and 40%, respectively, after radical radiotherapy. However, bowel function in the radical radiotherapy group only declined by about 20% in this time period.

Recent studies in the modern treatment era have also shown similar results. Katz et al. [59] compared QOL and functional outcomes between stereotactic body radiation and radical prostatectomy. Over a 36 month follow-up, radical prostatectomy showed significantly worse urinary and sexual function outcomes compared with radical radiotherapy and this was sustained throughout the study period. Bowel dysfunction, while initially worse in the radical radiotherapy group, was not significantly different to radical prostatectomy-treated men by 12 months. A contemporary series including men treated by robotic prostatectomy was reported by Van Tol-Geerdink et al. [60]. In this study, surgery was again found to have a greater adverse effect on urinary and sexual function compared with radical radiotherapy or brachytherapy. There was no difference in the bowel function domain between the three treatments, although cohort numbers were relatively small. Taken together, these data suggest that the impact on urinary and sexual function is apparently worse after radical prostatectomy than from radical radiotherapy. Bowel-related toxicity is a principal drawback of radical radiotherapy, but symptom score data from a number of studies suggest that it is not as bothersome to men compared with urinary and sexual dysfunction [36,59,60]. Bowel-related toxicity is also less bothersome with the evolution of more precise radiotherapy delivery. Modern image-guided radiotherapy and intensity-modulated radiotherapy, for instance, are designed to significantly reduce the risk of rectal toxicity [61]. The risk of secondary malignancies from radiotherapy has already been discussed above. In the context of high-risk disease, the effect of ADT given during radical radiotherapy is also important and has been shown to worsen functional outcomes as well as vitality scores [57]. Thus, although radical radiotherapy would seem to be more favourable than radical prostatectomy in terms of functional outcomes, there needs to be focused studies that explore the added effect of ADT both during treatment and after in this cohort of men. In parallel with this the effect of
adjuvant radical radiotherapy after radical prostatectomy on QOL and functional outcomes remains largely unmeasured and also needs more focused research.

**Salvage Therapy in Radical Therapy Failure and Related Morbidity**

HR-PC has the greater risk of primary radical therapy failure [62–65]. In radical radiotherapy when failure is local, salvage therapy is an important consideration for many men. Salvage therapy after radical radiotherapy is a complex area because of the variety of options available, including surgery, high-intensity focused ultrasound, cryotherapy or brachytherapy. All, however, are associated with significant risks of morbidity and adverse impact on QOL [66–68]. Incontinence rates are as high as 50%, while erectile dysfunction is almost universal [66]. The risk of major complications is also high, with fistula rates of up to 3% in some series [69]. The success rate of salvage therapy in eradicating residual disease is also mixed, with failure rates of about 50% regardless of treatment type and there is no good evidence of superiority of one modality over another [70,71]. The best outcomes from salvage therapy are in men who had low-to-intermediate-risk disease at the outset [72]. However, men with high-risk disease do not do well in this context, with much higher relapse rates after salvage therapy. When surgery fails, adjuvant radiotherapy has been shown to reduce biochemical relapse rates, but the benefit on CSM is debatable [73–75]. The place of salvage radical radiotherapy timing and concurrent ADT in this setting is also unclear and currently being explored through the UK RADICALS trial [76]. The addition of adjuvant radical radiotherapy to postsurgical men also carries the risk of side-effects from both treatments and is relatively poorly understood. Nevertheless, the option to have radical radiotherapy if surgery fails is an attractive pathway for many patients deciding on the initial primary treatment. Although the prospect of therapy failure and salvage is difficult to predict when choosing first treatment, it is a factor that should be considered in the general discussions with a patient, as is the possibility of requiring life-long ADT.

**Summary and a Proposed Approach to Treatment Selection**

It is clear that other factors apart from tumour characteristics have an important role in the decision-making process on primary radical therapy in HR-PC. There is compelling evidence that some of these factors, such as life expectancy and comorbidity, should already be taken into consideration when deciding on the best primary radical therapy. Other factors, such as functional outcomes and the potential need for salvage therapy, are more subjective and will depend on an individual’s personal perspective and priorities. The role of multiples of risk factors on treatment selection remains undefined and is worthy of focused research, particularly with regards to the precise sequencing of multimodality treatment.

There are currently no validated molecular/tissue biomarkers or clinicopathological variables to aid better prediction of outcome from radical radiotherapy or radical prostatectomy [11]. Contemporary risk models are also good at predicting outcome, but not therapy discrimination [15,77,78]. There is, therefore, an urgent need to prioritise research in this area to better inform the biological response to an individual therapy and to test their use in combination with current clinical risk models. The current state of biomarker research in this area and proposals for how this might be undertaken in the context of therapy selection has been recently reviewed elsewhere [11,12]. One exciting initiative in how genetic profiling may help guide radical therapy is the multicentre UK RAPPER study, which is seeking to determine if DNA polymorphisms can predict the extent and severity of radiation toxicity. *A priori* knowledge of an individual’s risk of toxicity may help guide radical radiotherapy planning and dosimetry and also, in the context of radical prostate therapy, help to select men who might have a better side-effect profile from surgery [79]. Data from studies of this nature and from biomarker research may in future to contribute to an individualised molecular profile used at diagnosis to help to select the best radical therapy option.

Presently, the clinical evidence from the published literature remains all that is available for clinicians to guide patients in the decision-making process. It is recognised, however, that the quality of this evidence, especially in the UK, is not strong, particularly with the lack of randomised controlled trials. In this context the current UK National...

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**Fig 1.** Proposed algorithm for radical treatment selection in prostate cancer (CI, co-morbidity index; LE, life expectancy; RP, radical prostatectomy; RT, radical radiotherapy).
Prostate Cancer Audit is seeking to collect robust data on the treatments and outcome of men with prostate cancer over a 5 year period [80]. Although the remit is wide, there will be a focus on the uptake of radical treatment, use of multimodal therapy, QOL measures and long-term survival. These data will provide valuable insight into real-life practice in the UK and allow comparisons of treatments across different outcome domains. The results from this work and other treatment studies, including ProtecT, are eagerly anticipated [81]. Until then, the current body of evidence may be useful in developing rational approaches to radical therapy selection when counselling patients. We propose one such approach in an algorithm (Figure 1). Ultimately, the patient’s decision will be a personal one, after an in-depth discussion with the clinician. However, in future it is almost certain that therapy selection in HR-PC and indeed prostate cancer as a whole will be guided by both molecular characterisation as well as a patient’s specific clinical context in the setting of personalised medicine.

References


