RADIATION ONCOLOGY—ORIGINAL ARTICLE

Long-term decision regret after post-prostatectomy image-guided intensity-modulated radiotherapy

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Conflict of interest: We disclose no conflicts of interest.

Submitted 11 June 2016; accepted 17 July 2016.

doi:10.1111/1754-9485.12508

Abstract

Introduction: Decision regret (DR) may occur when a patient believes their outcome would have been better if they had decided differently about their management. Although some studies investigate DR after treatment for localised prostate cancer, none report DR in patients undergoing surgery and post-prostatectomy radiotherapy. We evaluated DR in this group of patients overall, and for specific components of therapy.
Methods: We surveyed 83 patients, with minimum 5 years follow-up, treated with radical prostatectomy (RP) and post-prostatectomy image-guided intensity-modulated radiotherapy (IG-IMRT) to 64–66 Gy following www.EviQ.org.au protocols. A validated questionnaire identified DR if men either indicated that they would have been better off had they chosen another treatment, or they wished they could change their mind about treatment.
Results: There was an 85.5% response rate, with median follow-up post-IMRT 78 months. Adjuvant IG-IMRT was used in 28% of patients, salvage in 72% and ADT in 48%. A total of 70% of patients remained disease-free. Overall, 16.9% of patients expressed DR for treatment, with fourfold more regret for the RP component of treatment compared to radiotherapy (16.9% vs 4.2%, $P = 0.01$). DR for androgen deprivation was 14.3%. Patients were regretful of surgery due to toxicity, not being adequately informed about radiotherapy as an alternative, positive margins and surgery costs (83%, 33%, 25% and 8% of regretful patients respectively). Toxicity caused DR in the three radiotherapy-regretful and four ADT-regretful patients. Patients were twice as regretful overall, and of surgery, for salvage vs adjuvant approaches (both 19.6% vs 10.0%).
Conclusion: Decision regret after RP and post-prostatectomy IG-IMRT is uncommon, although patients regret RP more than post-operative IG-IMRT. This should reassure urologists referring patients for post-prostatectomy IG-IMRT, particularly in the immediate adjuvant setting. Other implications include appropriate patient selection for RP (and obtaining clear margins), and ensuring adequately discussing definitive radiotherapy as an alternative to surgery.

Key words: decision regret; IMRT; prostate cancer; radical prostatectomy; radiotherapy.

Introduction

Decision regret (DR) is a negative emotion experienced when a patient believes that their outcome may have been better if they had decided differently about their management approach.[1] In the management of localised prostate cancer, DR is particularly important to consider, given the very different management approaches available.[2]

Previous research has investigated DR after surgery or radiotherapy as the primary treatment choice,[2–9] however, there have been no published data on decision

regret for patients who have had both surgery and post-operative radiotherapy. Evaluation of DR in this group of men is particularly important due to the move towards 'multi-modal' therapy, where radical prostatectomy is undertaken with planned adjuvant or early salvage radiotherapy.

Our aim was to evaluate DR in a group of patients who were treated with both surgery and post-operative image-guided intensity-modulated radiotherapy (IG-IMRT), as well as DR specific to the individual treatment components of surgery, radiotherapy and androgen deprivation therapy (ADT). A secondary aim was to determine whether regret differed between patients given post-operative IG-IMRT in the immediate adjuvant vs salvage settings.

Methods

The study protocol received institutional ethics approval. Patients eligible for this study were men with histologically confirmed localised prostatic adenocarcinoma who had undergone a radical prostatectomy and also received post-operative IG-IMRT. All patients treated in our institution with a minimum of 5 years follow-up post-IG-IMRT were eligible. Excluded from the study were patients with either nodal involvement or distant metastases.

Each patient underwent pre-treatment staging which involved PSA assessment, clinical examination with digital rectal examination and staging computed tomography (CT) of the abdomen and pelvis and nuclear medicine bone scan.

Patients had fiducial marker insertion using three gold seeds placed into the prostate bed prior to radiotherapy planning scans.[10] All patients had magnetic resonance imaging (MRI) and CT simulation, with MRI–CT fusion to aid the planning process.[11] All patients were treated using departmental bowel and bladder filling protocols,[12,13] with daily target verification using either electronic portal imaging or cone beam imaging to ensure matching to the fiducial markers.[10] Patients were all treated using IMRT with the prescribed dose of 64 Gy (for planned adjuvant therapy) or 66 Gy (for salvage therapy) in 2.0 Gy fractions, using the www.EviQ.org.au prostate radiotherapy protocols.[14,15]

Patients with high-risk features (Gleason score 8–10, seminal vesicle invasion or gross recurrence) were offered 2–3 years of androgen deprivation using 3–4 month depots of GnRH analogues. Following radiotherapy, all patients are followed-up by the radiation oncology team at 3 months, then annually, with PSA done 3 monthly for the first 2 years and then 6 monthly. PSA failure post-radiotherapy was defined as a PSA rising above the pre-treatment PSA. All patients with PSA failure were re-staged with CT of the abdomen and pelvis, and bone scan. More recently, PSMA PET imaging was performed.[16] At each clinical attendance, toxicity was prospectively entered into our electronic medical record (Mosaiq) by the specialist or training registrar using the Common Toxicity Criteria. Also entered into Mosaiq was the patient's clinical status, including whether they were disease-free or had PSA, loco-regional or distant failure.

As part of standard institutional background reporting, patients were identified by Mosaiq as reaching 5 years from the end of radiotherapy, with an automated email to administration staff generating a list of these patients. As part of our conformity to national standards,[17] all of these patients were then mailed out a questionnaire evaluating toxicity and DR. Patients who did not respond were contacted to complete the questionnaire by telephone.

The questionnaire evaluated DR using Clarke's validated 2-question instrument.[1] Men were defined as regretful if they either indicated that it was true that they would have been better off had they chosen another treatment, or they said they wished they could change their mind about treatment at least some of the time. Men were scored as not being regretful if they were either unsure or rejected the notion that they would be better off with another treatment, and indicated that they wished they could change their mind no more than a little of the time. These questions were asked about their treatment experience overall and for the individual components of treatment (radical prostatectomy, radiotherapy and for relevant patients, androgen deprivation). Also included in the questionnaire were toxicity items, as well as a free text area where patients commented on why they were regretful (with more than one reason being allowed).

Data were analysed using SPSS v11.0 (Chicago, IL, USA). Univariate comparisons of categorical data were made using the chi-square or Fisher's exact test, while continuous variables were analysed with the Mann–Whitney *U* exact test. Variables included in the analysis were age, PSA at diagnosis, Gleason score (from the radical prostatectomy), overall stage, toxicity (worst grade of late genitourinary and gastrointestinal toxicity) and clinical status (i.e. disease-free vs any recurrence, whether biochemical or clinical) at time of last follow-up. A backward stepwise logistic regression for multivariate analysis of DR was also conducted. Confidence levels[18,19] were calculated using a published spreadsheet.[20]

Results

Seventy-one responses were received from 83 eligible patients (response rate of 85.5%). The median time from radical prostatectomy was 92 months (range: 66–200 months) and the median time from the end of radiotherapy was 78 months (range: 62–101 months). Patient demographics are shown in Table 1. Adjuvant IG-IMRT was used in 28% of patients, salvage in 72% and ADT in conjunction with IG-IMRT in 48% (7 of 20 adjuvant patients vs 27 of 51 salvage patients, P = n.s.). A total of 70% of patients remained disease-free, 16% had PSA-

Table 1. Patient demographics and outcomes

Age	Median	72
	Range	56–85
Care plan	Adjuvant	20 (28.2%)
	Salvage	51 (71.8%)
Pathological T stage	T2	32 (45.1%)
	T3	37 (52.1%)
	T4	2 (2.8%)
ADT	No	37 (52.1%)
	Yes	34 (47.9%)
Recurrence status	None	50 (70.4%)
	PSA only	11 (15.5%)
	Loco-regional/distant	10 (14.1%)
Worst GU toxicity	Grade I	31 (43.7%)
	Grade II	7 (9.9%)
	Grade III	0 (0%)
	Grade IV	0 (0%)
Worst GI toxicity	Grade I	32 (45.1%)
	Grade II	19 (26.8%)
	Grade III	2 (2.8%)
	Grade IV	0 (0%)

ADT, androgen deprivation therapy; GI, gastrointestinal; GU, genitourinary.

Table 2. Rates of decision regret

	Regretful *n* (%)	Not regretful *n* (%)
Overall decision regret	12 (16.9)	59 (83.1)
Regret for surgery	12 (16.9)	59 (83.1)
Regret for radiotherapy	3 (4.2)	68 (95.8)
Regret for ADT	4 (14.3)	24 (85.7)

ADT, androgen deprivation therapy.

only failure and 14% also had loco-regional and/or distant failures.

Twelve of 71 respondents (16.9%) were regretful of their overall treatment experience (Table 2). There was fourfold more DR for the radical prostatectomy component of treatment compared to IG-IMRT (16.9% vs 4.2%, $P = 0.01$, 99.4% confidence that patients were more regretful of surgery). Of patients receiving ADT, 14.3% had ADT-specific DR.

Patients were regretful of surgery due to toxicity, not being adequately informed about radiotherapy as an alternative, positive margins and cost of surgery (83%, 33%, 25% and 8% of regretful patients respectively). Toxicity was the cause of DR in the three radiotherapy-regretful and four ADT-regretful patients. Patients were more regretful overall, and of surgery, if they had salvage IG-IMRT vs adjuvant IG-IMRT (19.6% vs 10.0% for both overall and surgical DR, P = n.s., 86% confidence that there was more DR in the salvage group). Uni- and multivariate analyses found no significant impact of variables on DR overall, or for specific components of treatment.

Discussion

Decision regret is considered a valuable patient-centred outcome in the management of prostate cancer,[1] and is an important measure of treatment success.[12] Encompassing the quality of interaction between the physician and patient in the initial decision-making process,[1] DR reflects patient perceptions of treatment efficacy, toxicity and quality of life. Thus, research investigating the levels of DR with treatment techniques, and how it can be predicted and minimised, would seem to be important.

In the management of localised prostate cancer, DR is particularly important to consider given the very different management approaches available.[2] Men must consider whether they want active treatment at all, and if so, whether they choose the very different approaches of surgery, external beam radiotherapy or brachytherapy. Men may feel pressured to make hasty decisions, or may feel that they are being pushed towards one treatment over another. They may experience recurrence or toxicity, or have a lower quality of life after treatment. It is thus not surprising that men sometimes regret their decision about surgery or radiotherapy for prostate cancer. DR has been shown to occur not infrequently after treatment for localised prostate cancer[2–9] A recent meta-analysis demonstrated that men regret surgery more than radiotherapy,[2] with some studies finding up to 53% of men regret surgery.[4] The reason for these high levels of DR is multifactorial, and may be related to cancer recurrence (which could sometimes be a result of poor patient selection), toxicity and quality of life, a lack of balanced discussion of alternatives to surgery and the cost of treatment.

Although previous research has investigated DR after surgery or radiotherapy as the primary treatment choice, there has been no published data on DR for patients who have had both surgery and post-operative radiotherapy. This would seem to be a particularly important avenue of research due to the move towards 'multi-modal' therapy, where radical prostatectomy is undertaken with planned adjuvant or early salvage radiotherapy. The importance is also highlighted by the often poor rate of referral for adjuvant and salvage radiotherapy after radical prostatectomy, with one large population series finding only 9.4% of high-risk patients referred for adjuvant radiotherapy.[21] It seems apparent that urologists have concerns about toxicity and over-treatment, despite randomised trials finding improved QOL for patients receiving PPRT at least in the adjuvant setting.[22] Ultimately, it could be argued that urologists are concerned that patients who do undergo post-prostatectomy radiotherapy may live to regret their decision. In short, urologists may be concerned that their patients will experience DR.

Our research may help reassure clinicians considering a referral for post-operative IMRT. Overall, we found little DR for patients receiving both radical prostatectomy and

adjuvant or salvage IG-IMRT, with only 16.9% of patients regretful. This low rate of DR is highlighted by the fact that regret was lower than some studies of patients receiving surgery (including robotic prostatectomy) alone.[4,7–9] We note that none of our patients underwent robotic surgery, and it is uncertain how different types of surgery would influence DR relating to post-prostatectomy IG-IMRT. Of particular note for referring urologists and general practitioners, with over 5 years follow-up post-IMRT, only 4.2% of patients regretted their decision to have radiotherapy. We postulate that this extremely low rate of DR is due to a combination of good results (over 70% free of relapse and low rates of toxicity due to image-guided IMRT), thorough discussion of management options and potential radiotherapy toxicities before radiotherapy, and the fact that radiotherapy was provided at no cost to the patient (being delivered in public radiotherapy units). It is interesting that the 4.2% rate of DR for radiotherapy found in the current series of post-prostatectomy IG-IMRT is only slightly higher than the 1.4% level of DR found in our patients treated with definitive dose-escalated radiotherapy.[6]

It was very interesting to find that patients were much more regretful of their initial surgery than radiotherapy (16.9% vs 4.2%), and also slightly more regretful of surgery than of ADT (16.9% vs 14.3%). Toxicity was the main cause of DR after surgery, and it seems that patients rated their surgical toxicity as being much more of a cause of DR than their radiotherapy toxicity. We believe the message for urologists who have concerns about referring patients for post-operative radiotherapy is that it is extremely unlikely radiotherapy toxicity will add to the DR patients already experience due to surgical toxicity.

We also believe that our findings may impact on how care is delivered. One-third of regretful patients believe they were not adequately informed about radiotherapy as an alternative to surgery in the management of their initial localised prostate cancer. This concern has been raised previously,[23] and serves as a timely reminder that in order for patients to make informed decisions about the treatment of localised prostate cancer, they should be seen by both the urologist and radiation oncologist prior to any treatment. This is a key criterion for good management, and endorsed by national bodies.[24] From our current data, it is possible that failure to refer to a radiation oncologist may contribute to higher levels of DR. If this is true, there may be significant implications for urologists failing to refer patients to radiation oncologists, as it is thought that DR can result in future litigation.[25]

Patient selection for radical prostatectomy may also contribute to increased DR, given that some of our patients expressed DR due to positive margins. Previous population studies demonstrate that positive margins can occur in up to 27.6% of patients,[21] the vast majority of whom are never referred for post-prostatectomy radiotherapy.[21] Urologists should be aware that better patient selection, hence reducing positive margin rates, may also positively impact on the levels of DR that patients may experience after radical prostatectomy.

Finally, the cost of surgery was raised as a cause of DR by one patient, and anecdotally, this is not infrequently raised with the radiation oncologists in our institution. The financial toxicity of cancer therapy has been raised as a significant problem in Australia,[26] and further research into the association of cost and DR is warranted. Clinicians charging large out of pocket fees should be aware that this may impact on DR experienced by their patients.

In conclusion, we report decision regret in patients receiving radical prostatectomy and adjuvant or salvage image-guided IMRT. The extremely low levels of DR specific to radiotherapy should reassure referring doctors and hopefully lead to higher referral rates. Further research is required to better evaluate the causes of DR and the potential implications for treating specialists.

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