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Clinical Investigation: Genitourinary Cancer

Decision Regret in Men Undergoing Dose-Escalated Radiation Therapy for Prostate Cancer

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Summary

Decision regret (DR) is an important patient-centered outcome reflecting cure, toxicity, and quality of life. We evaluated DR after dose-escalated external beam radiation therapy. We found that 3.8% of patients expressed DR. Only 0.5% would not choose radiation therapy again; however, 8.4% would not choose the androgen deprivation component of treatment. This has implications for informed consent in any man considering his treatment options.

Purpose: Decision regret (DR) is a negative emotion associated with medical treatment decisions, and it is an important patient-centered outcome after therapy for localized prostate cancer. DR has been found to occur in up to 53% of patients treated for localized prostate cancer, and it may vary depending on treatment modality. DR after modern dose-escalated radiation therapy (DE-RT) has not been investigated previously, to our knowledge. Our primary aim was to evaluate DR in a cohort of patients treated with DE-RT.

Methods and Materials: We surveyed 257 consecutive patients with localized prostate cancer who had previously received DE-RT, by means of a validated questionnaire.

Results: There were 220 responses (85.6% response rate). Image-guided intensity modulated radiation therapy was given in 85.0% of patients and 3-dimensional conformal radiation therapy in 15.0%. Doses received included 73.8 Gy (34.5% patients), 74 Gy (53.6%), and 76 Gy (10.9%). Neoadjuvant androgen deprivation (AD) was given in 51.8% of patients and both neoadjuvant and adjuvant AD in 34.5%. The median follow-up time was 23 months (range, 12-67 months). In all, 3.8% of patients expressed DR for their choice of treatment. When asked whether they would choose DE-RT or AD again, only 0.5% probably or definitely would not choose DE-RT again, compared with 8.4% for AD ($P<.01$).

Conclusion: Few patients treated with modern DE-RT express DR, with regret appearing to be lower than in previously published reports of patients treated with radical prostatectomy or older radiation therapy techniques. Patients experienced more regret with the AD component of treatment than with the radiation therapy component, with implications for informed consent. Further research should investigate regret associated with individual components of modern therapy, including AD, radiation therapy and surgery.

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Introduction

Decision regret (DR) is a negative emotion experienced by some patients after making a choice about treatment, and it is an important patient-centered outcome (1, 2). It has been defined as a feeling of loss or distress over an action or inaction made under conditions of uncertainty (3). DR is thus of particular relevance for patients with localized prostate cancer. These men are often faced with the difficult task of choosing between several very different management options, and thus a degree of uncertainty is inherent in the choice made.

Several options are often available to these patients, including radical prostatectomy, external beam radiation therapy, brachytherapy, androgen deprivation (AD), and active surveillance. These options may differ in outcomes, including cure rates, toxicity, and quality of life (QoL). The long natural history of the disease and the generally good prognosis means that men who choose an active treatment must tolerate, sometimes for their remaining lives, treatment-related side effects (4). Although several studies have investigated DR in patients with localized prostate cancer, none that we are aware of have evaluated DR in patients who have been treated with modern radiation therapy techniques such as dose-escalated radiation therapy and image-guided intensity modulated radiation therapy (IMRT). Given the range of different approaches and the potential long-term toxicities, it is not surprising that up to 53% of patients with localized prostate cancer will regret their decision (2, 5-9), with rates shown to vary by treatment modality (9).

Given these findings, it is important to evaluate DR for new treatment techniques. As far as we know, no studies have assessed regret in patients undergoing modern external beam radiation therapy techniques. It is unknown how dose-escalated radiation therapy or IMRT would affect regret. Dose escalation has the benefit of increased biochemical disease-free survival (10, 11), which might reduce DR. However, dose escalation may increase treatment toxicity (12), with an associated adverse impact on QoL and thus DR. Newer techniques, such as IMRT and image guidance, are often used in conjunction with dose escalation. Image-guided IMRT may result in lower toxicity rates and an improvement in QoL, and therefore it could conceivably lead to lower rates of regret. Many patients treated with external beam radiation therapy are offered AD, and this could also affect rates of DR.

In addition, no reports have investigated DR for individual components of care for patients with localized prostate cancer, as far as we are aware. In particular, it is unknown how AD and radiation therapy individually affect DR. It would not be unreasonable to expect that if levels of regret sometimes differ between patients who have received surgery and those who have undergone radiation therapy (9), regret may also vary between individual components of a patient's treatment regimen. Given the very different toxicities of AD and radiation therapy, it would not be surprising if levels of regret differed between these components.

Our aim was to assess DR in a group of patients treated with dose-escalated radiation therapy. We also wished to evaluate regret specific to dose-escalated radiation therapy versus AD.

Methods and Materials

The study protocol received institutional ethics approval, and all patients gave informed consent to their participation. Patients eligible for this study were men with histologically confirmed localized prostatic adenocarcinoma who received dose-escalated external beam radiation therapy, either 3-dimensional conformal radiation therapy (3D-CRT) or IMRT. Excluded from the study were patients with either TNM-defined (13) nodal involvement or metastatic disease, or patients who received postprostatectomy adjuvant or salvage radiation therapy.

Each patient underwent pretreatment staging which involved assessment of prostate-specific antigen (PSA), clinical examination with digital rectal examination, and transrectal ultrasound guided core biopsy. Patients were classified as being at low risk if they had all of the following: T2a disease or less, a PSA less than 10 ng/mL, and a Gleason score of 6 or less. Patients were classified as being at high risk if they had any 1 of the following: T3 disease, PSA over 20 ng/mL, or Gleason score of 8 or more. All other patients were classified as being at intermediate risk. Patients with high-risk disease underwent computed tomography (CT) of the abdomen and pelvis and nuclear medicine bone scanning as part of their metastatic workup.

Patients who received IMRT had fiducial marker insertion with 3 gold seeds placed into the prostate before the radiation therapy planning scans. All patients underwent magnetic resonance imaging (MRI) and CT simulation, with MRI-CT fusion to aid the planning process. All patients were treated according to bowel and bladder filling protocols, with daily target verification using either electronic portal imaging or cone-beam imaging to ensure matching to the fiducial markers. Patients were all treated with either 3D-CRT or IMRT with the prescribed treatment plan of 1.8- to 2.0-Gy fractions over an 8-week period. The planned total to the planning target volume reference point ranged between 73.8 Gy and 76.0 Gy.

Patients with intermediate-risk or high-risk disease were also offered 3-monthly injections of AD. Patients at intermediate risk received 3 to 6 months of neoadjuvant AD, and patients at high risk received both neoadjuvant and 2 to 3 years of adjuvant AD. All patients receiving radiation therapy and AD were provided with verbal and written information that outlined the possible treatment-related toxicities.

Each participant was contacted initially by mail, and patients who did not respond were subsequently contacted by telephone and the questionnaire was resent by mail for those who agreed to participate. The mail-out invitation outlined the key purpose of our research, followed by a self-administered questionnaire.

Questions evaluated the level of a patient's DR with their treatment choice. This was measured with 2 validated questions from Clark et al (1): a man's wish that he could change the kind of treatment he had received, and his feeling that he would be better off if he had received another treatment. Our DR tool also incorporated 2 modified regret items as developed by Hamilton et al (14) that specifically looked at individual treatment modalities. This enabled individual evaluations of radiation therapy and hormone therapy upon analysis of results.

The DR instrument was evaluated by dividing the responses to each item into regretful and not regretful. We used the definition of regret formulated by Clark et al (1) Their first question was "During the past 4 weeks, how much of the time have you wished you could change your mind about the kind of treatment you chose for your prostate cancer?" Patients were classified as "regretful" if they responded "some of the time," "a good bit of the time," "most of the time," or "all of the time" and "not regretful" if they responded "a little of the time" or "none of the time." Their