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Clinical Investigation: Genitourinary Cancer

Prospective Preference Assessment of Patients' Willingness to Participate in a Randomized Controlled Trial of Intensity-Modulated Radiotherapy Versus Proton Therapy for Localized Prostate Cancer

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Summary

We undertook a qualitative research study to investigate patients' willingness to participate (WTP) in a randomized controlled trial (RCT) comparing intensity-modulated radiotherapy (IMRT) with proton beam therapy (PBT) for prostate cancer. We identified 21 factors that impacted WTP, which centered on: 1) altruism/desire to compare

Purpose: To investigate patients' willingness to participate (WTP) in a randomized controlled trial (RCT) comparing intensity-modulated radiotherapy (IMRT) with proton beam therapy (PBT) for prostate cancer (PCa).

Methods and Materials: We undertook a qualitative research study in which we prospectively enrolled patients with clinically localized PCa. We used purposive sampling to ensure a diverse sample based on age, race, travel distance, and physician. Patients participated in a semi-structured interview in which they reviewed a description of a hypothetical RCT, were asked open-ended and focused follow-up questions regarding their motivations for and concerns about enrollment, and completed a questionnaire assessing characteristics such as demographics and prior knowledge of IMRT or PBT. Patients' stated WTP was assessed using a 6-point Likert scale.

Results: Forty-six eligible patients (33 white, 13 black) were enrolled from the practices of eight physicians. We identified 21 factors that impacted patients' WTP, which largely centered on five major themes: altruism/desire to compare treatments, randomization, deference to physician opinion, financial incentives, and time demands/scheduling. Most patients (27 of 46, 59%) stated they would either "definitely" or "probably" participate. Seventeen percent (8 of 46)

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treatments, 2) randomization, 3) deference to physician opinion, 4) financial incentives, and 5) time demands/scheduling. Most (27/46, 59%) patients stated they would likely participate in such a RCT.

stated they would "definitely not" or "probably not" enroll, most of whom (6 of 8) preferred PBT before their physician visit.

Conclusions: A substantial proportion of patients indicated high WTP in a RCT comparing IMRT and PBT for PCa.

Keywords: Prostate cancer, Intensity-modulated radiotherapy, Proton beam therapy, Randomized controlled trial

Introduction

In 2010, the Institute of Medicine (IOM) noted that only half of National Cancer Institute Cooperative Group trials were completed (1). The reasons are multifactorial, including regulatory barriers, inadequate funding, suboptimal design, and poor accrual. It is estimated that <3% of adults in the United States with cancer participate in clinical trials (1). Notably, racial and ethnic minorities remain underrepresented (2). These trends underscore the importance of identifying factors that improve participation in randomized controlled trials (RCTs).

Prior efforts with randomization highlight the accrual challenges in North American prostate cancer (PCa) trials. SPIRIT randomized patients to either radical prostatectomy (RP) or brachytherapy. The study was closed in 2 years after only 56 patients elected to randomize (3). PIVOT, which compared RP and watchful waiting, randomized only 731 of 5023 eligible patients, far short of the 2000 target sample size (4). In contrast, PROTECT in the United Kingdom compared RP, conformal radiotherapy, and active monitoring. Before study initiation, investigators developed a pre-emptive intervention informed by qualitative research to improve accrual. More than 65% of eligible subjects consented to randomization, and acceptance of allocation improved from 65% in 2001 to 81% in 2005 (5).

Proton beam therapy (PBT) has become an increasingly prominent treatment modality. There is growing evidence demonstrating the clinical efficacy of PBT in PCa, although to date there is no randomized evidence comparing PBT with X-ray radiotherapies, such as intensity-modulated radiotherapy (IMRT) (6). As such, the Agency for Healthcare Research and Quality (7), IOM (8), National Cancer Institute (9), and Centers for Medicare & Medicaid Services (10) have called for randomized evidence to assess the relative clinical benefits and harms of PBT for PCa.

Nevertheless, patients' willingness to participate (WTP) in such an RCT is unknown. Because both modalities continue to receive substantial national media attention, many men with PCa have strong therapy preferences. Given the challenges of RCT accrual highlighted by the IOM and the particularly poor accrual in recent PCa RCTs, we undertook a qualitative research study to understand patients' motivations for and concerns about enrollment in an RCT of IMRT vs. PBT.

Methods and Materials

Study population

We recruited patients with clinically localized prostate adenocarcinoma at two tertiary care institutions with on-site proton therapy centers. We included men aged >18 years with histologically confirmed PCa and clinical T1c−T2b stage disease. Patients with the following Gleason score (GS) and prostate-specific antigen (PSA) criteria were eligible: GS 6 or 3 + 4 = 7 if PSA <10 ng/mL or GS ≤6 if PSA 10 ng/mL to <20 ng/mL. We excluded patients with a second or prior malignancy or any of the following PCa treatments: hormonal therapy, surgery (including orchiectomy), chemotherapy, pelvic radiation, or brachytherapy. The institutional review boards at both centers approved this study.

Recruitment

In this qualitative research study, we prospectively enrolled patients between October 2010 and April 2011. Investigators reviewed the medical records of patients scheduled with any of the genitourinary radiation oncologists. We used purposive sampling to ensure a diverse sample based on age, race, travel distance, and physician. A sample size was not determined *a priori* because enrollment was continued until theoretical saturation was reached (11) (*i.e.*, when additional interviews yielded no new information about patients' motivations or concerns).

Interviews

After an introduction to the study by the radiation oncologist at the end of the visit, study personnel trained in semi-structured interviewing techniques (J.J.P. and A.S.) obtained verbal informed consent and conducted audio-recorded interviews.

Using the methodology of prospective preference assessment (12), patients were read a description of a hypothetical RCT of IMRT vs. PBT (Appendix e1, available online); this was developed in conjunction with six genitourinary radiation oncologists at both institutions (J.E.B., J.P.C., J.A.E, S.M.H., N.V., and A.L.Z.,), a medical ethicist (S.D.H), and an expert in human subjects recruitment for radiotherapy clinical trials (D.W.B.). The RCT description explained the two alternative therapies, randomization, 350-subject sample size, study length, and follow-up. Importantly, patients were informed that they would still be offered IMRT or PBT if they chose not to participate in the RCT. Patients were afforded the opportunity to read this description before being asked questions to assess their understanding of the proposed RCT, including the concept of randomization. After clarifying any questions related to the study design, the interviewer asked a series of open-ended questions to understand the patient's motivations for and concerns about RCT participation. In addition, open-ended guiding questions were asked to encourage patients to thoroughly describe factors related to their participation (Table 1). Patients' answers were followed up with questions about specific