Original Study

Cost-effectiveness of the Decipher Genomic Classifier to Guide Individualized Decisions for Early Radiation Therapy After Prostatectomy for Prostate Cancer

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Abstract

It is not currently clear which patients will benefit from adjuvant radiation therapy after prostatectomy. A genomic classifier assay to estimate the individualized risk of prostate cancer progression would help physicians offer personalized decision-making for adjuvant therapy after prostatectomy. We present the results of a cost-effectiveness analysis that applies an individualized decision analysis framework to estimate the costs and outcomes for adjuvant therapy decisions after radical prostatectomy using a genomic classifier test (Decipher). Genomic classifier-based treatment decision-making was shown to be a cost-effective alternative compared with usual care and 100% usage of adjuvant therapy.

Background: Controversy exists regarding the effectiveness of early adjuvant versus salvage radiation therapy after prostatectomy for prostate cancer. Estimates of prostate cancer progression from the Decipher genomic classifier (GC) could guide informed decision-making and improve the outcomes for patients. **Materials and Methods:** We developed a Markov model to compare the costs and quality-adjusted life years (QALYs) associated with GC-based treatment decisions regarding adjuvant therapy after prostatectomy with those of 2 control strategies: usual care (determined from patterns of care studies) and the alternative of 100% adjuvant radiation therapy. Using the bootstrapping method of sampling with replacement, the cases of 10,000 patients were simulated during a 10-year time horizon, with each subject having individual estimates for cancer progression (according to GC findings) and noncancer mortality (according to age). **Results:** GC-based care was more effective and less costly than 100% adjuvant radiation therapy and resulted in cost savings up to an assay cost of $11,402. Compared with usual care, GC-based care resulted in more QALYs. Assuming a $4000 assay cost, the incremental cost-effectiveness ratio was $90,833 per QALY, assuming a 7% usage rate of adjuvant radiation therapy. GC-based care was also associated with a 16% reduction in the percentage of patients with distant metastasis at 5 years compared with usual care. **Conclusion:** The Decipher GC could be a cost-effective approach for genomics-driven cancer treatment decisions after prostatectomy, with improvements in estimated clinical outcomes compared with usual care. The individualized decision analytic framework applied in the present study offers a flexible approach to estimate the potential utility of genomic assays for personalized cancer medicine.

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Introduction

Each year in the United States, > 230,000 patients are diagnosed with prostate cancer.[1] One third of those patients will choose to undergo radical prostatectomy (RP).[2] On average, approximately 20% of prostate cancer cases will recur after RP.[3] The recurrence rates are greater, 40% to 60%, for patients with ≥ 1 adverse pathologic features.[4] For patients at high risk of recurrence, randomized controlled trials have shown that adjuvant radiation therapy (ART) to the prostate bed improves prostate-specific antigen (PSA) relapse-free survival[5-9] and might improve distant metastasis-free survival and overall survival[10] compared with observation. Alternatively, patients can be followed up with serial PSA testing after RP, with salvage radiation therapy (SRT) delivered at PSA recurrence.[11]

The comparative effectiveness of ART versus SRT is controversial,[12-15] and clinical trials are ongoing to directly compare ART and SRT. Currently, the clinical practice guidelines recommend that physicians offer ART to patients at high risk of recurrence after RP and that physicians assist patients in making a shared decision between ART and close observation with PSA testing and appropriate early use of SRT.[16,17] An alternative approach to decision-making would be to integrate tumor genomics-based estimates of prostate cancer progression. The Decipher genomic classifier (GC) assay (GenomeDx Biosciences, San Diego, CA) was developed to inform personalized post-RP treatment decisions and has been validated to provide individual estimates of risk of metastasis after RP for high-risk patients.[18,19] The Decipher GC assay has been shown to influence clinicians' recommendations for ART after RP.[20-22] Furthermore, it has been shown that GC-based post-RP treatment decisions might improve patient outcomes compared with usual care.[23]

Cost-effectiveness is an important consideration in the clinical implementation of a candidate molecular assay for cancer treatment decisions, because payers and policy-makers must consider the incremental value of the candidate assay when determining coverage.[24-26] We applied an individualized decision analysis framework to estimate the cost-effectiveness of the Decipher GC assay when used to guide personalized treatment decisions after RP. We investigated the cost-effectiveness of GC-based treatment decisions compared with 2 alternative strategies: (1) "usual care" adjuvant therapy usage rates derived from patterns of care studies[27-31]; and (2) complete (100%) usage of adjuvant therapy. This assessment uses a decision analysis model with individualized inputs for risks of distant metastasis (defined by the GC score) and noncancer mortality (defined by age at model entry). The model was designed to compare the modeled costs, life years (LYs), quality-adjusted life years (QALYs), and clinical outcomes during a 10-year time horizon for the 3 alternative post-RP therapy decision-making strategies for a cohort of patients with prostate cancer.

Materials and Methods

We present a Markov model to compare the costs and quality-adjusted life expectancy associated with usual care, GC-based care, and 100% usage of adjuvant therapy for men with prostate cancer in the post-RP setting. We compared GC-based treatment decisions to 2 alternative controls (complete [100%] usage and "usual care" usage [approximately 7% rate of ART usage and 4% rate of radiation therapy combined with hormonal therapy] determined from patterns of care studies[27-31]) because of the variability found in clinical practice and current controversy regarding adjuvant therapy after RP. After RP, patients have the option of pursuing adjuvant therapy: either radiotherapy or hormonal therapy, or both. The patients who do not receive adjuvant therapy have the option of undergoing salvage therapy if and when evidence of disease progression is found. For patients who have undergone treatment in the adjuvant or salvage setting, hormonal therapy is used for ≤ 2 years after recurrence or progression to metastasis.

We provide a cohort-based analysis of the post-RP decision-making process by evaluating the Markov model using Monte Carlo simulation. The model uses monthly transitions and has a 10-year horizon after RP. The model was run for 10,000 replications using the bootstrapping method of sampling with replacement. The state transition diagram is provided in Figure 1. The model was coded in C/C++, and validation of a similar model has been presented previously.[23] C/C++ was chosen instead of commercially available software to maximize the flexibility to create and vary the individual-level inputs for cohort simulation experiments. The cohort is described in the Supplemental Appendix (available in the online version).

Model Probabilities

The probabilities of treatment side effects and the transition probabilities among states were determined from estimates in published studies. The values used in the model and their citations are summarized in Table 1. The transition probabilities presented in Table 1 are annual estimates, although they were converted to monthly probabilities for use in the model. The risk of cancer recurrence for each simulated patient was determined from the individual GC assay results—the individual's risk of metastasis at 5 years. The monthly transition probabilities for developing biochemical recurrence (BCR) or metastasis were amended for each individual according to the proportion of deviation from the average 5-year risk of metastasis. The probability of death from other causes was determined from individual, age-dependent probabilities of death, with the probability of death from prostate cancer removed.[34]

The probability of treatment usage in the adjuvant and salvage settings was dependent on the setting analyzed: usual care, 100% adjuvant therapy, and GC-based care. Additional details are provided in the Supplemental Appendix (available in the online version).

Utilities

Our model incorporated decreases in utility due to cancer treatment, treatment side effects, and later stages of cancer. The utility values are presented in Table 1. When multiple utility values were applied, we multiplied the individual utility values to calculate the final utility value. The final utility values were summed to compute the QALYs during the 10-year horizon.

Costs

The costs were calculated in the model using the cost of radiotherapy and hormonal therapy, the cost of treatment of associated side effects, and the state-dependent cost of annual care for patients