

Health state utilities among contemporary prostate cancer patients on active surveillance

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Background: Active surveillance (AS) is the most rapidly expanding management option for favorable-risk prostate cancer (PCa). Early studies suggested substantial decrements in utility (quality of life weights) from disease-related anxiety. Our objective was to determine utilities for contemporary AS patients using different instruments.

Methods: We performed a systematic review of PubMed, PMC and OVID for utility measurements in modern AS patients. We then examined utilities among 37 men on AS participating in focus groups between 2015–2016 using the generic EurQol five dimensions questionnaire (EQ-5D-3L) and Patient Oriented Prostate Utility Scale (PORPUS), a PCa-specific instrument.

Results: The systematic review found previous studies with utilities for PCa treatment and historical watchful waiting populations, but none specifically in contemporary AS. In our AS population, the mean EQ-5D-3L score was 0.90 ± 0.16 (median, 1.00; range, 0.21–1.00) and PORPUS was 0.98 ± 0.03 (median, 0.99; range, 0.84–1.00). The Spearman correlation between the EQ-5D-3L and PORPUS was 0.87 ($P < 0.0001$), and 38% of patients had a difference > 0.1 between instruments.

Conclusions: Most contemporary AS patients had high utility scores suggesting that they perceive themselves in good health without a major decrement in quality of life from the disease. However, some patients had substantial differences in utility measured with generic versus disease-specific instruments. Further study is warranted into the optimal instrument for utility assessment in contemporary AS patients.

Keywords: Active surveillance (AS); prostate cancer (PCa); utilities; PORPUS; EQ-5D

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Introduction

For localized (non-metastatic) prostate cancer, radical treatment, such as surgery and radiation therapy, is often curative but may cause significant side effects such as impotence and urinary problems (1). However, in the era of widespread PSA screening, overdiagnosis is a significant issue (2). Many prostate cancers have a low risk of progression in the absence of treatment and may be managed conservatively.

Conservative management spans a spectrum from watchful waiting (WW), which involves minimal testing and no curative intent, to active surveillance (AS), which involves serial follow-up testing to offer selective delayed treatment to those with increasing disease burden over time. Several comparative-effectiveness models have shown that conservative management is a safe alternative and may reduce initial costs (3-5).

Although upfront conservative management has the potential to delay or avoid the need for treatment and its potential side effects, early studies reported a significant decrement in utility potentially from disease-related anxiety (6). However, over the past decade new data has emerged from large prospective cohort studies showing the long-term safety of AS, with very low rates of metastasis and prostate cancer death (7,8). Correspondingly, the use of AS has rapidly increased in both the United States and internationally (9). The Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry, which obtains data from urologic practices across the United States, reported that from 2010 to 2013 around 40% of low-risk prostate cancer patients were managed by AS or WW (10).

More recent data has shown a high quality of life among men in contemporary AS programs (11,12). Thus, we hypothesized that health state utilities (quality of life weights) may be different now than prior to the widespread use of AS. Our objective was to perform a systematic review of the published literature on utilities among contemporary AS patients. In addition, we directly examined utilities in an ethnically diverse group of AS patients using both a generic (EuroQol three level questionnaire, EQ-5D-3L) and prostate cancer-specific instrument (Patient ORiented Prostate Utility Scale, PORPUS). The EQ-5D-3L is a generic measure of health that has been validated in cancer patients (13). With only five questions, it has been deemed one of the shortest and least cognitively demanding utility assessment instruments (14). The EQ-5D covers mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The PORPUS was developed by Krahn *et al.*,

and validated by Ritvo *et al.*, to create a specific utility measure for prostate cancer patients (15,16). The PORPUS consists of 10 domains related to key dimensions of prostate cancer; pain, energy, social support, communication with doctor, emotional well-being, urinary leakage, sexual function, sexual interest, and bowel problems (14).

Methods

To assess health state utilities in contemporary AS patients, we first performed a systematic search of PubMed, PMC, and Ovid for English-language publications on “utility AND active surveillance”, and “utilities AND active surveillance” from inception through April 2016. We also searched for articles specifically using the EQ-5D and PORPUS instruments in AS populations with the following searches: “PORPUS AND active surveillance”, and “EQ-5D AND active surveillance”. Finally, we searched for “PORPUS and prostate cancer”, and “EQ-5D and prostate cancer” to find any additional articles using these questionnaires that may have included a subset of patients on AS. This search yielded a total of 518 unique results. After excluding based on title (n=500), abstract (n=7) and full-text review (n=11), this search did not find any data using these instruments to measure utilities in a modern AS population.

We addressed this gap in the literature by distributing the EQ-5D-3L and PORPUS to prostate cancer patients on AS from two clinical settings, NYU Langone Medical Center and the Manhattan Veterans Affairs Hospital. These surveys were completed as part of a larger qualitative study on AS that aimed to parse out the educational and informational needs of men on AS. A total of 235 men on AS from both institutions were identified through a query of the electronic health record and mailed invitations to participate in focus groups. Patients were eligible if they met the following criteria: (I) male between 30–89 years old; (II) diagnosed with prostate cancer; (III) had not undergone treatment. We conducted seven focus groups with 37 men on AS from October 2015 to March 2016, until thematic saturation was reached, wherein no new themes emerged. All participants completed both questionnaires prior to the focus group discussion. Descriptive statistics were used to examine the distribution of EQ-5D-3L and PORPUS scores, and a Spearman correlation was calculated between these instruments. Chi-square and Moody's test were used for statistical comparisons. All statistical analyses were performed using the statistical software package SAS (SAS Institute Inc., Cary, NC, USA). The study protocol was

Table 1 Patient demographics

	NYU patients (n=23)	VA patients (n=14)	Combined (n=37)
Age (median; range)	64 [48–80]	67 [61–84]	66 [48–84]
Race			
White	21 (91.3%)	3 (21.4%)	24 (64.9%)
Black	1 (4.3%)	10 (71.4%)	11 (29.7%)
Other	1 (4.3%)	1 (7.1%)	2 (5.4%)
Ethnicity			
Hispanic	1 (4.3%)	2 (14.3%)	3 (8.1%)
Non-Hispanic	22 (95.7%)	12 (85.7%)	34 (91.9%)
Education level			
Not a high school graduate	0 (0.0%)	2 (14.3%)	2 (5.4%)
GED	1 (4.3%)	1 (7.1%)	2 (5.4%)
High school graduate	1 (4.3%)	3 (21.4%)	4 (10.8%)
Associate's degree	0 (0.0%)	2 (14.3%)	2 (5.4%)
Some college	1 (4.3%)	2 (14.3%)	3 (8.1%)
4-year college graduate	6 (26.1%)	2 (14.3%)	8 (21.6%)
Graduate or professional school	14 (60.9%)	2 (14.3%)	16 (43.2%)
PSA at diagnosis (median; range)	5.2 (2.4–27)	4 (3–5.5)	4.9 (2.4–27)
Gleason at diagnosis (median; range)	6 (<6–7)	6 (<6–6)	6 (<6–7)
Years on AS (median; range)	3.4 (1.1–6.4)	4.2 (0.1–11.8)	3.7 (0.1–11.8)
Any complications from biopsy (% yes)	7 (30.4%)	2 (14.3%)	9 (24.3%)

approved by the IRB at New York University School of Medicine and the VA New York Harbor Healthcare System.

Results

Among the 37 focus group participants, the median age was 66, and racial background was 65% white, 30% black and 5% were of other race/ethnicities (*Table 1*). Twenty-two percent of participants graduated from a four-year university and 43.2% completed graduate or professional school. The median PSA at prostate cancer diagnosis was 4.9 (range, 2.4–27) and the median Gleason score was 6 (range, <6–7). The median length of time on AS at the time of the study was 3.4 years (range, 0.1–11.8 years).

All 37 patients completed the EQ-5D-3L and 36 of the patients completed the PORPUS (*Figure 1*). The mean score was 0.90 ± 0.16 on the EQ-5D-3L (median, 1.00; range, 0.21–1.00) and 0.98 ± 0.03 on the PORPUS (median,

0.99; range, 0.84–1.00). The correlation between the EQ-5D-3L and PORPUS was 0.87 ($P < 0.0001$), and 14 patients (38%) had a difference > 0.1 . There was no significant relationship between time on AS and utility scores, and no significant difference in scores between clinical settings. A bivariate analysis suggested no significant correlation between education level and utility score.

Evaluation of the individual items (*Table S1*) showed the highest (or most severe) item in the EQ-5D-3L was pain/discomfort (mean 1.35 ± 0.54), followed by anxiety/depression (mean 1.30 ± 0.57). None of the patients reported a decrement in the EQ-5D domain of self-care. In the PORPUS, the highest scores were for urinary frequency (mean 2.27 ± 0.77) and sexual function (mean 2.19 ± 0.80).

Discussion

Our results demonstrate a high overall correlation in the

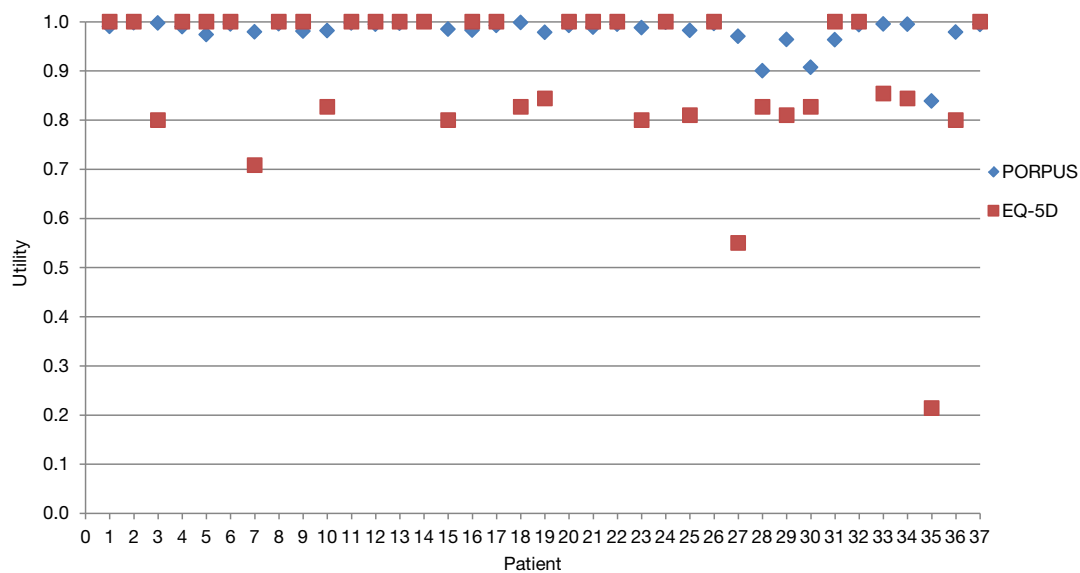


Figure 1 Active surveillance patient utility results using the EQ-5D-3L and PORPUS.

scores from EQ-5D and PORPUS in contemporary AS patients. However, there was a difference of more than 0.1 in 38% patients, and the most influential domains differed between instruments.

Precise utility estimates are very important for modeling studies of prostate cancer management, which are frequently used to guide clinical care and policy decisions. For example, a recent study by Roth *et al.* showed PSA screening is cost-effective when used in conjunction with conservative management of low-risk disease (17). In the main analysis, the authors used a utility decrement of 0.08 for “surveillance”, which was varied from 0.02 to 0.14. These utilities were drawn from a 2005 study including 162 men ages ≥ 60 (of whom 52% were diagnosed with prostate cancer) who were asked about three different watchful waiting states with a varying chance of cancer spreading (6). Although this is similar to the mean utility using the EQ-5D in our contemporary cohort, the PORPUS had a mean utility of 0.98 and only 2 patients had a decrement ≥ 0.1 . In the Roth study, sensitivity analyses showed that model results were most sensitive to the health state utility for the conservative management state (17). These combined findings suggest that the instrument used to assess utilities for AS patients may have a substantial impact on prostate cancer model results.

The PORPUS has more items overall, so each specific

item is not weighted as heavily as in the EQ-5D. For example, with all other domains perfect, a 3 for pain (middle category) brings the PORPUS to 0.99, and a 5 (maximum) results in a PORPUS score of 0.77. By contrast, with all other domains perfect, a pain score of 2 (middle score) brings the EQ-5D to 0.83, and a score of 3 (maximum) would result in a EQ-5D of 0.46. Although pain had the highest mean score on the EQ-5D in our patients, it is unclear whether this was related to prostate cancer or due to other comorbid issues. No patients reported a decrement in the self-care domain, suggesting that this item may have limited discriminatory utility in a contemporary AS population.

Meanwhile, PORPUS asks about several disease-specific domains that are not explicitly measured by the EQ-5D. Although the PORPUS also measures pain and anxiety/depression (worst scores in EQ-5D), the highest mean scores were instead for disease-specific urinary and sexual items. Although AS does delay or avoid the potential urinary and sexual side effects of radical treatment, it is important to recognize that it does not prevent the age-related progression of these issues. The prostate is a primary contributor to male lower urinary tract symptoms, and a long-term prospective cohort study of men undergoing radical prostatectomy found that men with significant urinary symptoms prior to surgery actually had an improvement in urinary quality of life

postoperatively (18). Acar *et al.* analyzed quality of life after various forms of prostate cancer treatment, demonstrating an inverse relationship between age and sexual function scores (19). In the subset of men on AS, they also found an increase in the use of incontinence aids over time. Overall, it is important for men choosing AS to recognize that they may still experience declines in urinary and sexual function over time, even in the absence of prostate cancer treatment.

Limitations of our study are that despite a racially diverse population, the sample size was small and these results may not be generalizable to other settings. Also, these utilities were not measured at the time of prostate biopsy, which may have a transient impact on quality of life. Despite these limitations, our systematic review demonstrated there is scant data on validated utility measures among current AS patients and how they may differ based on the instrument that is used. Thus, these preliminary findings provide novel data on utilities among current active surveillance patients, and how they differ using validated generic and disease-specific instruments.

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Footnotes

Conflicts of Interest: SL received honoraria for lectures from Astellas, GenomeDx Biosciences, MDx Health and Boehringer Ingelheim, consulting fees from Lilly, and reimbursed travel to conferences from Minomic and Astellas (unrelated to current study).

Ethical Statement: The study protocol was approved by the IRB at New York University School of Medicine and the VA New York Harbor Healthcare System.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Supplementary

Table S1 Means of PORPUS and EQ-5D items

Utilities in active surveillance patients	Mean (S.D.)
EQ-5D-3L items (high score is worse; range, 1–3)	
Mobility	1.14 (0.35)
Self-care	1.00 (0.00)
Usual activities	1.08 (0.36)
Pain/discomfort	1.35 (0.54)
Anxiety/depression	1.30 (0.57)
PORPUS items (high score is worse; range, 1–4/5/6)	
Pain	1.43 (0.65)
Energy	2.08 (0.76)
Social support	1.38 (0.79)
Communication with doctor	1.51 (0.73)
Emotional well-being	1.84 (0.87)
Urinary frequency	2.27 (0.77)
Urinary leakage	1.73 (0.80)
Sexual function	2.19 (1.24)
Sexual interest	2.08 (1.26)
Bowel problems	1.35 (0.54)