Side-effects of treatment for localized prostate cancer: are they valued differently by patients and healthy controls?

Ida J. Korfage, Harry J. de Koning, J. Dik F. Habbema, Fritz H. Schröder* and Marie-Louise Essink-Bot

Departments of Public Health and *Urology, Erasmus MC, University Medical Centre, Rotterdam, the Netherlands

Accepted for publication 20 October 2006

OBJECTIVES

To determine how men treated for localized prostate cancer and who had permanent side-effects, and healthy controls, would value five descriptions of health states associated with side-effects of treatment for localized prostate cancer, hypothesising that patients would value the health states as less detrimental than men with no prostate cancer.

PATIENTS, SUBJECTS AND METHODS

In previous research, patients with prostate cancer reported high generic quality-of-life scores after primary treatment, despite side-effects; it was suggested that these patients accepted the side-effects, i.e. urinary, bowel and sexual dysfunction, as 'part of the bargain' because they felt they were saved from a life-threatening disease. Thus, we asked 54 men who had been treated for localized prostate cancer and had permanent side-effects, and 53 healthy controls, to value five descriptions of health states. All respondents valued all descriptions using two valuation methods, a visual analogue scale (VAS, range 0–100) and time trade-off (TTO, range 0–1). The respondent functioning was assessed using the EuroQol-5D, completed with items on urinary, bowel and sexual function.

RESULTS

Patients and healthy controls had similar valuations for nine of the 10 comparisons (five health states by two methods). Valuations in both groups resulted in the same ranking order of states on the TTO and one exchange in rank order on the VAS.

INTRODUCTION

Prostate cancer is increasingly being detected in its early stages due to PSA testing of asymptomatic men. More men receive treatment for localized prostate cancer and subsequently many of them face the long-term side-effects, including urinary, bowel and sexual dysfunction [1–5]. However, when completing generic health-related quality-of-life (HRQoL) measures, such as the Short Form 36 [6], these patients typically report high scores [1,7–14], e.g. patients’ scores are higher than age- and sex-adjusted normal scores, or scores do not decrease significantly after treatment.

The discrepancy between high generic HRQoL scores and the high prevalence of urinary, bowel and erectile dysfunction (ED) after treatment suggests that not enough is known about what the side-effects mean to patients.

It seems implausible that side-effects are of no interest to the patients. Explanations for the discrepancy that have been proposed include a short follow-up, so that patients assessed still expect their side-effects to be temporary, the unresponsiveness of generic HRQoL measures to the impact of side-effects of treatment for localized prostate cancer [8,15], and ‘response shift’ [4], which denotes an adaptation to a changed health situation [16]. In a previous report we showed that men who had side-effects of treatment for localized prostate cancer took these as ‘part of the bargain’, as inevitable consequences of treatment for a life-threatening disease [15]. To corroborate this result, we asked a group of patients with prostate cancer who had been treated for localized disease and had long-lasting side-effects and a group of men with no prostate cancer to value descriptions of health states associated with the side-effects of treatment for localized prostate cancer.

Patients with a certain disorder often rate health states describing their disorder as higher, i.e. better, than people without that disorder [17]; the ‘have-not have’ discrepancy [18]. Therefore, we hypothesized that the survivors of prostate cancer would value the health states associated with treatment as less detrimental than men with no prostate cancer history. We assessed if such differences in judgement were present and if so, of what size.

CONCLUSIONS

When asked to value five health states associated with side-effects of treatment for localized prostate cancer, there was no difference in the valuation of erectile, urinary and bowel dysfunction between patients with permanent side-effects after treatment and healthy controls. More likely explanations for the high generic quality-of-life scores after primary treatment for prostate cancer are a response shift and insensitivity of generic health-related quality-of-life measures.

KEYWORDS

health-related quality of life, prostate cancer, time trade-off, visual analogue scale

© 2007 THE AUTHORS
the present study, we aimed at selecting 50 interview participants from this group. Patients were eligible for the interactive computer interview if they were aged ≤74 years and if they had urinary, bowel and/or ED since, but not before, treatment for localized prostate cancer. Subjects with no prostate cancer ('healthy controls') were included from an epidemiological survey assessing the prevalence of BPH [19] and were therefore known not to have BPH or prostate cancer. The healthy controls were eligible for participation in the interactive interview if they were aged ≤74 years.

We analysed longitudinal data on 5 years of follow-up in 314 patients with prostate cancer to arrive at a limited number of health states that typically represent the most frequently occurring severity levels of the side-effects, and their combinations, after radical prostatectomy or external beam radiotherapy. We used the format of the EuroQol-5D classification of health [20] as a framework for the descriptions. The standard EuroQol-5D classification consists of five statements (on mobility, self-care, usual activities, pain or discomfort, anxiety or depression, respectively) with three levels each (no/ some/ extreme problems). We replaced the 'pain or discomfort' statement in each description by three statements regarding urinary, bowel, and erectile function.

We arrived at five descriptions (Appendix); the descriptions of 'Man 1', 'Man 2' and 'Man 4' represent different situations with permanent side-effects after radical prostatectomy, 'Man 3' and 'Man 5' represent different situations after external beam radiotherapy. We presented the descriptions of Men 1–5 without mentioning the association with cancer or cancer treatment, to prevent the 'part of the bargain' effect of a cancer label on the valuations.

The valuation tasks were included in an interactive Internet-enabled self-reported valuation questionnaire through a self-developed generic (adaptable) Internet-tool, using PHP (version 4.0.1 and higher), MySQL (version 3.22 and higher), and JavaScript (version 1.3) [21]. The computer-based questionnaire (VIA©; Valuations Inter-Active) can be applied through the Internet and stand-alone, and ensured completeness of data. It consisted of four parts: (i) respondent's functioning; (ii) ranking of health state descriptions; (iii) valuation of descriptions of Man 1 to Man 5 on a visual analogue scale (VAS); (iv) valuation of descriptions of Man 1 to Man 5 by time trade-off (TTO).

In Part 1 we asked the respondent to classify his health on the EuroQol-5D self-classifier complemented with items on urinary, bowel and sexual function, and to provide an evaluation of his health on a VAS anchored at the lower end (0) by 'worst possible health state' and at the upper end (100) by 'best possible health state'. Ticks at 25, 50 and 75 were marked with numbers. The VIA software allowed for responses in increments of 1.

In part 2, respondents were asked to rank two sets of five descriptions of health states from best to worst. The first set comprised five generic descriptions of health states, ranging from very good to very bad, without mentioning urinary, bowel or sexual dysfunctions. The second set consisted of the descriptions of 'Man 1' to 'Man 5'. These ranking tasks were intended as 'warming up' for the real work in parts 3 and 4 (data not reported). In part 3 the descriptions of Men 1–5 were valued on a similar VAS as used in part 1 for the evaluation of own health. Part 4 consisted of the valuation of the descriptions of Men 1–5 using TTO; in a TTO task, respondents express their preference for a given suboptimal health state by considering the number of life-years they are hypothetically willing to sacrifice to attain perfect health. Hence, the valuation task included a hypothetical TO between length and QoL. In the present study we used an impersonalized version of the TTO, that was developed to elicit a relatively common-sense judgement about which of two people is better off, without forcing subjects to make a (hypothetical) treatment decision. Previous results of the impersonalized TTO were promising [22]. For the valuation of each 'Man n', we presented descriptions of two hypothetical persons; the first of 'Man n' with a life-expectancy of 10 years, and the second with no problem but with a life-expectancy of 5 years. We asked the respondent to indicate which man he would rather be. Depending on the choice of the interviewee, a new choice was offered, e.g. if a respondent preferred to be the healthy man with 5 years in perfect health over being 'Man n' with a life-expectancy of 10 years, the subsequent choice offered consisted of 'Man n' for 10 years or perfect health for 9 years. The number of healthy years offered was thus systematically varied using an oscillating procedure. The utility was equivalent to the ratio between the final choice of disease-free time and years in the suboptimal health state, i.e. 10; e.g. if a respondent chose 7.5 healthy years instead of 10 years as 'Man n’, the resulting valuation score for ‘Man n’ was 0.75. The software allowed choices in increments of 6 months, the equivalent of 0.05 on a 0–1 scale.

Patients with prostate cancer thus not only valued their health state, but a scale of five health states associated with side-effects of treatment for localized prostate cancer. The interactive interviews took place at the participant's home or at the university. An interviewer was present to assist with questions but otherwise remained unobtrusive.

Between-group differences in background characteristics and descriptive statistics on generic and prostate cancer-specific items were assessed using chi-square tests for categorical variables and Mann-Whitney U-tests for continuous variables. All VAS and TTO data were converted to scores of 0–1. Rank, mean scores and SIs were calculated for each group, health state and method. The statistical significance of differences between groups in valuations for each health state was determined using Mann-Whitney U-tests, with P < 0.01 taken to indicate significance. Power analysis showed that differences of 0.08 points on a scale of 0–1 between average group scores could be detected as significant with α = 5% and (1 – β) = 80%. Cohen’s effect sizes of differences between groups were assessed, with effect sizes designated 'small' if >0.2 but <0.5 [23]. The correlation between the VAS and TTO valuations for patients and the controls was calculated (Pearson correlation and the intraclass correlation coefficient, ICC).

RESULTS

In all, 63 of the original group of patients with prostate cancer fulfilled the criteria for the interactive computer interview. Four withdrew, one each because of refusal after initial consent, having moved house, having died, and being out of contact. Of the remaining men, 54 were interviewed; one interview had to be ended prematurely because of the patient's memory problems, and 53 were completed.
VALUES FOR THE SIDE-EFFECTS OF TREATMENT FOR LOCALIZED PROSTATE CANCER

Of 56 eligible controls, 53 were interviewed; one interview ended prematurely because the participant considered ‘deciding’ about lifetimes inappropriate and 52 interviews were completed. The mean completion time was 30 min. On average, the controls were younger than the patients (63 vs 67 years, \( P < 0.001 \)). The controls reported significantly better urinary, bowel and sexual function than the patients, and rated their health better (86 vs 74, \( P < 0.001 \), Table 1). Fig. 1 and Table 2 also show the VAS and TTO scores. The comparison for each health state description of mean VAS scores showed statistically insignificant differences between patients and healthy controls for Man 1, 3, 4 and 5.

Only the mean VAS scores for Man 2 differed significantly between patients and controls (65 vs 60, \( P = 0.03 \), Table 2). Differences per state for mean TTO scores were statistically insignificant for all five health state descriptions. Effect sizes of differences per health state description between groups were <0.2, except for the VAS valuation of Man 2 (Fig. 1); SDs were on average 28% larger in patients than in controls.

Ranking the health state descriptions of Man 1–5 using mean valuation scores resulted in the same ranking order for patients and controls if based on mean TTO scores. The ranking order based on mean VAS scores showed an exchange of Man 2 and Man 3 between patients and controls. Valuations in both groups and by each method resulted in the same order except for Man 3; both groups rated him best when they applied TTO, but as third (patients) or second (controls) based on the VAS value.

The Pearson correlations between the valuation scores of patients and the controls were 0.98 for the five VAS valuations, and 0.99 for the five TTO valuations. The ICCs were 0.98 for VAS and for TTO. Six patients and five controls (10% of the participants) were reluctant to deal in TTO; they never chose to be in perfect health with a shorter life-expectancy.

DISCUSSION

At a group level there were few to no statistically significant differences between men with and without prostate cancer in the valuation of prostate cancer-specific health states. Effect sizes of the differences in nine of the 10 valuations were ‘smaller than small’.

In previous studies, patients with a certain disorder typically reported better ratings for health states describing such a disorder than those without that disorder [17], i.e. the ‘have-not-have’ discrepancy [18]. Often cited examples include the study by Sackett and Torrance [24], where patients valued a dialysis-specific health state at 0.56, vs 0.39 for the general public, and the study by Boyd et al. [25], where the patients’ average estimate of a colostomy-specific health state was 0.92, vs 0.80 in the general public. Stewart et al. [26] measured utilities for prostate cancer health states in older men, and found that men who had ED or urinary incontinence rated these states as slightly

### TABLE 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients</th>
<th>Controls</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary leakage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no leakage</td>
<td>22 (41)</td>
<td>47 (90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>some leakage</td>
<td>28 (53)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>serious leakage</td>
<td>3 (6)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Bowel problems</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>no problems</td>
<td>35 (66)</td>
<td>49 (94)</td>
<td></td>
</tr>
<tr>
<td>some problems</td>
<td>17 (32)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>serious problems</td>
<td>1 (2)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Sexually active</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>yes</td>
<td>23 (43)</td>
<td>42 (81)</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>30 (57)</td>
<td>10 (19)</td>
<td></td>
</tr>
<tr>
<td>ED</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>yes</td>
<td>42 (79)</td>
<td>11 (21)</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>11 (21)</td>
<td>41 (79)</td>
<td></td>
</tr>
<tr>
<td>Mean (so):</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, years</td>
<td>67.1 (4.3)</td>
<td>62.7 (4.3)</td>
<td></td>
</tr>
<tr>
<td>EuroQol utility score of own health (0–100)</td>
<td>83 (28)</td>
<td>92 (11)</td>
<td>0.105</td>
</tr>
<tr>
<td>EuroQol assessment of own health (0–100)</td>
<td>74 (17)</td>
<td>86 (10)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Chi-square tests for categorical variables

FIG. 1. The VAS and TTO valuations by patients and controls.
better than men who had not had the specific problems. Also, a review study on the differences in valuation for hypothetical and actual health states between patients and other raters showed that in most of 38 studies the patients’ values were higher than those of other groups [27]. However, Smith et al. [28] reported TTO utilities of patients with prostate cancer treated by radical prostatectomy, and found that men who had urinary and sexual bother valued their health state significantly worse than men with no sexual or urinary bother (0.767 vs 0.923, \( P = 0.015 \)). Ubel et al. [29] explored several factors that might contribute to discrepancies between patients and the general public (although healthy controls might not be completely comparable to the general public), e.g. incomplete health-state descriptions, whereby subjects ‘complete the blanks’ according to their experiences or stereotypes, and the ‘focusing illusion’, whereby subjects are made to focus on those activities affected by the disease, while ignoring activities unaffected by it. According to Gilbert et al. [30] people tend to underestimate the duration of their affective reactions to negative events. These factors, if indeed present, all contribute to healthy persons evaluating health states as worse than patients would do. This formed the basis for our a priori hypothesis that the patients would value disease-specific health states as better than controls. However, there were no significant between-group differences in nine of the 10 valuations.

We asked both patients and controls to evaluate health states associated with prostate cancer treatment, and found only small differences at group level, as well as high correlations between groups (the Pearson and ICC were close to 1). We examined the possibility of a different result had there been more respondents; with four times as many the results of eight of 10 valuations would have been identical, meaning that there is no significant difference between groups of respondents.

The health state descriptions combined statements on generic and urinary, bowel and sexual function, and were thus not intended to assess if, e.g. bowel function was valued worse than erectile function. However, there was a striking difference between the VAS valuation of Man 1 with serious ED and Man 4 with serious urinary leakage (and some problems with usual activities). This suggests that serious ED was regarded as less bad than serious urinary leakage, but the strength of this suggestion is limited by the additional statement in Man 4’s description of ‘some bowel problems, moderate ED’.

In both groups the mean TTO values were higher than mean VAS values if re-scaled to 0–1. Compromise techniques such as TTO share conceptual advantages over rating-scale techniques, because they require people to hypothetically sacrifice one valuable commodity (e.g. life-expectancy in TTO) to gain another valuable commodity (e.g. QoL), such that they are indifferent between the two states [31]. Valuations by VAS have no (hypothetical) consequences for the respondents, such as fewer life-years to be lived. We are not the first to note that a VAS thus generates lower mean values than TTO [32,33]. However, Dolan and Sutton [31] found that the relationship between VAS and TTO scores depended on the severity of the state; TTO values were higher than VAS responses for mild states and lower for more severe states. The disease-specific health states to be valued in the present study can be considered as comparatively mild. Our findings are thus in line with those of Dolan and Sutton.

Remarkably, in both groups, different valuation methods led to different preferences for Man 3. This suggests a method effect, i.e. the outcome of health state preferences did not depend solely on the descriptions, but also on the method that was applied. Such a result was reported previously [32].

As expected, the controls reported significantly better prostate cancer-specific function than patients. As the controls were on average younger (63 vs 67 years), age might have played a role. However, differences between groups in, e.g. ED, were so large (80% in patients vs 20% in controls)
that age seems to be an insufficient explanation.

In the present study we found no indications of the 'have-not have' discrepancy. This suggests that other explanations for high generic QoL scores after primary prostate cancer treatment are more important, i.e. response shift and especially insensitivity of generic HRQoL measures.

In conclusion, patients with permanent side-effects after treatment for localized prostate cancer and healthy controls did not differ in their valuations of urinary, bowel or ED. No indications of the 'have-not have' discrepancy were found. This suggests that other explanations for high generic QoL scores after primary prostate cancer treatment are more important, i.e. response shift and especially insensitivity of generic HRQoL measures.

ACKNOWLEDGEMENTS

The authors thank all patients for participating in the study, E. Neeleman for the friendly cooperation in the development of the computer-based questionnaire, Dr F. Groeneveld of the Department of General Practice for the recruitment of men without prostate cancer, R. Frenken for conducting part of the interview sessions, and the Dutch Cancer Society for funding this study (EUR 2000–2329).

CONFLICT OF INTEREST


REFERENCES


12 Galbraith ME, Ramirez JM, Pedro LW. Quality of life, health outcomes, and identity for patients with prostate cancer in five different treatment groups. Oncol Nurs Forum 2001; 28: 551–60


21 Essink–Bot ML, Stuifbergen MC, Meerdink WJ, Looman CW, Bonsel GJ. Time trade-off valuations of health states: no effect of respondent age, but how about individual response patterns? 2006; in press


24 Sackett DL, Torrance GW. The utility of different health states as perceived by the general public. J Chronic Dis 1978; 31: 697–704


26 Stewart ST, Lenert L, Bhatnagar V, Kaplan RM. Utilities for prostate cancer
health states in men aged 60 and older. 

Med Care 2005; 43: 347–55


Correspondence: Ida J. Korfage, Department of Public Health, Erasmus MC, University Medical Center Rotterdam, PO Box 2040, 3000 CA Rotterdam, the Netherlands.
e-mail: i.korfage@erasmusmc.nl

Abbreviations: VAS, visual analogue scale; TTO, time-trade-off; ED, erectile dysfunction; HR(QoL), health-related quality-of-life; ICC, intraclass coefficient.

APPENDIX
A description of health states associated with permanent side-effects after treatment for localized prostate cancer (affected dimensions in italics for presentational reasons). Man 1, Man 2 and Man 4 represent health states after radical prostatectomy; Man 3 and Man 5 represent health states after external beam radiotherapy

MAN 1
- no problems in walking about;
- no problems with washing or dressing self;
- no problems with performing usual activities;
- no urinary leakage;
- no bowel problems;
- (almost) never an erection if wished for, sometimes not;
- not anxious or depressed.

MAN 2
- no problems in walking about;
- no problems with washing or dressing self;
- no problems with performing usual activities;
- no urinary leakage;
- no bowel problems;
- (almost) never an erection if wished for, sometimes not;
- not anxious or depressed.

MAN 3
- no problems in walking about;
- no problems with washing or dressing self;
- no problems with performing usual activities;
- no urinary leakage;
- some bowel problems;
- sometimes an erection if wished for, sometimes not;
- not anxious or depressed.

MAN 4
- no problems in walking about;
- no problems with washing or dressing self;
- some problems with performing usual activities;
- serious urinary leakage;
- no bowel problems;
- (almost) always an erection if wished for;
- not anxious or depressed.

MAN 5
- no problems in walking about;
- no problems with washing or dressing self;
- some problems with performing usual activities;
- no urinary leakage;
- serious bowel problems;
- (almost) never an erection if wished for;
- moderately anxious or depressed.