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Patients' perceptions of mortality risk for localized prostate cancer vary markedly depending on their treatment strategy

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Treatment choice for localized prostate cancer (PCa) is a controversial issue, and mortality risk is probably the most decisive factor in this regard. The study aimed to compare prostate-cancer-specific mortality risk estimates for different treatment options assigned by patients managed with active surveillance (AS), radical prostatectomy (RP) and patients who had discontinued AS (DAS). Patients initially managed with AS or RP ($N = 370$) were matched according to length of therapy. All patients completed mailed questionnaires assessing their mortality risk estimates (in %) and prostate-cancer-specific anxiety. Differences in risk estimates among the three treatment groups were analyzed using ANOVA, relationships of clinical and psychosocial variables with risk estimates using standard multiple regression. In all treatment groups, the prostate- cancer-specific mortality risk was overestimated. This applied whether it was the patient's own treatment or the alternative treatment option. RP patients assigned a mortality risk to AS that was almost three times higher than that assigned to RP (50.9 ± 25.0 *vs.* 17.8 ± 19.7, $d = 1.48$; $p < 0.001$). Anxiety was significantly associated with risk estimates for AS ($p = 0.008$) and RP ($p = 0.001$). Compared with clinical data that suggest that the prostate-cancer-specific mortality risk for AS is low and does not significantly differ from that for RP, patients strongly overestimated the mortality risk. This was most markedly so in RP patients, who drastically overestimated the benefits of RP compared to the risk of AS. This overestimation could increase overtreatment and should therefore be corrected by better patient education.

Introduction

For localized prostate cancer (PCa), the choice of treatment strategies, in particular the choice between the most invasive strategy, radical prostatectomy (RP) and the least invasive, active surveillance (AS), where intervention is not offered until a predefined histological or biochemical disease progression occurs, is a controversial issue. The most widely chosen treatment strategy in most European countries and the United States is RP, followed distantly by radiotherapy and AS.[1,2] Mortality is probably the most important factor on which the recommendation and choice of treatments are based. Therefore, patients can only make informed treatment choices if they assess the mortality risk that comes with the different treatment options realistically. In a review of seven large AS series, most of them including both intermediate and low risk tumors, the cancer-specific mortality risk was 0–1% (median of longest follow-up 6.8 years).[3] Recently published data of Klotz *et al.* that included both low-risk and intermediate risk categories[4] showed that the mortality rate remained low beyond 15 years. In this study, of 993 men 15 (1.5%) had died of prostate cancer and 149 men (15%) from other causes. And also recently, Tosoian *et al.*[5] reported prostate-cancer-specific mortality rates of 0.1% with a follow-up of 15 years within a prospective AS program including only very low-risk and low-risk patients. In summary, the cancer-specific mortality is probably 3% or less after 10–15 years, if AS is the primary choice.[6] However, there are four main reasons to assume that patients' risk estimates will be biased.[7] (*i*) Because RP is still framed as the "default"[8] in clinical practice, it is likely that patients estimate the cancer-specific mortality risk for AS significantly higher than that for RP. (*ii*) Numbers are often presented in a way that is difficult for patients to understand. Even for the physician,

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What's new?

Patients with localized prostate cancer typically must choose between invasive treatments, like radical prostatectomy (RP), and less-invasive strategies, including active surveillance (AS). It is probable that the strategy chosen is the one patients think is most likely to minimize risk of death. However, communicating risk probabilities to patients is a great challenge. Here, men on AS and after RP were asked to rate the risk of dying from localized prostate cancer. The results show that all men, irrespective of the chosen treatment, overestimated prostate cancer mortality risk by 20–50 absolute percentage points. The findings indicate a need for better patient education.

filtering the relevant numbers out of a vast array of data and interpreting them adequately is a challenge.[9] It is even more so for the patient.[10] (*iii*) Anxiety has been shown to increase the perception of vulnerability and is thus likely to inflate risk perceptions.[7] (*iv*) Once a decision is made, information that seems to confirm the patient's decision could be perceived as more useful and more positive than information that weakens the own decision, resulting in more favorable estimates for the chosen treatment compared with alternative treatments. To our knowledge, only one study asked AS patients about their self-estimated progression risk.[11] Therefore, the study aimed to compare prostate-cancer-specific mortality risk estimates for different treatment options assigned by patients managed with either AS or RP, which has not been studied before.

Patients and Methods

Procedure

This study was nested within the prospective, multicenter, observational HAROW study, which included 3,169 patients newly diagnosed with localized PCa between July 2008 and July 2013. The study has been described in detail elsewhere.[12] In the present study, of the 1,787 men, who had chosen RP as the primary treatment option, 378 were matched according to length of therapy to the 378 men whose primary treatment option was AS. The time interval between treatment decision and time of the interview ranged from 19 to 78 months (mean 47.9 ± SD 15.4). Sixty-six men fell into the high-risk category (according to d'Amico[13]) and were excluded to improve the balance between the two patient groups. The final sample consisted of 150 RP patients, 142 patients still on AS, and 78 patients, who had switched to invasive treatment (DAS, discontinued AS) (flowchart, Fig. 1).

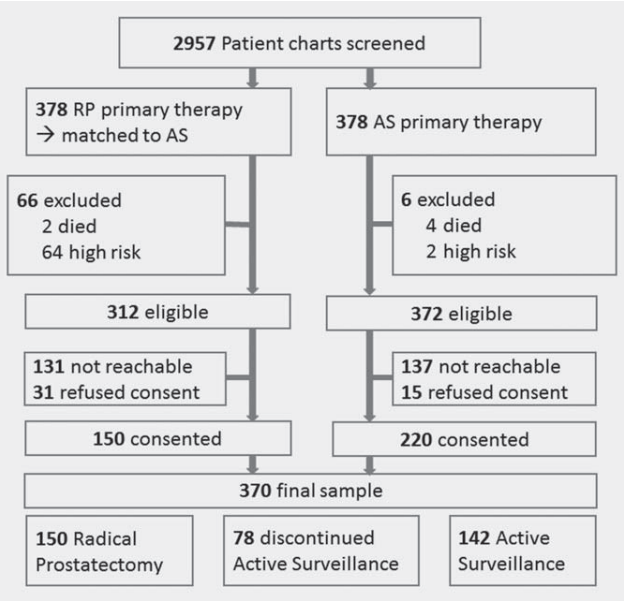

Figure 1. Flowchart of participants.

We obtained ethical approval from the Charité – Universitaetsmedizin Berlin (EA 1/242/13). Questionnaires were mailed to patients who had provided written consent.

Measurement

Clinical and sociodemographic baseline data were abstracted from case report forms. Prostate-cancer-specific anxiety was measured using the "Fear of Recurrence" subscale from the Memorial Anxiety Scale for Prostate Cancer (MAX-PC) with higher values reflecting higher levels of anxiety.[14] One example of the self-report 4-item subscale is "My fear of having my cancer getting worse gets in the way of my life." To assess numerical estimates, we asked men "How great, do you think, is the risk of dying from this disease, and not from another disease, given the below listed treatment strategies? Please provide your spontaneous estimate in percent." All patients were asked to provide risk estimates for both AS and RP.

Statistical analysis

We report means and standard deviations for metrically and ordinally scaled variables for the entire sample and for the treatment groups separately. For categorical variables, we display frequencies and percentages. Group comparisons for continuous variables were carried out using ANOVA to determine if the three patient groups differed significantly. Student's *t* test was used to analyze differences between two groups. For pairwise comparisons of risk estimates we also report Cohen's d as a measure of effect size. Using regression analyses, we examined the dependence of risk estimates on age, education, treatment group, length of therapy, PSA at diagnosis, risk category and anxiety. Collinearity diagnostics indicated no multicollinearity among the independent

Table 1. Sample characteristics

Characteristic	Total sample ($N = 370$)	AS ($n = 142$)	DAS ($n = 78$)	RP ($n = 150$)	p
Age, yrs, mean (SD)	66.6 (6.9)	68.8 (6.9)	66.9 (6.2)	64.4 (6.6)	<0.001
Higher education, *n* (%)	145 (39.4)	55 (39.0)	29 (37.2)	61 (40.9)	0.853
PSA at diagnosis (ng/mL), mean (SD)	6.14 (3.05)	5.47 (3.34)	5.84 (2.53)	6.93 (2.83)	<0.001
Tumor stage, *n* (%)					0.001
T1a-c	305 (82%)	126 (89%)	67 (86%)	112 (75%)	
T2a	40 (11%)	14 (10%)	8 (10%)	18 (12%)	
T2b	25 (7%)	2 (1%)	3 (4%)	20 (13%)	
Gleason score, *n* (%)					<0.001
4–6	292 (80%)	136 (97%)	71 (91%)	85 (58%)	
7a	61 (17%)	5 (4%)	7 (9%)	49 (33%)	
7b	13 (4%)	0 (0%)	0 (0%)	13 (9%)	
Risk classification,[1] *n* (%)					<0.001
Low risk	296 (80%)	125 (88%)	67 (86%)	104 (69%)	
Intermediate risk	74 (20%)	17 (12%)	11 (14%)	46 (31%)	
Length of therapy, months, mean (SD)	47.9 (15.4)	46.7 (15.3)	48.8 (15.2)	48.7 (15.7)	0.44
Anxiety,[2] mean (SD)	3.05 (2.77)	3.33 (2.64)	3.09 (2.89)	2.76 (2.80)	0.208

AS, active surveillance; RP, radical prostatectomy; DAS, discontinued active surveillance.
[1]Risk classification according to d'Amico.[12]
[2]Subscale "Fear of Recurrence", range: 0–12; SD, standard deviation; PSA, prostate-specific antigen.

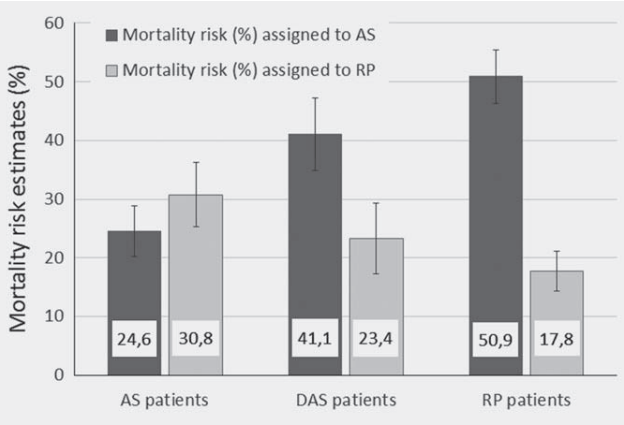

Figure 2. Differences in numerical estimates (in %) assigned by patients on AS, patients who discontinued AS, and RP patients for the mortality risk linked to AS and RP.

variables. An alpha level of $p < 0.05$ was considered statistically significant.

Results

The sample characteristics are shown in Table 1. AS patients and those who discontinued AS were on average older, had lower PSA values, more favorable tumor stages and Gleason scores. Accordingly, fewer RP patients (69%) were classified as low-risk as opposed to AS patients (88%) or patients discontinuing AS (DAS patients) (86%). Patient groups did not differ in education, length of therapy and anxiety.

Patients were asked to assign numerical estimates (in %) for the mortality risk linked to both AS and RP (Fig. 2).

Whereas AS patients' estimates for AS and RP differed only moderately (24.6 ± 22.4 *vs.* 30.8 ± 25.6, CI 95% = (-12.3, -1.1), $d = 0.26$; $p < 0.02$), RP patients assigned a risk to AS that was almost three times higher than that assigned to RP (50.9 ± 25.0 *vs.* 17.8 ± 19.7, CI 95% = (28.2, 38.5), $d = 1.48$; $p < 0.001$). DAS patients estimated the mortality risk of AS 1.8 times higher than that linked to RP (41.1 ± 23.6 *vs.* 23.4 ± 23.8, CI 95% = (12.3, 27.1), $d = 0.75$; $p < 0.001$).

Using standard multiple regression, we examined whether sociodemographic characteristics, clinical variables and anxiety were independently associated with mortality risk estimates. After controlling for all variables, treatment group, risk category and anxiety contributed significantly to the risk estimation of AS (Table 2). The direction of the relationship indicates that RP and DAS patients estimated the mortality risk of AS significantly higher than AS patients did. Within this model, 23.3% of the variability in risk estimates of AS was explained (adjusted $R^2 = 0.23$), almost exclusively by treatment group and anxiety. Table 3 displays the regression of risk estimates for RP on the same set of variables. Here, younger age, treatment group AS and higher anxiety independently contributed to the patients' risk estimates of RP.

Discussion

Across all treatment groups, men provided estimates of the risk of dying from prostate cancer that likely represent

Table 2. Predictors for the mortality risk assigned to active surveillance

	β	95% CI		p
Age (yrs)	0.107	−0.027	0.835	0.066
Higher education	−0.095	−10.779	0.627	0.081
Therapy length (months)	−0.035	−0.246	0.126	0.527
Treatment group RP	0.638	26.822	42.063	<0.001
Treatment group DAS	0.253	8.230	23.192	<0.001
Risk category (intermediate risk)	−0.124	−14.513	−0.023	0.049
PSA at diagnosis (ng/mL)	−0.113	−2.144	0.015	0.053
Anxiety	0.147	0.381	2.492	0.008

β, standardized regression coefficient; CI, confidence interval; RP, radical prostatectomy; DAS, discontinued active surveillance; PSA, prostate-specific antigen.

Table 3. Predictors for the mortality risk assigned to radical prostatectomy

	β	95% CI		p
Age (yrs)	0.159	0.118	0.944	0.012
Higher education	−0.109	−10.485	0.317	0.065
Therapy length (months)	−0.043	−0.245	0.114	0.475
Treatment group AS	0.165	0.890	16.168	0.029
Treatment group DAS	0.065	−3.933	10.888	0.356
Risk category (intermediate risk)	−0.029	−8.176	5.335	0.679
PSA at diagnosis (ng/mL)	−0.011	−1.152	0.965	0.861
Anxiety	0.195	0.650	2.618	0.001

β, standardized regression coefficient; CI, confidence interval; AS, active surveillance; DAS, discontinued active surveillance; PSA, prostate-specific antigen.

overestimates ranging from almost 20% to approximately 50% (see Fig. 2). The most noticeable overestimation occurred for RP patients estimating the mortality risk of AS. They assigned a 50% risk to AS, which was about three times higher than that assigned to RP, estimating that more than every second man choosing AS would die from prostate cancer and not from another disease.

Differences in risk estimates among treatment groups were independent of the respective risk category. Why do men, in the age of Internet, overestimate the prostate cancer-specific mortality risk so markedly? One reason may be that, since the introduction of PSA testing, the early recognition of prostate cancer has improved considerably. Currently, men with low-risk prostate cancer comprise up to 70% of those newly diagnosed.[15] Nevertheless, men may still have the many unfavorable courses of prostate cancer of previous generations in their minds. Moreover, the results of randomized trials that directly compare RP and AS have not been reported yet and clinicians have to rely on observational studies with all best-known limitations.[16] Despite these restrictions, the large overestimation of risk in light of the available, observational data demonstrates a clear failure of patient education. Physicians should make a great effort to not only inform about the different treatment options, but also to provide scientific information in the most transparent way possible. In this regard, it has been suggested to communicate natural frequencies rather than conditional probabilities, absolute risks rather than relative risks, and mortality rather than survival rates.[17] Additionally, it has been recommended to use simple tabular or visual displays including the number of diagnoses, death cases and side effects.[18]

Our results indicate a relationship between risk perception and anxiety. Risk perception is not merely a cognitive process, but also an affective one.[7,19] Our cross-sectional design does not reflect causal relationships, but it is likely that the perception of a high risk increases anxiety. Because anxiety generally affects treatment decisions[20] and may have an impact on adherence to AS,[21] it seems important to elicit the mechanism of a possible vicious circle of risk perception, anxiety and decision making.

Strengths and Limitations

To our knowledge, this is the first study on how PCa patients estimate the cancer specific mortality risk. Strengths of this study include one of the largest samples for the comparison of RP and AS, a high external validity by a multicenter

design and the inclusion of men who switched to curative treatment. This study has limitations. First, the cross-sectional study design does not allow for causal interpretation. For example, it is not possible to clarify the predictive priority of either anxiety or risk estimates across several time points. Second, people may assign higher risk estimates when they are uncertain. In this case, they would use the scale differently than experts.[7] In the interpretation of the data, we therefore focused on comparisons among the patient groups that are easier to interpret. Third, the reasons for discontinuing AS are likely to differ widely, but the number of DAS patients did not allow conducting reliable subgroup analyses. Fourth, our results may be highly population-dependent, because of factors such as differing national guidelines and varying patient awareness of AS. However, the recent commentary by Blumenthal-Barby *et al.*[8] on the way "toward ethically responsible choice architecture," which refers to America as well as to several European countries, suggests that the underlying problem is strikingly widespread.

Conclusion

RP patients strongly overestimate the benefit of RP and perceive the mortality risk of AS as much higher than do AS patients. This overestimation likely indicates a failure in patient education and could encourage aggressive treatment. Future studies need to show whether better patient education, for instance by providing more transparent information, helps patients with localized PCa to evaluate risks more realistically, reduces anxiety levels and ultimately leads to more informed decisions.

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Authors' Contributions

FK designed the study, carried out the research, analyzed the data and wrote the manuscript. LH contributed to the design of the study, and participated in the acquisition and interpretation of the data. KN performed the data analysis. JH helped to draft the manuscript. MS reviewed the manuscript for important intellectual content. CS conceived of the study and helped to draft the manuscript. WG participated in the design of the study, interpretation of the data, and reviewed the manuscript. All authors read and approved the final manuscript.

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