EUROPEAN JOURNAL OF CANCER 45 (2009) 2569–2573

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Do the risk factors of age, family history of prostate cancer or a higher prostate specific antigen level raise anxiety at prostate biopsy?

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ARTICLE INFO

Article history:
Received 4 February 2009
Received in revised form 9 March 2009
Accepted 17 March 2009
Available online 16 April 2009

Keywords:
Anxiety
Prostate biopsy
Prostate cancer
Risk factors
Screening

ABSTRACT

To date, little is known of the impact knowledge of personal risk factors has on anxiety in men undergoing biopsy tests for prostate cancer. This analysis explores anxiety scores of men at higher risk due to age, family history of prostate cancer and a higher prostate specific antigen (PSA) level when proceeding from PSA test to prostate biopsy. A prospective cohort of 4198 men aged 50–69 years with a PSA result of >3 ng/ml was studied, recruited for the Prostate testing for cancer and Treatment study (ProtecT). Anxiety scores at the time of biopsy were lower in older men ($p < 0.001$). No age group showed an increase in anxiety as the men proceeded from PSA testing to biopsy, although older men did not show the same level of decrease in anxiety as younger men ($p = 0.035$). There was no difference in anxiety scores at biopsy between men with or without a family history of prostate cancer ($p = 0.68$), or between those with a raised PSA of 10–<20 ng/ml compared to a PSA result of 3–<10 ng/ml ($p = 0.46$). Change in scores since the initial PSA test appeared unaffected by family history ($p = 0.995$) or by PSA result ($p = 0.76$). Within the context of a research study, the increased risk of prostate cancer through older age, having a family history of prostate cancer, or having a significantly elevated PSA level appears to have no detrimental effect on men's anxiety level when proceeding to biopsy.

1. Introduction

Testing for prostate cancer is controversial in the absence of evidence of benefit from randomised controlled trials, although such trials are currently underway.[1] Before a decision is made to proceed with a biopsy, there are several factors that have to be considered in conjunction with a raised prostate specific antigen (PSA) level, such as risk factors in predicting the likelihood of a positive result. These factors include age, ethnicity, family history of the disease, findings from digital rectal examination (DRE) and previous biopsy results.[2] Guidance from the United Kingdom's National Institute for Health and Clinical Excellence (NICE) encourages that risk factors should be discussed with men in order to make an informed decision on whether to have a biopsy test,[3] however a recent commentary identified that there are no data to determine the impact of these risk factors on patient's anxiety, nor on the decision making process to have a biopsy.[4]

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0959-8049/$ - see front matter
doi:10.1016/j.ejca.2009.03.016

Incidence and mortality of prostate cancer are strongly associated with age. Occurrence of prostate cancer in patients aged below 50 years is very low, with around 60% of cases registered in men over 70 years of age.[5] Prostate cancer also displays a familial pattern, with increased risk with a positive family history shown in numerous studies.[6] The awareness of the higher risk associated with family history is such that in the United States, it is recommended that men with a family history begin screening for prostate cancer with a PSA test between 40 and 50 years.[7] Positive predicted values for risk of prostate cancer at biopsy have been estimated from these associated risk factors, with a substantial increase in level of risk with multiple risk factors. At time of first biopsy, for white men with a PSA <4 ng/ml, a normal DRE and with no other risk factors, risk of prostate cancer at 50 years of age is predicted as 10%. For those aged 70 years, with a positive family history and a PSA level >10 ng/ml, the predicted risk of prostate cancer reaches around 80%.[8]

Creating a negative psychological response such as anxiety is an important consideration for any testing programme for disease. It has previously been suggested that receiving a raised PSA result and going on to have further testing for prostate cancer does not appear to have a detrimental effect on the measures of psychological health in the United Kingdom (UK),[9] with similar conclusions from a screening programme in the Netherlands.[10] However, it could be anticipated that knowledge of risk factors may increase anxiety for patients at higher risk, particularly after discovery of a raised PSA level. This has been indicated in studies of other cancer populations, where awareness of belonging to a risk group was associated with increased levels of distress and anxiety in women being screened for ovarian cancer. Around one-third of these women deemed at high risk due to a personal or family history of cancer reported high levels of cancer-associated anxiety, and approximately 18% had scores that fell into the clinical range for depressive symptoms.[11]

To date there is little known about whether anxiety in men being tested for prostate cancer changes throughout the course of the testing process specifically for those in higher risk categories. This current analysis examines anxiety levels of men undergoing a testing programme for prostate cancer and focuses on two of the commonly known risk factors: age and family history of prostate cancer. Anxiety at the time of the biopsy procedure is examined, and compared to the level recorded at attendance for the initial PSA test. The analysis aims to provide data for the unanswered question on whether being of higher risk impacts on anxiety at the biopsy testing stage.[4] Men with a raised PSA level of 3–<20 ng/ml are the group likely to be in decision of whether to undergo a prostate biopsy, with a higher PSA result equating to higher risk. We therefore also explore whether anxiety at the biopsy appointment is affected by PSA result.

2. Materials and methods

Data for this analysis were obtained from men aged 50–69 years, across nine sites throughout the UK, recruited as part of the Prostate testing for cancer and Treatment study (ProtecT), a randomised trial of treatment for localised prostate cancer[12] (ISRCTN number 20141297).

Anxiety was measured using the Hospital Anxiety and Depression Scale (HADS),[13] a questionnaire consisting of 14 statements to be rated on a four-point scale (0–3), designed to detect clinical cases of depression and anxiety. Seven items form a depression subscale and seven items an anxiety subscale. An overall anxiety score was calculated by addition of the responses to the individual anxiety items. A total score of 8 or more is considered to be of clinical significance.

After acceptance of an invitation to take part in the ProtecT study, men attended a nurse-led prostate check clinic, run at either their general practice surgery or local hospital. Men eligible for the study were offered a PSA test, administered by the study nurse. The HADS was completed on attendance at the clinic (before the PSA results were known), and age and the men's own recall of family history of cancer were recorded by study staff. Those men with a raised level of >3 ng/ml were invited by letter to attend their local urology hospital department for a transrectal ultrasound-guided biopsy (TRUS-B), DRE and second PSA test. On the day of the biopsy procedure, participants completed the HADS again as a component of the ProtecT trial questionnaire booklet.

The study group consisted of those men who had a biopsy following a raised PSA level, and had complete information on age, family history of prostate cancer, anxiety and PSA results. Of 5756 men who returned questionnaires at the biopsy stage, 4198 men had completed all the HADS anxiety items both at biopsy and on the previous questionnaire completed at the prostate check clinic. Within this sample, 4176 had complete data on family history and 4159 had a PSA result between 3 ng/ml and <20 ng/ml.

Approval for the ProtecT study was obtained from Trent Multi-centre Research Ethics Committee.

2.1. *Statistical analysis*

Very few men in the data set had more than one first degree relative affected with prostate cancer ($n = 7$) and so men were grouped by those with at least one affected relative (father or brother) and those with unaffected relatives. Age was examined as four 5-year age bands. For the analysis of anxiety in men grouped by PSA level, men with a result of 3–<10 ng/ml were compared to those with a result of 10–<20 ng/ml. Men with a PSA of >20 ng/ml were not examined due to the likeliness of advanced prostate cancer and hence being dealt with urgently by urologists, outside of the ProtecT study. Linear regression models with HADS anxiety score as the outcome measure were fitted using Stata® 10 (Stata Corp, College Station, TX; 2007). All models were adjusted for between-centre differences, the nine study centres being distinguished by the addition of eight dummy variables.

3. Results

For those men who were invited to attend a biopsy appointment but where there was no log of completed questionnaires ($n = 1984$) – indicating non-attendance for biopsy or non-completion of questionnaire at biopsy – risk factor profiles were comparable to those in our study cohort. Logistic regression analysis showed no difference for the cohort in age-group categories ($p = 0.395$); χ^2 analysis showed no difference for

family history groups ($p = 0.834$) or PSA result groups ($p = 0.435$). Within the cohort studied, the average time interval between men's attendance at the prostate check clinic (time of initial PSA test) and the biopsy invitation date was 54.8 days.

Mean anxiety scores at biopsy and the change in scores from those recorded at the initial prostate check clinic (before the PSA test) are presented in Table 1. At biopsy, a significant relationship between anxiety level and age was found, showing a lower level of anxiety with older age ($p < 0.001$). The change in anxiety score from first PSA test to the time of biopsy gave evidence of reducing anxiety in younger men while scores remain relatively stable in older men ($p = 0.035$). For family history, no significant difference in anxiety levels between those with affected relatives and the rest of the cohort was observed at biopsy ($p = 0.681$), and no association between family history and change in anxiety level between the two assessment points was found ($p = 0.995$). Those men with a higher PSA level at their initial blood test had comparable anxiety scores when attending for the biopsy appointment to those reported by men with a lower PSA level ($p = 0.459$). Change in anxiety scores reported by the men at biopsy from those reported at prostate check clinic (before they were aware of their PSA result) appeared unaffected by the PSA level ($p = 0.760$). A model mutually adjusted for age, family history and PSA result as well as recruiting centre led to the same conclusions for all three risk factors studied. Further analysis explored the anxiety levels of those men with combined risk factors – older age (>60 years) and a family history of prostate cancer ($N = 149$), older age and a higher PSA level (>10 ng/ml) ($N = 232$), and family history of prostate cancer with a higher PSA level ($N = 23$). Interaction tests suggest weak evidence of an increased effect of higher PSA on anxiety levels at biopsy ($p = 0.062$) and change in anxiety since PSA test ($p = 0.055$) in men with a family history of prostate cancer, compared to the effect of a higher PSA in men with no family history.

4. Discussion

It was recently stated that little is known about how the risk factors associated with a positive biopsy result impact on anxiety levels when men proceed from PSA testing to prostate biopsy.[4] We conclude that older age and a family history of prostate cancer appear to have no detrimental effect on anxiety between these two testing stages in the diagnosis of prostate cancer. With older age, anxiety levels overall are lower than those reported by younger men. Our findings also indicate that having a higher PSA level has little effect on anxiety in those recalled for biopsy. These results are suggestive that the screening process for prostate cancer affects men's anxiety very little; even at the biopsy testing stage and for those men who are aware that they are of greater risk of a positive result.

The sample studied was drawn from men involved in the ProtecT study, providing information from a large, multi-centre, community based population. This design was advantageous in having initial information of prostate cancer being relayed in a standardised format by research staff. However, there was no control over the knowledge gained by men prior to enrolment to the study or outside of the clinic visits, and data were not recorded on the level of awareness the men had of their risk. Furthermore, the current analysis examines only those responding to invitation for PSA testing within a designed study. Depending on the beliefs of men when making the decision to be screened, it may be reasonable to expect no change in anxiety between PSA testing and biopsy for those who have chosen to be tested. This hypothesis is

Table 1 – Anxiety scores compared between age groups (n = 4198), those with and without a family history of prostate cancer (n = 4176) and by PSA result (n = 4159).

	Score at biopsy Mean (SD)	Change in score since first clinic visit Mean (SD)	N (%)
Age group (years)			
50–54	5.49 (3.63)	–0.18 (2.46)	442 (11)
55–59	5.11 (3.60)	–0.18 (2.80)	1,042 (25)
60–64	4.85 (3.51)	–0.02 (2.66)	1,335 (32)
65–69	4.48 (3.39)	0.03 (2.60)	1,379 (33)
Difference in means per category increase[a] (95% CI)	–0.33 (–0.43, –0.22)	0.09 (0.01, 0.17)	
p	<0.001	0.035	
Affected first degree relatives			
None	4.87 (3.52)	–0.06 (2.66)	3,925 (94)
At least one	4.78 (3.56)	–0.06 (2.70)	251 (6)
Difference in means[a] (95% CI)	–0.09 (–0.54, 0.35)	–0.001 (–0.34, 0.34)	
p	0.68	0.995	
Initial PSA result (ng/ml)			
3–<10	4.85 (3.51)	–0.06 (2.66)	3,852 (93)
10–<20	4.97 (3.72)	–0.03 (2.76)	307 (7)
Difference in means[a] (95% CI)	0.16 (–0.26, 0.57)	0.05 (–0.26, 0.36)	
p	0.46	0.76	

PSA, prostate specific antigen; SD, standard deviation; CI, confidence interval.
a Adjusted for study centre differences.

supported by findings from qualitative research – that a biopsy is typically seen as the final step in a two-stage diagnostic process.[14] In addition, our analysis did not examine anxiety in those who chose not to have a biopsy (although previous research with men who refused a biopsy – approximately 12% – indicated no difference in anxiety compared with those accepting biopsy,[15]) neither did it incorporate anxiety levels of those not eligible for the trial, such as those over 70 years of age, or with a PSA result >20 ng/ml. Outside these study criteria and for those being investigated for prostate cancer unexpectedly, anxiety levels may vary. Caution must therefore be taken before generalising these findings to the wider population and in the context of the National Health Service (NHS).

The limited published research on anxiety levels of those at higher risk by age and family history generally examined anxiety levels at PSA test, whereas here we focus on these risk groups at a further stage in the testing process. The results of this analysis build upon findings of the Swedish cohort of the European randomised study of screening for prostate cancer (ERSPC), which reported a significant negative relationship between age and anxiety at biopsy, as well as concluding that most men with a family history of prostate cancer did not experience more anxiety when being tested compared to men with no family history.[16] Our current data add strength to these previous findings by using a more robust measure of anxiety – the HADS questionnaire – a tool that has been widely used for investigating anxiety in cancer populations. A potential weakness in this area of research is that it has been recognised that there is a need for a more sensitive and specific measure to detect anxiety in prostate cancer patients,[17] with substantial mood changes detected in qualitative research on men being tested for prostate cancer.[14]

The level of awareness of the risk factors within the study population should be taken into account when considering these results. Any anxiety associated with risk would be dependent on the individual's degree of knowledge and understanding of the risk factors. The significance of a raised PSA level is known as a prerequisite for further testing, although men in this study are informed that an increase in PSA can be caused by factors other than cancer. Surveys have found that not all men are aware of the risks of age and family history of prostate cancer, including some misconceptions of possible risk factors.[18,19] Aside from the information delivered at the initial PSA test, if no further information about the risk of age and family history is either provided or sought out when proceeding to biopsy, a consistent level of anxiety across groups might be expected. Likewise, the ProtecT study biopsy invitation letter informs men that their blood test showed a raised PSA level, but does not detail the PSA result. The standard ProtecT study information about risk factors is brief and only intended as a guideline for staff, therefore the depth of information given at the clinic appointments may have differed depending on the men's needs and interests. Our analysis controlled for any potential differences across the UK centres at which the men were tested and showed no significant variation in anxiety scores between the nine locations, though it is likely that the degree to which risk factor topics are discussed and the delivery of risk information will vary in clinical practice outside the study.

However, raised awareness is not just the influence in the consulting room; easily available online resources guide patients clearly to the risk factors of age and family history.[20–22] A raised PSA level and invitation for biopsy is a likely time point for men to investigate further for information on prostate cancer.[23] As internet usage becomes increasingly more common in the generation of men likely to be tested for prostate cancer, a wide variety of information regarding risk factors becomes readily available. In the attempt to create a balance between providing sufficient detail for the patient to make an informed choice on whether to proceed with testing whilst avoiding increased anxiety, it will therefore be increasingly important for healthcare professionals to be aware of the knowledge the patient has of the risk factors, and advise on the relevance to the individual. Research into increasing awareness of knowledge of the risk factors of cancer has shown no increase in anxiety in the general population,[24] although a review of intervention programmes in populations being screened for disease found insufficient data to report the effect that personalising risk information has on anxiety.[25]

In conclusion, our findings have shown that men at risk from prostate cancer by being of older age, having a family history of the disease, or having a higher PSA result do not report an increase in anxiety at the biopsy testing stage. This has significance for clinicians discussing risk information with men making a decision whether to undergo biopsy, as well as assessing potential side effects of a prostate cancer screening programme. Further research is needed to evaluate individuals' knowledge of risk factors whilst undergoing the testing processes, and to utilise a more sensitive measure of anxiety.

Conflict of interest statement

None declared.

Acknowledgements

The authors would like to acknowledge the tremendous contribution of all members of the ProtecT study research group. The ProtecT study is funded by the Department of Health NHS Health Technology Assessment Programme (Projects 96/20/06 and 96/20/99). The views and opinions expressed in this report are those of the authors and do not necessarily reflect those of the Department of Health. The funders had no involvement in this work.

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