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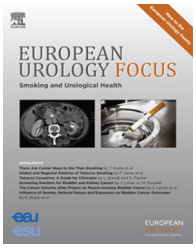

Prostate Cancer

Long-term Survival Outcomes for Men Who Provided Ejaculate Specimens for Prostate Cancer Research: Implications for Patient Management

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Abstract

Background: Determining whether men diagnosed with early prostate cancer (PCa) will live long enough to benefit from interventions with curative intent is difficult. Although validated instruments for predicting patient survival are available, these do not have clinical utility so are not used routinely in practice.
Objective: To test the hypothesis that volunteers who provided ejaculate specimens had a high survival rate at 10 and 15 yr and beyond.
Design, setting, and participants: A total of 290 patients investigated because of high serum prostate-specific antigen donated ejaculate specimens for research between January 1992 and May 2003. The median age at the time of ejaculation was 63.5 yr. 153 of the donors were diagnosed with PCa and followed up to December 31, 2013.
Outcome measurements and statistical analysis: Survival outcomes were compared with those for the whole population, as indicated by life expectancy tables up to 20 yr.
Results and limitations: Men in the PCa group had life expectancies comparable with values listed in life expectancy tables for the whole population. Overall, PCa-specific and relative survival were significantly better for men in the non-PCa and PCa groups in comparison with men diagnosed with PCa in Queensland during the same period. Relative survival for those aged 20–49, 50–64, and ≥65 yr was >100% for ejaculate donors and 81.5%, 82.7%, and 65.2%, respectively, for the Queensland Cancer Registry reference at 10 yr. These findings for this highly selected patient cohort support the hypothesis that an ability to provide an ejaculate specimen is associated with a high likelihood of surviving 10–20 yr after donation, whether or not PCa was detected.
Conclusion: Life expectancy tables may serve as a quick and simple life expectancy indicator for biopsy patients who donate ejaculate.
Patient summary: Life expectancy tables indicated survival of up to 20 yr for men who provided ejaculate specimens for prostate cancer research.

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1. Introduction

Selecting the most appropriate management for men with early prostate cancer (PCa) is beset by many uncertainties [1,2]. Prominent among these is predicting which patients will live long enough to benefit from interventions with curative intent given the long natural history of PCa and the age groups involved. In terms of survival, life expectancy of at least 10 yr is generally accepted as required to justify treatment and therefore testing [3,4].

Published evidence indicates that doctors are less than perfect in estimating survival [5]. In the Prostate Cancer Intervention versus Observation Trial (PIVOT) of radical prostatectomy (RP) and observation for localized PCa, 47.0% randomised to RP died during a median follow-up of 10.0 yr, compared with 49.9% assigned to observation; 5.8% died from PCa or treatment in the RP group compared with 8.4% in the observation arm [6]. In the randomised Swedish trial of RP versus watchful waiting (WW), 57.6% in the RP group and 70% in the WW group had died, 12.4% and 28.4%, respectively, from PCa, during a median follow-up of 13.4 yr [7]. Comparable outcomes have been observed following radiation therapy [8]. Daskivich et al [9] observed from the Surveillance, Epidemiology, and End Results-Medicare database that for 96 032 men aged >66 yr with early-stage PCa (Gleason ≤7) diagnosed during 1991–2007, 52% had life expectancy <10 yr, and nearly half had received aggressive treatment.

Although validated instruments are available for investigating general comorbidity-related deaths [10], none has become established in routine clinical use on a day-to-day basis, reflecting findings from a systematic review that found none of the life expectancy prediction tools available for localised PCa patients is sufficiently adequate to justify implementation into clinical practice [11]. It has recently become apparent that the onset of erectile dysfunction (ED) serves to herald fatal events from cardiovascular disease [12]. One large study reported a median time to death from a cardiovascular cause following the onset of ED to be 10 yr [13] since the reason for ED in the majority of cases is impaired arterial flow [12]. However, assessment of ED through patient histories and validated instruments is problematic because of the unreliability of patient reporting in questionnaires such as the International Index of Erectile Function (IIEF) [14,15].

We have been studying ejaculate as part of our early PCa research studies for many years, and hypothesised that these volunteers, all of whom had been vetted by urologists and were considered for treatment with curative intent should significant PCa be detected, would have a high survival rate, and that the ability to provide an ejaculate specimen would hence serve as a simple indicator of life expectancy. Thus, the aim of this study was to examine the survival outcomes for men who provided ejaculate specimens before 2003 for our research studies.

2. Patients and methods

2.1. Patients

Between January 1992 and May 2003, men referred to the Urology Unit of the Royal Brisbane and Women's Hospital (RBWH) (93%) or attending a urologist privately (7%) for investigation of abnormal prostate-specific antigen (PSA) with or without an abnormal digital rectal examination (DRE) were approached to volunteer a specimen of ejaculate for our research into early diagnosis of PCa. All were booked to have a diagnostic transrectal ultrasound (TRUS)-guided biopsy. Ejaculate specimens were provided before or 1 mo after biopsy.

2.2. Histology and PSA

Histologic diagnoses were obtained from the Queensland Cancer Registry and cross-checked with Queensland Health databases, institutional research files, and the files of relevant private pathology laboratories. Serum PSA levels before ejaculate donation and biopsy procedures were also obtained by interrogating the databases of Queensland Health and private Queensland pathology laboratories.

2.3. Patient outcomes

Dates and causes of death were obtained from the Queensland Health Hospital Business Corporate Information Services programme, Queensland Cancer Registry, patient hospital notes, relevant research databases, and private doctors' records, and were confirmed via the National Death Index.

2.4. Ethical approval

Human research ethics approval was given by the University of Queensland (project no. 2006000262) and from RBWH ethics committees (94/29; 1995/088B) with access to the Queensland Cancer Registry data approved by Queensland Health.

2.5. Measures

The cohort was stratified into three groups (biopsy positive, biopsy negative, and no biopsy performed) according to their biopsy status for PCa. PSA before ejaculate donation (<4 ng/ml, 4–10 ng/ml, and >10 ng/ml) and patient age at the time of ejaculation (modelled as a continuous variable but reported in categories of <50 yr, 50–65 yr, and >65 yr) were considered in the analyses and compared with Queensland population 10–yr survival data for PCa diagnoses during 1993–2003.

2.6. Statistical analysis

Survival times were taken from the date of ejaculate donation to the date of death or December 31, 2013, whichever came first. Men not known to have died by December 31, 2013 were considered alive, and therefore censored in the survival analysis. Median potential follow-up time was calculated using the reverse Kaplan-Meier method [16].

Our primary outcome of interest was all-cause survival. Kaplan-Meier survival curves were generated for the total cohort and stratified by biopsy status, PSA before ejaculate donation, and age group at the time of ejaculation.

In the absence of comparative data for men who did not provide ejaculate specimens during the study period, we used total population and cancer registry data as the comparison groups. Differences observed using this methodology are thus likely to be biased toward the null compared with the true value. We used relative survival to compare all-cause survival outcomes among the cohort with that for the age- and sex-matched population. The Ederer II method [17] was used to calculate expected survival.

While previous studies have used generalised linear models with a Poisson error structure to model excess mortality, convergence issues when the cohort mortality is less than for the general population [18] necessitated comparison of relative survival estimates for subgroups