No Detrimental Effect of a Positive Family History on Long-Term Outcomes Following Radical Prostatectomy

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Purpose: Overall 1 in 5 patients with prostate cancer has a positive family history. In this report we evaluated the association between family history and long-term outcomes following radical prostatectomy.

Materials and Methods: Patients treated with radical prostatectomy were identified from a German registry, and separated into positive first-degree family history vs negative family history (strictly negative, requiring at least 1 male first-degree relative older than 60 years and no prostate cancer in the family). Kaplan-Meier curves and Cox proportional hazards models were used for association analyses with biochemical recurrence-free and prostate cancer specific survival.

Results: Median followup for 7,690 men included in the study was 8.4 years. Of the 754 younger patients less than 55 years old 50.9% (384) had a family history compared to 40.4% of the older patients (2,803; $p < 0.001$). The 10-year biochemical recurrence-free (62.5%) and prostate cancer specific survival (96.1%) rates did not differ between patients with vs without a family history, nor between the younger vs older patient groups (all $p > 0.05$). Prostate specific antigen, pathological stage, node stage and Gleason score were the only significant predictors for biochemical recurrence-free survival, while pathological stage, node stage (all $p < 0.005$) and Gleason score (Gleason 7 vs 6 or less—HR 1.711, 95% CI 1.056–2.774, $p = 0.03$; Gleason 8 or greater vs 6 or less—HR 4.516, 95% CI 2.776–7.347, $p < 0.0001$) were the only predictors for prostate cancer specific survival.

Conclusions: A family history of prostate cancer has no bearing on long-term outcomes after radical prostatectomy.

Key Words: survival rate, prostatic neoplasms, prostatectomy, age factors, family

Abbreviations and Acronyms

PSA = prostate specific antigen

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AMONG all cancers prostate cancer has the highest rate of patients with a positive family history, with Swedish and German estimates near 20%. Other cancers, such as breast and colorectal, present with lower rates near 13%.[1,2] Because first-degree family history has been universally validated as an independent risk factor for prostate cancer, it has been included in worldwide risk prediction tools and genetic counseling platforms to facilitate patient decision making.[3–5] More recently, it has been observed that family history is more specifically associated with low grade

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(Gleason score less than 7) rather than high grade prostate cancer.[6] This distinction is relevant in an era of over detection, where active surveillance is emerging as a viable treatment alternative to radical prostatectomy for patients with low risk disease. There is a general perception that family history confers an increased lifetime risk of being diagnosed with prostate cancer, particularly when first-degree relatives have been diagnosed at an early age, such as less than 55 years.[7–9]

While some studies have reported an association between positive family history and prostate cancer specific mortality regardless of treatment,[8,9] those that have reported no association have generally had small sample sizes/low power and were also not stratified by treatment.[10] Radical prostatectomy remains a leading treatment option for prostate cancer, and may be even more likely among patients with a family history due to increased anxiety. In this investigation we assessed whether long-term outcomes after radical prostatectomy were diminished for patients with a first-degree family history, particularly among patients less than 55 years old.

PATIENTS AND METHODS

Since 1994 the German multicenter Familial Prostate Cancer study has recruited and surveilled patients with prostate cancer and their families to study the genetic/hereditary impact on long-term clinical outcomes.[11] As part of this long-term study participating clinics recruit patients diagnosed with prostate cancer independent of family history, and invite them to fill out demographic, clinical and family history questionnaires on an annual basis. Self-reported family history of prostate cancer is verified by histopathological reports of the patients and their affected relatives. Relatives diagnosed with prostate cancer are added to the study as soon as they are identified.

For this study patients who had undergone radical prostatectomy were identified from the database and those with a first-degree relative history of prostate cancer extracted (fig. 1). As a control group the patients with at least 1 male first-degree relative older than 60 years during followup and no history of prostate cancer in the family were chosen. This strict inclusion criterion eliminated men who had no first-degree relatives and, thus, whose family history status was missing. They represent a pure control group whose family history status is verified to be negative. This control group is referred to as strictly negative to differentiate it from the commonly used negative control group that also includes men with no first-degree relatives at all and, thus, is not fully verified. In addition to this study, only Valeri et al defined the sporadic group strictly by only including patients with at least 2 nonaffected brothers 50 years old or older.[12] However, to improve comparability to other family history studies that include all men with no record of family history regardless of family size or missing information, we performed an additional sensitivity analysis repeating the primary end point analyses in the expanded control group.

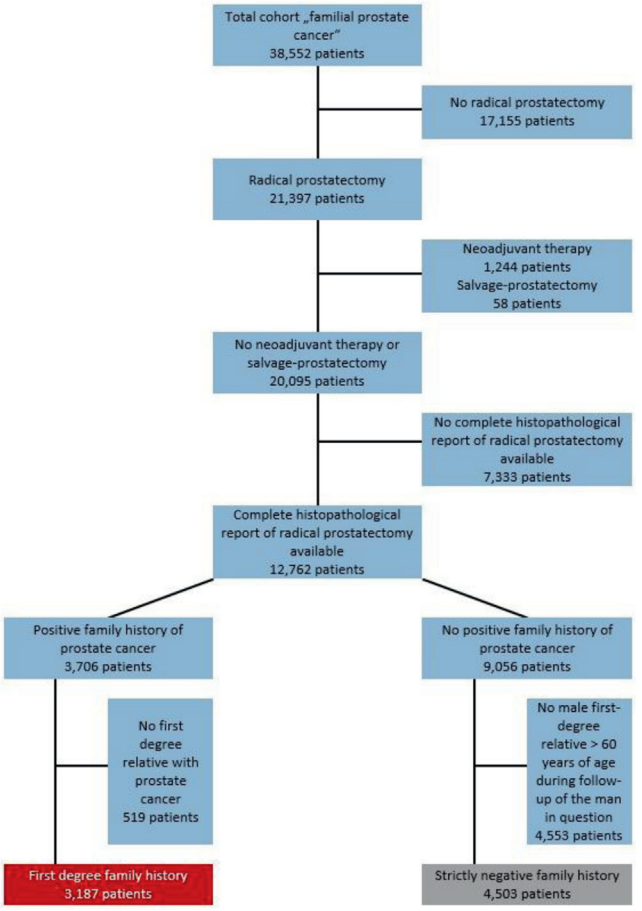

Figure 1. Selection of patients for inclusion in study

Clinical characteristics including PSA at diagnosis, clinical/pathological stage (all converted to the 2002 TNM system for patients diagnosed and treated before 2002) and pathological Gleason score were compared between the family history groups (first-degree vs strictly negative family history) and age groups (younger than 55 years vs older) using chi-square tests and Fisher's exact test for low counts. The nonparametric Wilcoxon test was used to compare age at radical prostatectomy and length of followup between the groups.

Kaplan-Meier curves were used to compare biochemical recurrence-free and cancer specific survival between the positive and strictly negative family history groups for all patients as well as for the younger and older patient groups separately. Univariate and multivariable Cox proportional hazard regression was used to assess the univariate and independent effect of each predictor on both survival end points. For the multivariable models the optimal fitting one was chosen as that which minimized the Bayesian information criterion. The minimal detectable hazard ratios for the positive vs strictly negative family history group effects on survival end points were calculated for a univariate Cox proportional hazards regression performed at the 0.05 statistical level (type I