Review: bias may contribute to association of vasectomy with prostate cancer

Question

Is the risk of prostate cancer increased in men with a history of vasectomy?

Data sources

Accounts from 1985 to 1996 were identified in MEDLINE, EMBASE/Excerpta Medica, and IME (Spanish Index Medicus) using terms relating to vasectomy, prostate, prostatic, and cancer. The bibliographies of relevant articles retrieved by the search were reviewed. Searches were also done in Research Activities published by the US Agency for Health Care Policy and Research and in the Spanish network of Research Transfer Offices.

Study selection

Epidemiological studies were selected if they measured the association between vasectomy and prostate cancer.

Data extraction

Data were extracted on study design, setting, and period; time during which research was done; sample size; instrument used for gathering exposure and outcome data; effect of measurement units; strength of association; and statistical methods. Possible sources of bias were confounding, selection, detection, nonresponse, regression to the mean, exposure recall, and disease misclassification. The methodological quality was assessed by two independent investigators.

Main results

A total of 14 studies were included (5 cohort studies and 9 case-control studies). An excess risk of prostate cancer was found in 11 studies; in 6 studies it was statistically significant. The weighted age-adjusted relative risk (RR) for prostate cancer across the 14 studies was 1.23 (95% confidence interval [CI] 1.01-1.49). The results of the studies varied widely. The sources of heterogeneity identified were type of design, study setting, presence of detection bias, and inadequate selection of controls. The weighted relative risk of prostate cancer in the cohort studies was 1.13 (95% CI 0.84-1.52) and in the case-control studies was 1.36 (95% CI 1.04-1.79). The RR of prostate cancer in the nine population-based studies was 1.12 (95% CI 0.96-1.32) and in the five hospital-based studies was 1.98 (95% CI 1.37-2.86). In studies in which detection bias was possibly present, the RR was 1.91 (95% CI 1.4-2.6); in those in which detection bias was less likely, the RR was 1.11 (95% CI 0.96-1.29). Studies with an adequate selection of controls had an RR of 1.11 (95% CI 0.94-1.31); those with possible selection bias had an RR of 2.24 (95% CI 1.42-3.54).

Conclusions

Meta-analysis of five cohort studies and nine case-control studies shows that there is an excess risk of developing prostate cancer in men who have had a vasectomy. Many sources of bias exist among the studies, however, leading to a probable overestimation of the association.

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Fertil Steril 1998;70:191-200.

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COMMENTARY

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Bernal-Delgado and colleagues have summarized data on the relation between vasectomy and prostate cancer from 14 epidemiological studies composed of more than 200,000 men. The authors made a comprehensive search for published studies (but did not include unpublished work), and they evaluated each study for potential bias. They tabulated the results separately for cohort and case-control studies (because case-control studies often show stronger associations than actually exist) and stratified studies for other potential sources of bias. The most rigorous studies generally showed only a weak association between vasectomy and prostate cancer.

The studies included in this meta-analysis investigated the relation between vasectomy and the diagnosis of prostate cancer, not the occurrence of prostate cancer. Men who have had vasectomies are more likely to seek regular medical care than men who have not, and they are therefore more likely to have screening for prostate cancer (Sackett's "diagnostic access" bias[1]). Because none of the included studies attempted to control for medical care-seeking behavior, there is likely an exaggerated association between vasectomy and prostate cancer.

Does this meta-analysis exonerate vasectomy? Not necessarily. Given the popularity of vasectomy (approximately 25% of men 40 to 60 years old in the United States have had one) and the high prevalence of prostate cancer (>18% of men in their 60s[2]), even a small increase in the risk of clinically evident disease could have a large effect on public health.

Future epidemiological studies will probably not resolve this issue; randomized trials are, of course, not an option. Understanding the pathophysiology of prostate cancer may be our best hope for resolving this and other thorny questions about its causes.

1 Sackett DL. Bias in analytic research. J Chronic Dis 1979;32:51-63.
2 Sheldon CA, Williams RD, Fraley EE. Incidental carcinoma of the prostate: a review of the literature and critical reappraisal of classification. J Urol 1980;124:626-631.