The association between vasectomy and prostate cancer: a systematic review of the literature


Authors' objectives
To evaluate the possible association between vasectomy and prostate cancer.

Searching
MEDLINE, EMBASE and IME (Spanish Index Medicus) were searched between 1985 and 1996 using the keywords 'vasectomy', 'prostate', 'prostatic', and 'cancer'. This was followed by manual retrieval using primary sources. The database of the Spanish network of Research Transfer Offices (DATRI) was also searched.

Study selection
Study designs of evaluations included in the review
Observational studies of case-control or cohort design, which mentioned an association between vasectomy and prostate cancer, were included. In the case of duplicate reports on the same study, only the most recent publication was included.

Specific interventions included in the review
Vasectomy. Vasectomy status was ascertained by the following methods: telephone interview, home interview, self-administered questionnaire, interview conducted by trained nurses, and hospital registries.

Participants included in the review
The participants included patients who had undergone vasectomy. The controls for the case-control studies included patients in the following diagnostic groups: other types of cancer including cancer of the skin, colorectal and lung cancer; digestive disorders, trauma; rehabilitation difficulties; urogenital disorders; and participants who were neighbours of the patients, from the same geographical area as the patients or who were randomly selected. The participants in the cohort studies were enrolled from the following sources: health check-up cohort; interventions for appendicitis or injuries; husbands of nurses who participated in a health study; specified professions; and the general population.

Outcomes assessed in the review
The outcome assessed was the incidence of prostatic cancer, as confirmed by histological diagnosis.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The methodological quality was assessed by considering the presence or absence of the following threats to study validity: confounding bias; adequacy of selection of controls; detection bias; regression to the mean bias; exposure recall bias; and disease misclassification bias.Two blinded authors evaluated validity according to the defined criteria, and any disagreements were resolved by consensus. Each study was classified as either category A, B, C or D using the validity criteria. A study classified as A shows possible bias; with B there is a minimisation strategy of certain bias; with C it is unlikely that internal validity is threatened; and for D, there is either no information to assess validity or the assessment is not applicable.

Data extraction
One author extracted the following data: the author; year of publication; study design; time during which the research was conducted; sample size; the instrument used for registering the variables; the effect of measurement units; strength of association and confidence limits; and statistical methods.
Methods of synthesis

How were the studies combined?
The random-effects model of DerSimonian and Laird (see Other Publications of Related Interest no.1) was used to estimate the relative risks (RR) of prostatic cancer adjusted for age, and the RR used in the multivariate analysis. The RR was also estimated using the hierarchical method (Bayesian random-effects model) assuming a gamma distribution of the parameters alpha (0.5) and lambda (0.5) as an a priori probability function (see Other Publications of Related Interest no.2).

How were differences between studies investigated?
The chi-squared test was used to assess heterogeneity. Heterogeneity was investigated by exploring the following potential sources: type of design, study base, presence of detection bias, and inadequate selection of controls.

Results of the review

Fourteen observational studies (N=221,238) were included: 9 case-control studies (N=14,334) and 5 cohort studies (N=206,904). Two of the cohort studies were prospective (N=68,331) and 3 were retrospective (N=138,573).

The results from the methodological evaluation were tabulated. In brief: all studies controlled for age; none controlled for time passed since vasectomy, or the age at which the vasectomy was performed; only 3 studies controlled for a history of prostate surgery; there was an inadequate selection of controls in several case-control studies; several studies were considered to have detection bias; the possibility of misclassification bias was present in 12 studies, which defined exposure from the interview onward; and all studies bar one used histological examination to diagnose the stage of cancer.

The age-adjusted RR was 1.23 (95% confidence interval, CI: 1.01, 1.49). Heterogeneity was found (chi-squared 56.31, d.f.=15, P<0.0001). A qualitative analysis also detected heterogeneity between the studies.

Investigation of heterogeneity.

Study design: the RR was 1.13 (95% CI: 0.84, 1.52) for cohort studies and 1.36 (95% CI: 1.04, 1.79) for case-control studies.

Study base: the population-based RR was 1.12 (95% CI: 0.96, 1.32) and the hospital-based RR was 1.98 (95% CI: 1.37, 2.86).

Selection bias: the RRs were 1.11 (95% CI: 0.94, 1.31) and 2.24 (95% CI: 1.42, 3.54) for adequate and inadequate selection of controls, respectively.

Detection bias: the RR was 1.11 (95% CI: 0.96, 1.29) for detection bias unlikely and 1.91 (95% CI: 1.4, 2.6) for doubt about detection bias.

Authors' conclusions

The empiric evidence available on the association between vasectomy and prostate cancer was of low quality, because of the numerous sources of bias that favoured overestimation of the effect of vasectomy. The available evidence does not justify a change in family-planning policies. In addition, it does not justify that individuals who have undergone vasectomy should be considered as a group at high risk for the development of prostate cancer.

CRD commentary

This clearly-presented review included a search of several databases. The validity of the primary studies was assessed and the results from this evaluation were given. Details of the methods used to extract the data and assess the validity were provided. Several potential sources of bias were discussed and investigated, and publication bias was assessed. Two models were used to estimate the overall RR, and there were brief descriptions of the primary studies, including the source of cohorts and controls. As the authors stated, the evidence was of low quality with a potential for bias.
The evidence presented supports the authors' conclusions, with the proviso that this lack of evidence does not indicate a lack of association.

**Implications of the review for practice and research**
Practice: The authors consider that the available evidence does not justify a change in family-planning policies, or consideration of individuals who have undergone vasectomy as a group at high risk for the development of prostate cancer.

Research: The authors did not state any implications for further research.

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**Other publications of related interest**

This additional published commentary may also be of interest. Millard PS. Review: bias may contribute to the association between vasectomy and prostate cancer. Evid Based Med 1999;4:92.

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