Diabetes Mellitus and Prostate Cancer Risk in Asian Countries: A Meta-analysis

Xiang-Ju Long1*, Shan Lin1, Ya-Nan Sun2, Zhen-Feng Zheng1

Abstract

Background/Aims: Diabetes mellitus (DM) is widely considered to be associated with risk of cancer, but studies investigating the association between DM and prostate cancer in Asian countries have reported inconsistent findings. We examined this association by conducting a detailed meta-analysis of studies published on the subject. Methods: Cohort or case-control studies were identified by searching Pubmed, Embase and Wanfang databases through May 30, 2012. Pooled relative risk (RR) with its corresponding 95% confidence interval (95% CI) were calculated using the random-effects model. Subgroup analyses were performed by the study type. Results: Finally, we identified 7 studies (four cohort studies and three case-control studies) with a total of 1,751,274 subjects from Asians. DM was associated with an increased risk of prostate cancer in Asians (unadjusted RR= 2.82, 95% CI 1.73–4.58, P < 0.001; adjusted RR= 1.31, 95% CI 1.12–1.54, P = 0.001). Subgroup analyses by study design further confirmed an obvious association. Conclusion: Findings from this meta-analysis strongly support that diabetes is associated with an increased risk of prostate cancer in Asians.

Keywords: Diabetes mellitus - prostate cancer - meta-analysis - Asian populations

Introduction

Diabetes mellitus (DM) and cancer are two common severe chronic diseases that lead to many deaths (Jemal et al., 2011; Nolan et al., 2011). Prostate cancer, a common cause of cancer mortality in men, is one of the most frequently diagnosed malignancies (Jemal et al., 2011). In developed countries, prostate cancer is the second most frequently diagnosed cancer, and the third most common cause of death from cancer in men (Damber and Aus, 2008). Identifying risk factors for prostate cancer is critically important to develop potential interventions and to expand our understanding of the biology of this disease (Foulkes, 2008; Hoffman, 2011; Mori et al., 2011). Besides, there are more than 250 million people with diabetes worldwide, and this number is expected to reach 380 million in 20 years (Nolan et al., 2011). Type 2 diabetes is an increasing epidemic in Asia, characterized by rapid rates of increase over short periods and onset at a relatively young age and low body mass index (Chan et al., 2009). Several studies have suggested that diabetes significantly increases the risk of different cancers, and the association between diabetes and cancer is of clear importance (Kasper and Giovannucci, 2006; Barone et al., 2008; McGrowder et al., 2012). In contrast with various other malignancies, published data obtained from population-based studies indicate that the risk of prostate cancer may have an inverse relationship with DM (Bonovas et al., 2004; Kasper and Giovannucci, 2006). However, previous meta-analysis only included studies from Caucasians, and there was no study from Asians (Bonovas et al., 2004; Kasper and Giovannucci, 2006). A few studies published recently investigated the association between DM and prostate cancer in Asian countries. But the findings from these studies were inconsistent (Li et al., 2010; Tseng, 2011; Hsieh et al., 2012; Lee et al., 2012). To provide more precise estimates for DM and prostate cancer risk in Asians, we performed a meta-analysis of observational studies including cohort studies and case-control studies.

Materials and Methods

Literature search and selection criteria
Cohort or case-control studies were identified by searching Pubmed, Embase and Wanfang databases through May 30, 2012. The search strategy used medical subject heading (MeSH) terms and keywords: diabetes or diabetes mellitus; and prostate cancer or prostate carcinoma. We also reviewed the reference lists to identify additional relevant studies. No language restrictions were imposed. All searched studies were retrieved, and their bibliographies were checked for other relevant publications. Studies were included in the meta-analysis if (1) studies from Asian countries; (2) cohort or case-control design; (3) one of the exposures was DM; (4) one of the outcome of interests was prostate cancer; and (5) relative risk (RR), odds ratio (OR), hazard ratio (HR) or
standardized incidence/mortality rate (SIR/SMR) with their corresponding 95% confidence intervals (95% CI) (or data to calculate them) were available. The major reasons for exclusion of studies were: (1) case-only studies; (2) review papers; (3) containing overlapping data. When more than one of the same patient population was included in several publications, only the most recent or complete study was used in this meta-analysis.

Data extraction

We extracted the following data from each study: the first author’s last name, publication year, year of the study conducted, country, sample size, participant characteristics (age and sex), methods of ascertainment of diabetes and outcome, the follow-up period, estimate effects with their 95% CIs, and covariates adjusted for in the analysis. When studies provided more than one RR according to the duration of diabetes before prostate cancer was diagnosed, we extracted and combined the RRs for individuals diagnosed with diabetes more than 1 year prior to the diagnosis of prostate cancer. We did not contact the prime investigators of these studies for further information.

Statistical analysis

We included studies in this meta-analysis reporting different measures of RR, OR, HR and SIR/SMR. To assess heterogeneity among studies, we used the I2 statistic, and a value more than 50% is considered that severe heterogeneity existed (Higgins et al., 2003). Pooled RR with corresponding 95% CI was derived with the method of DerSimonian and Laird using the assumptions of a random-effects model, which accounts for heterogeneity among studies (DerSimonian and Laird, 1986). Data were stratified into subgroups on the basis of study design, which was done to examine consistency across varying study designs with different potential biases. Publication bias was evaluated using the funnel plot and Egger’s test, and a P value of less than 0.05 was considered statistically significant (Egger et al., 1997). All statistical analyses were performed using STATA, version 1.0 (STATA, College Station, TX, USA). For all tests, a probability level of less than 0.05 was considered statistically significant.

Results

Studies characteristics

The primary computerized literature search identified 1227 records. Examination of these records yielded 9 potentially relevant publications for further review (Li et al., 2010; Tsugane and Inoue, 2010; Ganesh et al., 2011; Tseng, 2011; Chiou et al., 2012; Fukushima et al., 2012; Hong et al., 2012; Hsieh et al., 2012; Lee et al., 2012). After evaluation by reading full text carefully, two studies were further excluded including one case-only study (Chiou et al., 2012) and one review (Tseng, 2011). Finally, we identified 7 studies (four cohort studies and three case-control studies) with a total of 1,751,274 subjects (8480 prostate cancer cases) (Li et al., 2010; Ganesh et al., 2011; Tseng, 2011; Fukushima et al., 2012; Hong et al., 2012; Hsieh et al., 2012; Lee MY 2012).


<table>
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<tr>
<th>Study ID</th>
<th>RR (95% CI)</th>
<th>Weight</th>
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<tbody>
<tr>
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<td>55.89</td>
</tr>
<tr>
<td>Tseng DH 2011</td>
<td>14.80</td>
<td>14.80</td>
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<tr>
<td>Li Q 2011</td>
<td>13.81</td>
<td>13.81</td>
</tr>
<tr>
<td>Hsieh SK 2011</td>
<td>13.51</td>
<td>13.51</td>
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<tr>
<td>Tseng CH 2011</td>
<td>13.81</td>
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<td>Tseng CH 2011</td>
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NOTE: Weights are from random effects analysis

DM and prostate cancer risk

As shown in Figure 1, the pooled unadjusted RR with its 95% CI was 2.82 (95% CI, 1.73–4.58) for individuals with diabetes compared with individuals without diabetes or general population (P < 0.001), with significant heterogeneity among these studies (I² = 97.6%). When we restricted the meta-analysis to those studies controlled for potential confounders, the pooled adjusted RR with its 95% CI was 1.31 (95% CI, 1.12–1.54) for individuals with diabetes compared with individuals without diabetes or general population (P = 0.001), without obvious heterogeneity among studies (I² = 42.5%, Figure 2).

Subgroup meta-analyses by study design showed DM is associated with an increased risk of prostate cancer in both case-control studies and cohort studies (For cohort studies, see Figure 2).

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