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Review

The Relationship between Type 2 Diabetes and Breast Cancer Incidence in Differing Ethnic Groups

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ABSTRACT

In addition to rising type 2 diabetes and breast cancer incidence rates worldwide, diabetes may also increase breast cancer risk, and the association may vary by ethnicity. This review summarizes published data evaluating the association between diabetes and breast cancer in women of Asian, Hispanic and African American ancestry while considering a measure of obesity, body mass index (BMI). Published reports were identified through a search of PubMed and previous publications. Of 15 age-adjusted studies, 11 reported on Asian women from various countries, 3 on Hispanics and 1 on African Americans. The studies of Asian women described significant associations in 8 reports, with risk estimates of 1.5 to 8.4, but 3 were case-control studies and 6 did not adjust for BMI. The 3 case-control studies of Hispanic people included BMI, but only 1 detected a weak association between diabetes and breast cancer risk and was limited to postmenopausal women. The only study of African American women was a prospective cohort, and it showed no significant association between diabetes and breast cancer. In contrast to a 10% to 20% higher risk for breast cancer associated with diabetes reported for white women, there is little evidence for an association in Hispanics and African Americans. Although several studies of Asian women included in our review reported a higher risk for breast cancer with diabetes, methodologic shortcomings, such as lack of adjustment for obesity, use of a general population as controls, case-control design and small sample sizes, raise questions about the validity of the findings.

Mots clés :
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RÉSUMÉ

Les taux d'incidence du diabète de type 2 (DT2) et du cancer du sein sont en hausse dans le monde entier. En outre, le DT2 peut augmenter le risque de cancer du sein, et l'association peut varier selon l'origine ethnique. Cet article de synthèse résume les données publiées permettant d'évaluer l'association entre le DT2 et le cancer du sein chez les femmes d'ascendance asiatique, hispanique ou afro-américaine. Il aborde parallèlement une mesure de l'obésité, l'indice de masse corporelle (IMC). Une recherche sur le site PubMed et dans les publications antérieures a permis de recenser les comptes rendus publiés. Sur 15 études au cours desquelles des corrections ont été effectuées en fonction de l'âge des sujets, 11 ont été menées chez des femmes asiatiques issues de différents pays, 3 chez des femmes hispaniques et 1 chez des femmes afro-américaines. Huit comptes rendus d'études menées chez des femmes asiatiques font état d'associations significatives et d'un risque estimatif allant de 1,5 à 8,4; toutefois, trois études étaient de type cas-témoins et six ne comportaient aucune correction en fonction de l'IMC. Les trois études cas-témoins menées chez des femmes hispaniques tenaient compte de l'IMC, mais une seule a permis de déceler une faible association entre le DT2 et le risque de cancer du sein se limitant aux femmes en postménopause. La seule étude menée chez des femmes afro-américaines portait sur une cohorte suivie prospectivement et n'a révélé aucune association significative entre le DT2 et le cancer du sein. Alors que le risque de cancer du sein associé au DT2 est de 10 à 20 % plus élevé chez les femmes blanches, peu de signes d'une association ont été notés chez les femmes hispaniques et afro-américaines. Bien que plusieurs

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des études menées chez des femmes asiatiques incluses dans notre article de synthèse aient fait ressortir un risque plus élevé de cancer du sein associé au DT2, les lacunes méthodologiques telles que l'absence de correction en fonction de l'obésité, l'utilisation de la population générale en guise de témoin, le plan d'étude cas-témoins et la petite taille des échantillons soulèvent des questions sur la validité des conclusions qui en ont été tirées.

Introduction

The rising burden of type 2 diabetes affects populations around the world, but the prevalence of diabetes is 2 to 3 times higher in many non-Caucasian groups than in Caucasian groups (1–3). Breast cancer is the most common cancer among women worldwide (4). However, the incidence rates vary widely across populations, with the highest rates occurring in North America, Australia and Europe and the lowest rates occurring in large parts of Africa and Asia. Although the incidence rates have been stable in North America (5), rates in developing countries continue to rise (4). The prevalence of obesity is increasing at a rapid rate in all parts of the world (6,7) and constitutes the major modifiable risk factor for diabetes (8). At the same time, excess body weight is considered of the most important risk factors for postmenopausal breast cancer, along with levels of physical activity, hormone treatments and alcohol intake (9–12). For diabetes (3,13,14) and breast cancer (15,16), obesity appears to predict a higher risk for Asian women than for Caucasian women.

Considerable evidence suggests an association between diabetes and a higher breast cancer risk independent of obesity, but this question has been investigated primarily in Caucasian populations, as summarized in several meta-analyses (17–19). Two meta-analyses reported a nearly 20% higher risk for breast cancer in women with diabetes (17,19), while a larger review of 40 studies found a relative risk (RR) of 1.16 (95% CI 1.08 to 1.24) for body mass index (BMI)-adjusted studies as compared to 1.33 (95% CI 1.18 to 1.51) in studies that did not include BMI as a confounder (18). Studies reporting on the association between diabetes and breast cancer risk in differing geographic locations are contradictory. Whereas in 1 meta-analysis, diabetes was associated with similar risk for breast cancer in women with diabetes from Asia (RR 1.45; 95% CI, 1.07 to 1.97) compared with reports from North America (RR 1.12; 95% CI 1.06 to 1.18) and Europe (RR 1.19; 95% CI 1.08 to 1.31) (17), a more recent meta-analysis (19) showed a stronger association between diabetes and breast cancer in studies from Europe (RR 1.88; 95% CI 1.56 to 2.25) as compared to Asia (RR 1.01; 95% CI 0.84 to 1.21). As for biologic mechanisms, it has been hypothesized that ethnic differences in visceral fat and adipokines (20,21) or the adverse metabolic consequences of obesity on glucose control and chronic inflammation (22) may modify the relationship between diabetes and breast cancer risk. The goal of the current study was to explore how the association between diabetes and breast cancer risk differs among populations of Asian, Hispanic and African American ancestry.

Methods

We reviewed observational studies that examined the association between diabetes and breast cancer incidence by ethnicity. A summary of previous results in Caucasian populations was obtained from 3 meta-analyses (17–19). The publications for the current review were limited to English-language studies that were designed as case-control or cohort studies and provided risk estimates for the incidence of breast cancer in women with diabetes. The majority of reports were identified through a search in PubMed using the terms *breast*, *cancer*, *diabetes* and *risk* plus *Hispanic or Japan or Thailand or Latino or Black or African American or Asian or Chinese or Japanese or Indian or Filipino*. In addition, we examined the bibliographies in publications that included cancer sites other than breast (23–26). We summarized the results for women with Asian, Hispanic and African American ancestry separately and listed covariates that were included in each study. We were presented the risk estimates as forest plots taking into consideration adjustment of the statistical results for BMI. Depending on the study design, the risk estimates were presented as odds ratio (OR), hazard ratio (HR), relative risk (RR), incidence rate ratio (IRR), standardized incidence ratio (SIR) or mortality rate ratio (MRR).

Results

Of the total 170 publications identified (Figure 1), 166 articles were discovered in PubMed and 4 in published reports (23–26). After screening the abstracts of all records, we excluded 140 papers that were not relevant to our research question. Of the 30 publications examined as full articles, 15 reports (Table 1) were found to refer to epidemiologic investigations that examined the association between diabetes and breast cancer incidence or of breast cancer mortality as a surrogate of incidence (27).

Among the 11 investigations in differing Asian populations, 3 in Hispanics, and 1 in African American women (Table 1), we included 9 cohort and 6 case-control studies; 3 of the Asian cohorts used the general population as controls to estimate the relative risk for breast cancer. For the other 6 cohort studies, women without breast cancer served as comparison, while in the 6 case-control studies, controls were identified from population-based sources (3) or clinical settings (3). All risk estimates were adjusted for age, but 6 of the studies of Asians were not able to adjust the models for BMI. The inclusion of other potential confounding variables also varied across reports (Table 1). The number of breast cancer cases ranged from 36 to 1380, while the cohort sizes varied from 4155 women with diabetes (28) to more than 400,000 Korean health-plan members (23). All studies except 1 of Hispanic women (29), which also included non-Hispanic whites, were conducted uniquely within a single ethnic group.

Asians

Of the 11 reports concerning women of Asian ancestry (Figure 2), all but 3 investigations reported on East Asians; 4 were conducted in Japan (24–26,30), 2 in China (28,31) and 1 each in Korea (23), Taiwan (27), Thailand (32), Pakistan (33) and Asian Americans (women of Chinese, Japanese or Filipino ancestry) in California (34). All but 1 study reported breast cancer incidence, 1 had only breast cancer mortality as the outcome (27) and 1 showed risk estimates for incidence and mortality (23). Significant associations ranging between risk estimates of 1.5 and 8.4 were reported in 8 studies, but 6 of the studies were not adjusted for BMI (23,27,28,30–32). When looking at studies that adjusted for BMI, diabetes was a significant predictor of breast cancer in a case-control study of Asian Americans (34) and in Pakistan (33), with respective estimates of 1.66 (95% CI 1.12 to 2.45) and 2.96 (95% CI 1.30 to 6.30) but not in other studies of Asians (24–26). A large study of 182,542 Japanese women and 1380 breast cancer cases from 6 Japanese cohorts (26) reported a risk estimate of 0.98 (95% CI 0.69 to 1.38) for breast cancer associated with diabetes, though it reported