INTRODUCTION

Risk of cancer is affected by a number of environmental and lifestyle factors and by an interplay between these factors and genetic susceptibility. Over the past three decades, the prevalence of obesity and type 2 diabetes has been increasing in both developed countries and less developed areas along with an adoption of a Westernized lifestyle (see Chapter 2). It is well recognized that obesity dramatically increases the risk of type 2 diabetes. Moreover, there is an extensive body of epidemiological evidence that excess body weight considerably increases the risk of cancers at multiple sites (1). Herein we summarize the mounting epidemiological studies linking overweight, obesity, and diabetes with cancer incidence and mortality.

In view of the large number of epidemiological studies relating overweight and obesity to the risk of cancer, this chapter is based primarily on data from previous comprehensive reviews and meta-analyses, including (1) a quantitative review and meta-analysis by Bergström et al. (2), who summarized the epidemiological literature published between 1966 and 1997 investigating body mass index (BMI) (the weight in kilograms divided by the square of height in meters) in relation to the risk of developing cancer; (2) a comprehensive report by the International Agency for Research on Cancer (IARC) in 2002 (1); and (3) the Cancer Prevention Study II (3), a large prospective cohort study investigating the association of BMI with cancer mortality during 16 yr of follow-up of more than 900,000 adults in the United States.
In the review and meta-analysis by Bergström et al. (2), “normal weight” was defined as a BMI of 20–24.9 kg/m², “overweight” as a BMI of 25–29.9 kg/m², and “obesity” as a BMI of 30.0 kg/m² or more. In the Cancer Prevention Study II (3), BMI was categorized as follows: “normal weight” as 18.5–24.9 kg/m², “overweight” as 25.0–29.9 kg/m², “grade 1 overweight” as 30.0–34.9 kg/m², “grade 2 overweight” as 35.0–39.9 kg/m², and “grade 3 overweight” as 40.0 kg/m² or more, according to the recommendation by the World Health Organization (4).

REVIEW OF EPIDEMIOLOGICAL STUDIES

OVERWEIGHT AND OBESITY

Overweight and obesity have been associated with overall cancer incidence and mortality. In a Swedish population-based cohort of 28,129 hospitalized patients with any discharge diagnosis of obesity, there was an overall 33% excess incidence of cancer in obese individuals (25% in men and 37% in women) in comparison with the general population (5). In addition, the National Enhanced Cancer Surveillance System, a large Canadian population-based case-control study, showed that compared with normal-weight individuals (BMI < 25 kg/m²), those who were overweight (BMI between 25 and 30 kg/m²) had a 9% increased risk of cancer overall; obese individuals (BMI ≥ 30 kg/m²) had a 34% increased risk (6). The association of overweight and obesity with overall cancer mortality as well as mortality from specific cancers was examined in the American Cancer Prevention Study II (3) (see Tables 1 and 2). During 16 yr of follow-up of 900,000 participants, there were a total of 57,145 deaths from cancer. Compared with men with normal weight, the death rates from all cancers combined were 9% higher in men with a BMI between 30.0 and 34.9 kg/m² (grade 1 overweight), 20% higher for men with a BMI between 35.0 and 39.9 kg/m² (grade 2 overweight), and 52% higher for men with a BMI of 40.0 kg/m² or more (grade 3 overweight). The corresponding figures for women were 23, 32, and 62%.

DIABETES

In a Swedish cohort of 144,427 hospitalized diabetic patients, a total of 4919 men and 4742 women died from cancer during an average follow-up of 6.7 yr (7). This study showed that overall cancer mortality was approx 50% higher among the diabetic patients compared with the general population. However, because the analysis was not adjusted for obesity, the association between diabetes and overall cancer risk independent of the effect of obesity on cancer risk could not be distinguished.

Breast Cancer

OVERWEIGHT AND OBESITY

Breast cancer is the leading type of cancer in women both worldwide (21% of all cancers) (8) and in the United States (32% of all cancers) (9). The first epidemiological evidence of an association between excess body weight and increased breast cancer risk was obtained from a Dutch cohort study in 1974 (10). Findings from many subsequent epidemiological studies indicate that the relationship between excess body weight and risk of breast cancer varies by menopausal status (1). Whereas a positive association between body weight and risk of breast cancer has been observed in most studies of postmenopausal women, an inverse association has been noted in studies of premenopausal women (1).