The Role of Diet in Breast and Prostate Cancer Survival

Cancer is a leading cause of death worldwide. Breast and prostate cancer are two of the most common malignancies and contribute significantly to the societal and economic burden of cancer. Various ethnic and racial groups are affected differently by overall cancer incidence and mortality. Racial disparities are evident for breast cancer survival and both prostate cancer incidence and survival. The reasons for differences in cancer incidence and survival are not entirely clear. However, diet plays an important role in cancer prevention and survival and may also be implicated in racial and ethnic disparities. Ecologic, case-control, cohort, and randomized, controlled studies have demonstrated the benefits of a low-fat, high-fiber diet for breast and prostate cancer survival. A plant-based diet, generally low in fat and high in fiber, may offer survival benefits for both breast and prostate cancer. Further research is required to establish effective interventions that promote healthy dietary choices that enhance cancer survival. (*Ethn Dis.* 2007;17[suppl 2]:S2-18–S2-22)

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Hope R. Ferdowsian, MD, MPH; Neal D. Barnard, MD

From the Washington Center for Clinical Research (HRF), and Physicians Committee for Responsible Medicine (NDB), Washington, DC, USA.

Address correspondence and reprint requests to: Hope Ferdowsian; Washington Center for Clinical Research; 5100 Wisconsin Ave, NW, Suite 400; Washington DC 20016; 202-686-2210 ext. 347; 202-686-2216 (fax); hferdowsian@WashingtonCCR.org

Introduction

Cancer represents the fifth leading cause of death worldwide. An estimated 10 million people are diagnosed with some form of malignancy each year, and approximately seven million people die each year as a result. According to the World Health Organization, the number of new cases of cancer is expected to increase by 50% by 2020.[1] Cancer has historically been identified as a major health issue in industrialized nations. However, with the rapid rates of Westernization, cancer is increasingly viewed as a public health problem in developing countries. This trend is not surprising, since comparable lifestyles are associated with similar disease burdens.

In the United States, more than one million people are diagnosed with cancer each year. It is the leading cause of death in Americans >85 years of age.[2] Breast and prostate cancer are two of the most common malignancies and account for a significant portion of the burden, both in direct and indirect costs.

Various ethnic and racial groups are affected differently by overall cancer incidence and mortality. African American men have a 24% higher cancer incidence rate and 40% higher mortality rate, compared with Whites. African American women have a lower incidence rate but an ≈20% higher death rate compared with Whites for all cancer sites combined.[2]

Racial and ethnic disparities are particularly evident for breast and prostate cancer. The reasons for differences in cancer incidence and survival are not entirely clear. However, diet plays a key role in cancer prevention and survival and may also be implicated in racial and ethnic disparities.

Breast Cancer

Breast cancer is the most common cancer in women, excluding skin cancer, and accounts for >200,000 diagnoses per year. African American, Hispanic, and Native American women are disproportionately affected by breast cancer, more often present with advanced disease, and have poorer survival rates than do non-Hispanic White women. In the United States, five-year survival rates for African American women are ≈69%, compared with rates of 84% for White women, despite the lower incidence of breast cancer in African American women.[2] Proposed explanations for these disparities include differences in socioeconomic status, access to health care, lifestyle factors, and tumor characteristics. Recent research has suggested that genetic factors contribute to differences in breast cancer prognosis. Researchers have explored hormonal mediation of genetic factors and differences in p53 alterations.[3]

Diet and Breast Cancer Survival

Population studies have demonstrated a five-fold difference in breast cancer incidence between North American or European countries and Asian countries, which suggests a role of diet and lifestyle in cancer incidence. Studies have also shown increases in disease rates for immigrants from Japan to the United States. In population-based studies, women in Tokyo had 15% higher five-year survival rates, compared with women in Western countries, a finding that may be explained by an association between fat intake and treatment failure.[4] Obesity, partially determined by fat intake, increases the risk of breast cancer, recurrence, and death.[5–7]

Randomized, controlled studies have examined the role of diet in breast

cancer survival. The Women's Intervention Study (WINS) enrolled 2,437 postmenopausal women previously treated for breast cancer and randomly assigned them to either a low-fat dietary intervention group (≈20% of energy from fat) or a control group, whose participants were instructed to follow their habitual diets (deriving, on average, ≈40% of energy from fat). Risk of recurrent or new primary breast cancer was reduced in women who followed the low-fat diet (hazard ratio [HR] .76, 95% confidence interval [CI] .60–.98). The largest risk reduction (42%) was seen in women on the low-fat diet whose tumors did not respond to estrogen. This finding may be especially pertinent to African American women, for whom a significant tumor burden appears to be estrogen- and progestin-receptor negative.[3]

The Women's Healthy Eating and Living (WHEL) study is an ongoing randomized, controlled trial of 3,109 pre- and postmenopausal women previously treated for breast cancer. Women assigned to the dietary intervention were instructed to follow a diet that included five vegetable servings, 16 ounces of vegetable juice, three fruit servings, 30 g dietary fiber, and no more than 15%–20% of energy from fat per day. Using data from the WHEL study, Rock et al compared between-group differences in diet and hormone function in 291 of the study participants.[8] In the diet group, fat intake fell from 28% to 21% of calories within the first year ($P<0.001$), and fiber intake rose from 22 g/day to 29 g/day ($P<0.001$). In the control group, fat and fiber intake remained stable. The intervention group experienced a significant decline in baseline to one-year serum bioavailable estradiol concentration, compared with the control group. Bioavailable estradiol concentration fell from 41 pmol/L to 28 pmol/L in the intervention group, compared with a rise from 33 pmol/L to 36 pmol/L in the comparison group

($P<0.05$). Estradiol, estrone, and estrone sulfate concentrations fell in the intervention group, although results were not statistically significant for this subsample comparison. Separately, investigators examined the relationship between plasma carotenoid concentration, as a biomarker of fruit and vegetable intake, and the risk of a new breast cancer event among women assigned to the control group.[9] Women in the highest quartile of plasma carotenoid intake significantly reduced their risk of a new breast cancer event (HR .57, 95% CI .37–.89). The study controlled for potential confounders such as tumor stage and grade, hormone receptor status, chemotherapy, tamoxifen therapy, clinical site, age at diagnosis, body mass index (BMI), and plasma cholesterol concentration.

Body Weight and Breast Cancer Survival

One of the most well-established factors affecting breast cancer survival is body weight. Women with breast cancer who are near their ideal body weight at the time of diagnosis are more likely to survive, compared with women with higher body weights. Rock et al published a 2002 review of 26 studies published since 1990 on body weight and cancer recurrence or decreased survival in women previously diagnosed with breast cancer.[5] Seventeen studies showed that higher body weight was associated with increased risk, 7 studies showed no relationship, and 2 showed an inverse relationship between body weight and risk.

The relationship between body weight and recurrence risk appears relevant even at lower body weight ranges. In a 2006 study in Shanghai, Tao and colleagues demonstrated the relationship between BMI and survival in 1,455 women, aged 25–64, who had been previously diagnosed with breast cancer.[6] Women with a BMI <23 kg/m^2 had a five-year survival rate of 86.5%. Those with a BMI of 23–

25 kg/m^2 experienced survival rates of 83.8%. Those who had a BMI ≥25 kg/m^2 had a five-year survival rate of 80.1% ($P=.02$).

Proposed Mechanisms in Breast Cancer Survival

The association between lower body weight and increased survival may relate to hormonal activity. Increased endogenous and exogenous serum estrogen concentrations are associated with an increased incidence of breast cancer, particularly in postmenopausal women. Further, hormones may promote the late stages of carcinogenesis and facilitate malignant cell proliferation.[10] Fat tissue and high-fat, low-fiber diets contribute to increased blood levels of bioavailable estrogens, thereby increasing the risk of breast cancer and perhaps partially determining survival.[11] Women with more body fat have lower concentrations of sex-hormone binding globulin (SHBG), a protein that reduces the availability of circulating estrogens.

Studies have suggested that women of various races demonstrate differences in blood estrogen concentrations. In the Multiethnic Cohort Study, researchers identified racial differences in endogenous sex hormone profiles that might have contributed to the observed racial variations in breast cancer incidence.[12] After adjustment for potential confounders, African Americans had significantly higher estrone and estradiol levels compared with Whites, and Native Hawaiians had the highest serum concentrations of androstenedione, testosterone, and estrogens, and the lowest mean levels of sex hormone binding globulin, of all ethnic groups. These differences may influence survival as well. Increased estrogen levels in African American women may affect tumor growth characteristics, therefore influencing prognosis. Evidence suggests that a low-fat, high-fiber diet can significantly reduce estradiol and estrone sulfate concentrations in both

African American and Caucasian women.[8,13]

PROSTATE CANCER

Prostate cancer is the second most common malignancy in men in the United States; only skin cancer occurs more frequently. Although most cases progress slowly and may never become clinically apparent, the disease is the second-leading cause of cancer death in men and the most common cause of cancer death in male nonsmokers. Further, because of its strong association with age, the number of new cases and deaths from prostate cancer is expected to increase with the aging of the population.

Most prostate cancer cases are adenocarcinomas, with few isolated cases of transitional cell carcinoma. Evidence strongly suggests that hormonal and growth factors are important in the etiology of prostate cancer. In particular, research has demonstrated strong associations between serum testosterone and insulin-like growth factor I (IGF-I) concentrations and prostate cancer.

In addition to mortality risk, prostate cancer presents significant risk of morbidity as a result of primary tumor burden, metastasis, and adverse treatment effects. A small proportion of men present with symptoms of metastatic disease, including vertebral pain, renal failure secondary to ureteral obstruction, and weight loss. Erectile dysfunction, urinary incontinence, and bowel dysfunction are common consequences of surgery, radiation or androgen ablation.

African American men have an ≈60% higher incidence rate and a two-fold higher mortality rate from prostate cancer, compared with White men.[14] African American men generally have more advanced disease at diagnosis. The reasons for racial disparities in survival are largely unknown but likely involve an interaction among genetic, environmental, and social factors.

Diet and Prostate Cancer Survival

Prostate cancer risk appears to be increasing worldwide, a trend that may be due in part to the globalization of Western eating habits. Prostate cancer risk has been associated with higher meat and dairy intake and diets that are high in processed foods and low in fiber. Conversely, evidence is accumulating that a low-fat, vegetarian diet may help prevent prostate cancer and may play a role in its treatment.[15,16]

Ecologic, case-control, and cohort studies have identified associations between dairy product consumption and prostate cancer risk. Two large prospective US studies are illustrative. The Health Professionals Follow-Up Study of 47,781 health professionals showed that men who consumed more than two servings per day of milk increased their risk of cancer by 60%, as compared with men who consumed no milk per day (relative risk [RR] 1.6, 95% CI 1.2–2.1).[17] More than 80% of the milk that was consumed in the study was considered skim or low-fat. Giovannucci et al found that higher calcium intake was associated with the risk of advanced or fatal cancer ($P_{(trend)}$=.003).[18] Men who had a calcium intake of 1500–1999 mg/day were more likely to have fatal cancer, compared with men whose long-term calcium intake was 500–749 mg/day (RR 1.87, 95% CI 1.17–3.01). Men who consumed ≥2000 mg/day of calcium were more than two times as likely to have advanced or fatal cancer, compared with men whose calcium intake was <750 mg/day (RR 2.43, 95% CI 1.32–4.48). Chan et al showed that men in the Physicians Health Study who consumed >2.5 servings of dairy products per day had significantly increased risk of prostate cancer, compared with men who consumed no more than 0.5 servings (RR 1.34, 95% CI 1.04–1.71).[19]

In contrast, research has shown that a low-fat, vegan diet can prolong prostate cancer survival. Ornish et al followed 93 men with untreated prostate cancer for one year, after randomizing them to either a vegan diet or a control "standard" diet.[15] The vegan group experienced a 4% decrease in prostate-specific antigen (PSA) levels, whereas the control group experienced a 6% increase in PSA (P=.016). Six of 49 men in the control group required additional treatment, while none of the 44 men in the vegan group required additional treatment. Furthermore, the vegan diet inhibited prostate cancer cell growth microscopically. Saxe et al showed that an intervention that included a vegan diet increased the median PSA doubling time in men with prostate cancer from 6.5 months (95% CI 3.7–10.1) to 17.7 months (95% CI 7.8 to infinity) after only 4 months.[16]

Proposed Mechanisms in Prostate Cancer Survival

Several reasons could explain why a vegan diet improves indices of prostate cancer survival. A plant-based diet is generally low in fat, high in fiber, and high in nutrients that offer protection against cancer promotion. Intake of carotenoids, particularly lycopene, found in fruits such as tomatoes, watermelon, and pink grapefruit, is associated with a lower risk of prostate cancer.[20] Lycopene may reduce DNA damage and improve oxidative stress defense.[21] Cruciferous vegetable intake is associated with reduced risk for prostate cancer, perhaps because these foods can induce phase II detoxification enzymes, as well as cell-cycle arrest and apoptosis in prostate cancer cells.[22]

In contrast, non-vegan diets may promote prostate cancer growth. High-fat, low-fiber diets are associated with elevated blood testosterone concentrations, presumably either as a result of increased production or decreased excretion.[23] In turn, higher testosterone concentrations are associated with increased risk of prostate cancer.[24] Men who adopt low-fat, high-fiber diets show an ≈15% reduction in testosterone concentrations.[23]

Epidemiologic evidence suggests that prostate cancer risk increases with animal fat intake.[24] High intakes of certain animal fat-containing foods such as red meat and dairy products confer twice the risk for metastatic prostate cancer as do the lowest intakes.[25] Dairy products may contribute to increased prostate cancer risk by elevating circulating insulin-like growth factor I (IGF-I) concentrations. Because of their high calcium content, dairy product ingestion also depresses activation of vitamin D, which would otherwise maintain cellular differentiation.

DISCUSSION

Breast and prostate cancer are two of the most common malignancies in women and men, respectively. They exact an enormous cost in healthcare expenditures and in their effects on life expectancy and quality of life. Racial disparities are evident for incidence and survival for breast and prostate cancer, as well as many other forms of malignancy. Population studies, prospective studies, and clinical trials suggest that plant-based diets offer benefits for cancer prevention and survival, potentially countering these disparities.

The protective benefits of plant-based diets for cancer prevention and survival may stem from their high fruit, vegetable, and fiber content and lower content of fat, protein, calcium, and carcinogens. In the United States, the average daily fiber intake is 10–20 g/day, whereas intakes associated with low cancer rates are at least 30–40 g/day. Dietary fat increases adiposity and may increase production of sex hormones. The average diet in the United States contains more fat than the 30% of energy recommended by the National Cancer Institute. Whole grains, beans, legumes, fruits, and vegetables are both high in fiber and low in fat. Fruits and vegetables are also high in carotenoids, which are associated with reduced cancer risk. Lycopene, in particular, is found in tomatoes and tomato products, watermelon, and guava, and has powerful antioxidant properties. Fruits high in vitamin C and flavonoids, such as citrus fruits, inhibit tumor cell growth. Cruciferous vegetables contain flavones and indoles and lutein, which are thought to possess anti-carcinogenic properties. Vegetarians have higher serum carotenoid concentrations and consume more vitamin C, indoles, and fiber than meat eaters.

Increasing evidence suggests that simple dietary choices, particularly the use of plant-based diets, can both reduce cancer risk and lengthen cancer survival after diagnosis. Further research is required to establish dietary effects that influence prevention, effective interventions that promote healthy eating patterns, and policies that advance appropriate dietary choices.

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