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Part G. Section 7: Cancer

Introduction

In the United States, an estimated 45% of men and 38% of women will develop cancer in their lifetimes (1). Only 10% to 15% of cancers are due to an inherited genetic predisposition, and the remainder is thought to be due to lifestyle or environmental factors (2). The International Agency for Research on Cancer (IARC) estimates that 25% of cancer cases worldwide are due to overweight and obesity and a sedentary lifestyle (2). The most consistent associations between increased physical activity and reduced cancer risk have been observed for colon and breast cancers. Growing evidence supports a reduced risk of endometrial and lung cancers in physically active versus sedentary persons. A large number of studies have investigated the association between physical activity and prostate cancer and, in summary, have found no association between physical activity and risk of prostate cancer. Few data are available to determine whether physical activity affects risk of cancer at other sites.

A total of 1,437,180 new cancer cases and 565,650 deaths from cancers were projected to occur in the United States in 2008, and cancer is the leading cause of death for men and women younger than age 80 (1). A growing body of literature supports a role for physical activity in improving cancer prognosis and quality of life (3). Therefore, it is imperative to identify lifestyle factors that could be modified to reduce the impact of cancer.

Review of the Science

Overview of Questions Asked

This chapter addresses 3 specific questions:

1. What are the associations between physical activity and incidence of specific cancers? If an association exists, what is the dose-response pattern?

2. What are the effects of physical activity on cancer survivors, including late and long-term effects of treatment, quality of life, and prognosis?

3. What mechanisms explain the associations between physical activity and cancers?

Data Sources and Process Used to Answer Questions

This chapter reviews the available epidemiologic data on associations between physical activity and risks of specific cancers, the intervention study data on physical activity in cancer survivors, and the human experimental data on mechanisms that might explain the links between physical activity and cancer. The Cancer subcommittee began its literature review with the *Physical Activity Guidelines for Americans* Scientific Database, which includes publications since 1995 (see ***Part F: Scientific Literature Search Methodology***, for a full description of the Database). This search was augmented with MEDLINE searches of English-language articles using the terms "physical activity," "exercise," and "cancer." In addition, the subcommittee used several comprehensive literature reviews (2;4-8).

Because all of the studies that examined the association of physical activity with risk of cancer are observational epidemiologic studies, causality cannot be inferred. However, chance is unlikely as an alternate explanation because many of the results were statistically significant, particularly for colon and breast cancer.

Question 1. What Are the Associations Between Physical Activity and Incidence of Specific Cancers? If an Association Exists, What Is the Dose-Response Pattern?

Conclusions

A large body of epidemiologic data exists on the association between physical activity and the risk of developing various types of cancer. Although the direct evidence of these associations derives only from observational studies, randomized controlled trials (RCTs) have provided indirect evidence by examining the association of physical activity with markers of cancer risk, such as circulating levels of sex hormones, insulin, and cytokines.

The observational data are clearest for colon and breast cancer, with case-control and cohort studies supporting a moderate, inverse relation between physical activity and the development of these cancers. Individuals engaging in aerobic physical activity for approximately 3 to 4 hours per week at moderate or greater levels of intensity have on average a 30% reduction in colon cancer risk and a 20% to 40% lower risk of breast cancer, compared with those who are sedentary. A dose-response relation also is apparent, with risk decreasing at higher levels of physical activity. However, little information is available regarding what additional amounts and intensity of physical activity are associated with additional risk reductions; it also is unclear what the magnitude of the additional decrements in risk may be. The available evidence suggests that at least 30 to 60 minutes per day of moderate to vigorous intensity physical activity is required to significantly lower the risk of colon and breast cancer.

Compared with sedentary people, the available epidemiologic data suggest that active people have approximate reductions in risk of lung, endometrial, and ovarian cancers of

20%, 30%, and 20%, respectively. The data overall do not support associations of physical activity with prostate or rectal cancers. Too few data exist regarding the other site-specific cancers to make reasonable conclusions.

Rationale

Breast Cancer

Overall Associations

More than two dozen prospective cohort studies (9-34), and an even greater number of population-based case-control studies (35-71) have examined the relation between physical activity and breast cancer risk. These studies have primarily assessed the role of recreational physical activity on breast cancer risk. Overall, most studies suggest that physically active women have a lower risk of developing breast cancer than sedentary women. The majority of reported cohort studies (10-15;17;18;20-22;24;27;29;31-34) have reported a reduction in risk with physical activity ranging from 20% to 80%, and a number of population-based case-control studies (35-37;41-49;51;53;54;56;69-71) have reported reduction in risk ranging from 20% to 70%. In a meta-analysis of 23 studies focused on physical activity in adolescence and young adulthood, a summary relative risk (RR) estimate of breast cancer for highest versus lowest category of physical activity was 0.81 (95% CI 0.73-0.89), and each 1-hour increase of recreational physical activity per week was associated with a 3% (95% CI 0%-6%) risk reduction (72). A more extensive systematic review of recreational activity and breast cancer risk included 19 cohort and 29 case-control studies (73). The review concluded that evidence was strong that physical activity reduced risk of postmenopausal breast cancer by 20% to 80%, and that each additional hour of physical activity per week reduced risk for breast cancer by 6% (95% CI 3%-8%). They further concluded that the effect of physical activity on premenopausal breast cancer risk was a more modest 15% to 20% reduction.

The relevant lifetime periods for the effects of physical activity on breast cancer risk are not established. Lifetime recreational physical activity (35;51;54;64), adolescent physical activity (15;17;24;35;42;45;47), and physical activity at various life points (10-14;17;18;22;24;37;47;49;51;60) have been associated with lower breast cancer risk in several studies. Studies examining risk more broadly for specific decades of life also have observed an inverse association with some or all examined time periods (24;45;58;59). Furthermore, physical activity after menopause has been found to reduce breast cancer risk (12;22;24). Other studies that specifically looked at physical activity at various life periods have not found a reduced breast cancer risk with physical activity at any time (25).

Associations for Specific Subgroups

Within the United States, associations between increased physical activity and decreased breast cancer risk have been observed in multiethnic populations (24;70;71). These observations also hold true for specific racial and ethnic populations, including black (46;70), Hispanic (49;71), and Asian American women (56).

Results from some studies with sufficient numbers in subgroup populations suggest that the association with physical activity may be stronger in women without a family history of breast cancer than in those with a family history (22;34;51;69), although other large studies have found that women with as well as women without a family history of breast cancer had reduced risk of breast cancer with increasing physical activity (24;32). Several previous studies reported a greater reduction in risk with increasing physical activity among parous compared to nulliparous women (34;35). However, other studies have either observed the opposite finding with risk reduction greater in nulliparous women (32;44), or have found no effect modification of parity (24). One study found that physical activity may be more strongly associated with reduced risk of postmenopausal breast cancer in women who do not use menopausal hormones (22;71), though other studies found that physical activity effect did not change according to menopausal hormone use (16;24;32;40;64).

In 4 studies, researchers examined effect modification by adult weight gain (14;17;45;74), and 1 study reported a greater reduction in risk among women who had less than a 17% increase in adult weight (74). Several studies documented a greater reduction in risk among leaner women compared to heavier women (11;24;44;51), although other studies found that physical activity reduced risk of breast cancer in women with all levels of body mass index (BMI) (32;34).

Two cohort studies have addressed the effect of physical activity on breast cancer within the context of other variables related to energy balance, specifically adiposity and dietary energy intake. One study found evidence that premenopausal women who did not participate in vigorous activity, were overweight or obese (BMI greater than 25 kg/m^2), and had a relatively high calorie intake (more than 1,970 kilocalories per day, as determined from a food frequency questionnaire), had a statistically significant 60% increased risk of breast cancer compared with active, normal weight women with lower calorie intake (26). Another cohort study found that women with the highest quartile of energy intake, were obese, and participated in less than 4 hours per week of vigorous physical activity, had a RR of 2.1 (95% CI 1.27-3.45) compared with normal or overweight, active women who had the lowest quartile of calorie intake (31).

In hypothesizing about the reasons for the effects of energy balance on breast cancer risk, investigators speculate that, in addition to the potential role of obesity as an effect modifier, obesity possibly may be on the causal pathway between physical activity and postmenopausal breast cancer development. Specifically, physical activity reduces levels of adiposity, and subsequently reduces adipose tissue production of estrogen and testosterone, both of which can promote breast carcinogenesis or progression. However, most studies of

physical activity and breast cancer have adjusted for BMI as a proxy for adiposity, and an inverse association between physical activity and breast cancer risk persisted. Thus, it is likely that physical activity may have some effect on breast cancer risk independent of their mutual relation with adiposity.

Dose-Response Pattern

Several studies have tried to quantify the level of physical activity required for a decreased risk of breast cancer. Investigators have reported statistically significantly lower rates of breast cancer among women exercising at least 1 hour per week (14); exercising at least 3.8 hours per week (primarily vigorous exercise) (35); exercising to keep fit at least 4 hours per week (11); and exercising vigorously at least 7 hours per week (46). Other investigators have observed significantly lower rates among women expending at least 1,500 kilocalories per week (18) (approximately 4 hours per week of moderate-intensity activity); at least 15.3 metabolic equivalent (MET)-hours per week (approximately 4 hours per week of moderate-intensity activity) (41); and at least 17.6 MET-hours per week (4 to 5 hours per week of moderate-intensity activity) (74). Two reports from the same study found significantly lower rates of breast cancer only among women who exercised vigorously on a daily basis during the ages to 14 to 22 years (45;68). Finally, in a study where total physical activity over the lifetime was assessed, significantly lower breast cancer rates were seen in women who expended at least 47.5 MET-hours per week per year in total activity (48). The impact of these various levels of activity on reducing risk has varied from 20% to 40%. However, other studies that specifically looked at dose-response have had not found an effect of any dose of exercise on breast cancer risk (28;30). Overall, it appears that at least 4 to 7 hours per week of moderate to vigorous intensity physical activity is required to produce a statistically significant reduction in risk, although some evidence suggests greater reduction in risk with greater amount of activity, such that 1 hour per day of moderate or vigorous activity produces greater reduction in risk compared with the Surgeon General recommendation of 30 minutes per day on most days of the week (4).

Tumor Characteristics

The incidence of *in situ* breast cancer is largely influenced by prevalence of screening, and therefore it is important to examine the effects of physical activity on invasive breast cancer separately from that on *in situ* breast cancer. Furthermore, breast cancers consist of distinct biological subtypes that are strongly related to prognosis and that may differ in etiology including tumor responsiveness to hormones (i.e., estrogen and progesterone receptor [ER/PR] status positive or negative), and other tumor characteristics (e.g., Her2neu receptor status, and other proliferative indices). A few studies have separately examined the association between physical activity and *in situ* versus invasive breast cancer, however, very few have examined physical activity effects separately in hormone receptor positive or negative tumors, and none has considered other tumor characteristics. In one study, researchers examined the association between physical activity and breast cancer stratified by stage of disease and found risk reduction to be greater for localized invasive disease compared to either *in situ* or regional/distant breast cancer (54). A recent large cohort study

found a greater risk reduction for *in situ* (RR 0.69, *P* for trend 0.04) than for invasive breast cancer (RR 0.80, *P* for trend 0.02) (34). One case-control study focused specifically on in situ breast cancer, and found that risk of this stage of breast cancer was approximately 35% lower in women reporting any lifetime exercise activity compared with sedentary women (54). Two studies also reported risk ratios separately for ER/PR positive and negative tumors, but neither found a difference in risk by ER/PR subtype (18;75). A recent cohort study found that women who reported high versus low levels of physical activity at enrollment had a 13%, 33%, and 20% decreased risk of developing ER+/PR+, ER+/PR−, and ER−/PR− breast cancer, respectively (29). Another large cohort study found the greatest risk reduction from increased physical activity for ER−/PR− breast cancer (34). Most other studies have included too few women with hormone receptor negative disease to be able to assess the association of physical activity with risk of this subtype of breast cancer.

Type of Physical Activity

An association of sedentary occupations with increased risk of breast cancer has been documented in reports from some (11;17;27) but not other (76) prospective cohort studies. Published reports from some (43;47;48;53;61;77) but not other (41;44;52;55;56) population-based case-control studies also document an inverse association between occupational physical activity and breast cancer risk.

The effect of low-intensity activity (such as household activities, gardening, dancing, leisurely walking, or other activities with a MET score below 4) on breast cancer risk is still unclear, but may be of importance, particularly for postmenopausal breast cancer, as a large portion of activity among postmenopausal and elderly women is not vigorous. Although previous studies have examined the association between leisure-time physical activity, such as walking, biking, swimming, and aerobics, few studies have included the effects of other low-intensity activities, such as gardening, housework, or shopping, in their calculation of leisure-time physical activity. This may lead to an underestimation of true energy expenditure, especially among groups of women who do not have access to recreational or sports activity. In support of the importance of household activity, a recent large European cohort study found that for women in the highest versus lowest household activity quartile, risks for postmenopausal and premenopausal breast cancer were reduced by 19% (*P* for trend 0.0001) and 29% (*P* for trend 0.0003), respectively (33).

Prostate Cancer

Overall Associations

A number of epidemiologic studies have examined physical activity and prostate cancer risk (28;78-123), including 25 cohort studies (28;78;80-82;87-89;91-102;117;119-121;123) and 14 case-control studies (104-116;118). Several of the cohort studies (78;80;81;94;117) included prostate cancer mortality or advanced or metastatic prostate cancer as at least one endpoint. One study (91) also examined the association between cardiopulmonary fitness and risk of prostate cancer.

Of these studies, 19 found some suggestion for an inverse relation between physical activity and prostate cancer (80;81;87;89;91;93;94;96;97;101;102;104;105;109;112;113; 117;120;123). No overall association between physical activity and prostate cancer was found in 14 studies (28;82;88;95;98-100;106;108;110;114;115;119;121), and an increased risk of prostate cancer among physically active men was found in some studies (78;92; 107;111). The size of the association ranged from an 80% reduction in prostate cancer risk for the highest physical activity levels (113) to a 220% increased risk in one study (111).

Associations for Specific Subgroups

No consistent subgroup effects have been defined for demographic or health factors such as age, race/ethnicity, or BMI. A recent study found that, among men with a family history of prostate cancer, risk for those in the highest quartile of physical activity was reduced by 52%, compared to that for those in the lowest quartile of physical activity. Those without a family history had no risk reduction (115).

Dose-Response Pattern

Several studies have attempted to quantitate a dose-response association of prostate cancer risk with levels of physical activity (82;87;88;91-96;98;100-102;104-106;108-110; 112-118;120;121). A statistically significant trend toward decreasing prostate cancer risk with increasing physical activity level was observed in several studies (87;93;94;102;104; 105;113;118;120), although this was limited to advanced disease in two studies (120;124). In one study, a 74% reduction in prostate cancer risk was found in the highest compared to the lowest quartile of fitness level (91).

Type of Physical Activity

Occupational activity was associated with a decreased risk of prostate cancer in several studies (80;81;93;97;105;113;116) and recreational activity decreased risk of either overall or advanced prostate cancer in several additional studies (91;93;94;96;101;104;115;117). In one study, non-significant risk decreases were found for occupational and recreational activity but an increased risk was observed for household activity (115). No study differentiated between types of recreational activity, such as aerobic or resistance exercise, or to their subtypes such as jogging versus walking. Rather, activities were combined into measures of MET-hours per week, or to measures of frequency or total duration of activity per week.

Effect of Tumor Detection

One consideration for prostate cancer is the effect of screening. Prostate-specific antigen (PSA) screening for early detection became widespread in the United States in the 1990s. If physically active men also are more health conscious (i.e., they are more likely to be screened for prostate cancer), it may result in higher observed rates of prostate cancer among these men because of increased detection. This notion is supported by several cohort studies (94;117;120), which identified a reduction in risk of aggressive, metastatic, or fatal prostate cancer with increased physical activity level. In contrast, an investigation of physical

activity and prostate cancer, diagnosed in 1988 or earlier (before widespread PSA screening was available), among Harvard University alumni found an almost halving of prostate cancer incidence rates among men aged 70 years or older who expended at least 4,000 kilocalories per week in physical activity, compared with those expending less than 1,000 kilocalories per week (84). However, an updated analysis of these men, examining prostate cancer diagnosed after 1988, did not support the earlier observations (100). These inconsistent findings may have been due to bias arising from increased screening for prostate cancer among the most active men.

Colon Cancer

To examine the association between physical activity and colon cancer, the Cancer subcommittee searched the *Physical Activity Guidelines for Americans* Scientific Database. Because the association of physical activity with colon and rectal cancer appears different (see rectal cancer below), we did not include studies where colorectal cancer was the outcome of interest, as the relation between physical activity and colon cancer likely would be diluted. The search yielded 23 publications eligible for inclusion in the present report.

Overall Association

The 23 publications reviewed represented 12 prospective cohort studies (28;99;124-133) and 8 case-control studies (134-140). Four of these publications (137-140) pertained to different aspects of the same case-control study. The database represented by the 23 studies was large, including a total of 9,747 cases of colon cancer with approximately equal distribution between the sexes (4,933 in men and 4,814 in women). The studies were conducted in the United States (124-126;129;131;132;137-142), Europe (Denmark (28), Finland (99;127), Italy (143), Norway (133), Sweden (128) and Switzerland (136)), and Asia (China (134), Japan (130;135), and Taiwan (144)).

Overall, the studies consistently show an inverse association between physical activity and the risk of developing colon cancer, with 9 of the 12 cohort studies and 5 of the 8 case-control studies indicating significant, inverse associations with at least one domain of physical activity (e.g., occupational versus leisure-time) and/or in one sex. Across all the studies, the median RR, comparing most with least active subjects, was 0.7. More specifically, results were similar across the cohort studies (median RR = 0.8) and the case-control studies (median RR = 0.7), as well as for men and women (median RR in both sexes = 0.7). These findings, encompassing studies published in 1995 and later in the *Physical Activity Guidelines for Americans* Scientific Database , are comparable with findings from a recent review of the literature on physical activity and colon cancer risk that also included studies published before 1995 (145). In this recent review, the median RR, comparing most with least active subjects across all studies, also was 0.7 (median RR for men, 0.7; for women, 0.6).

For the prospective cohort studies, bias due to recall of physical activity is unlikely because physical activity was assessed before the development of colon cancer. Thus, any misclassification of physical activity is likely to be random, diluting associations rather than

causing spurious inverse relations. The results also do not appear to be confounded by other factors associated with colon cancer risk because many studies adjusted their findings for several factors, including BMI, smoking, alcohol, diet (e.g., energy intake, intake of calcium and folate intake of fiber, vegetables, and meat), use of aspirin, screening, menopausal status and use of menopausal hormone therapy, and family history of colon cancer. In particular, the findings appear independent of BMI, with most cohort studies (9 of 12) (28;124;125;127-130;132;133) adjusting for this factor, and continuing to observe significant inverse associations. However, fewer than half the case-control studies (3 of 8) adjusted for BMI. Finally, the inverse associations observed are supported by plausible biologic mechanisms. Thus, although the data on physical activity and risk of developing colon cancer are based on observational epidemiologic studies, the inverse associations indicated by these studies are likely to be real.

Associations for Specific Subgroups

Several studies have examined whether the association between physical activity and decreased colon cancer risk varies, depending on use of menopausal hormone therapy (125;131), various aspects of diet (125;139), or BMI (125;128;130;134;138;142). The findings have been inconsistent, with the most consistent being the suggestion that the adverse impact of high BMI on colon cancer risk may be ameliorated by higher levels of physical activity (134;138;142).

Several studies also have examined whether physical activity has a different association with colon cancers occurring at different subsites of the colon. The data have been equivocal, with some studies suggesting a larger magnitude of association for cancers occurring in the proximal colon (130;136;142), while others have reported greater associations for cancers of the distal colon (128;132). Most studies, however, have observed equivalent associations or unclear differences across proximal and distal sites of the colon (125;126;131;133;135;140;143).

Dose-Response Pattern

All but one (99) of the studies classified subjects according to at least 3 levels of physical activity, allowing investigators to assess dose-response. In the cohort studies, 7 of 11 studies with at least 3 physical activity levels reported significant, inverse trends between physical activity and colon cancer risk (124;126-128;130;132;133). For the case-control studies, 4 of 8 also observed significant, inverse trends between activity level and colon cancer risk (134;136;143;144). As discussed above, because of the many different methods used to assess and classify physical activity in these studies, it is difficult to ascertain the shape of the dose-response curve, apart from noting that a dose-response relation appears likely.

Types and Amount of Physical Activity

Most studies have assessed leisure-time and/or occupational physical activity only, with one study also assessing active commuting, in the form of walking or bicycling to work (134). Because of the different questionnaires used to assess physical activity and the different

categories used to group subjects in the studies, it is difficult to integrate the findings across the studies. Further, most studies presented their findings according to overall volume of energy expended, and data are sparse on specific kinds of activity associated with decreased colon cancer risk.

However, significantly lower risks of colon cancer have been observed with leisure-time physical activity (ordered in approximately ascending doses of physical activity) of at least twice a week for at least 10 minutes' duration (142), at least 4 hours per week of moderate-to-vigorous intensity recreational activity (131), at least 20 MET-hours per week of leisure-time activity (144), more than 21 MET-hours per week of leisure-time activity (132), 7 or more hours per week of recreational activities including walking (126) a median of 35.25 MET-hours per week of overall activity (130), a median of 46.8 MET-hours per week of leisure-time activity (124), and more than 94.3 MET-hours per week of active commuting (134). Additionally, the case-control study by Slattery and colleagues suggests that physical activity needs to be vigorous in intensity (137-140) to reduce colon cancer risk. Overall, these data suggest that 30 to 60 minutes per day of moderate-to-vigorous intensity physical activity may be needed to significantly lower the risk of developing colon cancer.

Rectal Cancer

In contrast to the associations observed between physical activity and colon cancer, the data on physical activity and risk of developing rectal cancer are far more mixed. More than half of the studies have reported no significant associations (99;126;130;133;143;144;146), with the remaining studies observing significantly lower risks (or of borderline significance) with higher levels of physical activity (127;128;135;136;140). In a recent review of the literature on physical activity and rectal cancer risk, the median relative risk, comparing most with least active subjects across all studies, was 1.0, indicating little association (130).

Additional Cancer Sites

The available evidence for an association of physical activity with reduced risk of lung, endometrial, ovarian, pancreatic, and other cancers is less complete than that for breast, prostate, colon, and rectal cancers. Therefore, the following sections present a general overview.

Lung Cancer

A review of the association of physical activity and lung cancer risk was included within a recently published book chapter (145). At the time of that review, 15 cohort studies and 6 case-control studies had been published, overall indicating a median of 20% reduced risk for lung cancer in the most versus the least active subjects. This present review focused on studies published between 1996 and 2006. Results indicate a 24% median reduction of lung cancer risk for the most versus least active subjects (101;147-156). As with the prior review, the reduction of risk was more obvious with case-control (median RR over 2 studies = 0.61) (154;156) than with cohort studies (median RR over 8 studies = 0.77) (101;147-153). The inverse relation of physical activity with lung cancer risk is similar for men (0.74, 8 studies

since 1996) (101;147;149-153;156) and women (0.75, 6 studies since 1996) (147-149;152;154;156).

Most of the studies on the association of physical activity and lung cancer adjust for cigarette smoking. However, even with this adjustment, the potential for residual confounding is quite high. Three studies have reported risk reductions specifically for current smokers, former smokers, or never smokers (148;150;155). The risk reduction in these studies is more similar for current and former smokers (median RR of 0.61 (148;150;155) and 0.59 (148;150), respectively) than for never smokers (median RR of 1.03 for 2 studies reporting for this subgroup) (148;155). As yet, evidence is too sparse to conclude that the reduction of lung cancer risk by physical activity is isolated to current and former smokers.

The question of whether the association of physical activity with lung cancer is due to residual confounding by smoking has been addressed in 2 ways: examining consistency of association across histologic subtypes of lung cancer and exploring the association in never smokers. Smoking is more clearly established as a risk factor for some histologic subtypes of lung cancer than others. Evidence links smoking more closely to small cell and squamous cell lung cancers than to adenocarcinoma of the lung. Therefore, one indirect approach to the question of whether the association of physical activity with reduced risk for lung cancer is due to residual confounding by smoking status is to evaluate whether the association is present for all histologic subtypes, including adenocarcinoma. Three studies to date have examined whether the association of physical activity is similar across most lung cancer histologic subtypes, as well as within sex. In men, the median relative risks for lung cancer for those who are most versus least active are 0.59, 0.96, 0.80, and 0.73 for small cell, squamous cell, adenocarcinoma, and other/nonspecified histologic types, respectively (147;149;156). In women, the median RR values for most versus least active among the same subtypes are 0.81, 0.77, 0.86, and 0.56, respectively (147;148;156). This evidence suggests that the physical activity association is present across histologic subtypes, including adenocarcinoma. Another approach to determining whether the overall association of physical activity and lung cancer is due to residual confounding by smoking is to study non-smokers. The RR (or odds radio) for non-smokers was 1.32 and 0.74 in the one cohort and one case-control study to report an association specifically for non-smokers (148;155). It also should be noted that the 39% risk reduction for most versus least active current smokers pales in comparison to the reduction of risk from quitting smoking. Smoking cessation remains the most important means to reduce lung cancer risk among smokers. That stated, it would be of interest to understand better the potential mechanisms by which physical activity may assist in marginally reducing lung cancer risk among current and former smokers. To our knowledge, no research has directly addressed this question.

Endometrial Cancer

A review of the association of physical activity and endometrial cancer risk was included within a recently published book chapter (145). At the time of that review, 4 cohort studies and 11 case control studies had been published, overall indicating a median relative risk of

0.70 for the most versus the least active subjects. An update of that review, focusing on studies published since 1996 reported a similar median RR (0.70) for the 15 most recently published studies, which included 7 cohort studies and 8 case-control studies (157-171). Of these more recent studies, 5 include relative risks that are adjusted for multiple variables but not for BMI (157-160;171). The median RR of 0.73 for these studies is similar to the results after adjustment for BMI, which was 0.70. This is important because the effect of physical activity on body weight has been hypothesized to mediate the purported association of physical activity with reduction of risk of endometrial cancer.

Another factor that should be accounted for in analyses is menopausal hormone therapy, given the potential causal link between use of unopposed estrogen therapy and increased risk of endometrial cancer. For example, the median RR from the 3 case-control studies that adjusted for menopausal hormone therapy was 0.70 (165;168;170) (no cohort studies published to date have adjusted for this factor) compared to a median RR of 0.68 for the 10 case-control and cohort studies that did **not** adjust for menopausal hormone therapy (157-164;169;171).

Overall, evidence indicates an inverse association between physical activity and incidence of endometrial cancer. Further, the lack of change in the median relative risks for studies that did versus did not adjust for BMI or menopausal hormone therapy may indicate that the association is not mediated through obesity or the generally healthy lifestyle commonly associated with exogenous hormonal exposure.

Ovarian Cancer

The association of physical activity with incidence of ovarian cancer was explored in a meta-analysis and systematic review published late in 2007 (172). This review concluded that a modest inverse association exists, with a weighted pooled RR of 0.81 (95% confidence interval was 0.72-0.92). Sensitivity analyses indicated no difference of findings when summarized studies did versus did not adjust for BMI (which may be on the causal pathway) and for exogenous hormone use (e.g., oral contraceptives).

Pancreatic Cancer

A total of 8 cohort studies (173-180) and 2 case-control studies (181;182) have examined whether physical activity may reduce incidence of pancreatic cancer. Case-control studies may be particularly biased for pancreatic cancer, given that at diagnosis most patients have advanced disease, are symptomatic, and often have recent weight loss. Four of the 10 cited case-control studies of pancreatic cancer adjusted for BMI in multivariate models. In the 5 cohort studies that did not adjust for BMI (173-177), the median relative risk for the association of physical activity with pancreatic cancer incidence was 1.21. One of the case-control studies provided an odds ratio (OR = 0.78) for men that was not adjusted for BMI (182). Both of the case-control studies provided odds ratios for women that were not adjusted for BMI; the average of these was 0.82 (181;182). In spite of this inconsistent evidence, when taken in combination with the observation of a weak positive association

with BMI (177;183), it remains possible that a level of physical activity sufficient for weight control would be associated with reduced incidence of pancreatic cancer.

Other Cancers

The potential for physical activity to reduce incidence of other cancers (e.g., thyroid, kidney, bladder, and hematopoietic) also has been studied. Reviews of these cancers are not included here because the data are too sparse to allow any conclusions regarding a potential relation with physical inactivity. Readers are referred to other reviews for an overview of results from these studies (2;145).

Question 2: What Are the Effects of Physical Activity on Cancer Survivors, Including Late and Long-Term Effects of Treatment, Quality of Life, and Prognosis?

Conclusions

A common definition of "cancer survivor" is any individual who has had a diagnosis of cancer, from the point of diagnosis and for the balance of life. Cancer survivors are a subset of the US adult population that is expected to grow substantively in the coming decades. As such, the role of physical activity in improving outcomes for cancer survivors is likely to increase in importance as well. Recently, data have been published regarding the effects of physical activity on health outcomes among persons who already have cancer. These studies suggest that physically active individuals with breast or colon cancer may have improved prognosis (i.e., fewer recurrences and deaths), compared with sedentary survivors. In addition, physical activity may play an important role in preventing, attenuating, or rehabilitating late and long-term effects of cancer treatment. Walking is a commonly prescribed form of exercise in the studies reviewed here and appears to have benefits on muscular strength and endurance, as well as quality of life. Dose-response effects and long-term outcomes are unknown for any outcomes from physical activity interventions in cancer survivors at this time.

Introduction

More than 10 million people in the United States are cancer survivors, and more than 16% of adults older than age 65 years are cancer survivors (184). The increasing success of cancer treatments has required a shift in focus toward new outcomes, such as preventing recurrence and mortality, and accommodating the unique medical and psychosocial needs of cancer survivors.

Cancer treatment typically includes some combination of surgery, radiation therapy, or chemotherapy, and may also include hormonal therapies, steroid treatment, immunotherapies, or monoclonal antibody treatment. Each of these therapies is associated with acute as well as late and long-term adverse physiologic and psychological effects. The terms "late effects" or "long-term effects" (185) are distinct in the timing of their onset. Late

effects are side effects or complications that are absent or subclinical at the end of therapy but that emerge after compensatory systems fail or some second insult (e.g., deconditioning) occurs that results in a clinically significant diagnosis that can be traced back to effects of treatment. An example of a late effect would be the diagnosis of a cardiac arrhythmia years after treatment with a cardiotoxic chemotherapeutic agent such as adriamyacin (186). Long-term effects are adverse effects or complications that appear during treatment and persist long afterward, for months, years, or the duration of life. Physical activity could be useful for preventing or attenuating some late and long-term effects of cancer treatments (Figure G7-1) (187), and may also be useful for prevention of recurrence or cancer mortality among cancer survivors.

Figure G7.1. Late and Long-Term Effects of Cancer Treatment That May Be Positively Affected by Physical Activity
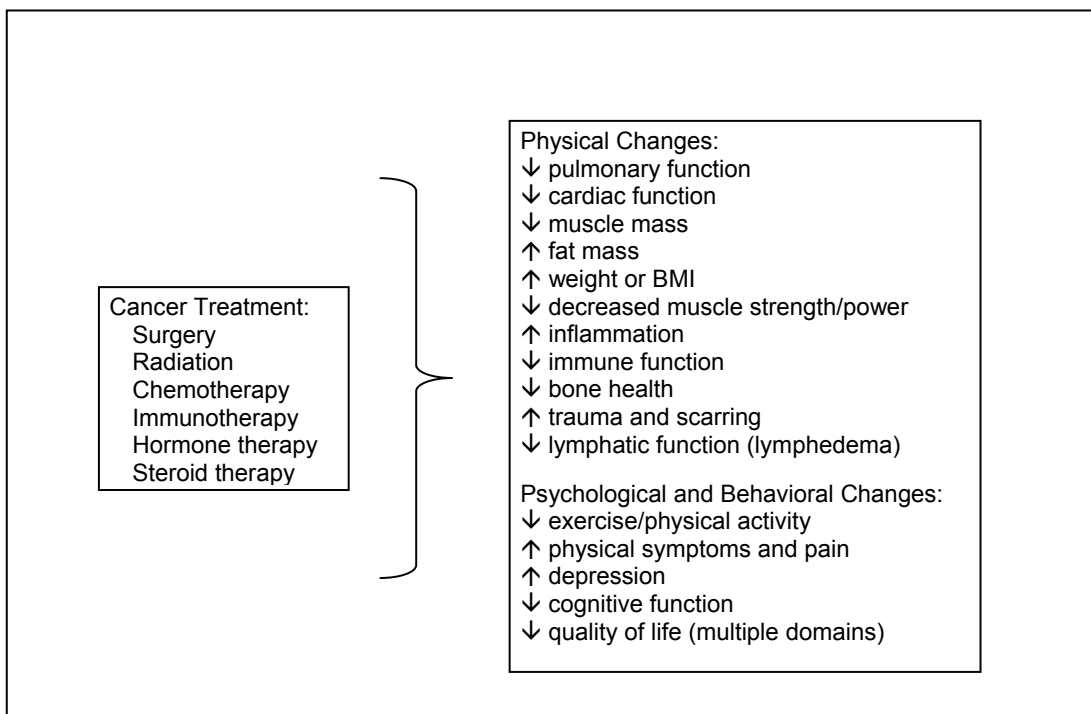
The acute effects of treatment and the potential for positive effects of physical activity during active cancer treatment are beyond the scope of this review, but have been reviewed elsewhere (188;189). Also not reviewed here are the late or long-term effects of childhood cancer treatment, as little research has been conducted in this area.

Rationale

Effects of Physical Activity on Cancer Recurrence and Mortality

Though few studies have been conducted on the role of physical activity in preventing cancer recurrence or reducing mortality, the consistent findings of a preventive effect

warrants comment. Data from the Nurses' Health Study were used to explore the dose-response association of physical activity with overall and breast cancer specific mortality, as well as recurrence, among 2,987 breast cancer survivors over a median of 96 months of follow-up (190). The results indicated a 29% decrease in overall mortality among women who did at least 3 MET-hours per week of aerobic activity after diagnosis, with minimal additional protection from greater levels of physical activity. The decrease in breast cancer-specific mortality and recurrence were 50% and 43%, respectively, in women who engaged in at least 9 MET-hours per week of physical activity compared with women who did less than 3. Additional benefits were small for activity levels greater than 9 MET-hours per week, which can be translated to 3 hours per week of walking at 2.5 miles per hour. Considerable evidence indicates that overweight, obesity, and weight gain are associated with breast cancer recurrence (191-193). These results are consistent with the hypothesis that physical activity reduces risk of mortality or recurrence among breast cancer survivors through weight control.

Evidence for a role of physical activity in colon and colorectal cancer survivorship comes from 2 recently published observational studies. One of these, the Nurses' Health Study, observed an inverse dose-response association of physical activity and overall and colorectal cancer-specific mortality in 554 women who had had a previous diagnosis of colorectal cancer. Women who engaged in at least 18 MET-hours per week of physical activity after diagnosis had a 61% and 57% reduced risk of colorectal cancer-specific and overall mortality, respectively, compared to women who did less than 3 MET-hours per week (194). A dose-response association of physical activity and colon cancer disease-free survival also was seen in the cohort of 832 male and female patients who participated in the CALBG trial (195). In this latter cohort, 18 MET-hours per week, or 6 hours of walking per week at 2.5 miles per hour, was associated with a 49% reduction in risk of recurrence (195).

Effects of Exercise on Prevention of Long-Term or Late Effects of Cancer Treatment

 A number of recent systematic reviews (188;196-205) as well as 2 meta-analyses (188;206) have recently been conducted on the effects of physical activity interventions on a variety of outcomes in cancer survivors. Readers interested in an in-depth discussion of the effects of exercise on cancer survivors are guided to these reviews. Below, the effects of exercise training on late or long-term effects is reviewed for outcomes for which there is the greatest amount of evidence and consensus and that may be most useful in guiding quantitative or qualitative behavioral recommendations for cancer survivors. Of the 22 controlled clinical trials published since 1995 and reviewed here, only 1 (207), examined a dose-response pattern of exercise training on any outcome, and none was noted. For each of the outcomes reviewed below, effects of walking programs are noted, if such data were available. Most of the studies reviewed were relatively short in duration (6 months or less); long-term effects are not yet known.

Physiologic Effects

Cardiorespiratory Fitness. Though the effect of physical activity on cardiorespiratory fitness has been long established (see *Part G. Section 2: Cardiorespiratory Health* for a detailed discussion of this topic), it is of particular relevance for cancer survivors given the cardiotoxic effects of several commonly used cancer treatment drugs and radiation to the chest (186;208). A meta-analysis published in 2005 indicated a strong weighted mean effect size of 0.65 (*P*=0.003) for cardiorespiratory fitness based on the 4 exercise interventions that had assessed this outcome in cancer survivors after treatment (188). Since this meta-analysis, 9 additional RCTs have assessed whether various of exercise interventions in cancer survivors improve cardiorespiratory fitness after treatment (209-217). All 13 studies have shown positive effects, and 11 showed statistically significant improvements on cardiorespiratory function tests ranging from a 6-minute walk test to maximal treadmill or cycle ergometer tests. All of these studies included breast cancer survivors, and most included only breast cancer survivors. Fitness improvements have been demonstrated in a variety of programs, including walking, yoga, tai chi chuan, exercise at home, and exercise at fitness facilities. For most of the studies, exercise doses used were 3 weekly sessions of 20 to 40 minutes in duration at moderate intensity.

Muscular Strength and Endurance. Observational evidence in small convenience-sample studies suggests that muscle mass may decrease and fat mass may increase after some breast cancer chemotherapy regimens (218). Cancer treatment may result in a decrease in activity (219), with subsequent deconditioning associated with muscle disuse. Therefore, it is important to determine whether exercise training improves muscular strength or endurance in cancer survivors. Six studies have examined the effects of some form of resistance training, tai chi chuan, or yoga on muscle strength or endurance (211-213;215;220;221). All of these studies were conducted in women who had completed breast cancer treatment. Five observed positive effects of training (211;213;215;220;221) and 4 reported statistically significant improvements (211;213;215;220) in strength or endurance tests.

Flexibility. Cancer surgeries may result in decreased range of motion with scarring or tissue trauma, and these changes may result in altered physical function. Six studies have examined the effects of exercise training on flexibility. Three assessed effects of aerobic exercise or yoga on lower body flexibility with the sit-and-reach test in breast and colon cancer survivors (207;215;222). All 3 showed improvements in flexibility, but only one (207) observed a statistically significant improvement comparing changes between treatment and control participants. Three other studies examined effects of tai chi chuan, dance and movement, or aerobic exercise and stretching on shoulder range of motion in breast cancer survivors (211;223;224). All 3 noted improvements, and 2 noted significant between-group differences in shoulder range of motion (211;223).

Lymphedema. Surgical removal or irradiation of lymph nodes results in damage to the lymphatic system that can result in an inability of the affected body part to manage fluid balance and temperature regulation. This damage may impair immune response and wound healing, as well as response to trauma or injury. Swelling and pain in the affected body part

can develop immediately after surgery and/or radiation or years later, making lymphedema a long-term risk among several types of survivors, including those with breast, head and neck, melanoma, genital cancers, lower gastrointestinal tract and bladder cancers. Lymphedema is considered a chronic condition, and occurs in 6% to 50% of breast cancer survivors, depending on number of nodes removed and intensity of radiation (225-227). Lower-limb lymphedema also occurs in 20% to 30% of cancer patients who have had lymph node removal or radiation in the groin or retroperitoneal lymph nodes (228-237). Four studies have examined the risk of lymphedema onset or worsening among breast cancer survivors by measuring changes in arm circumferences or symptoms resulting from exercise training (217;221;224;238). None of these studies has noted negative effects of aerobic or resistance exercise on arm circumferences or symptoms; evidence of possible benefit to the affected limb has not been examined. No studies of the safety or efficacy of exercise for cancer survivors with or at risk for lymphedema for cancer sites other than breast have been conducted.

Weight Change. Some breast cancer patients gain weight after diagnosis, and the associated changes in body composition may include decreased muscle mass and increased body fat, as suggested by a few convenience-sample studies (218). These effects have not been examined in population-based or clinical trial series of patients, nor in patients with other cancers. However, it is important to determine the effects of exercise training on body weight and body composition in survivors who have had any type of cancer treatment. The results of the 13 identified controlled trials conducted since 1995 indicate that, as for the general population, exercise may decrease percent body fat to a small degree, but has little to no effect on body weight in the absence of concurrent caloric restriction (188;207;210-215;217;222;239-241). (See *Part G. Section 4: Energy Balance,* for a detailed discussion of the association between physical activity, weight loss, and changes in body composition.)

Psychosocial and Symptom Effects

Quality of Life. The effect of exercise on health-related quality of life was examined in a systematic review and meta-analysis published in 2005 (188). This review concluded that evidence was strong for a positive effect of physical activity on quality of life in cancer survivors, though the weighted mean effect size of 0.30 was not statistically significant. Since the publication of that meta-analysis, an additional 10 studies have examined effects of physical activity on cancer survivors after treatment (209;213-217;223;224;240;242). Of these, all showed positive effects, and 8 indicated a statistically significant improvement in at least one quality of life indicator after a physical activity intervention. Overall, 10 out of 13 identified studies showed statistically significant improvements in quality of life resulting from a physical activity intervention after cancer treatment.

Fatigue. Cancer-related fatigue is distinct from ordinary types of fatigue in its persistence and severity (243). The effects of physical activity interventions on fatigue in cancer survivors (primarily breast cancer) have been tested in 8 studies since 1995. Of these 8 trials (207;209;210;214;216;222;239;244), 3 reported statistically significant improvements in fatigue after a program of aerobic exercise, walking, or cycling. Five other studies, most of

which focused on walking programs among breast cancer survivors during the time period after treatment, observed improvements, but not statistically significant improvements. The mechanisms through which physical activity may improve cancer-related fatigue are not yet fully understood (243).

Question 3: What Mechanisms Explain the Associations Between Physical Activity and Cancer?

Conclusions

A number of plausible mechanisms might explain the associations between physical activity and cancer risk and prognosis. Increased physical activity reduces adiposity, which may explain reductions in cancers that are associated with overweight and obesity, including postmenopausal breast, colon, endometrial, and other cancers. Increased physical activity is associated with reduced levels of sex hormones, which may explain a link between physical activity and hormone-related cancers such as breast and endometrial cancers. Another possible mechanism is through the effect of physical activity and inflammation and immune function. Finally, increased physical activity reduces insulin resistance, which could explain associations with risk for some cancers, such as colon cancer, that may be increased in individuals with insulin resistance or hyperinsulinemia.

Rationale

Physical activity could affect cancer risk or progression through several plausible mechanisms (245). Many of these mechanisms may act through the effects of physical activity on obesity, with resulting changes to circulating levels of adipokines, cytokines, insulin, and sex hormones. Other mechanisms may involve direct effects on target organs and tissues. The effects of physical activity on carcinogenesis or prognosis are likely to be multi-factorial and may be affected by many factors such as age, sex, and adiposity, in addition to physical activity specific factors such as type, duration, frequency, and intensity of physical activity.

Menstrual Factors and Sex Steroid Hormones

Several modifiable menstrual factors increase breast cancer risk, including early age at menarche, frequent ovulation, regular cycles, and late age at menopause (246). Women with elevated levels of estrogens and androgens have increased risk of developing breast cancer. In a combined analysis of 9 large cohort studies, postmenopausal women in the top quintile for various estrogens or androgens had approximately double the risk of developing breast cancer compared with women in the lowest quintile (247). Elevated levels of estradiol or testosterone in premenopausal women increase risk of breast cancer as well (248;249). Medications that block estrogen receptors or that prevent estrogen production in peripheral tissues have been a mainstay of treatment for women with estrogen receptor positive breast cancer (250). Women with elevated estrogen concentrations (unopposed by progesterone) are at an increased risk for endometrial cancer (251). In men, anti-androgen therapy

improves prostate cancer survival (252) and reduces overall incidence of the disease when tested as a preventive agent (253). However, recent evidence suggests that blood levels of androgens or estrogens are not related to prostate cancer risk (247), suggesting that only prostatic levels of sex hormones are relevant for prostate carcinogenesis or progression.

Premenopausal Women

The effect of physical activity on age at menarche, menstrual cycle function, and level of ovarian-produced sex steroid hormone levels in girls and young women are potential mechanisms for reduced breast cancer risk (254). Moderate-intensity physical activity may cause small changes in reproductive hormones in premenopausal women, but high intensity or volume of exercise sufficient to cause a negative energy balance may be required to induce menstrual dysfunction (amenorrhea, anovular cycles and luteal phase deficiency) with significantly decreased production of ovarian estradiol and progesterone (255-263).

Postmenopausal Women

In postmenopausal women, increased physical activity has been associated with decreased serum concentrations of estradiol, estrone, and androgens (264-266). The positive effect of physical activity is closely linked to body composition because the primary source of estrogen in postmenopausal women is from aromatization of androgen precursors in peripheral, mainly adipose, tissue. In a sub-sample from the Women's Health Initiative (WHI) Dietary Modification Trial, women with low self-reported physical activity had higher levels of estrone, estradiol, and free estradiol, and lower levels of sex-hormone binding globulin (which binds estradiol, making less available to target tissue) than did active women (265). The highest levels of estrogen were observed in women who were both below the median level for physical activity (i.e., less than 6.5 MET-hours per week, approximately less than 1.5 hours per week of brisk walking) and above the median BMI (i.e., at least 29 kg/m^2).

In an RCT, 173 overweight, sedentary postmenopausal women were assigned to a moderate-intensity aerobic exercise, 45 minutes per day, 5 days per week for 12 months or to a control group. A significant decrease in estradiol, estrone, and free estradiol was seen from baseline to 3 months in exercisers versus controls, with an attenuation of the effect at 12 months (267). However, in those women who lost body fat, the exercise intervention resulted in a statistically significant reduction in these estrogens at both 3 and 12 months. Similarly, in women who lost body fat, a statistically significant decrease in testosterone and free testosterone occurred in exercisers compared with controls (268). These intervention and observational studies results suggest that both increased physical activity and reduced body fat will produce the greatest protection against breast cancer by producing the greatest decrease in serum sex hormones.

Men

Chronically lowered testosterone concentrations have been reported in athletes, but this finding may require a threshold amount or intensity of physical activity to occur (269), and

the effects of moderate-intensity aerobic exercise on sex steroid hormones in men is not known. In a recent trial, 102 men aged 40 to 75 years were randomly assigned to a 12-month moderate to vigorous intensity aerobic exercise intervention (60 minutes per day, 6 days per week) or a control group (no change in activity) (270). Dihydrotestosterone (DHT) increased 14.5% in exercisers compared to 1.7% in controls at 3 months (P=0.04). At 12 months, DHT remained 8.6% above baseline in exercisers versus a 3.1% decrease in controls (P=0.03). Sex hormone binding globulin increased 14.3% in exercisers versus 5.7% in controls at 3 months (P=0.04), while at 12 months it remained 8.9% above baseline in exercisers compared to 4.0% in controls (P=0.13). No statistically significant differences were observed for testosterone, free testosterone, 3α-Diol-G, estradiol, or free estradiol in exercisers versus controls. Therefore, the association of physical activity with circulating hormone levels in men is still unclear.

Metabolic and Other Hormones

Insulin resistance has been linked to increased risk of breast, colon, pancreas, endometrial and stomach cancers (271). Higher cancer incidence and mortality also have been noted in those with type 2 diabetes or impaired glucose tolerance (271;272). Insulin can enhance tumor development by stimulating cell proliferation or inhibiting apoptosis (271). It also can regulate the synthesis and biological availability of sex steroid hormones, and inhibit hepatic synthesis of sex hormone binding globulin (271). Acute bouts of physical activity improve insulin sensitivity and increase glucose uptake by skeletal muscle for up to 12 hours (273), and chronic exercise training results in prolonged improvements in insulin sensitivity (274-276). Although body composition has been strongly associated with insulin sensitivity, exercise-induced changes in insulin sensitivity can occur from physical activity, independent of the changes in weight or body composition (273;274;277). An additive effect of resistance training to improve insulin sensitivity and glycemic control also has been proposed because skeletal muscle is a primary site of insulin resistance (273;278).

Women with elevated levels of prolactin are at increased risk of breast cancer (279), and a recent clinical trial found that increased physical activity levels as measured by increased VO_{2max} over 1 year in a moderate-intensity exercise intervention was associated with statistically significant reductions in prolactin levels in postmenopausal, overweight women (280).

Inflammation

Elevated levels of pro-inflammatory factors, such as C-reactive protein (CRP), interleukin (IL)-6, tumor-necrosis factor-α (TNF-α), and decreased levels of anti-inflammatory factors, such as adiponectin, have been linked with increased cancer risk (281). Physical activity may reduce systemic inflammation alone or in combination with body weight or composition through reducing macrophage or adipose cell production of inflammatory cytokines in adipose tissue, although exact mechanisms are unknown (278;282).

Although cross-sectional studies support an association between chronic physical activity and lower levels of the inflammatory markers CRP, serum amyloid A (SAA), IL-6 and

TNF-α in both men and women, intervention studies of exercise alone or exercise and diet combined have had inconsistent results, with some studies but not others showing reductions in these inflammatory markers (282).

Increases in adiponectin have been seen with physical activity interventions in the presence of significant weight loss (283). Shorter duration prospective physical activity and weight loss interventions have failed to alter adiponectin levels despite modest changes in body weight and body composition (278).

Immune Function

The immune system is thought to play a role in reducing cancer risk by recognizing and eliminating abnormal cells or through acquired and/or innate immune system components (284). The role of physical activity on immune factors related to cancer has been largely untested, but one hypothesis is that physical activity could improve the number or function of natural killer cells, which play a role in tumor suppression (282).

Bouts of physical activity have been shown to result in acute increases in a number of components of immune function (e.g., neutrophils, monocytes, eosinophils, and lymphocytes), followed by a dip below pre-exercise levels lasting up to 1 to 3 hours (285). For chronic physical activity, an inverted J-shaped dose-response relation between intensity of physical activity and immune function has been shown. Moderate physical activity results in enhanced immune function, but exhaustive exercise, overtraining, or high-intensity exercise may lead to immunosuppression, which may result in increased susceptibility to ailments such as upper respiratory infections (282). However, the current evidence on moderate-intensity physical activity from randomized controlled trials is inconclusive, with differences in components of the innate immune system noted in some, but not all, cross sectional studies that compare exercisers to non-exercisers. Randomized controlled trials of moderate physical activity show little effect on immune function (282).

Other Mechanisms

Physical activity also could mediate cancer risk through additional mechanisms, such as its effects on other body structures. For example, physical activity affects colon motility, leading to decreased transit time and, perhaps, reduced carcinogen exposure in the colon (254). In addition, physical activity has been hypothesized to affect various tissues leading to reduced carcinogenic prostaglandin (PG) production (286), although an RCT found no effect of a 12-month aerobic exercise intervention (1 hour per day, 6 day per week) on colon mucosal prostaglandins PGE2 or PGF2alpha in 202 men or women aged 40 to 75 years (287).

Overall Summary and Conclusions

Increased physical activity is associated with reduced risk of several cancers. Most evidence for this association is available for breast and colon cancers, although growing evidence

suggests an association between increased physical activity and reduced risk of endometrial and lung cancers. Overall, data suggest that 30 to 60 minutes per day of moderate-to-vigorous intensity physical activity may be needed to significantly lower the risk of developing breast and colon cancers. The effect of physical activity is larger for colon cancer (median reduction in risk of 30% across reviewed studies) compared with breast cancer (median reduction in risk of 20% across studies). A large part of the effect of physical activity on cancer is likely mediated through obesity and other hormonal and metabolic mechanisms. Randomized controlled trials have demonstrated effects of physical activity interventions on cancer risk factors, which further support a role of physical activity in reducing risk for cancer.

Strong evidence links increased physical activity in cancer survivors with improved quality of life and increased fitness. Less evidence is available regarding the effect of physical activity on cancer recurrence and survival. A 2006 publication from the American Cancer Society (3) states that although the current public health guidelines of 30 to 60 minutes of moderate-intensity aerobic exercise 5 times per week have not been studied systematically in cancer survivors, there is no reason to think that this would not also benefit survivors. Overall, results indicate that guidelines for cardiovascular exercise for cancer survivors who have completed treatment need not be different from those of the general population, and that particular physiologic and psychosocial effects of cancer and its treatments are positively affected by cardiovascular exercise, resistance training, and flexibility training.

Research Needs

Knowledge about the role of physical activity in reducing the risk of common cancers would benefit from additional evidence gathered from clinical trials. In the survivorship setting, clinical trials showing a benefit of physical activity interventions on reducing deaths, recurrences, and reducing the impact of late or long-term treatment effects, also would make a valuable contribution to our understanding of the needs of this growing population.

Other research needs include studies to clarify biological mechanisms linking physical activity to specific cancers in order to identify associations with less commonly studied cancers, define the shape of dose-response curve of the physical activity-cancer relation, determine the effect of low-intensity activities and accumulated bouts, and assess the effect of physical activity within specific population subgroups.

Additional observational epidemiologic research to identify the dose, type, and frequency of physical activity on risk of various cancer sites and subtypes is needed, in addition to identifying the effect of physical activity on risk of specific cancers within particular population subgroups including various race/ethnic, age, sex, and groups at elevated risk of cancer.

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