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TUTORIAL REVIEW

The role of physical activity in primary cancer prevention

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Abstract Few modifiable lifestyle factors have been shown to be associated with reduced cancer risk. For physical activity, more than 200 epidemiologic studies have provided evidence that its association with cancer risk is convincing for colon and breast cancers; probable for endometrial cancer; possible for prostate, gastric, and ovarian cancers; and insufficient for all other cancer sites. Relative risk reductions are in the range of 10–30 %. On the absolute scale, about 9–19 % of the most frequent cancers can be attributed to a lack of sufficient physical activity. As modifiable health behavior, exercise thus has a strong potential for primary cancer prevention and the evidence is sufficiently established to recommend physical activity as a means for the primary prevention of cancer. Current recommendations call for at least 30–60 min of moderate to vigorous activity daily. However, further research is needed to provide a stronger evidence base specifically for these recommendations. The exact type, dose, and timing of physical activity remain unclear but ongoing and planned research will elucidate these associations. In addition, possible biologic mechanisms whereby physical activity may influence carcinogenesis, independently and/or jointly with other factors of the energy balance equation, need further attention in future research.

Keywords Physical activity · Cancer · Primary prevention · Exercise

Introduction

Few modifiable lifestyle factors have been consistently shown to reduce cancer incidence. More than 200 epidemiologic studies in the past 30 years have investigated physical activity as a potential candidate for primary cancer prevention. Based on recently published reviews, a summary of the available evidence for major cancer sites will be given [2, 11, 12, 16]. Furthermore, some insights into current research and open issues for further research will be outlined.

Physical activity is a complex behavior and the assessment in any setting is challenging. To date, most of the evidence for cancer incidence is based on observational studies (case–control or cohort studies) conducted within different study populations. Physical activity exposure assessment was most frequently based on questionnaires with considerable variation in the quality and detail of data captured on timing, type, and dose of physical activity, hence, making direct comparisons of the data across these studies difficult. Randomized controlled exercise intervention trials have, so far, investigated intermediate markers for cancer risk only, limiting evidence to date to research regarding the underlying biologic mechanisms.

Summary of evidence by cancer sites

Physical activity and risk of colon, rectum, and gastric cancers

Particularly for colon cancer, a substantial body of evidence from observational epidemiological studies exists. For the past 10 years, scientific consensus from expert groups and reviews has existed and concluded that the association between physical activity and colon cancer incidence is convincing [5, 11, 12, 16]. A recent review and meta-analysis based on 52 studies, 24 population-based case–control studies, and 28 cohort studies, estimated a 24 % risk reduction, comparing the most versus least active individuals across all studies [14, 15]. Case–control studies reported with an average risk reduction of 31 % larger overall risk reductions

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than cohort studies (average risk reduction of 17 %) [15]. The majority of studies that examined dose–response relations between increasing activity and decreasing risk reported statistically significant, inverse trends [11]. There is some evidence that sustained activity over lifetime, activity done during adolescence and at various points in life are associated with the greatest reductions in colon cancer risk [14]. Overall, there is convincing, consistent, and strong evidence for an association with decreased colon cancer risk, particularly with high doses and intensities of physical activity [16].

In contrast to the associations between physical activity and colon cancer, there is little evidence for an association between physical activity and risk of developing rectal cancer [14]. Only two of 33 studies reported statistically significant risk reductions for rectal cancer [1, 10].

For gastric cancer, 19 studies have been published by now. In general, studies that used more detailed physical activity assessment methods tended to observe significant risk reductions, whereas studies with a more general assessment resulted in null associations. Thus, there are some indications that physical activity may be protective against total gastric cancer with more evidence for distal (noncardia) gastric cancer [12, 14].

For pancreatic cancer, the relation between physical activity and pancreatic cancer risk was examined in a recent systematic review and meta-analysis published in 2010 [9]. Overall, 28 studies, 22 prospective cohort, and six retrospective case–control studies were reviewed. There are some indications of an inverse relation between pancreatic cancer risk and higher levels of occupational and total physical activity, but evidence of such associations with recreational and other activity exposures is inconclusive.

Physical activity and risk of breast and gynecologic cancers

The etiology of these cancers is complex but there is now compelling evidence that physical activity is a key modifiable lifestyle factor that is associated with reduced breast cancer risk [8]. To date, 86 studies have analyzed some aspect of physical activity and its association with breast cancer. In total, 64 studies have demonstrated a risk reduction with increased levels of activity. When comparing the most to the least active participants in these studies, the average risk reduction is about 25 % and there is evidence for a dose–response effect in 40 of the 50 studies that investigated this issue. Both pre- and postmenopausal women experience a breast cancer risk reduction with physical activity but the association is somewhat stronger for postmenopausal (28 %) than premenopausal women (20 %).

There is consistent, strong, coherent, and biologically plausible evidence that physical activity reduces breast cancer risk in women, and that this holds presumably true for women of all racial groups, and of most BMI levels particularly if it is sustained over lifetime, of at least moderate intensity and regular in frequency and duration. The exact dose and type of activity needed to reduce breast cancer risk is not yet fully defined, as is the question whether this association holds true for all breast cancer subtypes as defined by hormone receptor status [13].

For endometrial cancer, there is also increasing evidence for an association with physical activity. This may be expected by the proximity in the etiologies of these cancers [3]. Overall, 28 studies have been conducted on endometrial cancer and 23 of them have shown a risk reduction with increased activity levels irrespective of how these have been defined. Half of these studies (n=14) have observed statistically significant risk reductions. The magnitude of the risk reduction is even stronger than found for breast cancer with an average of 30–35 % risk decreases amongst the most physically active study participants. Again, as with the breast cancer studies, the risk reductions were greater in case–control studies (33 %) than in cohort studies (25 %). In 13 of 20 studies, dose–response response analyses have been conducted, with 13 of 20 studies observing such a trend. Overall, the evidence is consistent, biologically plausible, and linear in the dose–response. Future research will provide more insights into the effect within population subgroups as defined by different racial and ethnic groups and women with different risk profiles.

For ovarian cancer, the evidence for a protective effect of physical activity on ovarian cancer is much weaker than for other female reproductive cancers with risk reductions, on average, of magnitude less than 10 % decreases for the highest versus lowest categories of activity [3].

Physical activity and risk of genitourinary cancers

For prostate cancer, the most recent review on physical activity and prostate cancer risk summarized the data from 19 cohort studies and 24 case–control studies published up to 2011. On average, a 10 % reduction in risk of total prostate cancer was reported for physical activity [7]. With average risk reductions of less than 10 % comparing high versus low levels of physical activity for renal cell cancer, effects of similar magnitude were observed, with stronger inverse association among women than men, among normal weight than overweight or obese individuals, and among older than younger individuals [6]. For bladder and testicular cancer, in contrast, current studies support that physical activity is not or only weakly associated with cancer risk [6].

Physical activity and risk of lung cancer

To date, 29 publications have reported on the association between physical activity and lung cancer risk [4, 11]. The

majority of studies support the fact that total and recreational physical activity reduces lung cancer risk by 20–30 % for women and 20–50 % for men, and there is evidence of a dose–response effect [4]. Thus, evidence is increasing that physical activity plays an etiological role in lung cancer risk reduction.

Gaps and future research perspectives

Current recommendations call for at least 30–60 min of moderate to vigorous activity daily [16]. Although remarkable progress has been made in this field particularly during the past 15–20 years, major gaps in scientific evidence remain. Some of them are: (1) further research is needed to provide a stronger evidence base specifically for these recommendations. The exact type, dose, and timing of physical activity remain unclear but ongoing and planned research will elucidate these associations. (2) Possible biologic mechanisms whereby physical activity may influence carcinogenesis need further and targeted attention in future research. This research should also aim to discern the joint and independent roles of physical activity and other factors related to the energy balance equation. (3) The assessment tools for physical activity have been crude and nonstandardized making direct comparisons or meta-analyses of these data challenging. (4) Few studies have examined any objective measures of activity or health-related fitness. These more quantitative, device-based measures of activity could provide a less biased and potentially more accurate assessment of current activity. However, possible limitations of these more objective measures are that longer-term activity cannot be assessed and some of these methods assess motion related to physical activity rather than the behavior itself. (5) For most of cancer sites, there has still been insufficient research done to determine the association between physical activity and cancer risk. (6) Limited research effort has yet been made to performing quantitative risk assessments in different populations by estimating the numbers of cancers nationwide or worldwide that may be attributable to physical inactivity. Assessments like this are urgently needed for health policy and health promotion planning in cancer prevention.

Conclusions

Overall, strong, consistent, and coherent evidence exists for an association between increased levels of physical activity and decreased risks of colon, breast, and endometrial cancers and somewhat less convincing evidence for an inverse association with lung and prostate cancers. For gastric, ovarian, and renal cancers, the evidence for a beneficial effect of activity on cancer incidence is weaker. For bladder and testicular cancers, the evidence is only suggestive of an association, and there is no association between activity and rectal cancer. Since too few studies have been conducted for the remaining cancer sites, there are too few studies to permit any comprehensive evaluations on the association between physical activity and cancer risk. Most research on physical activity and cancer prevention has emerged in the past 20 years, further studies are currently ongoing, thus it can be expected that the upcoming decades will bring further clarity on the nature of these associations. However, current evidence is available in such a quality that more evaluable research on how to increase physical activity in the general population needs to be realized.

Conflict of interest None.

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