

ORIGINAL ARTICLES

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Physical effort – an underused preventable method in colorectal cancer

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Abstract: Colorectal cancer prevalence is increasing worldwide. Modifiable risk factors are responsible for almost 50 % of cases and this could imply a huge potential of preventability. Among these factors the level of physical activity is of paramount importance. Physical activity has a positive impact on health status in general and it decreases the prevalence of various cancers including colorectal cancer. Physical activity decreases the prevalence of benign colorectal adenomas and it prolongs the disease free interval after surgery in colorectal cancer, thus increasing survival. The mechanisms involved are multiple: decreasing bowel transit time, regulating energy balance, decreasing peripheral insulin resistance, decreasing hyperinsulinism, antiinflammatory effects, increasing vitamin D production.

Keywords: colorectal cancer, physical activity, obesity, lifestyle modifications

Physical activity is a major and potentially modifiable component of life style, which may be able to highly influence the risk of main cancers. Hence, there are convincing evidence that an important benefit may be derived concerning risk reduction in endometrial cancer, colorectal cancer, breast cancer, prostate cancer, lung cancer and ovary cancer. It is estimated that in Europe in 2008 between 150000 and 300000 cases of cancer could have been prevented only by the way of maintaining a resonable level of physical effort in general population.[1]

A series of convincing observational data suggest that regular physical activity, be it occupational type or recreational type, protects against colorectal cancer (CRC)[1,2]. Around 60 studies

have been published till 2010 concerning the issue of physical activity and CRC.[2] A metaanalysis that included 21 studies stated a significant reduction of CRC risk by 27% in the group of subjects that performed vigorous physical activity as comparing with the group of sedentary subjects (RR 0.73, 95% CI 0.66-0.81).[3] The mechanism that may provide an explanation for the

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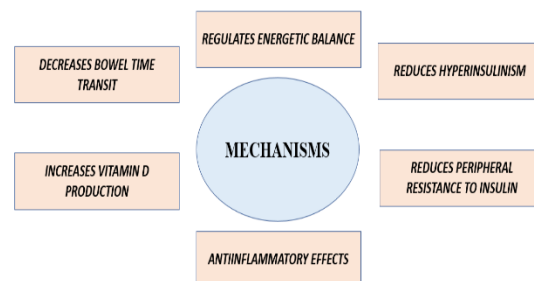
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relative protection of physical effort is currently unknown. There are no interventional type studies published yet to support the role of regular physical effort as preventive method in CRC.

In 2007 the results of a cohort study (Nurses' Health Study) has been published that enrolled 80,000 female subjects from 1986 with a 16 years follow-up. There have been diagnosed approximately 500 cases of CRC. A multivariate analysis that controlled the confounding factors represented by other risk factors for CRC concluded that there was a proportionate reversed relationship between physical effort and distal colonic cancer and, to a lesser extent, with proximal colonic cancer. Women situated in the highest percentile of recreational physical activity had a reduction of distal CRC risk by half as compared with women situated in the lowest percentile (RR=0.54, 95% CI 0.34-0.84). Risk reduction did not vary with body mass index (BMI), although former studies had suggested that physical activity had the greatest impact on CRC only in high BMI subjects. The level of physical effort to produce prophylactic benefits may be only minimal, as this study demonstrated. As such, even an hour of slight walking a week may reduce the risk of CRC by 31% (RR=0.69, 95% CI 0.45-1.03) as compared with women who do not report any kind of physical activity. This protective effect of slight walking reached a plateau at 2 hours a week (RR 0.64, 95% CI 0.41-1.00) as opposed to moderate and vigorous physical effort that was characterized by very clear dose-response relationship. The more alert slight walking rendered greater protective effect than slower slight walking (RR=0.43, 95% CI 0.17-1.05). Furthermore, 4 hours a week of moderate/vigorous physical effort may reduce the risk of CRC by 44% comparing with 1 hour a week (RR=0.56, 95% CI 0.33-0.94). Physical activity lessened

the risk of CRC regardless of the impact on BMI: this idea may imply that physical activity protects against CRC by a mechanism independent of that involved in resolution of obesity. The protective effect of physical effort validates at distance. The actual reduction of CRC risk is considerable only after several years. In conclusion, the authors of this study suggest that even minor physical effort may derive benefit on CRC risk reduction. Several mechanisms have been proposed. Thus, physical activity regulates energetic balance and intervenes in reduction of hyperinsulinism and peripheral resistance to insulin. Physical activity may intervene also through anti-inflammatory mechanisms. Moreover, the positive effects of physical effort may also be explained by reduction of obesity in spite of the data that demonstrated that physical activity may reduce the risk of CRC independent of the effect on obesity. Another proposed mechanism involves accelerating the peristalsis which reduces the contact time between intraluminal carcinogens and colonic mucosa. As a matter of fact, it is well known data that physical active individuals are more prone to sun exposure for longer periods of time which facilitates production of vitamin D that is associated with lessening the risk of CRC.[4]

Figure 1: Mechanisms involved in protective effect of physical effort on colorectal cancer risk



An epidemiologic study published in 2008 (NIH-AARP Diet and Health Study) shows interesting observations regarding the periods of an individual life when the

physical effort has the utmost impact on the risk of CRC. Thus, if the physical activity is performed in the age group 15-30 years the impact on CRC risk reduction will be minimal; on the other hand, if the physical activity is performed in the age group 30-39 years or throughout the whole life of an individual the reduction of CRC life-time risk will be maximal.[5]

Sedentarism is a globally important public health issue, especially in developed countries, in women, in old people and in low income individuals. Lack of physical activity is responsible of the increase in mortality rates especially from diabetes mellitus and heart diseases. To a comparable extent physical activity of moderate and vigorous intensity is associated with certain benefits regarding health status, including reduction of obesity risk, cardiovascular risk, stroke risk, risk of some types of cancers and decreasing in global mortality rate. Physical activity increases the probability to cease smoking, delays cognitive decline in old individuals, alleviates the adverse effects of stress, anxiety and depression. A study published in 2016 regarding the issue of physical activity status in the group of more than 50 years old individuals in USA the data are worrisome: 27% do not report any kind of physical activity outside working place in the last month; the prevalence of inactivity increases with age, reaching 35.3% in age group after 75 years; sedentarism is more prevalent in women than in men, in Afro-Americans than in Caucasians. Also, the prevalence of inactivity is decreasing with increasing in educational level and with decreasing in BMI.[6]

Lack of physical activity is the main cause of CRC being responsible of 14% of cases of CRC in USA; 12% of cases may be attributable to western diet, 12% to lack of daily administration of aspirin and 8% may be related to a family history of CRC.[6]

Sedentarism, especially that kind related to spending time in front of TV, is independently associated with increasing CRC risk. Hence, if one spends 9 hours in front of TV, as comparing with 3 hours or less, the risk of CRC will rise significantly by a RR=1.61 (95% CI=1.14-2.27).[5]

The relationship between physical activity, seden-

tarism and BMI is not to be changed even if one may exclude the contribution of age, race, family history of CRC, smoking and western diet.[6]

Several studies shows contradictory results concerning the issue of rectal localization of CRC. Cancer Prevention Study II indicates that moderate/vigorous physical activity in men and in women reduces the risk of rectal cancer by 30 %.[7] Many cohort studies did not find any kind of association between physical activity and rectal localization of CRC.[8,9]

A meta-analysis published in 2010, which included 20 studies on physical activity and colorectal benign adenoma, concluded that there was 16% reduction of the risk of these benign precursors of CRC if we compared active population with less active populations. Risk reduction was even more significant if we took into consideration polyps bigger then 1cm (31% risk reduction). It has been demonstrated in that way that physical effort might decrease the risk of CRC earlier in the stage of precursor lesions of oncogenic process.[10]

The role of physical activity as a protection factor in CRC is hardly known in general population. A study developed in USA that included 2000 subjects showed that only 15% of them are aware of this benefit of physical activity.[6] One similar study from Europe that included 21 countries indicated a 30% level of knowledge concerning this topic.[11] Several studies stated also that there was a close connection between the level of information concerning prophylactic benefits of physical effort in CRC and the increasing of the motivational status to produce life style changes that, in the end, will decrease the prevalence of CRC.[12,13,14]

Physical exercises represent a form of human activity that may benefit health more then it may inflict side effects. The most common side effects are musculoskeletal injuries. The least common side effects (sometimes more severe) are: cardiac arrhythmias, heart arrest and myocardial infarction. Generally, we may appreciate that the potential benefits of physical exercises highly surpass the potential risks. Moreover, it is considered that it is unnecessary to screen for coronary diseases prior to initiating physical activity if

the subject was asymptomatic and included in the low cardiovascular risk group.

One may consider mandatory that all healthy adult individuals to include in their life style moderate or vigorous physical exercises. The majority of authors agrees that the highest health benefits are provided by 150 minutes a week of moderate physical activity or by 75 minutes a week of vigorous physical activity. Nevertheless, adults that have a limited physical activity capabilities should remain active because it has been noticed that even if a modest amplitude of physical effort is exercised regularly health benefits will be significant.

Another epidemiologic studies suggest that physical activity may influence not only the risk of CRC but also it may prevent the recurrence of CRC after curative surgical treatment. All the data available resulted from observational type of studies; randomized and interventional studies are not published. Nevertheless, American Society of Oncology (ASCO) recently recommended that the surviveours of CRC should maintain an optimal weight, should perform daily physical exercises and should follow a healthy diet.[14] Futher on, there are some interesting results of a study published in 2006 that included 832 patients suffering from CRC stage III surgically treated and that followed a program of chemotherapy. It has been demonstrated that moderate physical activity performed for at least 300 minutes a week has increased the free disease interval with 45% and has improved by 29-36% the mortality rate of any cause.[16] The benefits have been dose dependent.

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In an observational study (unpublished data) that I have conducted in 2016, concerning the topic of CRC and its relationship with diabetes mellitus and other risk factors an important conclusion has been drawn.

A multivariate analisys in which the most acknowledged CRC risk factors have been included showed the statistical significance ($p < 0.05$) have been reached for smoking and physical activity only. This implies that by the way of increasing physical activity levels in general populations and by giving up smoking CRC „epidemics” could be fairly prevented.

Table 1: Multivariate analysis of risk factors in CRC

<i>Variable</i>	<i>Coefficient</i>	<i>Standard error</i>	<i>t Stat</i>	<i>p</i>
Age (years)	0.0014	0.0035	0.4087	0.68
BMI(Kg/m ²)	0.0031	0.0055	0.5650	0.57
Smoking	0.1273	0.0647	1.9658	0.05
Daytime nap (hours)	0.0150	0.0440	0.3404	0.73
Physical activity	-0.1334	0.0601	-2.2181	0.02

In conclusion, the preventable potential of CRC is high through the way of regular physical exercise and this may represent a very approachable solution to decrease the global burden of the disease. It is very important to stress that the target of decreasing the prevalence of CRC by physical exercise does not necessarily imply an impact on obesity, the benefits on CRC being independent from the benefits on BMI. A good level of motivation in general population through health politics is mandatory because the changes in life-style (level of physical activity, diet and smoking) are otherwise impossible to be reached.

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