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REVIEW ARTICLE

Selected risk factors of anal and rectal cancer

Wybrane czynniki ryzyka rozwoju raka odbytu i odbytnicy

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Abstract

Introduction and Objective. Malignant tumours of the anus and rectum represent a serious health issue in Poland and worldwide. In Poland in 2021, malignant rectal cancers accounted for 4.1% of cases in men and 2.4% in women, while cancers of the anus and anal canal made up 0.5% of all cancers. These tumours are classified within the group of colorectal cancers (C18-C21) according to ICD-10. Globally, they are the third most common cancer in men and the second most common in women. The aim of this article is to describe selected risk factors for the development of anal and rectal cancer based on available literature.

Review Methods. A literature review was conducted, focusing on articles related to anal and rectal cancer. The search was performed in two databases: Google Scholar and PubMed, using such key words as: cancer, anal cancer, rectal cancer, risk factors, HPV, microbiota, gut microbiota, constipation, fibre, obesity, physical activity, colorectal cancer. A total of 34 scientific articles from 2013–2023 were analyzed. No language restrictions were applied, and the selection of literature was made independently based on its relevance to the research topic.

Brief description of the state of knowledge. Factors that may increase the risk of developing anal or rectal cancers include age, a family history of cancer, smoking, HPV infection, obesity, low levels of physical activity, constipation, microbiota composition, and diet.

Summary. Despite their close anatomical proximity, anal and rectal cancers are two distinct conditions that differ in terms of etiopathogenesis, risk factors, prognosis, and treatment methods. Although cancer of the anal margin and anal canal is relatively rare, when combined with rectal cancer, they pose significant health risks. However, these cancers can be prevented by a properly informed healthy lifestyle

Key words

carcinoma, risk factors, rectal neoplasms, anal neoplasms

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Streszczenie

Wprowadzenie i cel pracy. Złośliwe nowotwory odbytu i odbytnicy stanowią poważny problem zdrowotny na świecie, w tym w Polsce. W 2021 roku nowotwory złośliwe odbytnicy stanowiły 4,1% przypadków u mężczyzn i 2,4% u kobiet, a rak odbytu i kanału odbytu 0,5% wszystkich nowotworów. Nowotwory te zaliczane są do grupy nowotworów jelita grubego (C18-C21) według ICD-10 są one trzecim najczęstszym nowotworem u mężczyzn i drugim u kobiet na świecie. Celem pracy było opisanie wybranych czynników ryzyka rozwoju raka odbytu i odbytnicy na podstawie dostępnej literatury.

Metody przeglądu. Przeprowadzono przegląd literatury. Poszukiwano artykułów dotyczących raka odbytu i odbytnicy. Wyszukiwanie przeprowadzono w dwóch bazach danych: Google Scholar i PubMed, używając słów kluczowych takich jak: „rak", „rak odbytu", „rak odbytnicy", „czynniki ryzyka", „HPV", „mikrobiota jelitowa", „zaparcia", „błonnik", „otyłość", „aktywność fizyczna", „rak jelita grubego". Przeanalizowano 34 artykuły naukowe z lat 2013–2023. Nie stosowano ograniczeń językowych, a wybór literatury został przeprowadzony samodzielnie na podstawie zgodności z tematem badania.

Opis stanu wiedzy. Czynnikami mogącymi zwiększać ryzyko rozwoju nowotworów odbytu lub odbytnicy jest starszy wiek, występowanie nowotworów w rodzinie, palenie tytoniu, infekcja wirusem HPV, otyłość, niski poziom aktywności fizycznej, zaparcia, nieprawidłowy skład mikrobioty oraz nieodpowiednia dieta.

Podsumowanie. Rak odbytu i odbytnicy, mimo że tworzą się w miejscach bliskich anatomicznie, są to dwa odrębne schorzenia różniące się pod względem etiopatogenezy, czynników ryzyka, rokowań oraz metod leczenia. Chociaż rak brzegu odbytu i kanału odbytu jest stosunkowo rzadkim nowotworem złośliwym, w połączeniu z rakiem odbytnicy stanowi poważne zagrożenie zdrowotne. Jednak nowotworom tym można zapobiegać poprzez świadome wybory dotyczące stylu życia.

Słowa kluczowe

czynniki ryzyka, rak, nowotwory odbytu, nowotwory odbytnicy

INTRODUCTION

Malignant tumours within the anus and rectum are a significant health issue of the modern world. In Poland, rectal and anal cancer represent a significant health issue, with a markedly higher incidence of rectal cancer compared to anal cancer, and rectal cancer constitutes a significant portion of malignant tumours [1,2]. Information regarding morbidity and mortality of anal and rectal cancer in Poland is presented in Table 1.

Due to the anatomical structure of the human body, both anal and rectal cancers have been classified by the International Classification of Diseases ICD-10 into the subgroup of colorectal tumours (C18-C21) [1]. Colorectal and anal cancer are the third most common cancer among men and the second most common among women (570,000 cases globally, about 9% of all cancer cases) [3]. These cancers are more prevalent in already developed countries [1].

Disease development is influenced by numerous risk factors, including age, family history of cancer and other genetic predispositions, tobacco smoking, pelvic, defecation disorders and chronic constipation, dietary patterns, low levels of physical activity, excess body weight, human papillomavirus infection (HPV), microbiota of the human body and changes in its composition.

The aim of the study was to describe selected risk factors of the development of anal and rectal cancer based on available literature, and investigates the risk factors due to their significant contribution to the development of anal and rectal cancer. The status of these cancers as global health concerns that can substantially elevate the risk of these conditions are also investigated. The risk factors are well-documented and widely discussed in the literature and are included in this comprehensive review of available publications.

Table 1. Morbidity and mortality of anal and rectal cancer in Poland in 2020 [2]

	Women		Men	
	Anal cancer	*Rectal cancer*	*Anal cancer*	*Rectal cancer*
Morbidity (% of all cancer cases)	0.3%	2.6%	0.1%	4.3%
Mortality (% of all cancer cases)	0.25%	3%	0.2%	4.1%
Absolute number, morbidity	192	1,931	83	3,126
Absolute number, mortality	115	1,345	129	2,213

MATERIALS AND METHODS

A literature review was conducted to explore the topic of risk factors associated with anal and rectal cancer. The search was performed in December 2023 using two scientific databases: Google Scholar and PubMed. The following key words were used during the search: cancer, anal cancer, rectal cancer, risk factor, HPV, microbiota, colonic microbiota, constipation, fibre, obesity, physical activity, colon cancer. A total of 78 articles were retrieved from Google Scholar and 150 from PubMed. The abstracts of the articles were reviewed, and those not relevant to the research topic were excluded. Ultimately, 49 scientific articles were selected for the review. The articles, published between 2013–2023, were analyzed to identify the most frequently occurring risk factors associated with anal and rectal cancer. No language restrictions were applied during the search process, but most of the selected studies were in either English or Polish. The selection process of articles was conducted individually, beginning with a review of key words and abstracts. Full-text analyses were performed for articles deemed relevant, leading to the final selection. The analysis of entire articles was conducted based on subjective relevance to the topic, i.e. the inclusion of data regarding specific risk factors for the development of anal and rectal cancer, rather than merely listing or briefly describing them. Original research articles were prioritized to provide robust evidence; however, literature reviews were also included to ensure a comprehensive understanding and to adequately describe specific risk factors. During the analysis of the available studies, the most frequently identified risk factors reported in the collected articles were selected and described. These factors formed the basis of the literature review and were thoroughly examined to effectively address the research problem.

Anal cancer – knowledge review. Anal cancer (ICD-10 code: C21, ICD-11 code: 2C00) is a rather rarely occurring malignancy, as it constitutes approximately 1–2% of all gastrointestinal cancers. It is more frequently diagnosed in women, among whom its risk increases with age, and is rare in women under the age of 40 [1,4,5]. The number of anal cancer cases has increased in recent decades, which may be an outcome of the liberalization of many sexual behaviours and the spread of high-risk variants of the HPV. In Poland in 2020, 279 individuals were diagnosed with anal cancer, with the highest number of cases observed in the age group of 65–69 years [1,6,7]. The most common form of anal cancer is squamous cell carcinoma (ASCC), which represents more than 80% of all anal cancer cases. For a correct diagnosis, a histopathological evaluation is necessary, which will eliminate the suspicion of other pathologies, such as adenocarcinoma, lymphoma, melanoma, or neuroendocrine tumours. Risk factors and treatment procedures are different for these pathologies and ASCC [8].

An important pre-cancerous lesion that may develop into ASCC is anal intraepithelial neoplasia (AIN), which is often neglected by gastroenterologists. It is speculated that AIN treatment in high-risk groups may prevent the development of ASCC, but there is no effective treatment method that could confirm this hypothesis. Moreover, most procedures are associated with many side-effects, which makes it difficult to develop optimal treatment procedures [8,9,10].

Patients with Human Immunodeficiency Virus (HIV) and/or Human Papillomovirus (HPV) are considered to be among those with higher risk, as well as patients with immune disorders, especially transplant recipients undergoing immunosuppressive therapy, as well as sexually-active men engaging in passive anal intercourse [6,7,11]. The risk of anal cancer increases with the duration of HIV infection, thus the increased survival rate among these patients may have contributed to the increase in anal cancer cases overall. Chronic proctological diseases, such as anal fistula or recurrent perianal abscess, are another important risk factor. For women, additional risk factors are tobacco smoking, intraepithelial neoplasia confirmed by cytological examination, and previous use of oral contraceptives [7,8,11].

Radical chemoradiotherapy (CRTH) is the first-line method used in the treatment of anal cancer. The chemotherapy

(CTH) includes two cycles of fluorouracil and mitomycin. However, it has been shown that the use of neoadjuvant or adjuvant CTH does not improve the results of therapy. Surgical treatment, especially abdominal-sacral amputation, is performed only in the event of CRTH failure, or in patients with contraindications for radiotherapy [1,4].

Rectal cancer – knowledge review. Rectal cancer (ICD-10 code: C20, ICD-11 code: 2B92) is one of the most common oncological diseases in Poland, and the incidence of this particular cancer is constantly increasing [5,12,13]. In Poland in 2020, 5,105 individuals were diagnosed with rectal cancer, with the highest number of cases observed in the age group 65–69 years [6]. Malignant tumours of the rectum (CD20) constitute about 35% of all malignant tumours of colorectal cancer (CD18-CD20). Histopathologically, the most common form of rectal cancer is adenocarcinoma (90% of cases), while squamous cell carcinoma is the least frequently diagnosed (0.3% of cases), and can be only diagnosed if the tumour mass is not connected to the anal canal [3,11,14].

Rectal cancer is challenging not only due to its anatomical location, but also due to the risk of recurrence, which is why it requires a different treatment approach than colon cancer [15]. The classification of rectal tumours has been developed based on anatomical considerations, and are recognized as changes occurring below the rectosigmoid junction. However, there are uncertainties regarding the definition of the rectum and, more specifically, how to define this position anatomically in a clinical context. Determining the correct location of the cancer may be difficult due to many factors, such as body size, gender, and imaging methods [15,16].

The group of people particularly susceptible to rectal cancer includes men, individuals over 60 years of age, and those genetically predisposed to tumours – with a family history of rectal cancer, polyposis syndrome, hereditary nonpolyposis adenomatosis and chronic inflammatory bowel disease [3,17].

Risk factors for rectal cancer are divided into three subgroups [1,3]:

1) Epidemiological risk factors – environmental (white people are more likely to develop rectal cancer), geographical factors (occuring more frequently in northern European countries) and lifestyle factors (increased risk through excessive body weight with low physical activity) tobacco smoking (increases the risk by 30–40%, depending on the patient's gender).
2) Diet-related risk factors – high-energy diet, low dietary fibre intake, inadequate intake of vegetables and fruits, and excessive consumption of red meat, animal fats and alcohol.
3) Intestinal risk factors – history of colorectal cancer, hereditary non-polyposis, adenomatosis, chronic inflammatory bowel diseases, history of adenomatous polyps.

The choice of appropriate treatment method depends on the clinical stage of the tumour, its location, and clinical assessment of its resectability. Patients undergo surgical treatment and subsequently evaluated to determine whether further treatment is necessary. If the patient is in a high-risk group for recurrence or is unable to undergo surgery, radiochemotherapy is administered. Contrariwise, when the tumour is immediately classified as 'non-resectable', the patient should receive radiation combined with chemotherapy before undergoing surgical intervention. Patients with contraindications to chemotherapy should only receive radiation therapy. Attempts to resection the tumour should occur regardless of its response to radiation, and the extent of resection should include tissues affected by cancer before radiation, as shown in the MRI (Magnetic Resonance Imaging) results [16,17].

Age as a risk factor. The risk of developing anal and rectal cancers increases with age. According to the 2021 report from the National Cancer Registry, a significant rise in incidence occurs in individuals over the age of 40, while the majority of cases are diagnosed in those over the age of 60 [6]. Epidemiological data suggests that individuals over the age of 65 have nearly three times the risk of developing cancers from the colorectal group, compared to those aged 50–64, and about thirty times the risk compared to those aged 25–49 [18].

The correlation between age and the incidence of these cancers is evident in developed countries, where an increase in the number of elderly people can be observed due to longer life expectancy. Additionally, older individuals are more susceptible to the development of these cancers due to prolonged exposure to other risk factors, such as viral infections or chronic inflammatory bowel conditions [19,20].

Family history of cancer. The occurrence of anal and rectal cancers in close family members significantly increases the risk of developing these cancers. This is due to hereditary genetic predispositions and lifestyle factors. Important information for assessing future colorectal cancer risk includes the age at which first-degree relatives were diagnosed, the number of family members diagnosed with these cancers, presence of other cancers in the family, and personal cancer history. Available epidemiological studies indicate that individuals with one affected first-degree relative, on average, have twice the risk of colorectal cancer compared to those with no family history [20,21].

Some clinical cases of these cancers result from hereditary conditions: familial adenomatous polyposis (FAP) is an autosomal dominant inherited syndrome of polyposis, characterized by the early appearance of numerous adenomatous polyps in the colon and rectum. In the case of anal cancer, genetic predispositions are not as significant, and greater emphasis is placed on infection with the HIV, HPV, and a history of cervical, vaginal, or vulval cancers [22].

Tobacco smoking. Tobacco smoking is a well-known risk factor for the development of many types of cancers, including those within the colorectal cancer subfamily. Available studies indicate that smokers have a 2–3 times higher risk of developing these cancers compared to non-smokers, and the risk increases with the dose and duration of exposure. Additionally, it is estimated that smoking contributes to approximately 12% of deaths from colorectal cancer [20].

Smoking tobacco is also associated with the occurrence of anal cancer, and increases the risk of developing the disease, as well as the probability of recurrence. The cancer risk originates from the composition of tobacco smoke, which contains a mixture of thousands of chemical substances, including those recognized as carcinogenic, such as heavy metals, aldehydes, and N-nitrosamines. These substances can damage DNA (Deoxyribonucleic Acid), leading to mutations

in the epithelial cells of the colon and the development of polyposis which, in turn, can progress into invasive adenocarcinoma [23]. Patients should be informed about the harmful effects of tobacco smoking to ensure better treatment outcomes [23].

HPV Infection. HPV is spreading worldwide at an alarming rate. To date, over 220 types of HPV have been discovered, with the majority capable of causing major health consequences, among them variants that lead to the development of various cancers [24]. The HPV variants have been divided into [25]:
- low-risk oncogenic types (6, 11, 40, 42, 43, 44);
- high-risk oncogenic types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59);
- non-cancerous types (1, 2, 3, 4, 7, 10).

HPV spreads through sexual intercourse, manual transmission of the virus from hands to genital organs, as well as through oral and anal routes. Vertical transmission is rare, but there is a correlation between the HPV DNA-positive mother and the possibility of transference to newborns [26].

The HPV virus, after penetration into cells, can remain latent or inactive even for years, which may be immunologically related. Most infections are asymptomatic and/or disappear of their own accord. The period from HPV infection to the development of cancer takes at least 5–10 years [26].

Development of genital warts (*condylomata acuminata*) is attributed to infection with low-risk variants of the human papillomavirus, such as HPV 6, 11, 42, 43, and 44. They are most likely to be found on the external genitalia, perineum, perianal area, and oral cavity [24]. Genital warts are recognized as another precursor lesions of cancer [27].

Infection with high-risk variants of the HPV initiates the development of anal cancer. Data suggests that over 90% of 12 million cases of anal cancer assessed in 2008 worldwide, were complications of local infection with HPV. Anal cancer is mostly related to HPV-16 and HPV-18 [24,28]. Despite increased overall survival in patients with anal cancer and HPV positivity, statistics show that over 33% of patients die within five years of diagnosis, with a five-year case-to-death ratio of 86% for women and 89% for men [28]. Contracting cancerous diseases associated with past chronic infection by high-risk types of HPV, such as cervical cancer, also increases the risk of developing anal cancer [1,4,7,11].

To reduce the risks of anal cancer and anal condyloma, the best strategy is HPV vaccination. Although current vaccines are prophylactic, it is worth underlining that studies have shown that among the high-risk population vaccinated against the HPV virus, a decrease in the incidence of AIN and anal cancers has been observed [7,8,11,25]. HPV vaccinations could help eliminate cases of anal cancer linked to the HPV virus, which constitute the majority of cases [9, 10, 24].

Obesity and low physical activity. Physical activity, or the lack of, may be a risk factor for the development of cancer and can also negatively influence patient prognosis. Available epidemiological data suggests that moderate physical activity reduces the chances of developing colorectal tumours [29]. Due to the anatomical structure, this also applies to oncological conditions of the rectum and anus [1]. It is possible that the relationship between the level of physical activity and the risk of cancer is a correlation rather than causation. Nevertheless, individuals leading a healthy and active lifestyle are less likely to suffer from obesity [29, 30] – a chronic disease characterized by the accumulation of fat tissue in the body [30]. Studies have shown that excess body weight predisposes to the development of cancer, including colorectal cancer, and consequently, cancer of the rectum and anus [1,30]. Obesity contributes to an increased risk of cancer through a number of molecular mechanisms, which are a direct result of the accumulation of fat tissue, as well as the presence of such disorders as hyperlipidaemia or hyperinsulinaemia, associated with the individual's lifestyle [30].

Adipose tissue is metabolically active secreting its hormones [30,31]:
- subcutaneous adipose tissue – secretion of leptin;
- visceral adipose tissue – synthesis of adiponectin, IL-6, tumour necrosis factor (TNF-α).

For individuals with normal body weight, leptin is a hormone responsible for regulating the feeling of fullness. Experimental studies have shown that in obese individuals, leptin concentration increases and acts in a mitogenic manner on the epithelial cells of the gastrointestinal tract. Excessive levels of leptin also promote the synthesis of free radicals [30,31].

Adiponectin is an anti-inflammatory compound secreted by adipose tissue [30]. In the body of an obese individual, it is present in reduced concentrations, decreasing the activity of the insulin/IGF-1 axis (insulin-like growth factor) and the mTOR pathway (mammalian target of rapamycin). Scientific studies suggest that this is a fundamental molecular pathway in the initiation and progression of tumours. Adipose tissue also synthesizes pro-inflammatory substances, including resistin, visfatin, and the previously-mentioned leptin. These pro-inflammatory cytokines increase the levels of tumour necrosis factor and IL-6, which are crucial in tumour progression [30,31].

Constipation (defecation disorders). Constipation is diagnosed when less than three bowel movements occur per week. Commonly, it refers to difficulties in defecation, passing stool involving excessive straining, passing hard stools, or experiencing a sensation of incomplete evacuation. Constipation has been divided based on etiological factors [32]:
- primary constipation – also known as functional, caused by disrupted functioning of the colon, pelvic floor and anal sphincter;
- secondary constipation – result from conditions such as colorectal cancer, rectal cancer, metabolic and endocrine disorders (e.g. diabetes), neurological diseases (including stroke), psychological disorders, eating disorders, myopathies (including muscular dystrophies).

The prolonged transit time of faecal matter contributes to the development of cancer in the organs of the excretory system, due to the long time period of direct contact of carcinogenic substances in the stool with the mucous membrane of the said system [33].

The gut microbiota and its metabolism play a crucial role in the physiology and pathology of constipation. This is a highly important risk factor for the development of colorectal cancer, and consequently, rectal and anal cancer, due to the fact that constipation can accelerate the carcinogenic process

through anatomical abnormalities, genetic mutations, or gene deletions [1,34].

A randomized study by Long Wu et al. suggests that constipation is a modifiable risk factor for colorectal cancer, and due to anatomical structure of the human body, rectal and anal cancer. Chronic constipation may lead to prolonged exposure to potential carcinogens in the colon which can promote tumour growth [35].

The chosen treatment approach for constipation is another significant factor. Patients dealing with slowed intestinal motility may use substances to expedite the defecation process. Additionally, chronic and severe constipation increases the risk of developing cancerous lesions [36]. Currently, there is a lack of sufficient scientific evidence to support the claim that constipation is a direct cause of colorectal, rectal or anal cancer [33].

Body microbiota. The body's microbiota is the collection of all eukaryotes (bacteria, viruses, fungi, and others) inhabiting various anatomical systems of the human body (digestive system, oral cavity, reproductive system, etc.). Gut microbiota refers to the eukaryotes that colonize the lower portion of the digestive system [37]. The mentioned microorganisms are crucial for many important functions of the body, such as maintaining proper functioning of the immune system, synthesizing nutrients and vitamins, or digestion of complex polysaccharides. The commensal microbiota residing in the human gut also encode various enzymes that can chemically alter ingested drugs. These modifications may result in activation, inactivation, toxification, changes in stability, reduced bioavailability, and increased excretion of the drugs. Any anomalies in the composition of microbiota will promote the development of various pathologies, including neurodegenerative, cardiovascular, metabolic, and gastrointestinal diseases. However, the influence of gut microbiota on the pathomechanism of diseases has yet to be fully clarified. [37–39].

Microbiota is directly connected to cancer as it influences the carcinogenesis process in the human body. Oncoviruses present in the microbiota induce the formation of tumours by integrating oncogenes into the human host genome [37]. The way in which the human microbiota contributes to the carcinogenesis process has been divided into three broad categories [37,40]:
- disruption of the balance between proliferation and death of the host's cells;
- regulation of the immune system and its reactions;
- influence on the metabolism of host-related factors, consumed comestible products and pharmaceuticals.

The composition of the microbiota also influences the risk of initiating carcinogenesis, as the presence of strains such as *B. fragilis*, *E. coli*, and *F. nucleatum* may induce the expression of pro-oncogenes and oncogenes, as well as the repair of abnormal and mismatched chromosomes, resulting in heterogeneous cell growth, adenomatous polyps, and ultimately cancer [34].

The International Agency for Research on Cancer (IARC) has identified 10 microorganisms as carcinogenic, such as eukaryotes, which are colonizing a significant percentage of the global population. However, the development of neoplastic changes will occur only in some individuals due to the host genotype [40].

The gut microbiota contributes to the development of clinical, cancerous disorders of the anus and rectum. Diet, as a customary way of eating, interacts with the gut microbiota and mutually modulates the risk of developing colorectal cancer [41,42].

Dietary factors. According to a report issued by the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR), low dietary fibre intake may increase susceptibility to cancer by the reduction of apoptosis and increase in proliferation [43]. Dietary fibre is a non-digestible soluble and insoluble carbohydrates (with three or more monomeric units), and lignin that is intrinsic and intact in plants. Isolated or synthetic non-digestible carbohydrates (with three or more monomeric units) are determined to have physiological effects that are beneficial to human health [44]. The anti-cancerous influence of fiber involves [45,46]:
- prevention of epithelial atrophy;
- improvement of the passage of food contents through the intestines, increasing stool volume and mass, which affects the shortening of the time potential carcinogens are in contact with the mucous membrane of the large intestine;
- acceleration of fermentation within the large intestine, resulting in the production of short chain fatty acids (SCFA), which promote apoptosis and inhibit proliferation;
- reduction of the pH of food contents;
- stimulation of the development of beneficial intestinal microbiota;
- production of butyrate by fermentation of soluble fibre, delays the proliferation of malignant cells, reduces inflammatory processes and promotes DNA regeneration;
- soluble fibre modifies the faecal microorganisms, and increases the number of saprotrophic bacteria which exert a beneficial effect on the intestinal microbiome by SCFAs while causing a decrease in pH and inhibiting pH-sensitive, and potentially pathogenic bacteria that could lead to potentially carcinogenic compounds.

The World Health Organization (WHO) recommends consumption of 2–40g of dietary fibre per day [45]. Individuals whose dietary pattern is chronically deficient in adequate fibre intake are at increased risk of developing anal and rectal cancer. A review study conducted by Jun Hu et al. indicates that dietary fibre shows a probable protective effect against colorectal and anal cancer [47].

A high-energy diet rich in animal fats and red meat, and low intake of vegetables and fruits, are a known risk factor for rectal cancer. A proper diet may exhibit protective effects against this cancer [1]. The low intake of vegetables and fruits is associated with deficiency of folate, carotenoids and vitamins, which causes the decrease in apoptosis and increase in proliferation, genome instability and increased inflammation. Excessive consumption of red meat contributes to the formation of N-nitroso compounds and exposure to nitrites. These factors result in decreased apoptosis, increased proliferation, increased inflammation and genomic instability. A high-calorie and fat-rich diet will contribute to the development of obesity, which is a well-known risk factor for the development of cancer, including anal and rectal cancer [43].

Alcohol is a known diet-dependent carcinogenic factor. The results of the European Prospective Investigation into Cancer and Nutrition (EPIC) study suggests that alcohol consumption

is also associated with an increased risk of developing rectal cancer [48]. Alcohol (ethanol alcohol) does not exhibit direct carcinogenic effects on the intestinal mucosa; however, acetaldehyde, which is produced during the metabolism of alcohol, has mutagenic and carcinogenic properties, playing a key role in the development of colorectal cancer. Additionally, it can reduce the absorption of B vitamins (B1, B2, B12, folic acid) and increase susceptibility to oxidative stress [48].

Calcium exhibits a protective effect against colorectal cancer. The anti-cancer mechanisms of calcium are diverse and include its influence on cell growth and the process of apoptosis. Calcium can inhibit carcinogenesis in the colon through its direct impact on cell proliferation, differentiation, and apoptosis, binding free fatty acids and bile acids, and modulating signalling pathways associated with colorectal cancer [49].

CONCLUSIONS

Anal and rectal cancers are diseases influenced by a variety of risk factors. In anal cancer, HPV infection in particular plays a crucial role. Genetic predispositions are also significant contributors, alongside lifestyle factors such as smoking, obesity, and an unhealthy, low-fibre diet. Additionally, bowel movement disorders, including chronic constipation or diarrhea, may further elevate the risk of these cancers. The likelihood of developing these conditions also increases with age, especially after the age of 50.

A summary of all the risk factors for the development of anal and rectal cancer described in the article are shown in Table 2.

Although cancer of the anal margin and canal is a relatively rare malignant tumour, together with rectal cancer, they pose serious threats to health that can be prevented through conscious lifestyle choices. Prevention strategies for these diseases should emphasize health education, the adoption of a healthy lifestyle, and widespread HPV vaccination.

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Table 2. Summary of key risk factors of anal and rectal cancer [1, 8, 18, 20-24, 28-30, 34, 35, 37, 41-43, 47]

Risk factor	Rectal cancer	Anal cancer
Age	Risk of developing anal and rectal cancers increases with age.	Epidemiological data suggests that individuals over the age of 65 have nearly three times the risk of developing cancers from the colorectal group, compared to those aged 50–64, and about 30 times the risk compared to those aged 25–49.
Family history of cancer	The age of cancer onset in first-degree relatives, the number of colorectal and other cancer cases in the family, as well as personal cancer history, are important factors in assessing the risk of developing colorectal cancer.	In the case of anal cancer, genetic predispositions are less significant.
Tobacco smoking	Smokers have a 2-3 times higher risk of developing these cancers compared to non-smokers. It is estimated that smoking contributes to approximately 12% of deaths from colorectal cancer.	Smoking tobacco is associated with the occurrence of anal cancer. It increases the risk of developing the disease as well as the probability of recurrence.
HPV Infection	In the case of rectal cancer, HPV infections are less significant.	Infection with high-risk variants of the HPV initiates the development of anal cancer. Anal cancer is mostly related to HPV-16 and HPV-18.
Obesity and low physical activity	Available epidemiological data suggests that moderate physical activity reduces the chances of developing colorectal tumours. The relationship between level of physical activity and the risk of cancer may be only a correlation, rather than causation. Excess body weight predisposes to the development of colorectal cancer.	Due to the anatomical structure, moderate physical activity may reduce the chances of developing cancer of the anus. Excess body weight may predispose to the development of anal cancer.
Constipation (defecation disorders)	Gut microbiota and its metabolism are a highly important risk factor for the development of colorectal cancer and, consequently, rectal (and anal cancer), since constipation can accelerate the carcinogenic process through anatomical abnormalities, genetic mutations or gene deletions.	Chronic constipation may lead to prolonged exposure to potential carcinogens in the colon, which can promote tumour growth.
Body microbiota	Microbiota is directly connected to cancer as it influences the carcinogenesis process in the human body. Oncoviruses present in the microbiota induce the formation of tumours by integrating oncogenes into the human host genome.	Gut microbiota contributes to the development of clinical, cancerous disorders of the anus and rectum.
Dietary factors	A high-energy diet, rich in animal fats and red meat, and a low intake of vegetables and fruits, are a known rectal cancer risk factor. A high-calorie and fat-rich diet will contribute to the development of obesity, which is a well-known risk factor for the development of cancer, including rectal (and anal) cancer.	Individuals whose dietary pattern is chronically deficient in adequate fiber intake are at increased risk of developing anal and rectal cancer.

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