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Review Article

A Descriptive Cross-Reference Study On The Impact Of Microbes On The Onset And Progression Of Colorectal Cancer In Humans.

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Abstract

Context: The purpose of this research is to identify the kinds of microbes that affect the development and progression of colorectal cancer (CRC) in people.
Techniques: When the malignancy was surgically removed from individuals with colorectal cancer, three swabs were obtained for microbiological analysis: one from the tumor's surface, one from the middle of the tumor tissue, and one from the surface of the healthy intestinal mucosa. Findings: Escherichia coli accounted for 70.5% of the microorganisms found in the colon's healthy mucosa, followed by Enterococcus species (47.7%) and Klebsiella/Enterobacter (20.5%). E. coli was the most common microorganism, accounting for 72.7% of the swabs taken from the tumor tissue's surface, followed by Enterococcus species. E. Coli accounted for 77.3% of the tumor tissue, followed by Enterococcus species (40.7%), Klebsiella (27%), and Pseudomonas aeruginosa (18.2%). In conclusion, some bacterial species can inhibit the growth of tumor tissue, while others can affect the onset and progression of cancer. Human stool samples examined microbiologically can stop CRC from developing.

Keywords : *Escherichia coli, Enterococcus species, Klebsiella, Enterobacter, Streptococcus gordonii, human colorectal cancer, Aeruginosa pseudomonas.*

INTRODUCTION

With an anticipated incidence rate of 935,173 deaths (IRD), or 9.0 per 100,000 persons, in 2020, colorectal cancer (CRC) is the second most prevalent cause of cancer mortality globally, behind lung cancer, according to the International Agency for Research on Cancer (IARC) [1]. Young adults (those under 55) had a yearly increase in CRC incidence rates of 1% to 2%. CRC was the fourth most common cause of cancer-related deaths in the 1990s for both men and women under 50, but it is currently the top cause for men and the second for women [2]. Over 1.9 million colorectal cancer (CRC) cases were reported globally in 2020, and nearly 0.9 million patients lost their lives to the disease.Alcohol use, smoking, obesity, sedentary lifestyle, poor diet (high consumption of red and processed meat and fat), psychological stress, gender, genetic predisposition, family history of colorectal cancer, abdominopelvic radiation, personal history of other diseases, and intestinal microbiota are some of the risk factors that may contribute to the development of colorectal cancer [3]. The collection of all microorganisms that live in the human body and play a significant part in and have an impact on other physiological systems is known as the homeostatic microbiome, or microbiota. Diabetes and decreased insulin secretion are two conditions that have been shown to emerge when the homeostatic microbiota is disturbed [4,5]. CRC development is directly linked to a decrease in gut microbiome diversity, where one species suppresses another [6]. According to specific analyses, the risk of colorectal cancer (CRC) was negatively correlated with gut Lachnospiraceae species, while the risk of CRC was positively correlated with Porphyromonadaceae species, the genus Lachnospiraceae UCG010, the genus Lachnospiraceae, and the genus Selimonas. These results imply that the gut microbiota and the risk of colorectal cancer are causally related [7]. By examining the microbial makeup of the mucosa on the surface of a healthy colon, the surface of tumor tissue, and in the center of tumor tissue, the study sought to identify the kinds of microorganisms in CRC patients that might have an impact on the growth and progression of tumor tissue.

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Material and Methods

At the Clinic for Digestive Surgery, UKCS, all patients with colorectal cancer had open procedure, medial laparotomy. For cancers of the right colon and hepatic flexure, a manual ileocolic termino-lateral anastomosis was created in two layers using right hemicolectomy and extended right hemicolectomy with digestive tract reconstruction, depending on the tumor's anatomical location and in compliance with oncological principles. Left hemicolectomy, upper rectal resection, low rectal resection with stapled colorectal termino-terminal anastomosis without protection, and colo-anal termino-terminal anastomosis with protective ileostomy were performed for carcinomas of the left colon and rectum, depending on the anatomical tumor location and disease stage.At most, one to two months elapsed between the time of the CRC diagnosis and the procedure. According to pathohistological results, CRC phases ranged from 1 to 3. The Ethics Committee on Human Research at UKCS authorized protocol number 420/25, which required informed consent from all research participants, and the committee found it to be acceptable. 44 patients between the ages of 26 and 87 (61.11 ± 08) were operated on starting in 2021; 25 of them were men and 19 were women.Every patient was white. Three swabs were obtained for the study: one from the colon's healthy mucosa, one from the tumor's surface, and one from the tumor's core following removal. To quantify the number of colonies cultivated, solid media were injected semi-quantitatively using the four-quadrant method. For 48 hours, the infected medium were incubated at 33C ± 2 C in both aerobic and anaerobic settings. There was a subculture of enrichment media. Standard microbiological techniques and the VITEK2 Compact system (bioMérieux, France) were used for identification. The VITEK-Compact system and the Kirby-Bauer method (Mueller-Hinton II agar plates [Torlak, Belgrade, Serbia]) were used to assess the sensitivity of isolated isolates. EUCAST criteria were used to interpret the results [8,9]. The specialized nature of the study and the data' percentage-based presentation precluded the use of statistical tests.

RESULTS

44 patients, aged 26–87 years (61.11 ± 08), were operated on starting in 2021; 25 of them were men and 19 were women. The results of this study's microbiological investigation of 132 samples from 44 individuals with colonrectal cancer (CRC) are shown in Table 1. Fifteen microbes in all were found. E. Coli accounted for 70.5% of the colon's healthy mucosa, with Enterococcus species (47.7%) and Klebsiella/Enterobacter (20.5%) following closely behind. Smaller percentages of the following bacteria were detected: Morganella morganii 4.5%, Citrobacter spp., Streptococcus gordonii 11.4%, Pseudomonas aeruginosa 13.6%, Proteus mirabilis 6.8%, and Kocuria kristinae 2.3% (Table 1). Swabs taken from the surface of tumor tissue were subjected to microbiological investigation, which revealed that E. The percentages of other microorganisms ranged from 2.3% to 11.4%. Shigella, Salmonella, and Candida were not found (Table 1, Graph 1). E. coli predominated in the core of tumor tissue, appearing in 77.3% of samples, followed by Enterococcus species (40.7%), Klebsiella (27%), and P. aeruginosa (18.2%). Smaller concentrations of other microorganisms ranged from 2.3% to 9.1% (Table 1). It's noteworthy to observe that, when comparing the three different swab types, the highest proportion of E. coli is found in the center of tumor tissue (77.3%), on the tumor surface (72.7%), and in healthy mucosa (70.5%). With 47.7%, 40.9%, and 47.7%, respectively, Enterococcus spp. came in second, followed by P. aeruginosa (13.6%), 20.5%, and 18.2%) and Klebsiella/Enterobacter (20.5%, 25%, and 27.3%).

DISCUSSION

Four types of bacteria—E. coli, Enterococcus spp., Klebsiella/Enterobacter, and Streptococcus gordonii—are identified by the analysis of the study's results. These bacteria are found in 70–10% of all three types of samples taken from the core of the tumor tissue, the surface of the tumor, and the surface of the healthy intestinal mucosa.

Escherichia coli

E. coli was the most common of these bacteria, showing up in almost 70% of patients on the surface of the tumor, the healthy intestinal mucosa, and inside the tumor tissue. E. Coli is a part of the saprophytic intestinal flora in both humans and animals, and it is also one of the most often found bacteria in medical oncology institutions. Digestion and the creation of some compounds, such vitamin K, depend on its presence. However, an overabundance of E. coli can cause a number of illnesses affecting the lungs, urogenital system, and gastrointestinal tract, as well as in extreme situations, sepsis and meningitis, if the microbiome's homeostasis is upset. Enteropathogenic, enterotoxic, and enteroinvasive strains of E. coli are the most common causes of these illnesses. Although they are usually rare, community-acquired E. coli infections can be found in cancer patients who do not exhibit any symptoms. Due to immunological inadequacies, cancer has been demonstrated to be a substantial risk factor for acquiring E. coli infections.

When E. coli causes diarrhea in cancer patients, neutropenic enterocolitis, a severe kind of diarrhea, should be taken into consideration. Patients who experience persistent diarrhea should be evaluated for colorectal cancer (CRC) because this condition may be a sign of intestinal cancer [10]. According

to recent reviews of the literature, intestinal microbiota dysbiosis is a risk factor for the development of colorectal cancer (CRC), and polyketide synthase-positive Escherichia coli (pks+ E. coli) is a major player in the pathophysiology of CRC [11]. Colibactin, a genotoxic protein produced by Pks+ bacteria, damages the DNA of host colonocytes. Furthermore, the intestinal epithelial barrier is disrupted, mucosal inflammation is induced, host immunological responses are modulated, genetic instability is promoted, and impact cell cycle dynamics, establishing an environment that is favorable for the development and spread of tumors [12]. In 1998, PCR analysis of biopsy samples revealed that E. coli was present in 60% of adenomas and 77% of CRC cases, while it was only present in 12% of nearby normal biopsies and 3% of normal control samples [13]. By directly interacting with host cancer cells, producing carcinogenic microbial metabolites, and secreting oncogenic virulence factors, the intestinal microbiota—which includes genera like Clostridium, Bacteroides, Enterococcus, and Escherichia—can promote colorectal carcinogenesis, according to recent research [13–16].

Enterococcus species

Enterococcus bacteria were found in the core of tumor tissue, on the surface of the tumor, and on the surface of the healthy intestinal mucosa in almost 40% of the patients examined (Table 1). Both people and animals have enterococci as a typical component of their intestinal flora. Among the most well-known enterococci are Enterococcus faecalis and Enterococcus faecium, which can lead to sepsis, urethritis, and endocarditis. Co-incubation with conditioned medium of Enterococcus faecalis boosted the proliferation of cultured colorectal cancer cells, demonstrating the link between Enterococcus and colorectal cancer. One important metabolite that E. faecalis produces is biliverdin (BV).

Enterobacter/Klebsiella

This bacterium was found in all three samples (on the surface of the tumor, on the surface of the healthy intestinal mucosa, and within the tumor tissue) in about 20% of the patients in this investigation. A common component of both human and animal flora, Klebsiella can be found in water, soil, plants, and insects. It can also colonize the mouth, nose, and intestines. Klebsiella species are opportunistic bacteria that can cause soft tissue infections, meningitis, diarrhea, pneumonia, urinary tract infections, sepsis, and peritonitis [19,20]. 4.3. Klebsiella/EnterococcusAbout 20% of the patients in this study had this bacterium in all three samples (on the tumor's surface, on the surface of the healthy intestinal mucosa, and inside the tumor tissue). Klebsiella is found in water, soil, plants, and insects and is a widespread part of both human and animal flora. Additionally, it can colonize the intestines, nose, and mouth. Soft tissue infections, meningitis, diarrhea, pneumonia, urinary tract infections, sepsis, and peritonitis are all possible outcomes of opportunistic bacteria called Klebsiella species [19,20].

Gordonii Streptococcus

In all three sample types, Streptococcus gordonii was found in about 10% of patients. Gram-positive S. gordonii bacteria are frequently detected in the oral cavity as saprophytic flora. Up to 70% of the bacterial biofilm that develops on clean tooth surfaces is made up of S. gordonii and similar species. Although S. gordonii is a harmless member of the saprophytic flora in the mouth, when systemically acquired, it can result in acute bacterial endocarditis [22]. Regarding the link between S. gordonii and colorectal cancer, one case of a patient with endocarditis and an advanced stage of CRC has been documented in the literature [23].

Aeruginosa pseudomonas

The intestinal mucosa contains about 13% of Pseudomonas, but up to 20% more of bacteria is present on the tumor's surface and in the tumor tissue. A common source of many systemic infections in hospitalized patients on long-term antibiotic or immunosuppressive therapy is the clinical bacterium Pseudomonas aeruginosa, which prefers wet settings. Data indicate that P. aeruginosa induces cancer cells to undergo apoptosis in human melanoma cell culture [25]. Azurin, a particular kind of protein produced by P. aeruginosa, has a detrimental effect on the proliferation and development of cancer cells in both human breast and melanoma cells [26,27].The pseudomonas Aeruginosa 4.5

About 13% of Pseudomonas is found in the intestinal mucosa, but up to 20% more bacteria are found in the tumor tissue and on the tumor's surface. The clinical bacterium Pseudomonas aeruginosa, which thrives in moist environments, is a frequent cause of several systemic infections in hospitalized patients receiving long-term antibiotic or immunosuppressive treatment.Evidence suggests that P. aeruginosa causes apoptosis in human melanoma cell culture [25]. P. aeruginosa produces a specific type of protein called azourin, which inhibits the growth and multiplication of cancer cells in human breast and melanoma cells [26,27].It is evident that its presence in some cancer types inhibits the proliferation of cancer cells. Since there is currently no evidence in the literature linking P. aeruginosa to colorectal cancer cells, we can only presume that Pseudomonas may benefit CRC patients and hinder the growth of CRC cells.It was intended that more patients would participate in this study. The COVID-19 pandemic struck during the research procedure's deployment, forcing us to halt clinic collaboration and the routine microbiological analysis of swabs.

CONCLUSION

A healthy person's homeostatic microbiota has a very complicated interaction with its microorganisms, and when that relationship is disrupted by a variety of causes, conditional infections and diseases, including colorectal cancer (CRC), can arise. While some bacteria (like Pseudomonas aeruginosa) can inhibit the growth of cancer cells, others (including Escherichia coli, Enterococcus species, Klebsiella/ Enterobacter, and Streptococcus gordonii) promote the formation and progression of colorectal cancer. Frequent examinations of the human stool's microbial makeup can both prevent colorectal cancer (CRC) and serve as a referral for more sensitive diagnostic techniques. Because of the saprophytic intestinal flora's microorganisms' competitive connection, in the future.

REFERENCES

1. Ferlay, J.; Ervik, M.; Lam, F.; Colombet, M.; Mery, L.; Piñeros, M.; Znaor, A.; Soerjomataram, I.; Bray, F. Global Cancer Observatory: Cancer Today. Available online: https://gco.iarc.fr/today (accessed on 10 October 2023).

2. Siegel, R.L.; Giaquinto, A.N.; Jemal, A. Cancer Statistics, 2024. CA Cancer J. Clin. 2024, 74, 12–49. [CrossRef] [PubMed]

3. Roshandel, G.; Ghasemi-Kebria, F.; Malekzadeh, R. Colorectal Cancer: Epidemiology, Risk Factors, and Prevention. Cancers 2024, 16, 1530. [CrossRef]

4. Nikolic, D. Diabetes Mellitus and Obesity as a Result of a Disrupted Homeostatic Microbiome. New Data on Etiopathogenesis of Diabetes Mellitus. Vojnosanit. Pregl. 2018, 75, 1110–1117. [CrossRef]

5. Nikolic, D.M.; Dimitrijevic-Sreckovic, V.; Ranin, L.T.; Stojanovic, M.M.; Ilic, I.D.; Gostiljac, D.M.; Soldatovic, I.A. Homeostatic Microbiome Disruption as a Cause of Insulin Secretion Disorders. Candida albicans, a New Factor in Pathogenesis of Diabetes: A STROBE Compliant Cross-Sectional Study. Medicine 2022, 101, e31291. [CrossRef] [PubMed]

6. Rebersek, M. Gut Microbiome and Its Role in Colorectal Cancer. BMC Cancer 2021, 21, 1325. [CrossRef]

7. Ma, M.; Zheng, Z.; Li, J.; He, Y.; Kang, W.; Ye, X. Association between the Gut Microbiota, Inflammatory Factors, and Colorectal Cancer: Evidence from Mendelian Randomization Analysis. Front. Microbiol. 2024, 15, 1309111. [CrossRef]

8. Ratnesh, K.; Jha, S.; Arya, A. Clinical and Bacteriological Profile of Abdominal Surgical Site Infections in an Indian Hospital. Bioinformation 2022, 18, 962–967. [CrossRef]

9. Rasilainen, S.K.; Juhani, M.P.; Kalevi, L.A. Microbial Colonization of Open Abdomen in Critically Ill Surgical Patients. World J. Emerg. Surg. 2015, 10, 25. [CrossRef]

10. Joob, B.; Wiwanitkit, V. Cancerous Patients and Outbreak of Escherichia coli: An Important Issue in Oncology. Asian Pac. J. Trop. Dis. 2014, 4, 204–206. [CrossRef]

11. Dougherty, M.W.; Jobin, C. Intestinal bacteria and colorectal cancer: Etiology and treatment. Gut Microbes 2023,15,2185028.[CrossRef][PubMed][PubMedCentral]

12. Sadeghi, M.; Mestivier, D.; Sobhani, I. Contribution of Pks+ Escherichia coli (E. coli) to Colon Carcinogenesis. Microorganisms 2024,12, 1111. [CrossRef] [PubMed]

13. Swidsinski, A.; Khilkin, M.; Kerjaschki, D.; Schreiber, S.; Ortner, M.; Weber, J.; Lochs, H. Association between Intraepithelial Escherichia coli and Colorectal Cancer. Gastroenterology 1998, 115, 281–286. [CrossRef] [PubMed]

14. Wong, S.H.; Yu, J. Gut Microbiota in Colorectal Cancer: Mechanisms of Action and Clinical Applications. Nat. Rev. Gastroenterol. Hepatol. 2019, 16, 690–704. [CrossRef]

15. Humphries, J.D. Integrin Ligands at a Glance. J. Cell Sci. 2006, 119, 3901–3903. [CrossRef]

16. Rubinstein, M.; Wang, X.; Liu, W.; Hao, Y.; Cai, G.; Han, Y.W. Fusobacterium Nucleatum Promotes Colorectal Carcinogenesis by Modulating E-Cadherin/β-Catenin Signaling via Its FadA Adhesin. Cell Host Microbe 2013, 14, 195–206. [CrossRef] [PubMed]

17. Louis, P.; Hold, G.L.; Flint, H.J. The Gut Microbiota, Bacterial Metabolites and Colorectal Cancer. Nat. Rev. Microbiol. 2014, 12, 661–672. [CrossRef]

18. Zhang, L.; Liu, J.; Deng, M.; Chen, X.; Jiang, L.; Zhang, J.; Tao, L.; Yu, W.; Qiu, Y. Enterococcus faecalis Promotes the Progression of Colorectal Cancer via Its Metabolite: Biliverdin. J. Transl. Med. 2023, 21, 72. [CrossRef]

19. Ermolenko, E.; Baryshnikova, N.; Alekhina, G.; Zakharenko, A.; Ten, O.; Kashchenko, V.; Novikova, N.; Gushchina, O.;Ovchinnikov, T.; Morozova, A.; et al. Autoprobiotics in the Treatment of Patients with Colorectal Cancer in the Early Postoperative Period. Microorganisms 2024, 12, 980. [CrossRef]

20. Bagley, S.T. Habitat Association of Klebsiella Species. Infect. Control Hosp. Epidemiol. 1985, 6, 52–58. [CrossRef]