American Journal of Infectious Diseases

Original Research Paper

Analysis of the Clinical Incidence and Correlation between Colorectal Cancer and Microorganisms

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Article history
Received: 13-05-2024
Revised: 26-05-2024
Accepted: 28-05-2024

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Abstract: In this single institution retrospective medical record review, patients diagnosed with colorectal cancer from the years 2018-2022 were evaluated to distinguish an associative linear relationship between diagnosed colorectal cancer and a positive result for the presence of an infectious microorganism. A total of 241 patients diagnosed with colorectal cancer accompanied by a test or order placed with the purpose of ruling out or identifying a microorganism were compiled. The data were analyzed on a linear model to determine association between the two variables and to further investigate trends associated with the presence of a dominant microorganism and the characteristics of the colorectal cancer. Based on the observed clinical incidence, the greatest presence of a dominant infectious microorganism occurred in patients with left sided colon cancers. Species evaluation within this cohort found similarity to microorganisms identified as common post-treatment infectious pathogens including *Escherichia coli*, *Enterococcus faecalis* and *Streptococcus* species. The apparent trend of a dominant microorganism within left sided colorectal cancers suggests clinical relevance when considering further treatment and management of infections within this population.

Keywords: Colorectal Carcinoma, Concurrent Infection, Colon Cancer Screening, Infectious Microorganisms

Introduction

Colorectal Cancer (CRC) is the fourth most prevalent cancer in the United States. In 2023 it is estimated approximately 150,000 individuals will be diagnosed with CRC (Siegel *et al*., 2023). Identifying and managing risk factors related to CRC has reduced the disease burden amongst diagnosed patients. According to the centers for disease control and prevention, the following are the most prominent risk factors and contributors to the development of CRC. Age, inflammatory bowel diseases (ulcerative colitis and Crohn's disease), genetic or epigenetic predisposition and lifestyle factors, including tobacco use, alcohol consumption, a high-fat low fiber diet and insufficient physical activity. The mechanism established in the development of CRC is most commonly the alteration of normal colonic epithelial cells to carcinoma through the adenoma-carcinoma sequence (Grady and Carethers, 2008).

The tumor microenvironment and how cancer cells interact and evade host defenses has been an important topic of discussion when considering CRC tumorigenesis (Schmitt and Greten, 2021). One prominent mechanism related to tumorigenesis is through the host's immune system. Signaling pathways associated with regulation of host immune responses and tumor suppression in early oncogenesis have been implicated with various members of the microbiome (Bauché and Marie, 2017; Daniel *et al*., 2017; Pang *et al*., 2018). Trends established within the tumor microenvironment have outlined associations with commensal and pathogenic organisms to certain locations and tumor types within the gastrointestinal tract (Zhong *et al*., 2020; Jin *et al*., 2021; Liu *et al*., 2022; Ternes *et al*., 2020). A prevalent confounding factor in the gut microenvironment of CRC is inflammation, unregulated microbial interactions and the inability to modulate immune anti-carcinogenic pathways (Elinav *et al*., 2013; Kim and Lee, 2022; Wang and Li, 2022; Lamaudière *et al*., 2023). A focus on the interplay between cancer cells and their interaction with the immune system may provide an essential avenue when treating patients with CRC.

Post-treatment infections are detrimental in long-term outcomes of CRC patients (Lawler *et al*., 2020). These

negative outcomes may be relevant in cases where non-surgical site infections occur as systemic inflammation has been noted to induce immunosuppressive and pro-carcinogenic pathways (Frigerio *et al*., 2021; Zeng *et al*., 2021; Hanus *et al*., 2021). Since specific tumor types and tumor location are relevant in CRC interaction with the hosts' immune system mediated through the tumor microenvironment, observing trends in CRC patients who have had post treatment infections confirmed through positive test results noting the presence of a microorganism may provide insight in further treatment of these patients.

Materials and Methods

This medical record review was approved by Cleveland Clinic's IRB and all information abides by the submitted research protocol and data collection sheet. A population of individuals who have been treated in Cleveland Clinic Weston Florida for their diagnosed CRC between February 1st, 2018 and February 1st, 2023, was compiled using Cleveland clinic's eResearch databank. The population pool ensured the individuals considered were over the age of 18 and under the age of 90 and had no actively treated autoimmune disorders during the period of interest. This population was then filtered for whether there was an order or test placed to the microbiology laboratory within the patient's medical record. The focus of this search included tests with the purpose of ruling out or identifying a microorganism during the period of interest. This was further filtered to ensure patients have not taken any course of antibiotics, excluding topical antibiotics, within the two-month time frame prior to the serological, histological, or laboratory test being collected and sent for testing. Information presented within the patients' medical record included testing facilities outside Cleveland clinic if pertinent to the inclusion criteria related to antibiotic administration. Information on the CRC including histological type, tumor size, location and differentiation as well as the type of order/test and corresponding result were entered into Cleveland clinic's Research Electronic Data capture (REDcap) database. The REDcap database allowed organization of CRC cases in a format where all cases were entered in a randomized order and assigned a new case number relevant only to this study.

Data Analysis

Study data were collected and managed using REDCap electronic data capture tools hosted at Cleveland Clinic (Harris *et al*., 2009; 2019). REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) An intuitive interface for validated data capture; (2) Audit trails for tracking data manipulation and export procedures; (3) Automated export procedures for seamless data downloads to common statistical packages; and (4) Procedures for data integration and interoperability with external sources. Data were analyzed using a linear model on Cleveland clinic provided statistical software.

Results

Population Characteristics

The study cohort included a total of 241 patients that comprised of 214 Adenocarcinomas, 7 mucinous Adenocarcinomas, 2 medullary carcinomas, 4 signet-ring cell carcinomas, 11 squamous cell carcinomas and 2 neuroendocrine carcinomas, with one Adenocarcinoma having neuroendocrine differentiation noted (Table 1). The population combined all individuals who were diagnosed with CRC that also had orders/tests placed with the purpose of ruling out and/or identifying microorganisms or being sent to the microbiology laboratory (Supplemental Fig. 1). Among the patients who fit the criteria, 101 had microbiology related orders and tests solely relating to the SARS-COV-2 virus. These cases will be noted (Supplemental Table 1), however they are not the focus of this investigation. Out of the remaining 140 cases that were not related to the SARS-COV-2 virus, 50.6% (n = 71) had a dominant microorganism present within a test result.

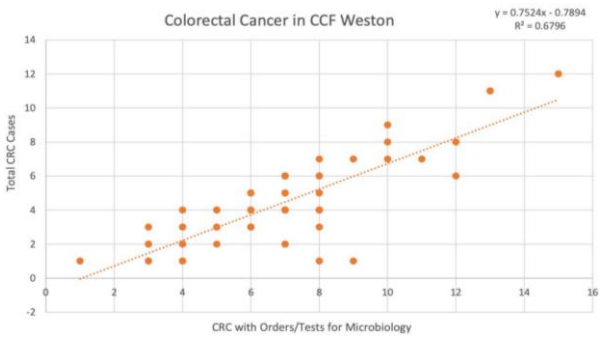
Linear Model Analysis

To determine a relationship between CRC cases and orders relating to microbiology a linear regression was run on the n = 378 cases of diagnosed CRC in Cleveland clinic's Weston campus and the n = 241 cases fitting the inclusion criteria. It was found that over the five-year period considered, CRC patients who have had orders or tests placed with the intent to identify or rule out a microorganism compared to the total number of patients diagnosed with CRC, were statistically significant in relation to each other ($p<0.001$) at the 95% confidence interval (Fig. 1a, Supplemental Fig. 1). Interpreting the residual plot for the total cases of CRC versus CRC cases with orders for microbiology displays data points not fitted around zero (Fig. 1b). This indicates the possibility of a relevant variable not being considered within this model. For the scope of this report, the variables within the limit of the approved data collection sheet are the only variables that have been included. It can be speculated that including patients without CRC that have had orders sent to the microbiology laboratory may influence the significance of this linear association.

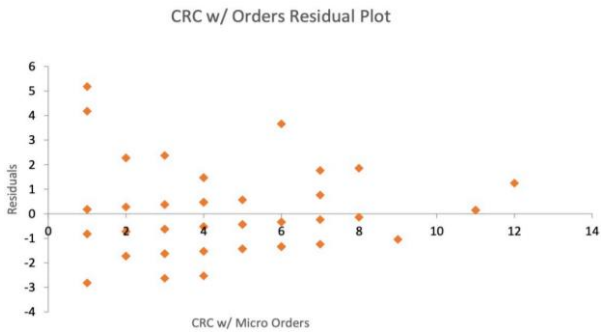
Table 1: Population demographics coordinated by CRC type

Demographics		Adenocarcinoma n = 228	Squamous cell carcinoma n = 11	Neuroendocrine carcinoma n = 2
Age (±SD)		62(13.22)	65(8.79)	68(0.5)
Sex	Male	131	5	
	Female	97	6	2
BMI (± SD) kg/m^2		27.87(7.76)	26.76(3.97)	37.22(13.54)
Location	Left	145	11	1
	Right	84*		1
Tumor Size (± SD) cm		3.88(2.38)	4.07(3.05)	6
TNM stage	pT1	29		
	pT2	46	2	
	pT3	92	2	1
	pT4	35	3	1
Differentiation	Poor	34		1
	Moderate	145**	7	
	Well	33	4	1

Figure legend: * One case had two tumors, each respectively located in the left and right colon ** the instance in which a case was classified as "moderate to poorly differentiated" is categorized under "moderate" in this table

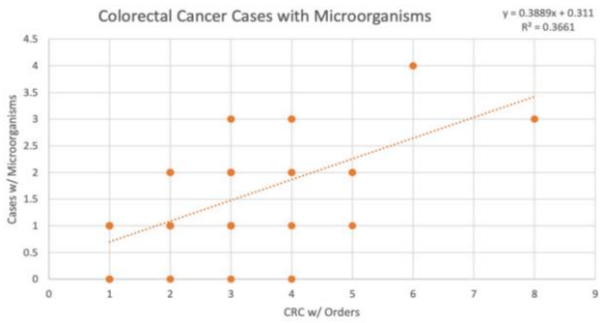


(a)

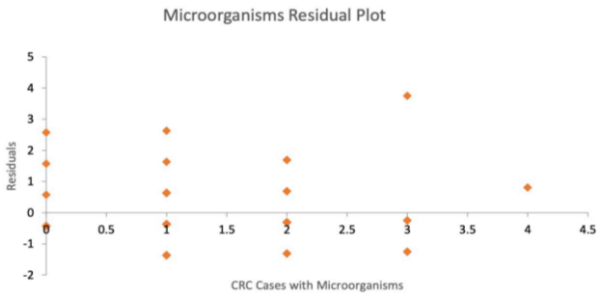


(b)

Fig. 1: Linear regression of total cases; figure legend: The regression analysis based on total CRC cases seen in the Cleveland clinic Weston campus from 2018-2022; (a) The linear regression scatter plot supporting 68% of all variability in the data set is explained by the regression model and; (B) The data presented on a residual plot



(a)



(b)

Fig. 2: Linear Regression of cases with microbiology association; figure legend: Regression analysis representative of the cases of CRC that have microbiology related orders correlated to cases presenting with organisms; (a) the linear regression representing 37% of variability within the model and (b) the residual plot presenting with a similar trend to the regression plot for CRC cases with orders placed where the residuals are not plotted around zero

DOI: 10.3844/ajidsp.2024.11.23

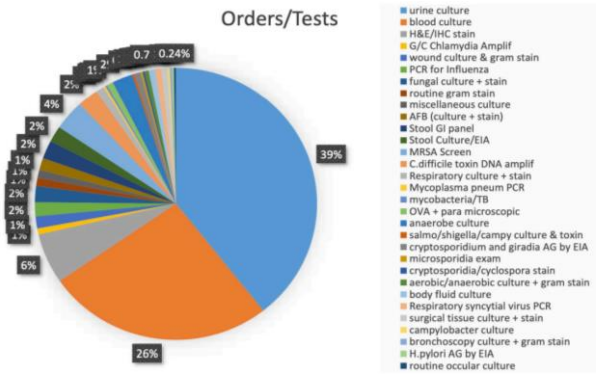


Fig. 3: Total tests ordered and listed corresponding to CRC cases; figure legend: A display of the proportion of tests/orders placed corresponding to the institutional nomenclature of the test/order conducted

The relationship between the n = 140 cases with microbiology related orders and n = 71 cases which had a dominant microorganism present was also plotted. The results of this linear regression analysis determined cases that had a dominant microorganism were significantly related ($p<0.001$) to the tests that had microbiology orders placed not relating to SARS-COV-2. Although this statistical significance is present between the two variables, the regression model explains 37% of variability (Fig. 2A and Supplemental Figure 2) and suggests more relevant variables in addition to a better fitting model need to be considered to provide meaningful analysis (Fig. 2B). This could include considering the (n = 101) SARS-COV-2 related cases that were omitted in this analysis, to account for the observations not represented in between the data points present.

Moreover, it can be speculated these residuals may be due to an increase and high importance of SARS-COV-2 related microbiology orders being placed during the year 2020 and therefore a decrease in the performance rate of the remaining tests. However, the data being presented cannot make definitive confirmation that SARS-COV-2 impacted patients who were diagnosed with CRC having a positive test result accompanying an identified microorganism (Eklöv *et al*., 2022; Blondeau, 2020). It is also relevant to note that although there was an increase in SARS-COV-2 related tests, diagnosis and treatment of CRC's did not decrease in comparison to previous years (Freund and Wexner, 2022).

Microbiology Tests/Orders and Dominant Microorganisms

Amongst the (n = 140) CRC cases that fit under the criteria of having orders and tests placed with the purpose of identifying or ruling out a microorganism or being sent to the microbiology laboratory, there were a total of 419 orders/tests placed. The most frequent and abundant tests were urine and blood cultures followed by H&E/IHC stains ordered on surgical specimens with the purpose of ruling out microorganisms within the tissue (Fig. 3). The largest amount of gathered data related to tests/orders in respect to CRC cases was observed under the Adenocarcinoma diagnostic category. Left colon Adenocarcinomas had approximately 50% more urine cultures ordered than in Right colon Adenocarcinomas. A similar trend was seen with blood cultures. The Right colon Adenocarcinomas displayed a greater incidence for respiratory/pulmonary related tests (Supplemental Table 2). These tests produced a total of 109 positive results for microorganisms present within the collected samples along with their respective frequency of result and identification (Fig. 4). This analysis does not include any SARS-COV-2 related tests despite their presence within the patient's medical record during the period of interest.

One prominent category discovered during data collection was observed when tests displayed a positive result, however there was no distinctive identification or further notation of this result. These instances fell under the category of positive test result with unspecified organism further referred to as 'not specified.' Another prominent category encountered was, a result although noted as a positive for the presence of microorganisms, was not a cause for concern due to microbiota present consisting of the normal flora found within the tested specimen type. These categories made up a total of 30 outcomes within the 109 positive results. These two categories will not be further analyzed as their results are nonspecific and do not provide insight into trends between dominant microorganisms and CRC.

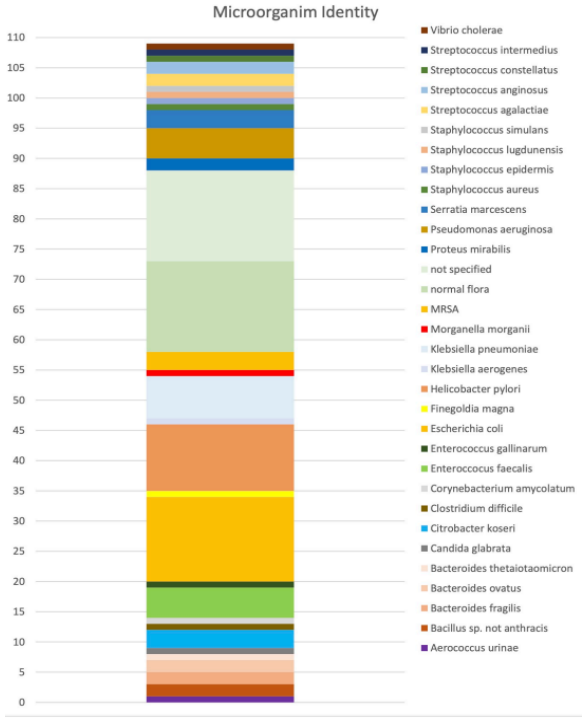


Fig. 4: Microorganism identities and abundance based on degree of identification; figure legend: Distribution of microorganism classification based on identification within a positive test result

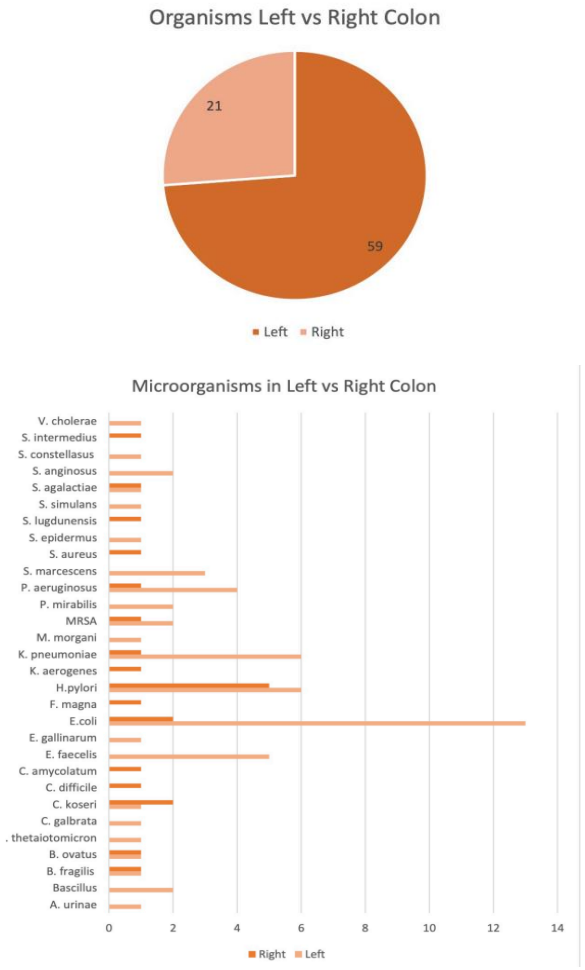


Fig. 5: Microorganism correlated to CRC location within GI tract figure legend: A representation of microorganism corresponding to location of CRC within the GI tract

The microorganisms with the highest prevalence within CRC cases were *Escherichia coli*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Staphylococcus*, *Streptococcus* and *Bacteroides*. Comparing these results to the cases that had orders/tests placed for microbiology, 65 were Adenocarcinomas, 3 were mucinous Adenocarcinomas, 2 signet-ring cell carcinomas and 2 squamous cell carcinomas, one of the Adenocarcinomas had neuroendocrine differentiation noted. The two previously mentioned neuroendocrine carcinomas did not have a dominant microorganism present. Left sided CRCs has a higher incidence of a corresponding positive test result for a dominant microorganism in comparison to the right side (Fig. 5a). Within the cases of Left sided CRCs *E. coli* was the most ubiquitous. In addition, although at a lower prevalence, both *Enterococcus* species appeared in test results of Left sided CRC's. The majority of the microorganisms that occur at a higher prevalence are correlated with cases of Left side CRC's. This is not true for *H. pylori*, *Staphylococcus*, *Streptococcus* and *Bacteroides* that are split evenly in both Right and Left sided CRC's (Fig. 5b).

Out of the 140 CRC cases, 71 patients produced a total of 109 positive test results. This indicates a number of patients with more than one infectious microorganism present within the period of interest. This is seen particularly in three CRC cases that have the most microbial presence within their reports. They comprise of the following organisms; *A. urinae*, *B. fragilis*, *B. ovatus*, *B. thetaiotaomicron*, *C. koseri*, *E. faecalis*, *E. coli*, *P. aeruginosa*, *P. mirabilis*, *S. simulans* and *S. anginosus*. One case, a Moderately differentiated mucinous Adenocarcinoma of the Left colon diagnosed in a Male over the age of 80 with a BMI greater than 30, had positive test results for 7 of these listed organisms. In comparison, the remainder of the positive test results were represented by a sole occurrence under one patient. This was seen with *E. gallinarum*, *K. pneumoniae* and some *Bacteroides*. The sole presence of *Corynebacterium amycolatum*, *Staphylococcus lugdunensis* and *Finegoldia magna* occurred in the same CRC case of a Moderately differentiated Adenocarcinoma in the right colon female with a BMI over 50 that also had a positive result for *Pseudomonas aeruginosa*. The sole presence of *Klebsiella aerogenes* was in an ocular sample. *Escherichia coli* was predominantly present in males with Moderately differentiated Adenocarcinoma in the Left colon (Table 2). Presence of *Helicobacter pylori* did not follow any trends based on cancer characteristics, sex, age or BMI. These findings introduce an avenue to further investigate patients who have more than one dominant microorganism as it is suggested these patients may have perturbed immune systems or immune regulatory pathways (Attiê *et al*., 2014).

Demographics and Social Determinants of Patients with Dominant Microorganisms

The 71 patients that had a positive test result with a dominant microorganism had an average age at time of diagnosis of 63 years (SD 13.9) and an average BMI of 29.08 kg/m^2 (SD 11.3). 39 were Male and 32 were Female. 36 had co-occurrent gastrointestinal diseases that included 3 ulcerative colitis, 1 Crohn's disease, 10 Type II Diabetes mellitus (T2D), 19 Gastroesophageal Reflux Disease (GERD), 5 that had both T2D and GERD and 2 other cooccurring GI disorders. These trends do not correlate with microorganism presence as the incidence of cooccurring GI disparities among the study population remained the same and concur with inflammatory bowel disorders classified as risk factors for the development of CRC. The additional factors discussed as risks for development of CRC involve social determinants of health including tobacco use, alcohol consumption, insufficient physical activity, diet and psychological adversity including depression and stress. This institution documents these factors through self-reported surveys and questionnaires at time of hospital admission.

Table 2: Microorganisms related to patient demographics and CRC characteristics

Organisms	Sex	Age (mean ± SD)	BMI (mean ± SD)	CRC type	Location	Tumor size (cm)(mean)	pTNM	Differentiation degree
**Aerococcus urinae*	Female Male: 1	81-85	33.23	mucinous Adenocarcinoma	Left: 1	4.40	pT2	Moderate
Bascillus	Female Male: 2	71-75	40.41(0.29)	Adenocarcinoma	Left: 2	2.00	pT1:2	Moderate
Bacteroides fragilis	Female Male: 2	69.5(12.02)	27.51(0.81)	Adenocarcinoma	Left: 1 Right: 1	2.50 2.50	pT2: 2	Moderate
Bacteroides ovatus	Female Male: 2	67(15.56)	26.41(0.76)	Adenocarcinoma	Left: 1 Right: 1	2.50	pT2	Moderate: 1 Well: 1
**Bacteroides thetaiotaomicron*	Female Male: 1	81-85	33.23	mucinous Adenocarcinoma	Left: 1	4.40	pT2	Moderate
Candida glabrata	Female Male: 1	71-75	27.62	Adenocarcinoma	Left: 1	7.50		Moderate
Citrobacter koseri	Female Male: 3	65(8.33)	30.29(3.83)	Adenocarcinoma	Left: 1 Right: 2	3.75	pT1:1 pT4: 1	Moderate: 1 Well: 2
Clostridium difficile	Female: 1 Male	46-50	21.1	Adenocarcinoma	Left: 1	2.30	pT3	Poor
**Corynebacterium amycolatum*	Female: 1 Male	66-70	50.1	Adenocarcinoma	Right: 1	4.00	pT2	Moderate
Enterococcus faecalis	Female: 1 Male: 4	55(15.68)	26.04(5.1)	Adenocarcinoma: 4 mucinous Adenocarcinoma: 1	Left: 5	4.14	pT2:1 pT3:3	Poor: 1 Moderate: 4
Enterococcus gallinarum	Female: 1 Male	66-70	22.5	Adenocarcinoma	Left: 1	3.40	pT4	Moderate
***Escherichia coli*	Female: 4 Male: 10	63(12.2)	27.75(7.03)	Adenocarcinoma: 12 mucinous Adenocarcinoma: 1 squamous cell carcinoma: 1	Left: 13 Right: 2	4.04	pT1: 2 pT2: 5 pT3: 3	Poor: 1 Moderate: 10 Well: 3 pT4: 3
**Finegoldia magna*	Female: 1 Male:	66-70	50.1	Adenocarcinoma	Right: 1	4.00	pT2	Moderate
Helicobacter pylori	Female: 5 Male: 6	57(10.1)	26.78(6.81)	Adenocarcinoma	Left: 6 Right: 5	4.35	pT1: 2 pT2: 1 pT3: 6	Poor: 2 Moderate: 6 Well: 1 pT4: 1
**Klebsiella aerogenes*	Female: Male: 1	66-70	30.71	Adenocarcinoma	Right: 1	5.00	pT2	Moderate
Klebsiella pneumonia	Female: 4 Male: 3	69(11.77)	26.53(2.38)	Adenocarcinoma	Left: 6 Right: 1	4.50	pT1: 1 pT2: 1 pT3: 3	Poor: 1 Moderate: 4 Well: 1 pT4: 1
Morganelli Morgani	Female: Male: 1	51-55	24.62	Adenocarcioma	Left:1	6.50	pT3	Moderate
MRSA	Female: 1 Male: 2	58(18.9)	41.38(2.06)	Adenocarcioma	Left: 2 Right: 1	5.90	pT3: 2 pT4:1	Poor: 1 moderate: 1 Well: 1
Proteus mirabilis	Female: 1 Male: 1	60.5(6.3)	22.55(4.7)	Adenocarcinoma	Left: 2	2.50	pT1	Well: 2
Pseudomonas aeruginosa	Female: 2 Male: 3	65(20.8)	32.13(11.16)	Adenocarcinoma: 4 Mucinous Adenocarcinoma: 1	Left: 4 Right: 1	4.58	pT2: 2 pT3: 3	Moderate: 5
Serratia marcescens	Female: Male: 3	81(12.4)	26.2(1.27)	Adenocarcinoma	Left: 3	5.07	pT2: 1 pT3: 1	Poor: 1 Moderate: 2 pT4: 1
* *Staphylococcus aureus*	Female: 1 Male:	86-90	20.7	Adenocarcinoma	Right: 1	7.00	pT2	Well
Staphylococcus epidermis	Female: Male: 1	76-80	30.4	Adenocarcinoma	Left: 1	4.50		Moderate
**Staphylococcus lugdunensis*	Female: 1 Male:	66-70	50.1	Adenocarcinoma	Right: 1	4.00	pT2	Moderate
**Staphylococcus simulans*	Female: Male: 1	86-90	33.23	Mucinous Adenocarcinoma	Left: 1	4.40	pT2	Moderate
Streptococcus agalactiae	Female: 2 Male:	57(2.83)	23.81(2.88)	Adenocarcinoma squamous cell carcinoma: 1	Left: 1 Right: 1	2.35	pT3 pT4	Moderate: 2
Streptococcus anginossus	Female: Male: 2	71(14.14)	30.66(3.64)	Adenocarcinoma Mucinous Adenocarcinoma	Left: 2	3.45	pT2: 2	Moderate: 2
**Streptococcus constellatus*	Female: Male: 1	86-90	26.52	Adenocarcinoma	Left: 1	6.50	pT4	Poor
**Streptococcus intermedius*	Female: Male: 1	61-65	24.25	Adenocarcinoma	Right: 1	5.00	pT4	Well
Vibrio cholera	Female: 1 Male:	61-65	19.23	Adenocarcinoma	Left: 1	2.5	pT1	Well

Figure legend: Well to moderately differentiated is categorized under moderately differentiated the cases that tested positive for *E. faecalis* one of the adenocarcinomas is noted to have neuroendocrine differentiation

* Indicates one patient tested positive for these microorganisms and this result was not shared by any other patients

** Indicates adenocarcinoma has two tumors and both are located in the Left colon

During data collection, information regarding status of these social determinants was included to investigate whether trends can be observed from the total study population compared to those cases with a dominant microorganism. 84% of the study population had information present regarding tobacco use. This institution records tobacco use in three categories. Low risk, indicating the patient has never used a tobacco product, medium risk indicating the patient is a former user of tobacco products and high risk indicating the patient currently uses tobacco products. A comparison of tobacco usage yields no distinct trends regarding this risk factor in relation to having a positive result of a microorganism. Although not determinative of any result or analysis it is interesting to note the patient that tested positive for the greatest number of microorganisms was classified under low risk of tobacco use. Additional consideration of social determinants including alcohol consumption, physical activity, depression, stress and food security cannot be included as sufficient analysis between the total study population and those with dominant microorganisms is not accurately reflective based on the volume of unreported values for these social determinants at the time of CRC diagnosis.

Discussion

Colorectal cancer cases in Cleveland clinic's Weston Florida campus were compiled to determine whether there was a correlation between clinical presentation of a dominant microorganism within the patients' medical record and the formal diagnosis of CRC during a 5-year period. There was statistical significance observed in both linear regression plots. The COVID-19 virus may have been involved in exogenous factors revolving around the laboratory procedures instated during the pandemic, presumably the collection of samples and ordered tests. Strengthening this model to emulate linear models associated with progression of cancer alongside tests placed will clarify the full scope of infection and cancer relationships (Sung *et al*., 2022; Vuik *et al*., 2019).

Evaluating the tests placed during the period of CRC diagnosis displayed Left-sided colon Adenocarcinomas had the greatest prevalence of urine and blood cultures ordered when compared to Right CRC's, which had a greater prevalence of respiratory/pulmonary related tests. This distinction of focused testing provides avenue for further investigation if location of the malignant lesion influences immune pathways leaving specific body systems more susceptible to infection (De Renzi *et al*., 2021; Teimoorian *et al*., 2018). Left colon Adenocarcinomas consisted of a greater representation in tests that had a positive result for a microorganism indicating infection during or post cancer treatment. This study's population pool was compared to a previously established study population of CRC cancers in Cleveland clinic by Hanumant *et al*. (2019). The similarities between the demographics and cancer characteristics of that cancer patient population and this study's patient population indicated the trend of left sided CRC cases was based on the presence of a dominant microorganism rather than population characteristics. This could indicate a correlation between left sided CRC tumors and greater risk of infections. This can be attributed to a variety of factors including but not limited to the GI microenvironment, composition and structure of the microbiome, tumor type and interactions with host immune system in this area of the colon (Zhong *et al*., 2020; Baran *et al*., 2018).

Conclusion

Although presence of a dominant microorganism within patients that have CRC does not explicitly display correlation, the findings suggest clinical relevance. From a clinical standpoint the incidence of a dominant microorganism is more likely to occur in Left sided CRC tumors and may be useful to clinicians in the management of these infections (Braumüller *et al*., 2022; Tripathy *et al*., 2021). This is especially vital for patients that have more than one dominant infectious microorganism as these patients have a decreased likelihood for survival and overall lower quality of life. Inclusion of prebiotics, probiotics and the Fecal Microbiota Transplantation (FMT) procedure in post CRC treatment have been suggested as efficient methods for lowering the risk of infection by modulating a variety of anti-oncogenic immune pathways (Fong *et al*., 2020; Kaźmierczak-Siedlecka *et al*., 2020). Prospective studies including an in-depth consideration of microorganisms within the tumor microenvironment and association to immune responses can provide further insight on the relevance of pathogenic microorganisms to colorectal cancer oncogenesis and treatment.

Limitations

The results of the linear regression analysis correlation indicate there are variables not accounted for. This may include the inclusion of the sequence in which the CRC diagnosis was made versus the positive result for an infectious organism listed in the data, infections that occurred in patients without CRC during the same period or the effects the COVID-19 pandemic may have had on the microbiology lab. The results from the microbiology related orders and tests were also limited to the available services within the microbiology department. Some microorganisms are not culturable in the hospital laboratory setting. An example of this is seen in stool cultures and GI panels as these tests identify enterotoxins related to common food-borne or opportunistic pathogens rather than the identification of the organism itself. Patient demographics and social

determinants of health was collected via self-surveys. This method of documentation was optional and resulted in these factors being undocumented in the majority of cases collected in this study.

Acknowledgment

The authors would like to thank Cleveland Clinic's Pathology laboratory for the time and resources allocated to the authors during the researching and publication of this article. The authors did not receive any outside financial support or assistance.

Funding Information

The authors have not received any financial support or funding to report.

Author's Contribution

Kalia Koutouvalis: Conceptualization, formal analysis, data curation, resources, investigated, written-original drafted.

Pablo Augusto Bejarano: Supervision, visualization, validation, written-review and edited.

Ethics

This study has been approved by the Cleveland clinic institutional review board, study number 23-300, as exempt human subject research for which the research involves only information collection and analysis.

Competing Interests

There are no competing interests.

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Supplemental Table 1

CRC Case	Sex	Order/Test	BMI	Histological type	Location	Tumor size (cm) pTNM	Differentiation	Co-occuring GI Disorde
1	Male	Expedited COVID 19, CORONAVIRUS (S	21.10	Adenocarcinoma	Left	pT4		
2	Female	Two pre procedure and pre operative	30.60	Adenocarcinoma	Left	0.7 pT1	Well differentiated	
3	Male	Two pre procedure and pre operative	22.10	Adenocarcinoma	Left	pT4	Moderately differentiated	
4	Female	Expedited COVID-19	22.38	Intramucosal adenocarcinoma	Right			GERD
5	Female	Coronavirus (SARS cov 2 access labs), p	21.50	Adenocarcinoma	Right	1 pT3	Moderately differentiated	GERD
6	Female	COVID-19 PCR nasopharynx (bio-ref), C	30.12	Adenocarcinoma	Left	2.5 pT2	Ulcerative Colitis	
9	Male	Expedited COVID-19	26.96	Adenocarcinoma	Right	3.5 pT3	Moderately differentiated	GERD
10	Male	Pre procedure and pre operative COVID	24.10	mixed neuroendocrine carcinoma-ade	Left			
11	Female	Pre procedure and pre operative COVID	23.90	Adenocarcinoma	Left	pT1	Well differentiated	
12	Male	Pre procedure and pre operative COVID	26.00	Adenocarcinoma	Left	15 pT4	Moderately differentiated	
13	Female	Pre procedure and pre operative COVID	37.50	Adenocarcinoma	Left	0.4 pT1	Moderately differentiated	GERD
15	Male	2019 coronavirus, coronavirus (sars c	24.13	Adenocarcinoma	Left	3.5 pT2	Moderately differentiated	GERD
16	Female	Two pre procedure and pre operative	25.99	Adenocarcinoma	Right	4 pT4	Moderately differentiated	
17	Male	Coronavirus (SARS cov 2 access labs), p	26.89	Adenocarcinoma	Left	1 pT1	Moderately differentiated	GERD
18	Male	Coronavirus (SARS cov 2 access labs), e	28.12	Adenocarcinoma	Left		Moderately differentiated	
19	Female	CCIRH rapid COVID-19, COVID-19 PCR na	25.60	Adenocarcinoma	Left	5.5 pT3	Moderately differentiated	
21	Female	Four 2019 coronavirus, expedited cov	24.20	Adenocarcinoma	Left	5.5 pT3	Moderately differentiated	Type II diabetes mellitus
23	Female	Pre procedure and pre operative COVID	19.77	signet-ring cell carcinoma	Left	3 pT4	Poorly differentiated	
24	Male	Two 2019 coronavirus, pre procedure	29.70	Adenocarcinoma	Left		Moderately differentiated	
25	Female	Two pre procedure and pre operative	25.00	Adenocarcinoma	Left	4.3 pT3	Moderately differentiated	
26	Male	COVID-19 PCR nasopharynx (BIOREF)	28.94	Adenocarcinoma	Left	0.8	Moderately differentiated	Type II diabetes mellitus
27	Male	Pre procedure and pre operative COVID	32.20	Adenocarcinoma	Right	4.2 pT1	Well differentiated GERD	
28	Female	Expedited COVID-19	29.10	mucinous Adenocarcinoma	Left	1.8 pT2		
29	Male	Pre procedure and pre operative COVID	36.78	Adenocarcinoma	Right	0.4 pT3	Well differentiated GERD	
30	Male	Pre procedure and pre operative COVID	30.20	Adenocarcinoma	Left			GERD
31	Female	Pre procedure and pre operative COVID	31.16	Adenocarcinoma	Right	4.5 pT2	Moderately differentiated	
32	Female	Pre procedure and pre operative COVID	23.60	Adenocarcinoma	Left		Moderately differentiated	
33	Female	Three pre procedure and pre operative	19.10	squamous cell carcinoma	Left	3.4 pT2	Moderately differentiated	
34	Male	Pre procedure and pre operative COVID	25.10	squamous cell carcinoma	Left	0.4	Moderately differentiated	
35	Female	Expedited COVID-19	23.68	neuroendocrine carcinoma	Right	6 pT3	Poorly differentiated	
36	Female	Expedited COVID	28.30	Adenocarcinoma	Right	1.5 pT1	Moderately differentiated	
37	Female	Coronavirus (SARS cov 2 access labs)	22.30	Adenocarcinoma	Right	4.5 pT4	Moderately differentiated	
38	Female	COVID-19 PCR nasopharynx (BIOREF)	23.60	Adenocarcinoma	Left	5.5 pT3	Well differentiated	
39	Female	Expedited COVID-19, coronavirus (sars	30.80	Adenocarcinoma	Left	3 pT2	Well differentiated Ulcerative Colitis	
40	Male	Two coronavirus (SARS cov 2 access lab	28.00	mucinous adenocarcinoma	Left	4.5 pT3		GERD
41	Male	Three coronavirus (SARS cov 2 access la	30.40	Adenocarcinoma	Left	0.3 pT3	Moderately differentiated	Type II diabetes mellitus
42	Female	Coronavirus (SARS cov 2 access labs), p	33.20	Adenocarcinoma	Left	0.7 pT2	Moderately differentiated	
43	Male	Pre procedure and pre operative COVID	27.10	squamous cell carcinoma	Left	3 pT2	Moderately differentiated	GERD
45	Male	Expedited COVID-19	23.70	Adenocarcinoma	Left	5.5 pT3	Moderately differentiated	GERD
46	Female	Expedited COVID-19	24.24	mucinous adenocarcinoma	Right	5 pT3	Poorly differentiated	GERD
47	Female	Pre procedure and pre operative COVID	28.91	Adenocarcinoma	Right	4.5 pT3	Moderately differentiated	
48	Male	Expedited COVID-19	26.10	Adenocarcinoma	Right	1.5 pT2	Moderately differentiated	
49	Male	Pre procedure and pre operative COVID	26.20	Adenocarcinoma	Left	3 pT3	Moderately differentiated	
55	Male	Coronavirus (SARS cov 2 access labs), s	24.50	Adenocarcinoma	Left	3.5 pT3	Moderately differentiated	Type II diabetes mellitus
56	Male	2019 coronavirus, two coronavirus (s	30.40	Adenocarcinoma	Right	4 pT2	Moderately differentiated	GERD
57	Male	SARS cov 2 rapid result antigen test	26.80	Adenocarcinoma	Left	2.5 pT1	Moderately differentiated	
58	Male	Expedited COVID-19	27.12	Adenocarcinoma	Left	3 pT4	Moderately differentiated	GERD
59	Male	Four sars-cov-2 molecular POCT COVID	28.30	Adenocarcinoma	Left	4 pT3	Poorly differentiated	
60	Male	Expedited COVID-19, two sars-cov-2 PC	28.90	Adenocarcinoma	Left	4 pT3	Moderately differentiated	Type II diabetes mellitus
61	Male	Pre procedure and pre operative COVID	30.40	Adenocarcinoma	Left	4.5 pT2	Moderately differentiated	GERD
62	Female	Two sars-cov-2 RNA pre procedure an	21.14	Adenocarcinoma	Left	2.5 pT3	Moderately differentiated	
64	Female	2019 coronavirus, three pre procedur	28.50	Adenocarcinoma	Left	4.5 pT3	Poorly differentiated	
66	Male	Two sars-cov-2 RNA, expedited COVID1	38.20	Adenocarcinoma	Left	5 pT3	Moderately differentiated	Type II diabetes mellitus
68	Male	Expedited COVID-19, pre procedure and	27.40	Adenocarcinoma	Left	3.5 pT3	Moderately differentiated	GERD
69	Male	Expedited COVID-19, 2019 coronavirus	42.80	mucinous adenocarcinoma	Right	5 pT3	Moderately differentiated	
73	Female	Pre procedure and pre operative COVID	48.00	Adenocarcinoma	Left	3 pT2	Moderately differentiated	
75	Male	2019 coronavirus, pre procedure and	20.50	Adenocarcinoma	Right	7 pT4	Well differentiated	
76	Male	2019 coronavirus	27.83	Adenocarcinoma	Right	7.5 pT3	Moderately differentiated	GERD
77	Male	Pre procedure and pre operative COVID	24.65	Adenocarcinoma	Left	7 pT4		
79	Male	SARS-cov-2 PCR	21.70	Adenocarcinoma	Left	3.2 pT2	Moderately differentiated	
80	Female	2019 coronavirus, coronavirus (sars c	27.21	Adenocarcinoma	Left	2 pT2	Moderately differentiated	GERD
81	Female	SARS-cov-2 RNA, expedited COVID-19, c	24.55	Adenocarcinoma	Left			GERD
84	Female	Coronavirus (SARS cov 2 access labs)	21.10	Adenocarcinoma	Left	7 pT4	Poorly differentiated	
85	Male	Pre procedure and pre operative COVID	30.50	Adenocarcinoma	Left	4.5 pT2	Moderately differentiated	
93	Female	2019 coronavirus, pre procedure and	20.98	Adenocarcinoma	Left	6 pT4	Moderately differentiated	GERD
103	Female	Pre procedure and pre operative COVID	19.90	Adenocarcinoma	Left	1.8 pT2	Moderately differentiated	
113	Male	Expedited COVID-19, two SARS cov 2 PCR	28.10	Adenocarcinoma	Right	8.5,2 pT3,pT1	Moderately differentiated, well differe	Type II diabetes mellitus & GERD
114	Male	Expedited COVID + flu A/B, four pre pr	31.74	Adenocarcinoma	Right	3.8 pT3	Moderately differentiated	GERD
115	Male	Pre procedure and pre operative COVID	27.67	Adenocarcinoma	Left	3 pT2	Poorly differentiated	
117	Male	Pre procedure and pre operative COVID	31.31	Adenocarcinoma	Right	4.5 pT4	Moderately differentiated	GERD
119	Male	Expedited COVID, expedited COVID + flu	29.35	Adenocarcinoma	Left	2.5 pT2	Poorly differentiated	
121	Female	Expedited COVID-19	24.40	Adenocarcinoma	Right	4.6 pT3	Moderately differentiated	
124	Male	Two expedited COVID-19,	26.23	medullary carcinoma	Right	11 pT3		
126	Male	2019 coronavirus, pre operative and	30.00	Adenocarcinoma	Left	3.5 pT3	Poorly differentiated	Type II diabetes mellitus & GERD
130	Male	Two expedited COVID,	23.00	Adenocarcinoma	Right	10 pT3	Moderately differentiated	
136	Female	Two expedited COVID	18.11	Adenocarcinoma	Left	2 pT2	Moderately differentiated	Type II diabetes mellitus
137	Female	Pre procedure and pre operative COVID	21.80	Adenocarcinoma	Right	1.5 pT1	Moderately differentiated	
142	Female	Expedited COVID-19	24.80	Adenocarcinoma	Right	2.8 pT3	Moderately differentiated	
146	Male	Three H&E/IHC stains, coronavirus (sa	28.30	Adenocarcinoma	Right	3.5 pT3	Moderately differentiated	
149	Male	Expedited COVID-19	31.34	Adenocarcinoma	Left	2.5	Poorly differentiated	GERD

DOI: 10.3844/ajidsp.2024.11.23

Supplemental Table 1

152	Male	Two expedited COVID-19	23.47	Adenocarcinoma	Left	2 pT3		GERD
153	Male	Two 2019 coronavirus, COVID-19 PCR n	27.67	Adenocarcinoma	Left	3.5 pT1	Moderately differentiated	
161	Female	Two coronavirus (SARS cov 2 access lab	32.65	Adenocarcinoma	Left	2.5 pT2	Moderately differentiated	GERD
164	Female	Coronavirus (SARS cov 2 access labs), t	24.80	Adenocarcinoma	Left	2.5 pT2	Moderately differentiated	GERD
172	Male	Pre procedure and pre operative COVID	29.07	Adenocarcinoma	Right	2.5 pT4		
178	Male	Two expedited COVID-19, two pre proce	26.05	Adenocarcinoma	Right	6.2 pT4	Moderately differentiated	Type II diabetes mellitus
179	Female	Expedited COVID-19, pre procedure and	26.15	Adenocarcinoma	Left	4 pT4	Moderately differentiated	GERD
181	Male	SARS-cov-2	26.62	Adenocarcinoma	Left	1 pT2	Moderately differentiated	Type II diabetes mellitus
182	Female	Expedited COVID-19, Sars-Cov-2	30.73	squamous cell carcinoma	Left	2	Poorly differentiated	
187	Male	Coronavirus (SARS cov 2 access labs), e	24.74	Adenocarcinoma	Left	4.5 pT2	Moderately differentiated	GERD
195	Male	Expedited COVID-19, two COVID-19 PCR,	18.19	Adenocarcinoma	Left	1.6 pT4		GERD
205	Male	Two expedited COVID, two coronavirus	34.67	Adenocarcinoma	Right	0.3	Moderately differentiated	
206	Male	2019 coronavirus, expedited COVID-19	30.06	squamous cell carcinoma	Left	10.2 pT3	Moderately differentiated	GERD
207	Female	Two CCIRH rapid COVID	25.90	Adenocarcinoma	Left	4.1 pT1	Moderately differentiated	GERD
208	Female	Expedited COVID, pre procedure and p	17.12	Adenocarcinoma	Left	5 pT2		GERD
211	Male	Coronavirus (SARS cov 2 access lab) pre	21.80	Adenocarcinoma	Left		Moderately differentiated	
215	Male	Three pre procedure and pre operative	34.31	Adenocarcinoma	Left	6 pT2	Moderately differentiated	
217	Male	Expedited COVID-19, two coronavirus (s	22.78	Adenocarcinoma	Left	5 pT4	Moderately differentiated	GERD
219	Male	Two expedited COVID-19, 2019 coronav	30.73	squamous cell carcinoma	Left	4 pT4	Moderately differentiated	Type II diabetes mellitus
229	Male	Expedited COVID-19, rapid SARS-COV-2	31.20	Adenocarcinoma	Left	4.5 pT3	Moderately differentiated	
239	Female	Pre procedure and pre operative COVID	34.57	Adenocarcinoma	Left	0.1 pT1	Well differentiated	

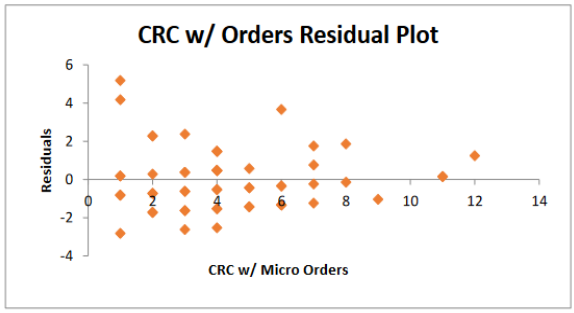
SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.824359
R Square	0.679567
Adjusted R Square	0.673521
Standard Error	1.649641
Observations	55

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	305.879407	305.8794	112.4013	1.04716E-14
Residual	53	144.2296839	2.721315		
Total	54	450.1090909			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*ower 95.0%*	*Upper 95.0%*
Intercept	2.915196	0.434532994	6.708802	1.33E-08	2.043633076	3.786759	2.043633	3.786759
X Variable 1	0.903171	0.08518915	10.60195	1.05E-14	0.732303266	1.074039	0.732303	1.074039

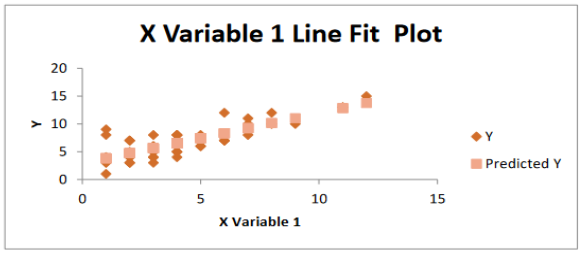


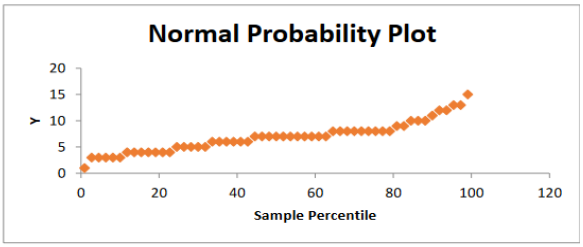
RESIDUAL OUTPUT

Observation	*Predicted Y*	*Residuals*	*idard Residuals*
1	6.52788	1.47211986	0.900768
2	5.624709	0.375290923	0.229635
3	4.721538	-1.721538014	-1.05338
4	6.52788	0.47211986	0.288883
5	5.624709	0.375290923	0.229635
6	3.818367	-0.818366951	-0.50075
7	4.721538	2.278461986	1.394156
8	5.624709	2.375290923	1.453404
9	4.721538	2.278461986	1.394156
10	5.624709	-0.624709077	-0.38225
11	3.818367	0.181633049	0.111138
12	4.721538	-1.721538014	-1.05338
13	3.818367	4.181633049	2.558677
14	6.52788	0.47211986	0.288883
15	3.818367	5.181633049	3.170562
16	4.721538	-0.721538014	-0.4415
17	3.818367	-0.818366951	-0.50075
18	6.52788	-2.52788014	-1.54677
19	6.52788	-1.52788014	-0.93489
20	3.818367	0.181633049	0.111138
21	6.52788	0.47211986	0.288883
22	8.334222	-1.334222265	-0.81639
23	5.624709	-1.624709077	-0.99413
24	4.721538	0.278461986	0.170387
25	6.52788	-1.52788014	-0.93489
26	6.52788	0.47211986	0.288883
27	5.624709	-2.624709077	-1.60602
28	8.334222	-0.334222265	-0.20451
29	6.52788	1.47211986	0.900768
30	3.818367	-2.818366951	-1.72452
31	7.431051	-1.431051202	-0.87564
32	7.431051	0.568948798	0.348131
33	12.85008	0.14992242	0.091735
34	8.334222	-1.334222265	-0.81639
35	5.624709	-1.624709077	-0.99413
36	9.237393	1.762606672	1.078512
37	10.14056	-0.140564391	-0.08601
38	12.85008	0.14992242	0.091735
39	6.52788	1.47211986	0.900768
40	8.334222	-1.334222265	-0.81639
41	7.431051	-1.431051202	-0.87564
42	9.237393	-1.237393328	-0.75714
43	7.431051	-0.431051202	-0.26375
44	10.14056	1.859435609	1.13776
45	5.624709	0.624709077	0.38225
46	9.237393	-0.237393328	-0.14526
47	13.75325	1.246751358	0.762868
48	6.52788	-0.52788014	-0.323
49	7.431051	-0.431051202	-0.26375
50	9.237393	0.762606672	0.466627
51	6.52788	-0.52788014	-0.323
52	8.334222	3.665777735	2.243033
53	11.04374	-1.043735454	-0.63865
54	8.334222	-0.334222265	-0.20451
55	4.721538	-0.721538014	-0.4415

PROBABILITY OUTPUT

Percentile	*Y*
0.909090909	1
2.727272727	3
4.545454545	3
6.363636364	3
8.181818182	3
10	3
11.81818182	4
13.63636364	4
15.45454545	4
17.27272727	4
19.09090909	4
20.90909091	4
22.72727273	4
24.54545455	5
26.36363636	5
28.18181818	5
30	5
31.81818182	5
33.63636364	6
35.45454545	6
37.27272727	6
39.09090909	6
40.90909091	6
42.72727273	6
44.54545455	7
46.36363636	7
48.18181818	7
50	7
51.81818182	7
53.63636364	7
55.45454545	7
57.27272727	7
59.09090909	7
60.90909091	7
62.72727273	7
64.54545455	8
66.36363636	8
68.18181818	8
70	8
71.81818182	8
73.63636364	8
75.45454545	8
77.27272727	8
79.09090909	8
80.90909091	9
82.72727273	9
84.54545455	10
86.36363636	10
88.18181818	10
90	11
91.81818182	12
93.63636364	12
95.45454545	13
97.27272727	13
99.09090909	15





Supplemental Figure 1

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.605074
R Square	0.366115
Adjusted R Square	0.353437
Standard Error	1.162915
Observations	52

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	39.05456972	39.05457	28.87861	2.01971E-06
Residual	50	67.6185072	1.35237		
Total	51	106.6730769			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*ower 95.0%*	*Upper 95.0%*
Intercept	1.426015	0.288499323	4.942871	9.05E-06	0.846546896	2.005483	0.846547	2.005483
X Variable 1	0.94151	0.175201135	5.373882	2.02E-06	0.589608422	1.293412	0.589608	1.293412

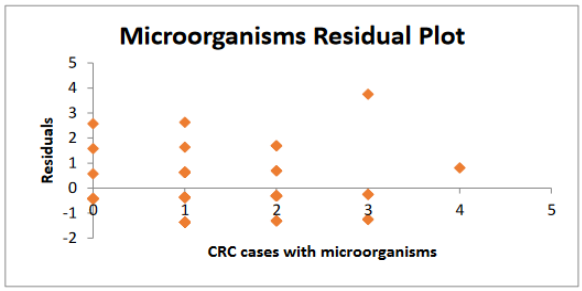
DOI: 10.3844/ajidsp.2024.11.23

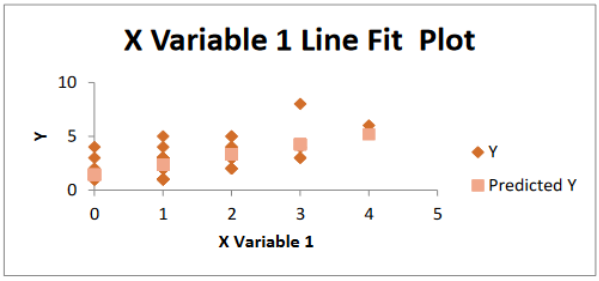
RESIDUAL OUTPUT

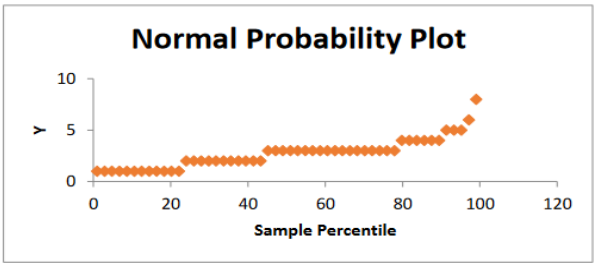
Observation	Predicted Y	Residuals	Standard Residuals
1	2.367525	0.632474902	0.549282
2	3.309035	-1.309035356	-1.13685
3	2.367525	-1.367525098	-1.18765
4	2.367525	0.632474902	0.549282
5	1.426015	0.573985159	0.498486
6	2.367525	-1.367525098	-1.18765
7	2.367525	-0.367525098	-0.31918
8	3.309035	-0.309035356	-0.26839
9	1.426015	-0.426014841	-0.36998
10	2.367525	-0.367525098	-0.31918
11	2.367525	-1.367525098	-1.18765
12	3.309035	-1.309035356	-1.13685
13	2.367525	-1.367525098	-1.18765
14	1.426015	-0.426014841	-0.36998
15	2.367525	-1.367525098	-1.18765
16	3.309035	-1.309035356	-1.13685
17	1.426015	-0.426014841	-0.36998
18	3.309035	-0.309035356	-0.26839
19	2.367525	0.632474902	0.549282
20	1.426015	-0.426014841	-0.36998
21	2.367525	0.632474902	0.549282
22	2.367525	1.632474902	1.417747
23	2.367525	-0.367525098	-0.31918
24	2.367525	-1.367525098	-1.18765
25	2.367525	0.632474902	0.549282
26	1.426015	-0.426014841	-0.36998
27	4.250546	-1.250545613	-1.08606
28	2.367525	0.632474902	0.549282
29	2.367525	-0.367525098	-0.31918
30	1.426015	1.573985159	1.366951
31	3.309035	1.690964644	1.468544
32	2.367525	-0.367525098	-0.31918
33	2.367525	0.632474902	0.549282
34	3.309035	1.690964644	1.468544
35	2.367525	2.632474902	2.286212
36	3.309035	0.690964644	0.600079
37	4.250546	-1.250545613	-1.08606
38	3.309035	-0.309035356	-0.26839
39	3.309035	-0.309035356	-0.26839
40	3.309035	-0.309035356	-0.26839
41	4.250546	-0.250545613	-0.21759
42	2.367525	-0.367525098	-0.31918
43	2.367525	-0.367525098	-0.31918
44	4.250546	3.749454387	3.25627
45	3.309035	-0.309035356	-0.26839
46	2.367525	0.632474902	0.549282
47	3.309035	0.690964644	0.600079
48	4.250546	-0.250545613	-0.21759
49	1.426015	2.573985159	2.235416
50	5.192056	0.807944129	0.701671
51	3.309035	-0.309035356	-0.26839
52	2.367525	-1.367525098	-1.18765

PROBABILITY OUTPUT

Percentile	Y
0.961538462	1
2.884615385	1
4.807692308	1
6.730769231	1
8.653846154	1
10.57692308	1
12.5	1
14.42307692	1
16.34615385	1
18.26923077	1
20.19230769	1
22.11538462	1
24.03846154	2
25.96153846	2
27.88461538	2
29.80769231	2
31.73076923	2
33.65384615	2
35.57692308	2
37.5	2
39.42307692	2
41.34615385	2
43.26923077	2
45.19230769	3
47.11538462	3
49.03846154	3
50.96153846	3
52.88461538	3
54.80769231	3
56.73076923	3
58.65384615	3
60.57692308	3
62.5	3
64.42307692	3
66.34615385	3
68.26923077	3
70.19230769	3
72.11538462	3
74.03846154	3
75.96153846	3
77.88461538	3
79.80769231	4
81.73076923	4
83.65384615	4
85.57692308	4
87.5	4
89.42307692	4
91.34615385	5
93.26923077	5
95.19230769	5
97.11538462	6
99.03846154	8







Supplemental Figure 1

Supplemental Table 2: Outline of the representation of the microbiology tests ordered corresponding to the CRC type and location

CRC histological type	Urine culture	Blood culture	H&E/ IHC stain	G/C chlamydia Amplif	Wound culture & gram stain	PCR for Influenza	Fungal culture + stain	Routine gram stain	Miscellaneous culture
Adenocarcinoma									
Left	98	72	10	2	3	5	5	2	4
Right	41	29	15	1	2	2	3	1	
Medullary adenocarcinoma									
Left									
Right	7								
Mucinous adenocarcinoma									
Left	4	6			1			1	
Right	1								
Signet-Ring cell Adenocarcinoma									
Left	3								
Right	5								
Squamous Cell Carcinoma									
Left	6	2							
Neuroendocrine Carcinoma									
Left									
Totals	165	109	25	3	6	7	8	4	4

Supplementary Table 2: Continuation

CRC histological type	AFB (culture + stain)	Stool GI panel	Stool Culture/ EIA	MRSA Screen	C. difficile toxin DNA amplify	Respiratory culture + stain	Mycoplasma pneum PCR	Mycobacteria/ TB	OVA + para microscopic
Adenocarcinoma									
Left	4	9	5	8	6	2	1	1	2
Right	2		2	6	3	2			
Medullary adenocarcinoma									
Left									
Right									
Mucinous adenocarcinoma									
Left									1
Right									
Signet-Ring cell adenocarcinoma									
left									
right				1					
Squamous Cell Carcinoma									
Left									
Neuroendocrine Carcinoma									
Left									
Totals	6	9	8	15	10	4	1	1	3

Supplementary Table 2: Continuation

CRC histological type	Anaerobe culture	Salmo/shigella/ campy culture & toxin	Cryptosporidium and giardia AG by EIA	Microsporidia exam	Cryptosporidia/ cyclospora stain	Aerobic/ anaerobic culture +gram stain	Body fluid culture
Adenocarcinoma							
Left	6	1	2	1	1	1	1
Right	4		1				2
Medullary adenocarcinoma							
Left							
Right							
Mucinous adenocarcinoma							
Left						1	
Right							
Signet-Ring cell adenocarcinoma							
Left							
Right							
Squamous Cell Carcinoma							
Left							
Neuroendocrine Carcinoma							
Left							
Totals	10	1	3	1	1	2	3

Supplementary Table 2: Continuation

CRC histological type	Respiratory syncytial virus PCR	Surgical tissue culture + stain	Campylobacter culture	Bronchoscopy culture + gram stain	*H. pylori* AG by EIA	Routine occular culture
Adenocarcinoma						
Left						
Right	3	3	1	1	1	1
Medullary adenocarcinoma						
Left						
Right						
Mucinous adenocarcinoma						
Left						
Right						
Signet-Ring cell adenocarcinoma						
Left						
Right						
Squamous Cell carcinoma						
Left						
Neuroendocrine carcinoma						
Left						
Totals	3	3	1	1	1	1