

RESEARCH ARTICLE

Editorial Process: Submission:02/25/2024 Acceptance:08/02/2024

Evolution of Colorectal Cancer Trends and Treatment Outcomes: A Comprehensive Retrospective Analysis (2019-2023) in West Kazakhstan

Nauryzbay Imanbayev^{1*}, Yerbolat Iztleuov², Arip Koishybaev³, Nurgul Kereyeva⁴, Anar Tulyayeva¹, Dinara Zholmukhamedova⁴, Azamat Zharylgapov⁴

Abstract

Objective: To determine the demographic and clinical characteristics of individuals diagnosed with colorectal cancer. **Methods:** A retrospective study was conducted on 650 patients diagnosed with colorectal cancer in West Kazakhstan from 2019 to 2023. Statistical analysis was performed to explore the relationships between various factors and outcomes, using significance tests and regression techniques. **Results:** The study included 650 colorectal cancer patients, with 59.7% males and 40.3% females. Age distribution showed 63.1% between 24-65 years and 36.9% over 65, with no gender-based age differences. Nationality significantly influenced patient composition (63.8% Kazakh, 36.2% Russian, $P=0.03$). KRAS mutations (76.0% negative) and tumor morphology (40% adenocarcinoma, $P=0.02$) displayed varied associations. Univariate logistic regression revealed links between demographic/clinical factors and cancer outcomes. Multivariate analysis emphasized age, stage of cancer, expansion, involvement of lymphatic and metastasis in cancer progression. Nomogram predictive modeling incorporated gender, tumor form, stage, and infiltration. Evaluation in a validation cohort showed good differentiation ($AUC=0.6293$) and calibration. The findings provide insights into colorectal cancer demographics, progression, treatment, and mortality, aiding personalized interventions. **Conclusion:** this study reveals critical insights into demographics, treatment, and prognosis. Emphasizing the complexity of CRC, the study highlights age, gender, and tumor characteristics' impact on progression and mortality. A developed nomogram model offers clinicians a practical tool for personalized treatment decisions, enhancing prognosis discussions with patients.

Keywords: Colorectal neoplasms- disease trends- treatment outcome- retrospective studies- Kazakhstan

Asian Pac J Cancer Prev, 25 (8), 2773-2785

Introduction

Colorectal cancer ranks third in terms of worldwide prevalence, accounting for around 10% of all cancer cases [1]. Furthermore, it ranks as the top second cause of cancer-related fatalities on a global scale. Colorectal cancer mostly affects adults aged 50 and older, posing a huge danger to public health worldwide by greatly influencing illness and death rates. Tackling this widespread and alarming problem is essential for efficient healthcare administration and preventive measures [2]. Gaining a comprehensive understanding of the complex relationship between multiple factors that affect colorectal cancer trends, as well as appreciating the characteristics of the disease, treatment options, and factors that predict outcomes, is crucial for improving patient care and maximizing clinical results. In light of the current

situation, it is crucial to carry out thorough investigation in order to understand and unravel these complex processes [3]. There are multiple variables that have an impact on the progression of colorectal cancer, which is a multifaceted disease [4]. As a result, it is essential to conduct a thorough evaluation that takes into account patient demographics, characteristics of the tumor, treatment modalities, and variables that influence the prognosis [5]. This research aims to examine the therapeutic patterns, trends, clinico-pathological features, and other contributing elements that shape the landscape of colorectal cancer therapies in West Kazakhstan.

Local staging of colorectal cancer as assessed by MSCT and histological findings are consistent. This correlation is positive and strong, showing great agreement. The results imply that colonography MSCT tests may improve local stage T2 colorectal cancer detection [6]. Calculating the

¹Department of oncology, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan. ²Department of Radiologists of the NJSK ZKMU named after M. Ospanov, MC NCJSC Marat Ospanov Western-Kazakhstan Medical University, Kazakhstan. ³Department of Oncology of the NJSK ZKMU named after M. Ospanov MC NCJSC Marat Ospanov Western-Kazakhstan Medical University, Kazakhstan. ⁴Department of Oncology, MC NCJSC Marat Ospanov Western-Kazakhstan Medical University, Kazakhstan. *For Correspondence: nauryzbai92@mail.ru

photoluminescence intensity is one of the steps involved in establishing whether or not the small bowel is viable in the experiment [7]. MRI is a crucial tool in the realm of medicine. In order to generate comprehensive pictures of the interior structures of the human body, magnetic resonance imaging machines make use of radio waves and strong magnetic fields. These images are helpful in the diagnosis and comprehension of a variety of illnesses [8]. In concert with the ever-evolving understanding of CRC, the significance of tailored therapeutic approaches cannot be overstated [9]. This necessitates a thorough exploration of the surgical treatment patterns that underscore the clinical management of CRC patients within the studied timeframe [10]. Colonoscopy is the gold standard for CRC screening due to its ability to detect and remove precancerous polyps. Regular colonoscopies have been shown to reduce CRC incidence and mortality by allowing for early intervention. The fecal occult blood test (FOBT), including guaiac-based FOBT and fecal immunochemical tests (FIT), detects hidden blood in the stool, which can be an early sign of CRC. Positive results from these tests often lead to further diagnostic procedures like colonoscopy [11,12].

It is crucial to recognize the diverse approaches employed by surgeons in pelvic organ prolapse treatment. The various surgical techniques utilized, depending on the surgeon's expertise, aim to maximize patient satisfaction and restore pelvic organs to their original positions, as indicated by previous research [13]. This underscores the importance of understanding and adapting surgical strategies within the evolving landscape of colorectal cancer trends and treatment outcomes in the specified region during the specified time frame. The journey toward optimized outcomes is incomplete without an exploration of prognostic markers that guide clinical decision-making [14]. Therefore, an intricate examination of prognostic indicators associated with CRC within cohort will provide valuable insights into the diverse trajectories that CRC can assume [15].

Precise anticipation of the path and consequences of colorectal cancer is essential for improving clinical judgment and optimizing patient treatment. Conventional prognostic models sometimes focus on certain clinical indications. To improve overall patient outcomes in colorectal cancer, it is crucial to combine varied elements and build more nuanced and accurate prognostic models. This will provide a more thorough knowledge of the illness and its effects [16]. Within this particular framework, the integration of sophisticated prediction techniques such as the nomogram model shows great potential [17]. Nomograms provide a comprehensive method for predicting outcomes, taking into account several factors at the same time and offering an individualized evaluation of risk [18]. By using multivariate logistic regression, these results may provide a precise evaluation of the probability of certain outcomes for an individual [19]. Integrating predictive models into clinical practice has the capacity to improve the accuracy and efficacy of treatment regimens. This allows for customized therapies that consider the complex effects of several variables on the course and death of colorectal cancer. Hence, the present investigation

not only enhances the overall comprehension of colorectal cancer patterns and features, but also emphasizes the need of precise prognostication in directing treatment choices and eventually enhancing patient results. This research seeks to analyze a comprehensive dataset of patients treated at West Kazakhstan between 2019 and 2023 in order to understand the complex nature of colorectal cancer (CRC) in this particular location. This undertaking is emphasized by a methodical technique that conforms to accepted criteria in medical research, guaranteeing the precision and dependability of present discoveries.

The study aims to comprehensively assess the effect of demographical factors on progression of colorectal cancer, focusing on key indicators such as tumor stage, infiltration, lymphatic node involvement, metastasis, and mortality. Analyses reveal associations between age, gender, and nationality with various aspects of cancer progression, shedding light on the multifaceted nature of colorectal cancer. The study investigates the significance of KRAS mutation status in influencing cancer progression and mortality. Additionally, an exploration of the relationship between demographic characteristics and cancer treatment utilization highlights the role of metastatic status in treatment decisions. Building on these findings, a nomogram predictive model is developed, incorporating demographic factors and tumor characteristics to estimate mortality probabilities. Performance of the predictive model is assessed in a validation cohort, demonstrating its ability to differentiate and categorize outcomes in real clinical contexts. The nomogram's clinical utility is underscored by its potential impact on treatment decisions and its role in facilitating informed patient conversations about prognosis and mortality risk.

Materials and Methods

Study design

A retrospective cohort studies

Study place

The research was carried out in the region of West Kazakhstan, which includes the territories of West Kazakhstan Province. The study was specifically conducted at the West Kazakhstan Marat Ospanov Medical University and affiliated healthcare institutions.

Sample Size

The study involved a cohort of 650 patients diagnosed with colorectal cancer in West Kazakhstan. Among these patients, those identified as Russians are individuals of Russian ethnicity living in Kazakhstan. They form a distinct ethnic group within the region.

Study duration

2019 to 2023

Data Collection

A pretested questionnaire was used to collect data from the medical records of all eligible patients. Patient eligibility for the study required a verified colorectal cancer (CRC) diagnosis in the hospital's pathology registry, with treatment or diagnosis occurring between 2019 and 2023. Exclusions comprised metastatic lesions,

recurrent CRC, and invasive tumors from nearby organs. The first stage was conducting a retrospective cohort research using data from the Pathology Registry. This dataset included extensive patient information, such as demographics, background, age at diagnosis, tumor location, and pathological diagnosis.

Eligibility

Patients eligible for the study had to possess a verified diagnosis of colorectal cancer with recorded information in the hospital's pathology registry. Additionally, they should have received a diagnosis or treatment for CRC during the period from 2019 to 2023. Those with lesions from distant malignant tumors, those with recurring colorectal cancer, and those whose lesions were invaded by malignant cancer from nearby body organs were not allowed to participate in the research.

Outcome variables

CRC Character

CRC character refers to the clinical and demographic characteristics of colorectal cancer, including tumor morphology, stage, depth of invasion, lymph node involvement, and presence of metastasis. These factors collectively define the initial presentation and classification of colorectal cancer in patients.

CRC Progression

CRC progression refers to the advancement of colorectal cancer from its initial diagnosis to more severe stages, including increased tumor size, deeper invasion into surrounding tissues, and the spread to lymph nodes or distant organs.

CRC Treatment

CRC treatment refers to the therapeutic interventions administered to colorectal cancer patients, including surgery, chemotherapy, radiotherapy, and targeted therapies. It evaluates the factors influencing the likelihood and type of treatment received.

CRC Related Mortality

CRC related mortality refers to deaths attributable to colorectal cancer, considering factors such as age, gender, nationality, genetic mutations (e.g., KRAS), and tumor characteristics.

CRC Related Survival

CRC related survival refers to the duration of survival after a diagnosis of colorectal cancer, taking into account the influence of clinical and demographic factors.

Statistical Analysis

The study employed IBM SPSS Statistics 26 for statistical analysis to explore the relationships between independent and dependent variables. The analytical framework was guided by the Union for International Cancer Control's Manual of Clinical Oncology. To ensure robust findings, a power analysis was conducted to determine the requisite sample size for detecting significant demographic associations with

desired outcomes, adhering to a conventional statistical power threshold of 0.80 or higher. The power analysis incorporated parameters such as anticipated effect sizes of relationships, significance level (alpha), and desired statistical power. The established power analysis indicated that a sample size of 180 participants would be sufficient to detect significant correlations with the specified statistical power. Presentation of the data involved tabular and graphical representation, with descriptive statistics expressed in terms of frequency and relative frequency.

Inferential statistics were harnessed through the application of the Chi-square test and multivariate logistic regression techniques. The Chi-square test was employed to assess associations between categorical variables, while multivariate logistic regression allowed for the examination of the simultaneous impact of multiple independent on dependent variable. A significance level of $p < 0.05$ was adopted, signifying statistical significance. Consequently, any p-value below this threshold was considered indicative of a statistically significant relationship between variables. This comprehensive approach ensured a rigorous examination of the data, facilitating the identification and interpretation of meaningful associations within the context of the study's objectives.

Nomogram for Predicting Mortality

Our thorough investigation of 650 cases began with univariate logistic regression to identify colorectal cancer mortality risks. Multivariate logistic regression models used clinically relevant variables with P-values below 0.05. During model development, a backward stepwise selection strategy with a P-value admission threshold of 0.1 and a retention condition of 0.05 was applied. Models containing 70% random instance samples were shown as nomograms. Discrimination and calibration studies evaluated prediction performance. Performance of the model to distinguish CRC survival was assessed using the area under the ROC curve. In the Hosmer Lemeshow test, calibration confirmed the model probability alignment with observed outcomes. GraphPad Prism 9.5.1.733 was used for AUC assessments, with a statistical significance of $P < 0.05$ in all tests. Internal validation happened on 30% of occurrences.

Results

Distribution of study Characteristics

Table 1 outlines the socio demographic and baseline clinical feature of colorectal cancer patients, offering valuable insights into the distribution of key variables among the studied population. The cohort consists of 650 patients, with a slight predominance of males (59.7%) over females (40.3%). Age distribution reveals that 63.1% fall within the 24-65 years old range, while 36.9% are older than 65. Notably, there is no significant age-based difference between genders ($P=0.965$). Nationality appears to influence the patient composition significantly, with 63.8% being Kazakh and 36.2% Russian ($P=0.03$). KRAS mutation status exhibits no significant gender-based disparity ($P=0.86$), and the majority of patients (76.0%)

Table 1. Patients Demographics and Baseline Clinical Features

Variables	Sub category	Frequency	Male (Percentage)	Female (Percentage)	P-value
Gender		650 (100)	388 (59.7)	262 (40.3)	-
Age	24-65 years old	410 (63.1)	245 (59.8)	165 (40.2)	0.965
	>65 years old	240 (36.9)	143 (59.6)	97 (40.4)	
Nationality	Kazakh	415 (63.8)	257 (61.9)	158 (38.1)	0.03
	Russian	235 (36.2)	131 (55.7)	104 (44.3)	
KRAS mutations	Positive	156 (24.0)	94 (60.3)	62 (39.7)	0.86
	Negative	494 (76.0)	294 (59.5)	200 (40.5)	
Tumor morphology	Adenocarcinoma with low, middle and high-grade	260 (40.0)	158 (60.8)	102(39.2)	0.02
	Others	390 (60.0)	230 (59.0)	160 (41.0)	
Stage of tumor	First Stage	462 (71.1)	277 (60.0)	185 (40.0)	0.07
	Last stage	188 (29.9)	111 (59.0)	77 (41.0)	
Tumor infiltration	Low tumor infiltration (Mucosa + Submucosa layers)	282 (43.4)	171 (60.6)	111 (39.4)	0
	High tumor infiltration (Mucosa + Submucosa + Muscle + Serosa layers)	368 (56.6)	217 (59.0)	151 (41.0)	
Lymphatic nodes involvement	≤3 lymph nodes	457 (70.3)	272(70.1)	185(29.9)	0.02
	>3 lymph nodes	193 (29.7)	116 (29.9)	77 (29.4)	
Metastasis	Positive	542 (83.4)	322 (59.4)	220 (40.6)	0.04
	Negative	108 (16.6)	66 (61.1)	42 (38.9)	
Treatment	surgical resection + chemotherapy	319 (49.1)	184 (47.4)	135 (51.5)	0.01
	surgical resection + radiation therapy	331 (50.9)	204 (61.6)	127 (38.4)	
Mortality	No	423 (65.1)	254 (60.0)	169 (40.0)	0.08
	Yes	227 (34.92)	134 (59.0)	93 (41.0)	

test negative for KRAS mutations. Tumor morphology shows a statistically significant difference, with 40% having adenocarcinoma with low, middle, and high-grade features (P=0.02). tumor stage, tumor infiltration,

involvement of lymphatic, and metastasis demonstrate varying distributions, providing an overview of the disease progression within the cohort. Treatment modalities also exhibit significant differences (P=0.01), highlighting the

Table 2. Patients Demography and Tumor Characteristics

Variables	Sub category	Odd Ratio (95% CI)	P-value
Age	24 - 65 years	0.122 (0.345, 0.921)	0.041
	older than 65		
Gender	Male	0.182 (0.695, 1.421)	0.973
	Female		
Nationality	Kazakh	0.390 (.236, 1.086)	0.81
	Russian	0.001 (0.401, 0.741)	
KRAS mutations	Positive	1.102 (0.827, 1.467)	0.506
	Negative		
Tumor morphology	Adenocarcinoma	1.020 (0.839, 1.239)	0.002
	Others	0.987(0.868, 1.123)	
Stage of tumor	First Stage	1.021(0.922, 1.131)	0.686
	Last stage	0.950 (0.743, 1.216)	
Tumor infiltration	Low	1.106 (0.919, 1.330)	0.283
	High	0.927 (0.810, 1.062)	
Lymphatic nodes involvement	≤ lymph nodes	1.051(0.947, 1.168)	0.03
	>3 lymph nodes	0.890 (0.701, 1.131)	
Metastasis	Positive	0.991(0.923, 1.063)	0.01
	Negative	1.049 (0.734, 1.499)	

Table 3. The Effect of Demographic Features on the Progression of CRC

Variables	Sub category	Odd Ratio (95% CI)	P-value
Age (years)	24-65	0.423 (0.52, 0.856)	0.04
	>65		
Sex	Male	0.745 (0.253, 1.425)	0.42
	Female		
Nationality	Kazakh	1.238 (0.998, 1.125)	0.74
	Russian		
KRAS	Positive (mutations)	1.024(0.774, 1.345)	0.02
	Negative (mutations)		
Morphology of Tumor	Adenocarcinoma	1.046(0.862, 1.269)	0.04
	Others		
Tumor Stage	First Stage	1.011(0.915, 1.118)	0.02
	Last stage		
Tumor infiltration	Low	1.04(0.869, 1.246)	0.667
	High		
Lymphatic nodes involvement	≤3	0.993(0.897, 1.099)	0.06
	>3s		
Metastasis	Positive	0.988(0.922, 1.059)	0.02
	Negative		

diverse therapeutic approaches employed, with surgical resection and radiation therapy being slightly more prevalent. The mortality rates, while not statistically significant ($P=0.08$), show a trend, with 34.92% of patients succumbing to the disease.

CRC Character and Demographic Features

The findings of the univariate regression analysis are shown in Table 2. This study uncovered a variety of links between demographic and clinical factors, as well as the influence these connections had on important outcomes within our research group. A lot of factors, like the type of tumor, its stage, how deeply it has invaded,

whether it has spread to lymph nodes, and whether it has metastasized, were strongly linked to clear odds ratios and confidence intervals. On the other hand, the correlations between gender, country, and the presence or absence of a KRAS mutation were either less different or did not have statistical significance. These results shed light on the multifaceted character of colorectal cancer, drawing attention to the critical elements that have the potential to greatly impact both the clinical manifestations of the illness and its consequences.

CRC Progression and Demographic Features

Table 3 outlines the results of univariate logistic

Table 4. Influence of Demographic Characteristics on Cancer Treatment

Variables	Sub category	Odd Ratio (95% CI)	P-value
Age (year)	24-65	0.977 (0.866, 1.103)	0.712
	>65		
Sex	Male	0.936 (0.824, 1.062)	0.305
	Female		
Nationality	Kazakh	0.956 (0.851, 1.073)	0.446
	Russian		
Morphology of Tumor	Adenocarcinoma	0.991 (0.821, 1.196)	0.923
	Others		
Tumor Stage	First Stage	0.977 (0.885, 1.077)	0.636
	Last stage		
Tumor infiltration	Low	0.994 (0.834, 1.185)	0.950
	High		
Lymphatic nodes involvement	≤3	0.926 (0.730, 1.173)	0.523
	>3		
Metastasis	Positive	0.895 (0.835, 0.960)	0.002
	Negative		

Table 5. Impact of Demographic Characteristics on CRC Mortality

Variables	Sub category	Odd Ratio (95% CI)	P-value
Age (year)	24-65	1.038 (0.913, 1.180)	0.566
	>65	0.942 (0.769, 1.154)	0.624
Sex	Male	1.017 (0.890,1.162)	0.801
	Female	0.975 (0.802,1.185)	0.867
Nationality	Kazakh	1.089 (0.960,1.235)	0.174
	Russian	0.865 (0.7021,0.64)	0.203
KRAS	Positive (mutations)	1.043 (0.781,1.393)	0.776
	Negative (mutations)		
Morphology Tumor	Adenocarcinoma	1.086 (0.887,1.329)	0.02
	Others	0.948 (0.833,1.078)	0.007
Tumor Stage	First Stage	0.966 (0.873,1.069)	0.007
	Last stage	1.091(0.843, 1.411)	0.046
Tumor infiltration	Low	0.905 (0.756,1.083)	0.002
	High	1.082 (0.936,1.251)	0
Lymphatic nodes involvement	≤3	1.016 (0.914,1.129)	0
	>3	0.964 (0.754,1.234)	0.001
Metastasis	Positive	1.030 (0.716,1.481)	0
	Negative		

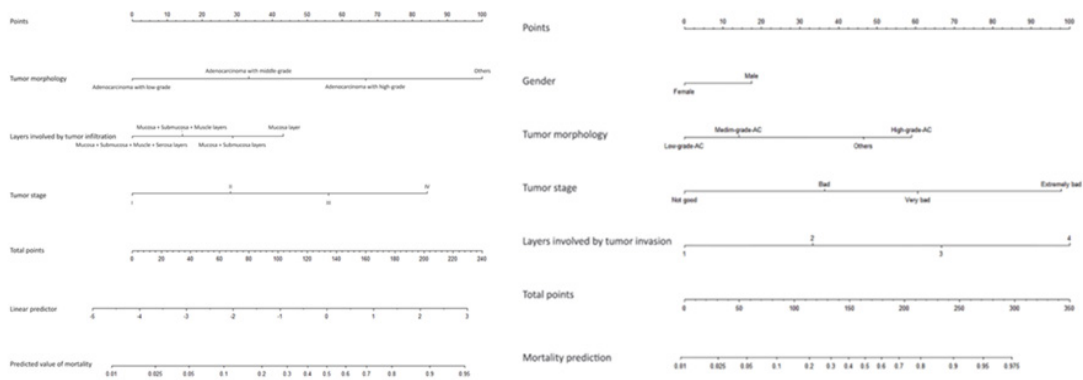


Figure 1. CRC Mortality Prediction Nomograms

regression. Age emerged as a significant factor influencing cancer progression, with individuals aged 24-65 years showing a decreased in risk (p=0.04) as compared to those over 65 years. Gender did not exhibit a statistically significant association, with males and females having ORs of 0.745 (95% CI: 0.253-1.425, p=0.42). Nationality (Kazakh or Russian) did not demonstrate a significant

impact on cancer progression, with Kazakh nationality having an OR of 1.238 (95% CI: 0.998-1.125, p=0.74), and Russian nationality having an OR of 0.852 (95% CI: 0.652-1.523, p=0.64). KRAS mutations displayed a marginally significant association (p=0.02), with positive mutations yielding an OR of 1.024 (95% CI: 0.774-1.345). Tumor morphology, tumor stage, tumor infiltration,

Table 6. CRC and Demographic Traits

Variables	Sub category	Odd Ratio (95% CI)	P-value
Morphology Tumor	Adenocarcinoma	1.032 (0.745,1.429)	0.03
	Others		
Tumor Stage	First Stage	0.935 (0.658,1.327)	0.02
	Last stage		
Tumor infiltration	Low	1.216 (0.880,1.680)	0.04
	High		
Lymphatic nodes involvement	≤3	0.824 (0.582,1.167)	0.03
	>3		

Table 7. Impact of Demographic Characteristics on Cancer Progression

Variables	Sub category	Odd Ratio (95% CI)	P-value
Lymphatic nodes involvement	≤3	0.997(0.680,1.462)	0.002
	>3		
Metastasis	Positive	1.156(0.724,1.846)	0.005
	Negative		

Table 8. Influence of Demographic Characteristics on CRC Mortality

Variables	Sub category	Odd Ratio (95% CI)	P-value
Sex	Male	0.969(0.701,1.339)	0.09
	Female		
Morphology Tumor	Adenocarcinoma	1.037(0.749,1.434)	0.07
Tumor Stage	First Stage	0.934(0.658,1.324)	0.01
	Last stage		
Tumor infiltration	Low	1.195(0.867,1.648)	0.03
	High		

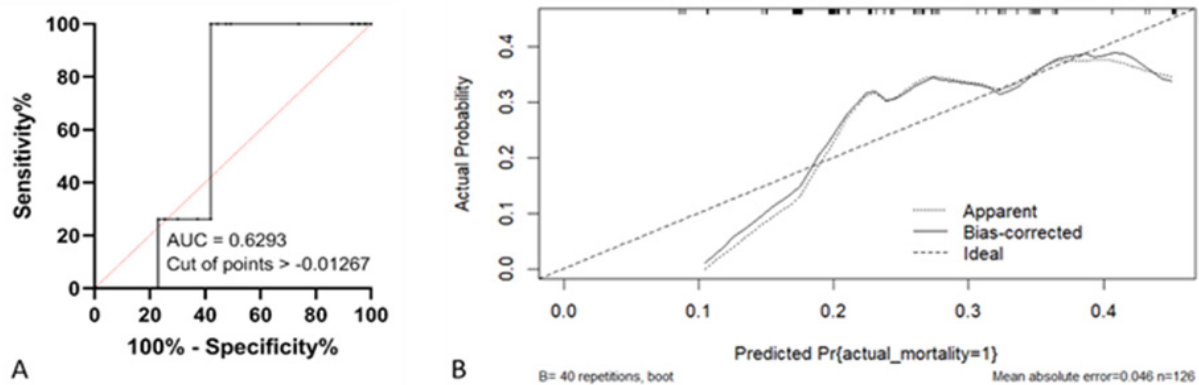


Figure 2. (A) Receiver Operating Characteristic (ROC) Curves (B) Calibration Plots.

lymphatic node involvement, and metastasis showed varying degrees of association with cancer progression, each accompanied by corresponding ORs, 95% CIs, and p-values. These statistical findings contribute crucial insights into the demographic determinants of colorectal cancer progression, offering a basis for targeted interventions and personalized treatment strategies.

CRC Treatment and Demographic Characteristics

Table 4 outlines the results of univariate logistic regression and showing that regarding age, the study found that individuals aged 24-65 years old had a slightly lower odds ratio (0.977) of affecting cancer treatment compared to those over 65 years old (OR = 1.038). Gender showed no significant impact on cancer treatment, with male and female patients having odds ratios of 0.936 and 1.103, respectively. Similarly, nationality did not seem to play a significant role, as Kazakh and Russian patients had odds ratios of 0.956 and 1.083, respectively. Morphology of Tumor, stage of tumor, infiltration, lymphatic nodes involvement, and metastasis were also assessed. None of the variables demonstrated a statistically significant impact on cancer treatment, as their respective p-values

were above conventional significance thresholds (typically 0.05). Notably, the presence of metastasis showed a significant impact, with a p-value of 0.002, indicating that patients with negative metastasis had a considerably higher odds ratio (1.764) compared to those with positive metastasis (OR = 0.895). Interestingly, the interpretation of the odds ratios reveals that patients without metastasis (negative) have 1.764 times odds of receiving cancer treatment as compared to those having metastasis (positive). This implies that the absence of metastasis is associated with a significantly increased likelihood of undergoing cancer treatment, highlighting the importance of considering metastatic status in the assessment and management of CRC patients.

CRC Related Mortality and Demographic Characteristics

Table 5 outlines the results of univariate logistic regression and shows that age, a crucial factor in cancer outcomes, reveals that individuals of age group 24-65 years exhibit an OR of 1.038 (CI: 0.913, 1.180) with a insignificant p-value of 0.566, while those above 65 years of age have an OR of 0.942 (CI: 0.769, 1.154) with a p-value of 0.624. Gender does not significantly impact

mortality, as males show an OR of 1.017 (CI: 0.890, 1.162), and females exhibit an OR of 0.975 (CI: 0.802, 1.185). Nationality, particularly Kazakh and Russian, indicates a non-significant impact on mortality. Notably, KRAS mutations, a genetic factor, show no significant association (p-value = 0.776). Tumor morphology is significant, with adenocarcinoma associated with an OR of 1.086 (CI: 0.887, 1.329) and a p-value of 0.020, while other morphologies have a lower OR of 0.948 (CI: 0.833, 1.078) with a p-value of 0.007. The tumor stage, infiltration, lymphatic nodes involvement, and metastasis all demonstrate varying degrees of significance, highlighting the complex interplay of these factors in colorectal cancer-related mortality. In summary, the findings suggest that age, tumor morphology, stage, and several other factors contribute to colorectal cancer-related mortality, providing valuable insights for prognosis and potential targeted interventions in clinical settings.

CRC and Demographic Characteristics

Table 6 presents the results of multivariate logistic regression and shows that the odds ratio for adenocarcinoma is 1.032 with a 95% CI of 0.745 to 1.429, and the p-value is 0.03. This suggests a marginal association with adenocarcinoma, although the result is not statistically significant. In terms of tumor stage, the odds ratio for the first stage is 0.935 with a 95% CI of 0.658 to 1.327, and the p-value is 0.02. This indicates a lower likelihood of being in the first stage compared to the last stage, and the association is statistically significant. Regarding tumor infiltration, the odds ratio for low infiltration is 1.216 with a 95% CI of 0.880 to 1.680, and the p-value is 0.04. Although the odds ratio suggests an increased likelihood of low infiltration, the result is not statistically significant. Finally, for lymphatic nodes involvement, the odds ratio for ≤ 3 lymph nodes are 0.824 with a 95% CI of 0.582 to 1.167, and the p-value is 0.03. This implies a decreased likelihood of involvement when ≤ 3 lymph nodes are affected, and the association is statistically significant. In summary, the multivariate logistic regression analysis reveals varied impacts of demographic characteristics on different cancer features, with some associations being statistically significant while others are not. These findings contribute valuable insights into the complex relationships between demographics and cancer characteristics.

CRC Progression and Demographic Characteristics

Table 7 offers a comprehensive analysis of the factors linked to colorectal cancer (CRC) progression, using multivariate logistic regression to examine the influence of lymphatic node involvement and metastatic status. In this case, CRC progression is defined as the growth of cancer, which includes an increase in the number of affected lymph nodes and presence of metastasis.

Patients were divided into two groups depending on the number of lymph nodes affected: one group had 3 or less affected lymph nodes, and another group had more than 3 affected lymph nodes. The odds ratio (OR) for patients with 3 or fewer involved lymph nodes is 0.997 (95% CI: 0.680, 1.462). This OR is close to 1 which means that the chance of cancer progression among patients

with 3 or fewer involved lymph nodes is almost equal to those having more than three involved lymph nodes. In this comparison, the reference category was patients with more than three involved lymph nodes. However, despite showing nearly similar chances of progression according to OR; it achieved statistical significance at p-value = 0.002 indicating that even such a slight difference cannot be attributed to random variation alone but may reflect some relationship between CRC development and number of lymph nodes involved. Patients were divided into two groups based on their metastatic status, either positive or negative for metastasis. The OR for patients with positive metastasis is 1.156 (95% CI: 0.724, 1.846), compared to those without metastasis (the reference group). This OR suggests a slightly elevated likelihood of cancer progression for patients with positive metastasis. The p-value of 0.005 is statistically significant, indicating that the observed association between metastasis and cancer progression is unlikely to be due to random variation. This underscores the significance of metastatic status in predicting the progression of CRC.

The outcome being assessed in this analysis is the progression of CRC. This includes things like an increase in the number of affected lymph nodes and the presence of metastasis. The ORs reported are derived from a multivariate logistic regression model, which considers multiple variables simultaneously to provide a more accurate assessment of the relationship between each factor (lymphatic node involvement and metastatic status) and the outcome (CRC progression). The results of this analysis show how important it is to consider lymphatic node involvement and metastatic status in predicting CRC progression. The statistical significance of the findings (p-values of 0.002 and 0.005 for lymphatic node involvement and metastasis, respectively) underscores that these associations are not random. This further emphasizes the importance of these factors in evaluating CRC progression by clinicians as well as the need for rigorous statistical methods to validate and interpret such associations.

In conclusion, multivariate logistic regression analysis shows that both lymphatic node involvement and metastatic status are significant predictors of CRC progression. These findings have important implications for clinical management and treatment planning for patients with CRC, which necessitates a thorough assessment and consideration of these factors.

CRC Related Mortality and Demographic Characteristics

Table 8 outlines the result of multivariate logistic regression and shows that in terms of gender, the odds ratio for males is 0.969 (95% CI: 0.701, 1.339) with a p-value of 0.09, suggesting a non-significant trend towards decreased mortality compared to females. Tumor morphology, specifically adenocarcinoma, exhibits an odds ratio of 1.037 (95% CI: 0.749, 1.434) and a p-value of 0.07, indicating a borderline non-significant association with mortality. The stage of tumor presents interesting findings, with the first stage showing an OR of 0.934 (95% CI: 0.658, 1.324) and a p-value of 0.01, suggesting a potential protective effect against mortality. Conversely,

the last stage does not reach statistical significance, indicating a more complex relationship between tumor stage and mortality. Tumor infiltration demonstrates an odds ratio of 1.195 (95% CI: 0.867, 1.648) with a p-value of 0.03 for the “Low” category, suggesting a non-significant inclination towards increased mortality compared to the “High” category.

Nomogram Predictive Model

Figure 1 shows death probability is predicted by the model. After multivariate logistic regression, we built a nomogram model that includes gender, tumor form, stage, and infiltration as risk factors. The cumulative score was the total of component scores. After drawing a vertical line from the calculated score to the Mortality axis, the anticipated mortality probability was determined. Suppose a patient with high-grade cancer scores 25. Three levels of infiltration contribute 15 points to this patient's score. The tumor is stage IV, scoring 82.5 points. A 72.5% mortality probability is projected for this patient's 203.75 score. This estimated statistic might influence treatment decisions and enable informed patient conversations.

Predictive Model Evaluation

Evaluation of the model's performance included determining how well it could differentiate between different things and how well it could calibrate. As a consequence of the creation of the ROC curves shown in Figure 2A, the validation cohorts had an AUC of 0.6293. Taking into consideration these facts, it can be concluded that the model has a good capacity to differentiate and categorize in real clinical contexts. In addition, the calibration of the model was investigated by means of the Hosmer-Lemeshow test, which resulted in a Hosmer-Lemeshow chi-square value of -287.45 with 5 degrees of freedom. Further proof of the correctness of the evaluation is provided by the calibration curve, which is shown in Figure 2B. There is a significant degree of concordance between the 208 predicted probabilities and the observed probabilities, as shown by the value of $P = 1$.

Discussion

The persistence of CRC as a global health issue compels us to delve into its many intricacies in order to get a more understanding. This study was conducted at the West Kazakhstan Medical University. The aim of this research was to examine the patterns of colorectal cancer, pathological, clinical features, treatment, and prognostic variables, among patients treated from 2019 to 2023. The detailed consideration of the data yielded valuable insights into the intricate nature of this ailment. The analysis of demographic factors revealed the significant impact of age, gender, and country on several aspects of CRC therapy and outcomes. Notably, those over the age of 65 had a notable inclination towards reduced disease advancement, which corresponds with the results of a study emphasizing the link between older age and a less aggressive nature of colorectal cancer [20].

However, the discovery that female patients had a decreased likelihood of cancer progression contradicted

the findings with other study. The disparities among the both genders underscore the intricate interplay of factors that impact the outcomes of colorectal cancer. Similarly, an examination of gender related disparities in colorectal cancer occurrence, screening participation, methods of diagnosis, disease progression, and survival underscores the significance of understanding gender disparities in colorectal cancer [21]. The study proposes that implementing more focused treatments might enhance the prevention and early detection of diseases, ultimately resulting in improved outcomes for patients. A recent investigation on inequalities in colorectal cancer risk based on sex and gender revealed that women had a higher susceptibility to colon cancer on the right-side compared to males. This kind of cancer is linked to a more severe form of neoplasia when compared to the colon cancer on the left-side [22]. This research highlights the need of using gender-specific approaches in screening, treatment, and preventative procedures to enhance patient outcomes.

The analysis deemed it crucial to investigate the clinico-pathological characteristics of colorectal cancer, such as morphology of the tumor, stage, infiltration, lymph node involvement, and metastasis. Surprisingly, the morphology of the tumor was shown to be strongly correlated with the occurrence of cancer and the predicted outcome. The progression of the disease was shown to have significant adverse associations with adenocarcinoma (high and middle grade) situations. These results are similar to the results found in another study that highlights the importance of tumor differentiation in terms of prognostic value [23]. Furthermore, these findings, showing correlation between the tumor stage and the and disease progression are similar to previous studies [24]. Another research offers evidence that supports the novel understanding of how tumor infiltration impacts the progression of the illness. This contributes to the ongoing discourse on the prognosis of colorectal cancer [25]. The intricate interplay between clinical factors demonstrates a comprehensive comprehension of colorectal cancer prognostication.

The research revealed that age plays a crucial role in cancer advancement, with those between the ages of 24 and 65 exhibiting a lower risk compared to those who are 65 years or older. This discovery aligns with previous research that has shown that increasing age is the primary and most significant determinant for cancer, both in general and for many specific forms of cancer [26]. The prevalence of cancer increases beyond the age of 50, regardless of mutations seen in these malignancies and the fact that cancer may be detected at any age [27]. The anticipated rise in cancer cases presents significant problems to the healthcare system, particularly around midlife, which is a crucial stage for both cancer susceptibility and prevention. The statistical results provide important insights into the demographic factors that influence the course of colorectal cancer. This information may be used to develop targeted interventions and tailored treatment options. The current study finding is similar to the existing literature on the impact of age, tumor stage, and lymph node involvement on the development of colorectal cancer, when compared to earlier studies [28,29]. However, the correlations found

between tumor and cancer progression provide new perspectives, necessitating more investigation.

The research determined that factors such as age, gender, country, and numerous tumor features did not have a substantial influence on cancer therapy, with the exception of the occurrence of metastasis. Absence of metastases was correlated with a much higher probability of receiving cancer therapy. This discovery emphasizes the significance of taking into account the metastatic status while evaluating and treating cancer patients within the framework of the research. When engaging in discussions with other researchers, it is crucial to take into account the wider body of evidence about the influence of age on cancer therapy. Prior research has shown that cancer clinical trials tend to have a disproportionately low participation rate among older persons, namely those aged 65 and above, despite this age group accounting for approximately 50% of all cancer patients. The lack of adequate representation may impact the capacity to apply treatment results to a wider community and hinder the creation of evidence-based methods for this specific group [30].

The mentioned research emphasizes the importance of age, tumor form, stage, and several other parameters in relation to death caused by colorectal cancer. The death rates for all malignancies combined exhibit a significant correlation with age, with the greatest rates seen among the elderly population. Individuals in the age group of 65 years and above constitute 58% of newly identified cancer cases in industrialized nations [31]. Research done in Finland revealed that cancer may be classified as an age-related ailment due to the fact that the occurrence of most malignancies escalates with age, particularly accelerating around middle age. Enhancing the patient's quality of life is a crucial objective, and some prevalent forms of cancer have a high likelihood of being cured if identified promptly and managed in accordance with optimal methods [32].

The results pertaining to the diverse effects of demographic characteristics on various cancer features align with previous research that employed logistic regression analysis to examine the association between demographic factors and cancer outcomes. For instance, a study investigating the susceptibility to colorectal cancer in the relatives (1st degree) discovered odds ratios ranging from 1.23 for individuals with hyperplastic polyps to 1.44 for those with tubulovillous adenomas [33]. This research elucidates that the correlation between demographic parameters and cancer outcomes is contingent upon the particular form of cancer and the attributes of the population under investigation. Separate research examined the correlation between preoperative variables and the occurrence of adenocarcinoma or high-grade dysplasia by using both univariate and multivariate logistic regression models. The research revealed a lack of consistency between the findings of the univariate regression and multiple logistic regression. This emphasizes the need of taking into account numerous variables when evaluating the association between demographic features and cancer outcomes [34].

The present research further revealed the importance of involvement of lymph node and metastasis in predicting

the course of cancer. These are the same results as found in another study emphasizing the significance of comprehending the mechanisms by which tumor cells spread to lymph nodes and the impact of lymph node metastasis on the prognosis and treatment of cancer patients [35]. Ultimately, these data emphasize the statistical importance of involvement of lymphatic node and metastasis in forecasting the advancement of cancer.

The tumor stage exhibits intriguing results, with the first stage showing an OR of 0.934 and a p-value of 0.01, indicating a possible safeguarding impact against death. In contrast, the last stage does not achieve statistical significance, suggesting a more intricate correlation between tumor stage and death. This discovery aligns with research that identified a higher likelihood of death in people with more progressed stages of colorectal cancer [36]. To summarize, the results of the colorectal cancer study align with previous research indicating higher mortality rates in males compared to females. Additionally, the study reveals a nuanced connection between tumor stage and mortality. It emphasizes the significance of evaluating tumor morphology and infiltration in order to accurately assess the mortality risk of patients with colorectal cancer.

A nomogram model that predicts the chance of death in individuals with colorectal cancer is an invaluable tool for guiding treatment choices and improving patient consultations. Various research has focused on creating prediction models for mortality caused by colorectal cancer, highlighting the importance of these tools in clinical settings. Research published in the British Journal of Cancer in 2020 created and verified a prognostic model to determine the likelihood of mortality from colorectal cancer within 90, 180, and 365 days following diagnosis. The model used integrated national cancer and death statistics to forecast mortality, with the objective of rectifying the imprecision and lack of clarity in physicians' prognostications of cancer survival [37]. A separate study used clinicopathologic and genetic information to create a Bayesian risk prediction model for predicting the likelihood of death from colorectal cancer. The model successfully determined the significant factors in predicting the stage classification and mortality of colorectal cancer. It highlighted the need of using diverse data sources to provide precise forecasts [38]. In addition, research published in BMC Surgery in 2023 sought to create a nomogram model for predicting the post-surgical overall survival of patients with colorectal cancer. The research emphasized the significance of nomogram models in forecasting patient outcomes and directing therapeutic decision-making [39]. These studies emphasize the use of prediction models, such as nomograms, in guiding therapeutic choices and enhancing patient care in the setting of colorectal cancer. Utilizing such models may assist healthcare practitioners in calculating death probability, customizing treatment approaches, and participating in well-informed conversations with patients on their prognosis and care alternatives.

This study significantly enhanced the decision making by health professional through a nomogram derived from the results of multivariate logistic regression

analysis. This novel method considers a diverse array of sociodemographic, clinical and pathological variables to provide a precise assessment of the probability of mortality in individuals diagnosed with colorectal cancer. Significantly, the predictions generated by the nomogram align well with the existing body of research. The recognition of tumor morphology, tumor stage, and lymph node infiltration as crucial prognostic indicators, for instance, aligns with the outcomes of prior investigations [16,40]. The broad range of applications of nomogram offers clinicians a valuable tool to create personalized treatment plans and have informed discussions with patients on prognosis and therapeutic choices.

Limitations

It is important to recognize certain constraints in the present investigation. Conducting the research retrospectively may have initially resulted in the incorporation of inherent biases and inadequate data. Furthermore, the present sample was obtained from a single institution, thereby restricting the generalizability of the results to a wider range of organizations and demographics. Moreover, it is conceivable that the research duration does not include the long-term consequences or current improvements in therapy. Although there are certain limitations, the present extensive research offers useful insights into the prognosis of colorectal cancer and the variables that influence the course of the illness.

In conclusion, the extensive retrospective cohort research carried out at West Kazakhstan Medical University provides important information on several aspects of colorectal cancer (CRC), including demographic and clinico-pathological features, treatment patterns, and prognostic variables. The results highlight the intricate nature of CRC and underline the need for customized therapies and individualized tactics in clinical practice. The research emphasizes the substantial influence of age, gender, and tumor features on the advancement of cancer and death rates. The recognition of age as a crucial determinant in the advancement of cancer implies that therapies targeted at certain age cohorts may provide more efficacious outcomes. Furthermore, the intricate interaction between gender and tumor features highlights the significance of gender-specific approaches in screening, treatment, and preventive measures. The study's investigation of clinico-pathological features, including tumor morphology, stage, lymph node infiltration, and metastasis, yields vital data for prognosticating cancer advancement. The established correlations between these characteristics and death emphasize the need for a subtle approach in making treatment choices. The lack of metastasis as a prognostic factor for a higher probability of receiving cancer therapy underscores the need of evaluating the metastatic status in patient evaluation and care. The research has made a noteworthy addition by creating a nomogram model, which provides doctors with a useful tool to assess the likelihood of death using various demographic and clinico-pathological parameters. This breakthrough has the capacity to direct clinical decision-making, enabling the implementation of treatment regimens that are

tailored to individual patients. Additionally, it facilitates well-informed talks with patients about their prognosis and available therapeutic alternatives.

Author Contribution Statement

All authors contributed equally in this study.

Acknowledgements

I extend my heartfelt gratitude to all those who have played a pivotal role in the successful completion of this study, "Evolution of Colorectal Cancer Trends and Treatment Outcomes: A Comprehensive Retrospective Analysis (2019-2023) in West Kazakhstan." Special thanks to the participants, whose willingness to share experiences enhanced the comprehensiveness of our findings. I acknowledge the medical professionals, researchers, and healthcare staff for their contributions to data collection and analysis. Thanks also to friends and family for their unwavering encouragement. To everyone who contributed, directly or indirectly, your efforts have enriched the quality of this research, contributing to the ongoing dialogue on colorectal cancer trends and treatment outcomes. Thank you all.

Ethical Declaration

The study was carried out after getting the approval from the Ethical Committee. Due to the retroactive nature of this inquiry, the Ethics Committee waived the need for written informed consent.

References

1. Marcellinaro R, Spoleitini D, Grieco M, Avella P, Cappuccio M, Troiano R, et al. Colorectal Cancer: Current Updates and Future Perspectives. *J Clin Med.* 2024;13:40. <https://doi.org/10.3390/JCM13010040>.
2. Klimeck L, Heisser T, Hoffmeister M, Brenner H. Colorectal cancer: A health and economic problem. *Best Pract Res Clin Gastroenterol.* 2023;66:101839. <https://doi.org/10.1016/j.BPG.2023.101839>.
3. Chen K, Collins G, Wang H, Toh JWT. Pathological Features and Prognostication in Colorectal Cancer. *Curr Oncol.* 2021;28:5356-83. <https://doi.org/10.3390/CURRONCOL28060447>.
4. Cascianelli S, Barbera C, Ulla AA, Grassi E, Lupo B, Pasini D, et al. Multi-label transcriptional classification of colorectal cancer reflects tumor cell population heterogeneity. *Genome Med.* 2023;15:1-17. <https://doi.org/10.1186/S13073-023-01176-5/FIGURES/6>.
5. Alese OB, Zhou W, Jiang R, Zakka K, Huang Z, Okoli C, et al. Predictive and Prognostic Effects of Primary Tumor Size on Colorectal Cancer Survival. *Front Oncol.* 2021;11:728076. <https://doi.org/10.3389/FONC.2021.728076/BIBTEX>.
6. Langko JM, Atmaja MHS, Wiratama PA, Ferristuti W. Compatibility of Local Staging (T) Colorectal Cancer in Multi-Slice Computed Tomography (MSCT) with Histopathology: a Retrospective Study. *FM.* 2023;2:12-9. <https://doi.org/10.57125/FEM.2023.09.30.02>.
7. Horditsa V, Grynchuk F, Besaha R. The determining the photoluminescence intensity for assessing of the small bowel viability in the experiment. *FM.* 2023;2:20-8. <https://doi.org/10.57125/FEM.2023.09.30.03>.

8. Tsekhmister YV, Stepanenko VI, Konovalova T, Tsekhmister BY. Analysis of Physicochemical Natures of Modern Artifacts in MRI. *Int J Online Biomed Eng.* 2022;18:89-100. <https://doi.org/10.3991/IJOE.V18I03.25859>.
9. Hense C, Schelper M. Combating the Compounding Effects of Chronic Disease [Internet]. Springer, Cham; 2022 [cited 2024 Jun 9]. Available from: https://doi.org/10.1007/978-3-031-04836-4_10.
10. Yap S, He E, Egger S, Goldsbury DE, Lew J Bin, Ngo PJ, et al. Colon and rectal cancer treatment patterns and their associations with clinical, sociodemographic and lifestyle characteristics: analysis of the Australian 45 and Up Study cohort. *BMC Cancer.* 2023;23:1-13. <https://doi.org/10.1186/S12885-023-10528-8/FIGURES/3>.
11. Joseph DA, King JB, Dowling NF, Thomas CC, Richardson LC. Vital Signs: Colorectal Cancer Screening Test Use — United States, 2018. *MMWR Morb Mortal Wkly Rep.* 2020;69:253-9. <https://doi.org/10.15585/MMWR.MM6910A1>.
12. Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2021;325:1965-77. <https://doi.org/10.1001/JAMA.2021.6238>.
13. Meirmanova A, Bi str T. Different treatment tactics of the pelvic organ prolapse according to the type and the degree of the prolapse: A narrative review. *FM.* 2022;1:33-44. <https://doi.org/10.57125/FEM.2022.03.25.04>.
14. Ramirez-Rodriguez JM, Martinez-Ubieto J, Muñoz-Rodes JL, Rodriguez-Fraile JR, Garcia-Erce JA, Blanco-Gonzalez J, et al. Surgical treatment for colorectal cancer: analysis of the influence of an enhanced recovery programme on long-term oncological outcomes—a study protocol for a prospective, multicentre, observational cohort study. *BMJ Open.* 2020;10. <https://doi.org/10.1136/BMJOPEN-2020-040316>.
15. Li C, Zhang D, Pang X, Pu H, Lei M, Fan B, et al. Trajectories of Perioperative Serum Tumor Markers and Colorectal Cancer Outcomes: A Retrospective, Multicenter Longitudinal Cohort Study. *EBioMedicine* 2021;74. <https://doi.org/10.1016/j.ebiom.2021.103706>.
16. Krogue JD, Azizi S, Tan F, Flament-Auvigne I, Brown T, Plass M, et al. Predicting lymph node metastasis from primary tumor histology and clinicopathologic factors in colorectal cancer using deep learning. *Commun Med.* 2023;3:1-9. <https://doi.org/10.1038/s43856-023-00282-0>.
17. Ma Y, Li J, Tan X, Cai M, Zhang X, Ma J. Dynamic Nomogram Based on the Metastatic Number and Sites and Therapy Strategies Predicting the Prognosis of Patients with Metastatic Cervical Cancer. *Int J Womens Health.* 2022;14:1807–19. <https://doi.org/10.2147/IJWH.S386689>.
18. Wang Y, Zhou C-W, Zhu G-Q, Li N, Qian X-L, Chong H-H, et al. A multidimensional nomogram combining imaging features and clinical factors to predict the invasiveness and metastasis of combined hepatocellular cholangiocarcinoma. *Ann Transl Med.* 2021;9:1518-1518. <https://doi.org/10.21037/ATM-21-2500>.
19. Goodman ZT, Casline E, Jensen-Doss A, Ehrenreich-May J, Bainter SA. shinyDLRs: A Dashboard to Facilitate Derivation of Diagnostic Likelihood Ratios. *Psychol Assess.* 2022;34:558-69. <https://doi.org/10.1037/PAS0001114>.
20. Cheong C, Oh SY, Kim YB, Suh KW. Differences in biological behaviors between young and elderly patients with colorectal cancer. *PLoS One.* 2019;14:e0218604. <https://doi.org/10.1371/JOURNAL.PONE.0218604>.
21. Baraibar I, Ros J, Saoudi N, Salvà F, García A, Castells MR, et al. Sex and gender perspectives in colorectal cancer. *ESMO Open.* 2023;8:101204. <https://doi.org/10.1016/J.ESMOOP.2023.101204>.
22. Petrick JL, Barber LE, Warren Andersen S, Florio AA, Palmer JR, Rosenberg L. Racial Disparities and Sex Differences in Early- and Late-Onset Colorectal Cancer Incidence, 2001–2018. *Front Oncol.* 2021;11:734998. <https://doi.org/10.3389/FONC.2021.734998/BIBTEX>.
23. Jurescu A, Dema A, Văduva A, Gheju A, Vița O, Barna R, et al. Poorly differentiated clusters and tumor budding are important prognostic factors in colorectal carcinomas. *Bosn J Basic Med Sci.* 2022;22:164. <https://doi.org/10.17305/BJBMS.2021.6110>.
24. Pyo J-S, Choi JE, Kim NY, Min K-W, Kang DW. Prognostic Implications of Intratumoral Budding in Colorectal Cancer: Detailed Analysis Based on Tumor-Infiltrating Lymphocytes. *J Clin Med.* 2024;13:134. <https://doi.org/10.3390/JCM13010134>.
25. Malki A, Elruz RA, Gupta I, Allouch A, Vranic S, Al Moustafa AE. Molecular mechanisms of colon cancer progression and metastasis: Recent insights and advancements. *Int J Mol Sci.* 2021;22:1-24. <https://doi.org/10.3390/IJMS22010130>.
26. Berben L, Floris G, Wildiers H, Hatse S. Cancer and Aging: Two Tightly Interconnected Biological Processes. *Cancers (Basel).* 2021;13:1–20. <https://doi.org/10.3390/CANCERS13061400>.
27. Laconi E, Marongiu F, DeGregori J. Cancer as a disease of old age: changing mutational and microenvironmental landscapes. *Br J Cancer.* 2020;122:943-52. <https://doi.org/10.1038/s41416-019-0721-1>.
28. Alexander MS, Lin J, Shriver CD, McGlynn KA, Zhu K. Age and Lymph Node Positivity in Patients With Colon and Rectal Cancer in the US Military Health System. *Dis Colon Rectum.* 2020;63:346-56. <https://doi.org/10.1097/DCR.0000000000001555>.
29. Lewis SL, Stewart KE, Garwe T, Sarwar Z, Morris KT. Retrospective Cohort Analysis of the Effect of Age on Lymph Node Harvest, Positivity, and Ratio in Colorectal Cancer. *Cancers.* 2022;14:3817. <https://doi.org/10.3390/CANCERS14153817>.
30. Keim-Malpass J, Alcalá HE. Association of Age at Cancer Diagnosis and Clinical Trial Participation. *JAMA Netw Open.* 2021;4. <https://doi.org/10.1001/JAMANETWORKOPEN.2020.37573>.
31. Hashim D, Carioli G, Malvezzi M, Bertuccio P, Waxman S, Negri E, et al. Cancer mortality in the oldest old: a global overview. *Aging (Albany NY).* 2020;12:16744. <https://doi.org/10.18632/AGING.103503>.
32. Tanskanen T, Seppa KJM, Virtanen A, Malila NK, Pitkaniemi JM. Cancer Incidence and Mortality in the Oldest Old: A Nationwide Study in Finland. *Am J Epidemiol.* 2021;190:836-42. <https://doi.org/10.1093/AJE/KWAA236>.
33. Song M, Emilsson L, Roelstraete B, Ludvigsson JF. Risk of colorectal cancer in first degree relatives of patients with colorectal polyps: nationwide case-control study in Sweden. *BMJ.* 2021;373:877. <https://doi.org/10.1136/BMJ.N877>.
34. Pilleron S, Soto-Perez-de-Celis E, Vignat J, Ferlay J, Soerjomataram I, Bray F, et al. Estimated global cancer incidence in the oldest adults in 2018 and projections to 2050. *Int J Cancer.* 2021;148:601-8. <https://doi.org/10.1002/IJC.33232>.
35. Ji H, Hu C, Yang X, Liu Y, Ji G, Ge S, et al. Lymph node metastasis in cancer progression: molecular mechanisms, clinical significance and therapeutic interventions. *Signal Transduct Target Ther.* 2023;8:1-33. <https://doi.org/10.1038/s41392-023-01576-4>.
36. Abancens M, Bustos V, Harvey H, McBryan J, Harvey BJ. Sexual Dimorphism in Colon Cancer. *Front Oncol.* 2020;10:607909. <https://doi.org/10.3389/FONC.2020.607909>.

FONC.2020.607909/BIBTEX.

37. Cowling TE, Bellot A, Boyle J, Walker K, Kuryba A, Galbraith S, et al. One-year mortality of colorectal cancer patients: development and validation of a prediction model using linked national electronic data. *Br J Cancer*. 2020;123:1474-80. <https://doi.org/10.1038/s41416-020-01034-w>.
38. Zhao M, Lau MC, Haruki K, Väyrynen JP, Gurjao C, Väyrynen SA, et al. Bayesian risk prediction model for colorectal cancer mortality through integration of clinicopathologic and genomic data. *NPJ Precis Oncol*. 2023;7:1-13. <https://doi.org/10.1038/s41698-023-00406-8>.
39. Peiyuan G, xuhua H, Ganlin G, Xu Y, Zining L, Jiachao H, et al. Construction and validation of a nomogram model for predicting the overall survival of colorectal cancer patients. *BMC Surg*. 2023;23:1-12. <https://doi.org/10.1186/S12893-023-02018-2/FIGURES/7>.
40. Mainenti PP, Stanzione A, Guarino S, Romeo V, Ugga L, Romano F, et al. Colorectal cancer: Parametric evaluation of morphological, functional and molecular tomographic imaging. *World J Gastroenterol*. 2019;25:5233. <https://doi.org/10.3748/WJG.V25.I35.5233>.



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.