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ORIGINAL ARTICLES

Characteristics, Effect of Histological Grade and Localization on the Prognosis of Colorectal Cancer. A retrospective Study.

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Abstract

Background: Colorectal cancer is the third most deadly cancer and the fourth most frequent in the world according to GLOBOCAN 2018. The number of new cases is growing up, which may also be related to lifestyle. Many studies have shown a difference in the number of males and females, correlation of localization, stage, and grade with prognosis.

Material and Methods: In our study were included operated cases with colorectal cancer in University Hospital Center "Mother Theresa" during the period from January 1, 2016 to December 31, 2017.

In our study, the total number of patients enrolled is 334. In the end was evaluated the correlation between histological grade, stage, and localization with prognosis.

Results: From the study resulted that males were affected more than females by colorectal cancer.

The average age of diagnosis of colorectal cancer is 63.9 (±12.4) years. Moderately differentiated adenocarcinoma, histological grade II and pathological stage pT3N0Mx after TNM are predominant.

The commonest localization is the rectum. Disease-free survival is better in stages I and IIa than in other stages, least favorable in poorly differentiated adenocarcinoma.

Conclusion: In Albania, patients diagnosed with CRC showed a low survival rate specific to cancer.

The type of histology, the stage of the cancer, and the level of CEA at diagnosis and the type of treatment a patient received significantly determine the mortality rate.

Therefore, cancer screening programs can help to detect the disease at an early stage and initiate timely available treatments in order to extend the life expectancy of CRC patients.

Keywords: colorectal cancer, histological grade, disease-free survival.

Introduction:

Worldwide, there were approximately 24.5 million cases and 9.6 million deaths in 2017 from Cancer, which continues to be the second leading cause of morbidity and mortality [1].

Colorectal cancer (CRC) ranks third in incidence and second leading cause of cancer deaths in both sexes worldwide, with nearly 2 million new cases and more than one million new deaths by 2020 [2], which accounts for 10% and 9.4% of all cancer cases and deaths respectively.

Previously, cancer was considered a disease of high-income countries, however, now evidence shows that they are also becoming a major public health issue in low- and middle-income countries (LMIC).

Global studies have shown that lifestyle changes, urbanization, cultural changes (physical inactivity and unhealthy dietary habits) and increased life expectancy at LMIC may be possible reasons for the increase in cancer cases [3, 4, 5].

Improving individual income and economic growth in LMICs has shifted the dietary pattern towards an increased

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intake of fat, sugar and packaged foods of animal origin [6].

From 2007 to 2017, the largest increase (52%) of cancer incidence was observed in countries with the Medium Socio-Economic Development Index (SDI) [1].

In our study were included operated cases with colorectal cancer in University Hospital Center "Mother Theresa" during the period from January 1, 2016 to December 31, 2017.The total number of patients included in the study for both years is 334. The year 2016 has a total number of 153 cases, whereas the year 2017 has a total number of 181 cases. Of these cases, 158 of them are females, accounting for 47.3% of cases and 176 are males, accounting for 52.7% of cases, (Fig. 1) with a significant difference between them ($p < 0.01$). (Tab. 1)

Variables	*No. of cases*	*% of cases*	P
Gender			
Females	158	47.3	**0.3**
Males	176	52.7	
Age, M (SD)	63.9 (12.4)	[21-93]	
Age groups, years			
≤30	7	2.1	
31-40	6	1.8	
41-50	31	9.3	**<0.01**
51-60	75	22.5	
61-70	105	31.4	
>70	110	32.9	
Year			
2016	153	45.8	
2017	181	54.2	

Table 1 - Epidemiologic data of patients

Incidence of colorectal cancer in our study in according of the age-groups and gendes were as follow: In the age group < 30 years are 7 (2.1%) patients; In the age group 31-40 years are 6 (1.8%) patients; In the age group 41-50 years are 31 (9.3%) patients; In the age group 51-60 years are 75 (22.5%) patients; In the age group 61-70 years are 105 (31.4%) patients; In the age group >70 years are 110 (32.9%) patients, with a significant difference from other age groups, (*p<0.01*) (Fig. 2)

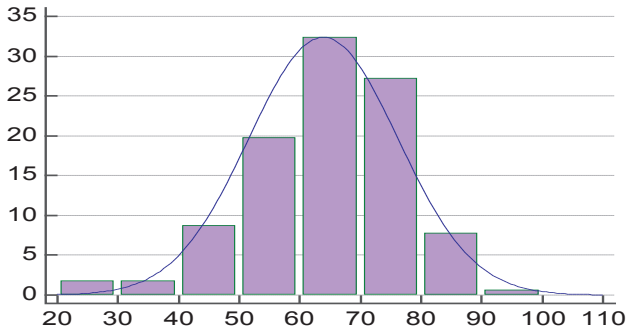

Figure 1 Distribution of Age of patients in histogram

In our study, the predominant age of patients diagnosed with colorectal cancer is age group 61-70 and >70 years with a significant difference from other age groups.

The average age of patients in our study is 63.9(12.4 %) years, ranging from 21 to 93 years.

In our study, it is noticed an increased incidence after the sixth decade of life (22.5%), with a peak in the seventh (31.4%) and eighth (32.9%) decades.

In Albania, as in most other countries, the incidence starts growing during the fifth decade of life. So, we can say that the risk of developing colorectal cancer increases with age.

This is related to long-term exposure to risk factors, as well as to an almost 10-year period of transformation of a precancerous lesion into cancer. Over 90% of patients with colorectal cancer are diagnosed over the age of 50 years, with an average age of about 64 years.

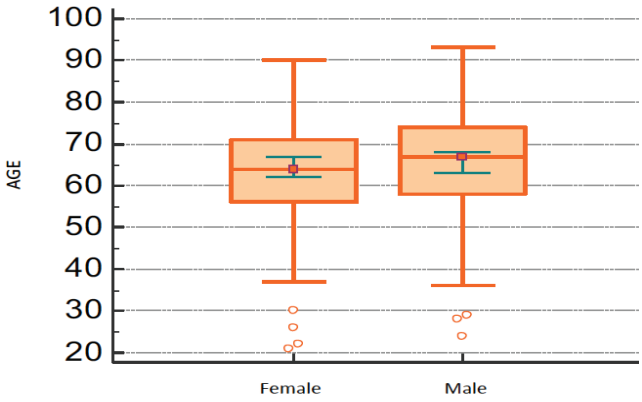

Figure 3. Comparison of average age according to gender

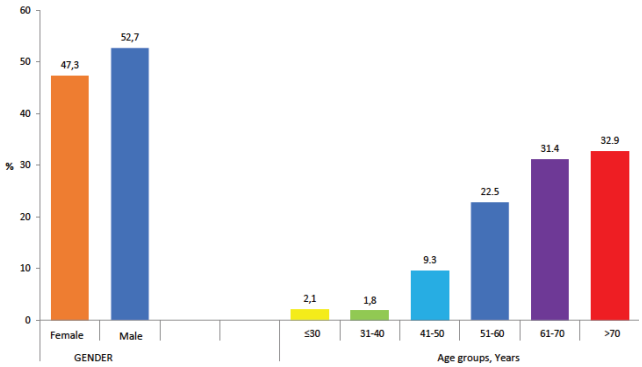

Figure 2 Distribution of data in according to gender and age group

In our study, the average age of females (M=62.9 ± 12.4) is younger compared with the average age of males (M=64.7 ± 12.2), but without a significant difference between them (t=1.3, p=0.2).

The data of our study do not support the data of the studies above, because the average age of females/males does not have a significant difference between them. The above-mentioned studies have a larger number of cases included in the study, compared with ours, and this could be the reason why the results do not match.

Years	Gender				Total	
	Female		Male			
	No. of cases	*% of cases*	*No. of cases*	*% of cases*	*No. of cases*	*% of cases*
2016	78	51.0	75	49.0	153	45.8
2017	80	44.2	101	55.8	181	54.2
Total	158	100	176	100	334	100

Table 2. Distribution of cases according to gender and years of study

In the year 2016, in our study were diagnosed 153 patients with colorectal cancer. 78 (51%) of them were females, whereas 75 (49%) were males. (Tab 2)

In the year 2017 were diagnosed 181 patients with colorectal cancer. 80 (44.2%)of them were females and 101(55.8%) were males. (Tab 2)

During the year 2016, it is noticed a slightly increased number of females diagnosed with colorectal cancer than males. In the year 2017, it is noticed a larger number of males compared with females diagnosed with colorectal cancer.

Anyway, there was not found a significant difference according to gender between the two years of study (p=0.2). (Tab 3)

Age Group	Year		P
	2016	2017	
≤30	2 (1.3)	5 (2.8)	
31-40	2 (1.3)	4 (2.2)	
41-50	17 (11.1)	15 (8.3)	
51-60	34 (22.2)	42 (23.2)	
61-70	55 (35.9)	49 (27.1)	0.2
>70	43 (28.1)	66 (36.5)	

Table 3. Distribution of cases according to age group and years of study

What is striking in this distribution is the fact that during the year 2016, as well as during the year 2017, the age groups with the highest incidence are the age groups 61-70 years and >70 years. However, there was not found a significant difference comparing the age groups between the two years (p=0.2) (Tab 3)

This shows again that colorectal cancer, despite the changes in incidence values undergone in recent years, remains an old age disease with a peak over 60 years.

There was not found a significant difference comparing the age groups between the two years (p=0.2).

In our study, it is noticed this kind of distribution of cases according to histological diagnosis: with the least number of cases is poorly differentiated adenocarcinoma with mucinous focuses 2 (0.6%), moderately differentiated adenocarcinoma with mucinous focuses 11(3.3%), mucinous adenocarcinoma of the colon 37(11%), well-differentiated adenocarcinoma 38(11.4%), poorly differentiated adenocarcinoma 39(11.7%) and moderately differentiated adenocarcinoma with a number of cases clearly higher than other diagnoses 207 (62%) of all histological diagnoses.(Tab 4)

The predominant diagnosis: moderately differentiated adenocarcinoma in 62% of patients, with a significant difference from other diagnoses (p<0.01).

Diagnosis	*No. of cases*	*% of cases*
Poorly differentiated adenocarcinoma	39	11.7%
Poorly differentiated adenocarcinoma with mucinous focuses	2	0.6%
Well-differentiated adenocarcinoma	38	11.4%
Moderately differentiated adenocarcinoma	207	62.0%
Moderately differentiated adenocarcinoma with mucinous focuses	11	3.3%
Mucinous adenocarcinoma of the colon	37	11.0%
Total	334	100.0

Table 4. Distribution of cases according to histological diagnosis

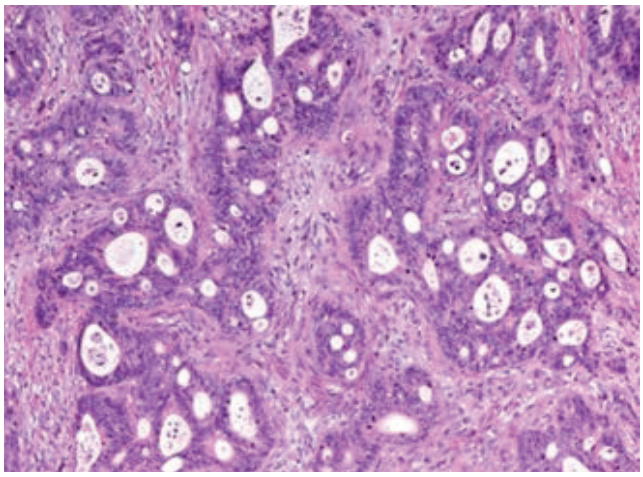

Figure 4. Moderately differentiated adenocarcinoma. Glandular component 50-95% of the tumor. Glands lose their regularity and it is noticed a loss of nucleus polarity. (H&E stain, original magnification x100)

The table 5 shows the correlation between diagnosis and gender.

Our study includes 2 (1.3%) of cases with poorly differentiated adenocarcinoma with mucinous focuses (females); 11(3.3%) of cases with moderately differentiated adenocarcinoma with mucinous focuses [3 (1.9%) females, 8(4.5%) males]; 36 (10.8%) of cases with mucinous adenocarcinoma of the colon [17 (11.4%) females, 19 (10.8%) males]; 38 (11.4%) of cases with well-differentiated adenocarcinoma [15 (9.5%) females, 23(13.1%) males]; 39 (11.7%) of cases with well differentiated adenocarcinoma [21 (13.3%) females, 18 (10.2%) males], and 207 (62%) of cases with moderately differentiated adenocarcinoma [99 (62.7%) females, 108 (61.4%) males]. (Tab 5)

There was not found a significant difference regarding the distribution of cases according to gender (p=0.3) during the evaluation of statistical data.

Moreover, even in the literature was not found any correlation between histopathological diagnosis and gender.

Diagnosis	Gender				Total	
	Female		Male			
	No. of cases	*% of cases*	*No. of cases*	*% of cases*	*No. of cases*	*% of cases*
Poorly differentiated adenocarcinoma	21	13.3	18	10.2	39	11.7
Poorly differentiated adenocarcinoma with mucinous focuses	2	1.3	0	0	2	0.6
Well-differentiated adenocarcinoma	15	9.5	23	13.1	38	11.4
Moderately differentiated adenocarcinoma	99	62.7	108	61.4	207	62.0
Moderately differentiated adenocarcinoma with mucinous focuses	3	1.9	8	4.5	11	3.3
Mucinous adenocarcinoma of the colon	17	11.4	19	10.8	36	10.8
Total	158	47.3	176	52.7	334	100

Table 5. Distribution of cases according to histological diagnosis and gender

Grade	No. of cases	% of cases
Grade 1	41	12.3
Grade 2	220	65.9
Grade 3	73	21.9
Total	334	100.0

Table 6. Distribution of cases according to histological grade

In our study we have recorded 12.3 % of cases are of grade 1, most of them 65.9% are of grade 2 and 21.9% are of grade 3, with a significant change between them (p<0.01) (Tab 6)

The table and the graph above describe the grouping of patients according to histological grade. In our study there are; Grade 1 - well-differentiated adenocarcinoma 41 (12.3%) cases; Grade 2 - 220 (65.9%) cases; Grade 3 - 73 (21.9%) cases.

Some other studies describe Grade 1 and 2 as low grade, whereas Grade 3 as high grade.

The histological grade is related to histological diagnosis.

In our study, the largest number of patients have the diagnosis of moderately differentiated adenocarcinoma(G2) and this group belongs to histological Grade 2. (Tab 6)

The table 7 show the distribution of cases according to histological grade and gender.

Grade 1 has a number of 41 (12.3%) of cases, with a female/male ratio of 17/24; Grade 2 has a number of 220 (65.9%) of cases, with a female/male ratio of 102/118; Grade 3 has a number of 73 (21.6%) of cases, with a female/male ratio of 39/34.

There was not found a significant difference between histological grade and gender (p=0.4) during the study of statistical data. (Tab 7)

Moreover, even in the literature was not found any correlation between histological grade and gender.

Grade	Female		Male		Total	
	No. of cases	*% of cases*	*No. of cases*	*% of cases*	*No. of cases*	*% of cases*
Grade 1	17	41.5	24	58.5	41	12.3
Grade 2	102	46.4	118	53.6	220	65.9
Grade 3	39	52.8	34	47.2	73	21.6
Total	158		176		334	100

Table 7. Distribution of cases according to histological grade and gender

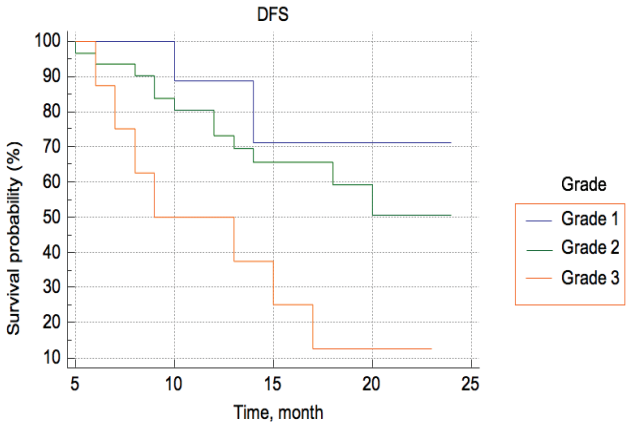

Figure 5. Progression-free survival according to histological grade

Progression-free survival is studied in survival analysis with Kaplan-Meier curves for the period 2016-2018 and results to be higher in cases with histological grade 1 and grade 2, with a significant difference to grade 3 (p=0.01). This is supported by other studies, too.(Fig 5)

Localization	No. of cases	% of cases
Colon	2	0.6
Colon dexter	92	27.5
Colon sinister without rectum	100	29.9
Rectum	140	41.9
Total	334	100.0

Table 8. Distribution of cases according to anatomic localization

Localization in the rectum predominates in 41.9% of cases, with a significant difference to other regions (p<0.01). The unit "colon" indicates that the anatomic localization of the tumor was not specified by the surgeon. Anyway, the value of only 2 unspecified cases, does not impact our study.

In our study, 92 (27.5%) of cases with colorectal cancer are localized in colon dexter, 100 (29.9%) of cases are localized in colon sinister (not rectum); and 140 (41.9%) of cases are localized in rectum. (Tab 8)

The predominant location of colorectal cancer is the rectum, with a significant difference from other regions.In this study, around 50% of colorectal cancer is localized in the rectum, whereas the remaining part is localized in different regions of the colon.We can say that based on our study and the studies mentioned above, the most frequent localization of colorectal cancer is the left colon and specifically the rectum. (Tab 9)

Localization	No. of cases	Average	SD (Standard deviation)
(1) Colon Dexter	92	64.76	11.91
(2) Colon Sinister without rectum	100	63.27	12.53
(3) Colon	2	70.50	10.60
(4) Rectum	140	63.57	12.52

Table 9. Comparison of average age according to tumor localization

The table and graph above show the distribution of cases in our study according to the average age and tumor localization. It is noticed that the average age is approximate for all three tumor locations. Localization in colon dexter has an average age of 64.76. Localization in colon sinister has an average age of 63.27. Localization in the rectum has an average age of 63.57. Only the two cases of unspecified location have an older average age of 70.50, but this does not affect the results of our study. (Tab 9)

It was not found a significant difference in the average age of patients according to localization.

It was not found a significant difference in the localization of disease according to gender (p=0.5). The table above shows the distribution of cases in our study according to localization and gender, 44 (47.8%) females and 48(52.2%) males have the localization of the tumor in colon dexter; 45 (45%) females and 55(55%) males have the localization of the tumor in colon sinister, and 69(49.3%) females and 71(50.7%) males have the localization of the tumor in the rectum.

Males are more affected in comparison with females 156/176 in all three anatomical regions, but without a significant difference between them (p=0.5).

Progression-free survival according to tumor localization. In the analysis of survival with Kaplan-Meier curves, it was not found a significant change in progression-free survival according to tumor localization (p=0.3). (Fig. 6)

So, based on the data of our graph there is no difference in progression-free survival between the right-side cancer and the left side cancer.

The staging of disease is made according to the Tumor, Node, Metastasis (TNM) system, founded and standardized by the American Joint Committee on Cancer (AJCC). In our study, staging is done according to AJCC 8th edition .[8]

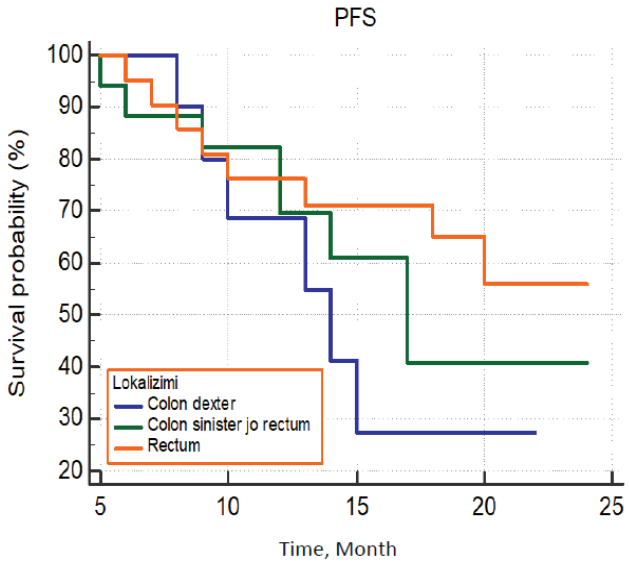

Figure 6. Progression-free survival according to tumor localization

The table 11 shows the distribution of cases involved in the study according to the stage of the disease, as fellow; Stage I includes 35(10.5%), Stage IIA includes 147 (44%); Stage IIIA includes 5(1.5%); Stage IVA includes 2(0.6%); Stage IIB includes 2 (0.6%); Stage IIIB includes 137 (41%); Stage IIC includes 2 (0.6%); Stage IIIC includes 4 (1.2%) of the total cases.

In our study predominate patients in stage IIA (44% of cases) and stage IIIB (41%) with a significant difference from other stages.

Patients in stage IIA (44%) and stage IIIB (41%) predominate, with a significant difference from other stages ($p<0.01$).

Localization	Female		Male		Total	
	No. of cases	*% of cases*	*No. of cases*	*% of cases*	*No. of cases*	*% of cases*
Colon	0	0	2	1.1	2	0.6
Colon dexter	44	47.8	48	52.2	92	27.5
Colon sinister without rectum	45	45.0	55	55.0	100	29.9
Rectum	69	49.3	71	50.7	140	41.9
Total	158	100	176	100	334	100

Table 10. Distribution of cases according to tumor localization and gender

Stage	No. of cases	% of cases
I	35	10.5
II A	147	44.0
III A	5	1.5
IV A	2	0.6
II B	2	0.6
III B	137	41.0
II C	2	0.6
III C	4	1.2
Total	334	100.0

Table 11. Distribution of cases according to TNM

The table 12 shows the distribution of cases according to TNM stage and gender.

The distribution of cases in our study is as follows:Stage I, female/male ratio 12/23 with female predomination; Stage IIA, female/male ratio 71/76 with a mild predomination of males; Stage IIIA, female/male ratio 1/4 with male predomination.; Stage IVA, female/male ratio 1/1; Stage IIB, female/male ratio 1/1; Stage IIIB, female/male ratio 69/68; Stage IIC, female/male ratio 1/1; Stage IIIC, female/male ratio 2/2.

There was not found a significant difference in the relation between TNM stage and gender (p=0.7) from the analysis of statistical data in our study.

The table 13 shows the distribution of cases according to TNM stage and histological and is evaluated the correlation between them.

Based on the data in the table, it is noticed that histological Grade 2 predominates in stages I and II, whereas Grade 3 predominates in stage IIIB.

It was found a significant difference in the distribution of patients according to histological grade and stage (p<0.02) from the analysis of statistical data.

Grade 3 predominates in stage IIIB (47.4%) compared with the other two grades.

The data of our study indicate that stage IIIB, which is an advanced stage of disease with involvement of regional lymph nodes from carcinomatous metastasis, has a significant correlation with histological grade 3 which is poorly differentiated adenocarcinoma, supporting the results of the study above.

There was not found a significant difference in the distribution of patients according to localization and TNM stage (p=0.4).

The table 14 show the distribution of patients in the study according to tumor localization and disease stage and is evaluated the correlation between them. What stands out from the distribution of the data is that the most frequent localization for all TNM stages is the rectum, but without a significant difference from other localizations.

Stage	Females		Males		Total	
	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases
I	12	34.3	23	65.7	35	10.5
II A	71	48.3	76	51.7	147	44.0
III A	1	20.0	4	80.0	5	1.5
IV A	1	50.0	1	50.0	2	0.6
II B	1	50.0	1	50.0	2	0.6
III B	69	50.4	68	49.6	137	41.0
II C	1	50.0	1	50.0	2	0.6
III C	2	50.0	2	50.0	4	1.2
Total	158	47.3	176	52.7	334	100

Table 12 Distribution of cases according to TNM stage and gender

Stage	Grade 1		Grade 2		Grade 3		P
	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases	
I	7	17.9	26	11.9	2	2.6	**<0.01**
II A	16	41.0	100	45.7	31	40.8	
III A	0	0	5	2.3	0	0	
IV A	1	2.6	0	0	1	1.3	
II B	0	0	1	0.5	1	1.3	
III B	15	38.5	86	39.3	36	47.4	
II C	0	0	1	0.5	1	1.3	
III C	0	0		0	4	5.3	

Table 13. Distribution of cases according to TNM stage and histological grad

Stage	Colon		Colon dexter		Colon sinister without rectum		Rectum		P
	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases	
I	0	0	6	6.5	8	8.0	21	15.0	0.4
II A	2	100	41	44.6	50	50.0	54	38.6	
III A	0	0	2	2.2	1	1.0	2	1.4	
IV A	0	0	0	0	2	2.0	0	0	
II B	0	0	1	1.1	1	1.0	0	0	
III B	0	0	39	42.4	37	37.0	61	43.6	
II C	0	0	0	0	1	1.0	1	0.7	
III C	0	0	3	3.3	0	0	1	0.7	

Table 14. Distribution of cases according to tumor localization and TNM stage

In the survival analysis of our study with the Kaplan-Meier curves it is observed that the progression-free survival is higher in cases with stages I and IIA with a significant difference from other stages ($p<0.01$). In the TNM classification, the greatest number of cases belongs to stage pT3N0Mx or stage IIA with 114 cases or 34.1% of the total number with a significant difference from other stages ($p<0.0001$). (Fig. 7)

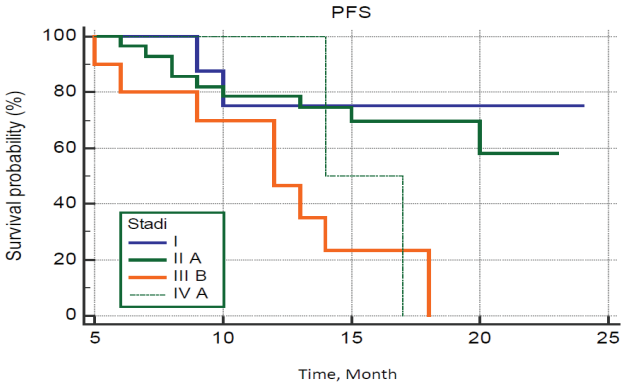

Figure 7. Progression-free survival according to TNM stage

Discussions

The incidence of colorectal cancer in Albania is lower than in neighboring countries and similar to that in Greece and may be related to the Mediterranean diet.[9]

In our study were included operated cases with colorectal cancer in University Hospital Center "Mother Theresa" during the period from January 1, 2016 to December 31, 2017.The total number of patients included in the study for both years is 334. The year 2016 has a total number of 153 cases, whereas the year 2017 has a total number of 181 cases. Of these cases, 158 of them are females, accounting for 47.3% of cases and 176 are males, accounting for 52.7% of cases, (Fig. 1) with a significant difference between them ($p < 0.01$). (Tab. 1)

Suzana Manxhuka-Kerliu et al. in their study found as Colorectal cancer in general was more frequent in men than in women 60,4% vs. 39,59%.[10]

Albania has a lower incidence of colorectal cancer than neighboring countries with a rate of 9/100000 for males and 7.9/100000 for females and a mortality rate of 4.8/100000 and 4/100000, respectively. Anyway, these figures are not very accurate because the hospital registry data are incomplete and screening programs are not performed. [7]

Bray F et al. in their study[11] in 2018, shown in about 576,000 and 521,000 men and women, respectively, are projected to be diagnosed with colon cancer. This incidence constitutes a 1.51% cumulative risk of colon cancer among men age 0–74 years, and a 1.12% risk among women. About 430,000 men and 274,000 women are expected to be diagnosed with cancer of the rectum. Their cumulative, lifetime risks are 1.2% and 65%, respectively [11]

By comparisonof our data, with those of a study conducted by *Ema Altobelliet al.* [12] on performing screening programs in countries outside the EU, it results that Albania has a low CRC incidence rate, 9.0 among men and 7.9 among women, and an equally low mortality rate, respectively 4.8 and 4.0 but the hospital-based disease registries provide non-excellent data quality. [12]

Ferlay et al. in their[13] study have this data as fellow, CRC is more incident among men than women and 3–4 times more common in developed than in developing nations. Age-standardised (world) incidence rates per 100,000 of CRC in both sexes is 19.7, in males is 23.6, and in females is 16.3. [13]

In our study, the predominant age of patients diagnosed with colorectal cancer is age group 61-70 and >70 years with a significant difference from other age groups.

The average age of patients in our study is 63.9 years (12.4 %), ranging from 21 to 93 years.

In our study, it is noticed an increased incidence after the sixth decade of life (22.5%), with a peak in the seventh (31.4%) and eighth (32.9%) decades. In Albania, as in most other countries, the incidence starts growing during the fifth decade of life. So, we can say that the risk of developing colorectal cancer increases with age.

But *Widdison et al,* [14] and *Teng et al.* [15] in their study separately discover that Colorectal cancer was previously thought to solely affect the elderly, however recent studies published in the US, Canada and Europe have revealed a dramatic change in the pattern of the raised incidence rate among young adults. [14, 15]

In according the *Howladeret al.* [15]The risk of CRC

increases with age; the median age at diagnosis for colon cancer is 68 in men and 72 in women; for rectal cancer it is 63 years of age in both men and women.[16] As a result of rising CRC incidence rates in younger age groups coincident with declining rates in older age groups, the proportion of cases diagnosed in individuals younger than age 50 increased from 6% in 1990 to 11% in 2013.[16]Most of these cases (72%) occur in people who are in their 40s. [17]

According to the *Zahir Ahmed et al.* [18]the usual trend of males having a higher incidence than females for developing colorectal cancer changes during the sixth decade of life and indicates an increased incidence in females after 60 years.

What supports this fact is that during this period females experience menopause and the decrease of female hormones is a risk factor for colorectal cancer. In addition, during this age, females are more prone to weight gain and a sedentary lifestyle.

In our study, the average age of females (M=62.9 ± 12.4) is younger compared with the average age of males (M = 64.7 ± 12.2).

Virostko et al. [19] analyzed and try to determine if specific populations have the greatest rise in rates of CRC in younger adults. Similar trends in the proportion of cases diagnosed before age 50 were seen in men and women. [19]

Also, the incidence and mortality of colorectal cancer in populations over 65 years old are higher in women than those in men implying that colorectal cancer is a major health threat among older women. [20]

According to a study conducted by Tokyo University in Japan[20], it was found that in patients younger than 70 years, the female/male ratio was low, but increased with age.

It was also found that the chances of developing proximal colorectal cancer increased with age, whereas that for rectal cancer decreased. Even here, some studies have suggested a correlation between reduced endogen secretion of female hormones and the occurrence of proximal colorectal cancer in older women. Other studies have shown an increased expression of estrogen receptors in the right colon epithelium compared with that of the left colon, and as a consequence of this, the reduced level of estrogen in menopause stimulates the development of right colon cancer. [21]

The data of our study do not support the data of the studies above, because the average age of females/males does not have a significant difference between them. The above-mentioned studies have a larger number of cases included in the study, compared with ours, and this could be the reason why the results do not match. [21]

In our study, it is noticed this kind of distribution of cases according to histological diagnosis: in most of the cases was moderately differentiated adenocarcinoma with a number of cases clearly higher than other diagnoses 207 (62%) of all histological diagnoses, (Tab 4)with a significant difference from other diagnoses ($p<0.01$).

The results of two studies conducted by *Sherri L. Stewart et al.*[22] on the distribution of pathological diagnosis of colorectal cancer in USA and a study conducted by *Suzana Manxhuka Kerliuet al.*[10] in the year 2019, from the University of Pristina support the result of our study regarding the degree of spreading of moderately differentiated adenocarcinoma. So, based on the results of these studies, we can say that moderately differentiated adenocarcinoma constitutes the largest number of cases of adenocarcinoma, both in developed countries as well as in less developed ones.

Our study showed that the most common localization of colorectal cancer is the left localization, especially rectal cancer.

Meanwhile, the data in Albania show that the distribution of colorectal cancer on the right side as well as on the left side is similar for both genders, different from the study of *Sung-Eun Kim et al.*[23] which shows that cancer in women is more prone to be in the right side. One of the reasons for this result is the lower number of cases in the study compared with other studies*Kevin J. Moore et al.*[24] which could be insufficient to conclude.

There was not found a significant difference in the relation between TNM stage and gender ($p=0.7$) from the analysis of statistical data in our study.

Cheung WY et all [25] considers gender a modest prognostic factor in patients with early stages of cancer, especially in older ones, and conventional therapy for localization of cancer indicates a better prognosis in females than males.

The table 14 show the distribution of patients in the study according to tumor localization and disease stage and is evaluated the correlation between them. What stands out from the distribution of the data is that the most frequent localization for all TNM stages is the rectum, but without a significant difference from other localizations.

Our study does not support the results of two studies made by Cassia B. Wang et al. [25] in the years 2018 and 2019 which show that right colon cancer has a worse prognosis.

In our study, rectal adenocarcinoma has a greater frequency in all TNM stages. Compared with the two studies above, the sample examined in our study is very small and this could be one of the reasons why the results do not match. [26]

In the survival analysis of our study with the Kaplan-Meier curves it is observed that the progression-free survival is higher in cases with stages I and IIA with a significant difference from other stages ($p<0.01$). In the TNM classification, the greatest number of cases belongs to stage pT3N0Mx or stage IIA with 114 cases or 34.1% of the total number with a significant difference from other stages ($p<0.0001$).

The data of our study comply with many other studies as; Yanal Alnimer et al. [27] Mouna Trabelsi et al. [28]

The dimensions of the primary tumor have prognostic significance[29]

Anyway, TNM staging does not always indicate a positive correlation between prognosis and survival. Frequently, cases that are in the same TNM stage have a different progress of disease with different prognosis and survival from each other. This shows that in addition to the characteristics of the tumor, the internal characteristics of the patient's body also intervene in the prognosis of the disease and the survival from the disease.[30]

In our study, no significant difference was observed between the patient's age and tumor localization. One of the reasons is the fact that in our country, routine colonoscopy examinations are not performed, and this leads to delayed diagnosis in both proximal and distal cancers. One reason may be the small number of cases we have included in the study.

Conclusions

Men are affected more than women by colorectal cancer. The predominant age of patients affected by colorectal cancer is 61-70 years and over 70 years. The average age is 63.9 (± 12.4) years. Disease-free survival is longer in stage I and stage IIa of the disease.

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