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## THE DIFFERENCE BETWEEN LEFT AND RIGHT COLON CANCER PATIENTS' CHARACTERISTICS - SINGLE CENTER EXPERIENCE

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### Summary

*Objectives:* The purpose of the study was to determine the difference in time until the appearance of relapse or metastases in patients treated for colorectal cancer, depending on the location of the tumor in the left or right colon at the Oncology Clinic of Clinical Medical Centre Osijek between 1<sup>st</sup> January 2010 and 31<sup>st</sup> December 2012.

*Study design:* historical prospective study

*Material and methods:* Study included patients whose data were recorded from medical archive at the Oncology Clinic of Clinical Medical Centre Osijek. The data on patients' deaths were recorded from the Registry Office of the Republic of Croatia.

*Results:* The study included 272 patients, 160 (58.8%) men and 112 (41.2%) women. According to the location, left sided colon tumor was discovered in 211 (77.6%) patients and right-sided in 61 (22.4%). The median age was 67 years. Right-sided colon tumors are considerably larger with median diameter of 6 cm, with median number of 16. Median of time until the appearance of the metastases is 20 months (interquartile range is from 8 to 29 months); marked time being shorter in right-sided colon tumors. Positive outcome of the treatment was achieved in 205 (75.4%) patients, with no significant difference in comparison to the colon cancer localization. By using Kaplan-Meier analysis of patients' survival rates, a total 5-year survival rate of 72% was achieved in right-sided colon tumor in comparison to 62% in patients with the left-sided colon tumor.

*Conclusion:* This study confirms that there is a difference in colorectal cancer according to its localisation. Patients with right-sided colorectal cancer are older, the carcinoma is larger, the time until the appearance of a relapse or a metastases is shorter in right sided colon cancer while 5-year survival rate is lower in left sided colon cancer.

KEYWORDS: *colorectal cancer, oncology, colon*

### RAZLIKA IZMEĐU KARAKTERISTIKA BOLESNIKA S KARCINOMOM LIJEVOG I DESNOG KOLONA - ISKUSTVO JEDNE USTANOVE

#### Sažetak

*Cilj Istraživanja:* Utvrditi razliku u vremenu do pojave recidiva ili presadnica kod bolesnika liječenih zbog kolorektalnog karcinoma ovisno o smještaju u lijevom ili desnom kolonu u pacijenata liječenih na Zavodu za onkologiju, KBC-a Osijek od 1. siječnja 2010. do 31. prosinca 2012.

*Nacrt studije:* Povijesno prospektivna studija

*Materijal i metode:* U istraživanje su uključeni ispitanici čiji su podatci preuzeti iz arhive medicinske dokumentacije Zavoda za onkologiju KBC-a Osijek, podatci o smrti pacijenata preuzeti su od nadležnog Matičnog ureda Republike Hrvatske.

*Rezultati:* U istraživanje je uključeno 272 pacijenta, od kojih je 160 (58,8 %) muškaraca i 112 (41,2 %) žena. Prema lokalizaciji, lijevostrani tumor kolona ima 211 (77,6 %) bolesnika, a desnostrani njih 61 (22,4 %). Središnja dob pacijenta (medijan) je 67 godina. Značajno su veći u promjeru desni tumori kolona, medijana 6 cm. Medijan vremena do pojave metastaza iznosi 20 mjeseci (interkvartilnog raspona 8 do 29 mjeseci), pri čemu je značajnije kraći kod desnih tumora kolona. Pozitivan ishod liječenja imalo je 205 (75,4 %) bolesnika, bez značajne razlike u odnosu na lokalizaciju tumora kolona. Kaplan – Meierovom analizom preživljenja promatranih bolesnika podijeljenih prema lokalizaciji, dobiveno je petogodišnje ukupno preživljenje 72 % za tumor u desnom kolonu, u odnosu na 62 % kod bolesnika koji su imali tumor u lijevom kolonu.

*Zaključak:* U ovom istraživanju potvrđeno je da postoji razlika u kolorektalnom karcinomu s obzirom na njegov položaj. Pacijenti s desnim kolorektalnim karcinomom su starije dobi, tumor je veći u promjeru, vrijeme do pojave presadnica ili recidiva je kraće, te je petogodišnje preživljavanje manje.

*Ključne riječi:* kolorektalni karcinom, onkologija, kolon

## INTRODUCTION

Colorectal cancer is the third most frequent malignant tumor in the world. The newer studies indicate that tumors behave differently, depending on their position – left or right. An historical - prospective study has been carried out in which various parameters were examined. These are the parameters of the carcinoma itself and its behaviour in the left or right colon, as well as the behaviour of left and right colon cancer according to difference in sex, TNM characteristics, time until the appearance of metastases or recidive, age limit and patients' survival rate (1,2,6).

The colon was developed from the primitive gut. The development of the primitive gut and its derivatives is divided into four segments: esophagus, foregut, midgut and hindgut. The colon has different development because it was developed from the mid and hindgut. After the development ended, the midgut starts distally from the entry of gallbladder into the duodendum and it ends at the boundary between proximal 2/3 and distal 1/3 of the transverse colon, and through its whole length it is supplied by blood from *a. mesenterica superior*. From the hindgut develops distal 1/3 of the colon, descending colon, sigmoid colon, rectum and the lower half of the anal canal (3).

The frequency of the carcinoma itself rises simultaneously with the industrial development of each country. The highest incidence rates are recorded in New Zealand, the USA, Canada and Great Britain, while low rates are registered in African countries, Asia and some parts of South

America. In the Republic of Croatia the incidence and mortality rates are similar to the median values in developed countries. In 2012 the incidence rate of colorectal cancer was 44,2/100000 in men, and 24,7/100000 in women; the mortality rate in men was 26,7/100000, and in women 24,7/100000. Colorectal cancer is among ten most common causes of death in Osijek-Baranya county; it was ranked fourth with 158 deaths in 2016 (1,4,5,10,11).

The cause of colorectal carcinoma itself, as well as of many other malignant diseases, remains unknown. However, it is known that certain factors can have an enormous influence on its development. Risk factors such as old age, nutrition rich in fat, but poor in fibres, contributes to the appearance of colorectal cancer. Genetic factors such as family adenomatose polyposis of the colon also add to its appearance (1,2).

Hereditary predispositions, inflammatory intestine diseases, especially ulcerative colitis, as well as patients who have already had a colorectal carcinoma and have undergone surgery, have a greater risk of developing this carcinoma (1,2).

Pathological-anatomically speaking, most commonly it is an adenocarcinoma, localized in rectum and sigmoid colon, around 73%, rarely in ascending colon, around 14%. and in transverse colon, around 10%. According to gradus, we distinguish well differentiated, moderately differentiated and poorly differentiated. For clinical purposes the greatest influence has a pathohistological classification, which was introduced in 1930 by Dukes i Gordon-Watson (1,2,7).

**MATERIAL AND METHODS**

Study includes patients whose data were taken from medical archive at the Oncology Clinic of Clinical Medical Centre Osijek. The data on patients' deaths were taken from the Registry Office of the Republic of Croatia. 272 patients were involved from 2010 to 2012, including 2012

**RESULTS**

In the research 272 patients were involved from 2010 to 2012, including 2012, 160 (58,8 %) men and 112 (41,2 %) women. According to tumor localization, left colon cancer had 211 (77,6 %) patients, and right colon cancer 61 patients (22,4 %). Table 1 is showing clinical-pathological and demographic data (Table 1.). In the research colon transversum was used as the border between left and right colon.

Table 1. LOCALIZATION OF COLON CANCER ACCORDING TO PATIENTS' GENDER AND AGE

	Number (%) of patients according to localization of colon cancer			P*
	Right colon cancer	Left colon cancer	Total	
<b>Gender</b>				
Men	35 (57,4)	125 (59,2)	160 (58,8)	0,88
Women	26 (42,6)	86 (40,8)	112 (41,2)	
<b>Patients' age</b>				
to 50 years	5 (8,2)	17 (8,1)	22 (8,1)	0,09
51 – 60	7 (11,5)	57 (27)	64 (23,5)	
61 – 70	22 (36,1)	57 (27)	79 (29)	
71 – 80	23 (37,7)	72 (34,1)	95 (34,9)	
81 years and older	4 (6,6)	8 (3,8)	12 (4,4)	
<b>Total</b>	<b>61 (100)</b>	<b>211 (100)</b>	<b>272 (100)</b>	

\*Fisher's exact test

Median age was 67 years (interquartil range from 58 – 74 years) at the range from 31 to 88 years. Most patients, 95 (34,9 %) were between 71 and 80 years old. Right colon cancer is significantly larger, median value 6 cm (interquartil range from 4,5 to 7 cm) at the range from 2 cm to 13 cm (Mann – Whitney U test, P = 0, 008), as well as the number of examined lymph nodes, median value 16 (interquartil range from 10 to 22) (Mann – Whitney U test, P < 0, 001). The number of infiltrated lymph

nodes is not significantly different according to colon cancer localization (Table 2.)

The highest number of patients, 214 (78,7 %), had T3 stage of the primary tumor, and in 157 (57,7 %) patients, regional lymph nodes not invaded. Lymphovascular invasion was not present in 221 (81,3 %) patients. There were no significant differences according to the colon cancer localization in terms of regional or local invasion (Table 3)

Table 2. PATIENTS' AGE, THE SIZE OF CANCER AND THE NUMBER OF EXAMINED AND INVOLVED LYMPH NODES

	Median (interquartil range) according to colon cancer localization			P*
	Right colon cancer	Left colon cancer	Total	
Patients' age (years)	70 (62,5 – 75)	66 (57 – 74)	67 (58 – 74)	0,17
The tumor size (cm)	6 (4,5 – 7)	5 (4 – 6)	5 (4 – 6, 5)	<b>0,008</b>
The number of examined lymph nodes	16 (10 – 22)	10 (7 – 16)	10,5 (8 – 18)	<b>&lt; 0,001</b>
The number of involved lymph nodes	0 (0 – 4)	0 (0 – 2)	0 (0 – 2)	0,31

\*Mann – Whitney U test

Table 3. T IN STAGE AND THE LYMPHOVASCULAR INVASION ACCORDING TO COLON CANCER LOCALIZATION

	Number (%) of patients according to colon cancer localization			P*
	Right colon cancer	Left colon cancer	Total	
<b>Primary tumor stage(T)</b>				
T1	1 (1,6)	2 (0,9)	3 (1,1)	0,88
T2	10 (16,4)	37 (17,5)	47 (17,3)	
T3	49 (80,3)	165 (78,2)	214 (78,7)	
T4	1 (1,6)	7 (3,3)	8 (2,9)	
<b>Regional lymph nodes (N)</b>				
N0- negative regional lymph nodes	34 (55,7)	123 (58,3)	157 (57,7)	0,11†
N1	10 (16,4)	53 (25,1)	63 (23,2)	
N2	17 (27,9)	35 (16,6)	52 (19,1)	
<b>Lymphovascular invasion</b>				
Not present	52 (85,2)	169 (80,1)	221 (81,3)	0,46
Present	9 (14,8)	42 (19,9)	51 (18,8)	
<b>Total</b>	<b>61 (100)</b>	<b>211 (100)</b>	<b>272 (100)</b>	

\*Fisher's exact test; †χ<sup>2</sup> test

Table 4.

THE EXISTENCE AND LOCALIZATION OF METASTASES ACCORDING TO COLON CANCER LOCALIZATION

	Number (%) of patients according to localization of colon cancer			P*
	Right colon cancer	Left colon cancer	Total	
<b>Existence of metastases</b>				
Yes	7 (11,5)	20 (9,5)	27 (9,9)	0,63
No	54 (88,5)	191 (90,5)	245 (90,1)	
Total	61 (100)	211 (100)	272 (100)	
<b>Localization of metastases</b>				
Liver	5/7	13/19	18/26	0,92
Lungs	0	2/19	2/26	
Peritoneus	0	1/19	1/26	
Other	1/7	2/19	3/26	
Liver and lungs	1/7	1/19	2/26	
Total	7/7	19/19	26/26	

\*Fisher's exact test

Table 5.

TUMOR STAGE AND GRADUS ACCORDING TO THE COLON CANCER LOCALIZATION

	Number (%) of patients according to the colon cancer localization			P*
	Right colon cancer	Left colon cancer	Total	
<b>Tumor stage</b>				
I	6 (9,8)	31 (14,7)	37 (13,6)	0,65
IIA	28 (45,9)	86 (40,8)	114 (41,9)	
IIB	0	3 (1,4)	3 (1,1)	
IIC	0	1 (0,5)	1 (0,4)	
IIIA	2 (3,3)	4 (1,9)	6 (2,2)	
IIIB	14 (23)	56 (26,5)	70 (25,7)	
IIIC	4 (6,6)	11 (5,2)	15 (5,5)	
IVA	6 (9,8)	19 (9)	25 (9,2)	
IVB	1 (1,6)	0	1 (0,4)	
<b>Gradus</b>				
I	25 (41)	77 (36,5)	102 (37,5)	0,17*
II	24 (39,3)	108 (51,2)	132 (48,5)	
III	12 (19,7)	26 (12,3)	38 (14)	
Total	61 (100)	211 (100)	272 (100)	

\*Fisher's exact test; \*χ<sup>2</sup> test

Metastases were found in 27 (9,9 %) of patients, and the most frequent localization of the metastases is in liver in 18/26 of patients (Table 4).

Regarding the tumor stage, the highest number of patients, 114 (41,9%), had stage IIA, and 70

(25,7 %) has stage IIIB. According to the tumor grading system, 102 of tumor patients (37,5%) had grade I, 132 (48,5%) grade II, and 38 (14%) grade III. There was no significant difference regarding colon cancer localization in terms of grade or stage (Table 5).

Most patients received adjuvant therapy was administered (189 patients; 69,5%). From the total number of 152 (80,4%) patients, who received chemotherapy only, there are significantly more patients with right colon cancer, while those with left colon cancer received radiotherapy or chemoradiotherapy (Fisher's exact test, P < 0,001) (Table 6).

Table 6.

PATIENTS ACCORDING TO THE ADJUVANT THERAPY AND COLON CANCER LOCALIZATION

	Number (%) of patients according to the colon cancer localization			P*
	Right colon cancer	Left colon cancer	Total	
<b>Adjuvant therapy</b>				
Yes	44 (72,1)	145 (68,7)	189 (69,5)	0,64
No	17 (27,9)	66 (31,3)	83 (30,5)	
<b>Type of adjuvant therapy</b>				
Chemotherapy	44 (100)	108 (74,5)	152 (80,4)	0,001
Radiotherapy	0	2 (1,4)	2 (1,1)	
Chemo-radiotherapy	0	35 (24,1)	35 (18,5)	
Total	44 (100)	145 (100)	189 (100)	

\*Fisher's exact test

The time median until the occurrence of metastases is 20 months (interquartile range from 8 to 29 months). The time median is significantly shorter in the right colon cancer group of patients. (Mann – Whitney U test, P = 0, 007) (Table 7).

Table 7.

TIME (MONTHS) UNTIL THE APPEARANCE OF METASTASES ACCORDING TO TUMOR COLON LOCALIZATION

	Median (interquartil range) according to the colon tumor localization			P*
	Right colon cancer	Left cancer colon	Total	
Time (months) until the appearance of metastases	8 (4 – 23)	20 (12 – 37)	20 (8 – 29)	0,007

\*Mann –Whitney U test

Recurrences or metastases had 88 (32,4 %) patients, 22 (34,9 %) operated patients and 45 (72,6 %) received chemotherapy (Table 8.).

Table 8.  
THE APPEARANCE OF METASTASES ACCORDING TO TUMOR COLON LOCALIZATION

	Number (%) of patients according to the colon cancer localization			P*
	Right colon cancer	Left colon cancer	Total	
<b>Recurrence or metastases</b>				
Yes	21 (34,4)	67 (31,8)	88 (32,4)	0,76
No	40 (65,6)	144 (68,2)	184 (67,6)	
Total	61 (100)	211 (100)	272 (100)	
<b>Surgical treatment of metastases</b>				
Yes	4 (33,3)	18 (35,3)	22 (34,9)	> 0,99
Ne	8 (66,7)	33 (64,7)	41 (65,1)	
Total	12 (100)	51 (100)	63 (100)	
<b>Chemotherapy of metastases</b>				
Yes	9 (81,8)	36 (70,6)	45 (72,6)	0,71
No	2 (18,2)	15 (29,4)	17 (27,4)	
Total	11 (100)	51 (100)	62 (100)	

\*Fisher’s exact test

A positive outcome was observed in 205 (75,4 %) patients, without any significant difference according to the colon cancer localization (Table 9)

Table 9.  
PATIENTS REGARDING THE TREATMENT OUTCOME AND CANCER LOCALIZATION

	Number (%) of patients according to the colon cancer localization			P*
	Right colon cancer	Left colon cancer	Total	
<b>Outcome</b>				
Survived	42 (68,9)	163 (77,3)	205 (75,4)	0,18
Died	19 (31,1)	48 (22,7)	67 (24,6)	
Total	61 (100)	211 (100)	272 (100)	

\*Fisher’s exact test

Cancer localization does not show a statistically significant influence on the overall survival rate (Mantel-Coxox, P = 0,10). Kaplan–Meier survival analysis of the patients divided according to localization shows an overall five-year survival rate of 62% in patients with right colon cancer compared to 72% in patients with left colon cancer.

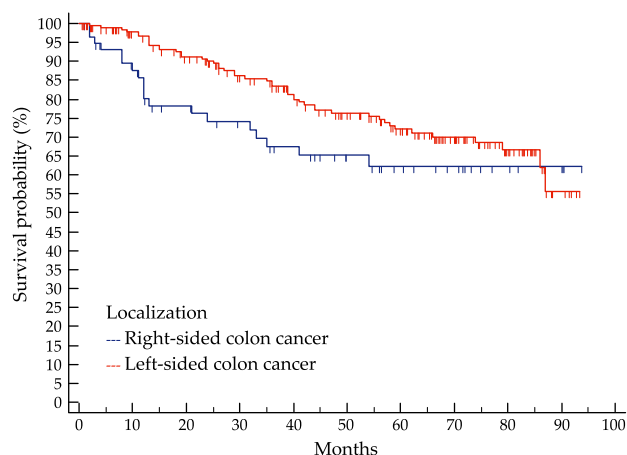


Figure 1. Kaplan-Meier graph – influence of the cancer localization on the total survival rate

### Statistical analysis

We used MedCalc Statistical Software version 18.2.1 (MedCalc Software, Ostend, Belgium; <http://www.medcalc.org>; 2018) for statistical analysis.

### DISCUSSION

This study included 272 patients treated at the Institute for Oncology of the Clinical Medical Centre in Osijek in three years. Of the total number of patients, 42% were women. Left colon cancer was three times more prevalent than the right colon cancer, which is similar to available registry data (HZJZ). There was no difference in localization when considering patient’s gender.

Right sided colon cancer was diagnosed in older patients and was larger at diagnosis compared to left sided colon in this cohort. Mika’s study showed that right colon cancer is larger in diameter and that patients who have it are older. That difference in age and size seems related with the difference in clinical manifestations, where right colon cancer is clinically more silent and harder to diagnose than the left colon cancer(31).

On the other hand right sided colon had more lymph nodes harvested during surgery, but without significant difference in tumour involved lymph nodes when compared to leftside colon cancer. However, the involvement of lymph nodes in N1 stage is in favour of the left colon cancer, while in the N2 stage is in favour of the right colon cancer. The lymphovascular invasion did not

show any significant difference according to the localization of the tumor itself. Moreover, when comparing stages according to TNM classification of tumors, again no difference was found.

As opposed to these results, many studies prove that the right colorectal cancer is more often in an advanced stage, whereas the left colorectal cancer is diagnosed in earlier stages (3,4,8,9,12).

Also, there is a difference in cancer differentiation (gradus). The right colorectal cancer shows a poorer differentiation in comparison to the left colon cancer, 19,7 % to 12,3 %. This result corresponds to the Dae Ro Lima's study conducted in South Korea in which more patients (13,5%) with right colon cancer show a poor differentiation compared to patients (4,3%) with the left colon cancer. The difference could arise from the different embryonal basis of the left and right colon development (31).

Time median to recurrences or metastases was 20 months. We observed a significant difference regarding the left and right colon cancer: the right colon tumors have a shorter time to recurrences or metastases development which is similar to literature data (3,4,8,9,12,19-2 -26, 29,31,32).

A positive treatment outcome in the survey had 205 patients, which makes 75%, with no significant difference according to the colorectal cancer localization. Cancer localization does not show a statistically significant influence on the overall survival rate (Mantel – Cox,  $p=0,10$ ).

However, Kaplan – Meier survival analysis of the patients divided according to localization, shows a overall five year survival rate in 62% of patients with right colon cancer in comparison to 72% in patients with left colon cancer.

Glebov's study shows that a microsatellite instability is more often in the right colorectal cancer, while a chromosomal instability is characteristic for left colorectal cancer. Moreover, Glebov and his associates discovered that over 1000 genes have a different expression in right and left colorectal cancer (5). The biology of left and right colon cancer is rather complex, but gradually reveals different surgical and treatment options according to its analysis (12-18,25,26,31,32).

## CONCLUSIONS

1. There is a difference in colorectal cancer behaviour according to the localization itself noticeable in this study.

2. There is a difference in time to metastases or recurrences regarding the localization: this period is much shorter for the right colon cancer than for the left colon cancer.
3. There is a difference in the total five year survival rate according to the cancer localization, and this total five year survival rate is 72% in patients with left colon cancer in comparison to 62% in patients with right colon cancer.
4. There is no statistically significant difference in the cancer localization according to the gender.
5. There is no statistically significant difference according to the TNM staging.

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