



Prognostic Factors of Recurrence and Survival in Operated Patients with Colorectal Cancer

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ABSTRACT

BACKGROUND:

The recurrence of colorectal cancers is considered to be one of the greatest post-surgical complications that is affected by various factors. This study was designed to investigate the prognostic factors that affect the recurrence and survival of patients with colon and rectal cancers.

METHODS:

A retrospective study was performed on 380 patients with colorectal cancers who underwent surgery were enrolled in the study (152 patients with colon cancer and 228 patients with rectal cancer). Preoperative serum albumin level, type of surgery, tumor size, differentiation grade, proximal, distal and radial, and marginal involvement, the total number of excised lymph nodes, the number of involved lymph nodes, and tumor stage were recorded. Also, the incidences of recurrence and metastasis were recorded during the study.

RESULTS:

380 patients with a mean age of 57.11 years were enrolled in the study. 152 patients with an average age of 57.57 years were diagnosed as having colon cancer. Recurrence and metastasis occurred in two patients (1.3%) and five patients (3.3%), respectively. 18 patients (11.8%) died because of colon cancer. 228 patients with a mean age of 56.81 had rectal cancer. Recurrence was seen in 19 patients (8.3%) and metastasis in 33 patients (14.5%). 38 patients (16.7%) died because of rectal cancer. Tumor size and involved lymph nodes were independent prognostic factors for the recurrence and metastases of colon cancer. Only involved lymph nodes were associated with death due to colon cancer. Independent prognostic factors for rectal cancer metastasis include serum albumin level and age. The total number of excised lymph nodes was the only predictor of tumor recurrence and death in rectal cancer. The median survival times of colon and rectal cancers were 90 and 110 months, respectively.

CONCLUSION:

The size of the tumor and the number of involved lymph nodes were independent prognostic factors for recurrence and metastasis of colon cancer. Also, the number of involved lymph nodes was associated with colon cancer-related deaths. In the case of rectal cancer, serum albumin levels and age predicted metastases. Only the total number of excised lymph nodes had a reverse relationship with recurrence and rectal cancer-related death.

KEYWORDS:

Colorectal Neoplasms; Neoplasm Recurrence; Neoplasm metastasis; Lymphatic metastasis; Survival

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INTRODUCTION

Colorectal cancers are one of the most common cancers,^{1,2} and about one million new cases occur each year.³⁻⁵ Colorectal cancers are the third most common cancer and the second leading cause of death from cancers.⁵⁻⁷ The risk of this disease is estimated at 5% per person throughout life.⁴ Surgical treatment is considered the best treatment for colorectal cancer.^{6,8} About 50% of patients are completely treated with surgical and other procedures, but treatment options are more limited in people with metastases.⁴ Metastases and local recurrence were associated with high mortality and morbidity rates.^{8,9}

Local recurrence occurs in 4-30%, and even 40% of patients^{9,10} and significantly reduces the quality of life, with a 5-year survival rate of about 25%,^{11,12} Generally, the 5-year survival in the early stages of colorectal cancers is more than 90%, in an area with lymphatic nodal involvement of up to 65%, and in metastatic cases, it reaches less than 10%.⁴

In previous studies, different factors such as histologic grade, T stage, the ratio of involved lymph nodes to total excised lymph nodes,^{2,13} preoperative carcino-embryonic antigen (CEA),^{14,15} neutrophil to lymphocyte ratio (NLR),^{3,16} tumor site^{5,7,17} obesity,¹⁸ genetics,^{4,19} tumor stage,^{8,19} male sex, alcohol us,⁸ surgical quality, pathologic features such as lymphatic invasion, margin positivity or lack of infiltration of lymphocytes^{8,11} have been introduced as prognostic factors for recurrence and survival in patients with colorectal cancer. Local and systemic recurrence occurs in approximately one-quarter of patients with colorectal cancer and is considered a failure factor in the treatment and a poor prognostic factor.⁶ So, recognizing the determining factors of prognosis and relapse is very important. Therefore, the present study retrospectively investigated the prognostic factors affecting the recurrence and survival of patients with colon and rectal cancers.

MATERIALS AND METHODS

Data collection began after receiving ethical approval from the local Ethics Committee. Patients who underwent surgery from 21 March 2013 to 20 March, 2016 with the diagnosis of colorectal cancers at Shahid Faghih Hospital in Shiraz (Iran) were evaluated retrospectively. All of these patients were examined by colonoscopy, and the

pathological diagnosis was confirmed before surgery. Patients with metastases, bone and para-aortic lymph node involvement, and uncertain pathological reports were excluded from the study.

Due to the different properties of colon and rectal cancer, the gathered data on colon and rectal cancer were evaluated independently. Patients' demographic characteristics, including age and sex, albumin level (for measuring physical and nutritional status), and preoperative data, including chemotherapy and radiotherapy, were extracted from the patients' records. Then, the type of operation, the size of the mass in cm, its degree of differentiation (well, moderately, and poorly), proximal, distal and radial, and marginal involvement, the total number of excised lymph nodes, the number of involved lymph nodes, and tumor stage were recorded based on TNM staging. In the end, the duration of the follow-up of the patients and recurrence or metastasis of the tumor were investigated, and the obtained data entered the analysis process.

Data analysis

Data were analyzed using SPSS software version 21. The categorized variables were compared by the two-sided Pearson or Fisher exact test, and quantitative variables were compared by the t test. The Kaplan-Meier test was used to calculate survival. Also, univariate and multivariate analyses were performed using the Cox proportional hazards regression model. A *P* value of 0.05 was deemed statistically significant.

RESULTS

152 patients, of 189 patients with colon cancer and 228 patients of 297 patients with rectal cancer, were enrolled in the study. Of the 380 patients in the study, 170 were women (44.7%), and 210 were men (55.3%). The mean age of the patients was 57.11 ± 14.27 years (median=58). The mean albumin level was 3.12 ± 2.00 (median=4.00). The average tumor size was 3.97 ± 2.26 cm (median=4cm). 211 patients (55.5%) had a history of radiotherapy. In terms of differentiation, well, moderate, and poor differentiation were reported in 209 (55%), 64 (16.84%), and 25 (6.57%) cases, respectively. Also, 82 cases (21.6%) were reported as undifferentiated. The mean number of excised lymph nodes was 8.44 ± 7.33 (median=7), and the mean number of involved lymph

nodes was 0.99 ± 3.04 (S.E=0.17, median=0, and range=0-33). Proximal marginal involvement was not observed in any cases, but in two patients (0.5%), there was distal marginal involvement, and in six patients (1.6%), there was a radial marginal involvement. 174 patients (45.8%) were operated on by laparotomy, and 206 patients (54.2%) were surgically treated by laparoscopy. Recurrence and metastasis were observed in 21 patients (5.5%) and 38 patients (10%), respectively. The mean follow-up period was 34.76 ± 24.93 months (median=30). At the end of the study, 299 patients (78.7%) were free of disease, and 24 patients (6.3%) were alive with cancer. Also, 56 patients (14.7%) died due to cancer, and one patient (0.3%) died for other reasons.

Colon cancer

Table one demonstrates colon cancer patient's features. 152 patients (76 men) with an average age of 57.57 ± 14.53 years (range of 26 to 87 years, median=59) were diagnosed as having colon cancer. Radiotherapy was performed only in five patients (3.3%) before surgery. The mean albumin level was 1.98 ± 2.15 mg/dL (standard error (S.E)=1.17). The mean tumor size was 4.63 ± 2.42 cm (median=4.5). The lymphatic invasion was observed in 42 patients (27.6%). The mean number of lymph node excision was 10.04 ± 8.55 (median=9), and the mean number of involved lymph nodes was 1.48 ± 4.32 (S.E=0.38). The tumor differentiation was well-differentiated in 88 cases (57.9%), moderately differentiated in 26 cases (17.1%), poor differentiated in 10 cases (6.6%), and undifferentiated in 28 cases (18.4%). There was no proximal and distal marginal involvement, and only two patients (1.3%) had radial marginal involvement. 80 patients (52.6%) underwent laparotomy, and 72 patients (47.4%) underwent laparoscopy. Recurrence and metastasis occurred in two patients (1.3%) and five patients (3.3%), respectively. At the end of the study, 119 patients (78.3%) were alive without disease, 14 patients (9.2%) were alive with the disease, and 18 patients (11.8%) died of cancer. In addition, a patient died for unrelated reasons.

The average number of involved lymph nodes ($P < 0.001$), relapse rate ($P < 0.001$), and metastasis ($P = 0.001$) were significantly higher in patients who died with colon cancer. The tumor had a worse degree

of differentiation in dead patients ($P = 0.001$). Most dead patients had undergone laparotomy ($P = 0.023$) (Table 1).

Rectal cancer

As shown in table two, 228 patients (134 men) with a mean age of 56.81 ± 14.11 years (range of 25 to 94 years, median=57) had rectal cancer. Radiotherapy was performed for 164 patients (71.9%) before the surgery. The mean albumin level was 4.31 ± 0.76 mg/dL (median=4.30). The mean rectal mass size was 3.48 ± 2.00 cm (median=3.5). The lymphatic invasion was observed in 41 patients (18%). The mean number of lymph nodes removed was 5.85 ± 5.99 (S.E: 0.39, median=5), and the average number of involved nodes was 0.65 ± 1.58 (S.E=0.11), respectively. The tumor differentiation was well-differentiated in 121 cases (53.1%), moderately differentiated in 38 cases (16.7%), poorly differentiated in 15 cases (6.6%), and undifferentiated in 54 cases (23.7%), respectively. There was no proximal marginal involvement. However, distal and radial marginal involvements were observed in two (0.9%) and four (1.8%) cases, respectively. 94 patients (41.2%) underwent laparotomy, and 134 patients (58.8%) underwent laparoscopy. Recurrence was seen in 19 patients (8.3%) and metastasis in 33 patients (14.5%). At the end of the study, 180 patients (78.9%) were alive without disease, 10 patients (4.4%) were alive with the disease, and 38 patients (16.7%) died of cancer. The incidence of recurrence and metastasis in the patients who died was significantly higher ($P < 0.001$) (Table 2).

Factors affecting recurrence, metastasis, and survival

Cox analysis showed that tumor size (Chi-square=4.86, $P = 0.027$) and involved lymph nodes (Chi-square=8.22, $P = 0.016$) were independent factors of prognosis for the recurrence of colon cancer. Prognostic factors for colon metastases included tumor size (Chi-square=25.986, $P = 0.009$) and involved lymph nodes (Chi-square=29.52, $P = 0.003$). Only involved lymph nodes were associated with death due to colon malignancy (Chi-square=4.82, $P = 0.028$). Independent prognostic factors of rectal cancer metastasis include serum albumin level (Chi-square=7.97, $P = 0.005$) and age (Chi-square=5.20, $P = 0.023$). The total number of excised lymph nodes was the only predicting

Table 1: Data comparison of patients with colon cancer on the basis of clinical outcome

Factors	Alive patients	Dead patients	P value	
Age	57.18±14.11	60.44±17.55	0.37	
Sex	Male	11 (61.1%)	0.31	
	Female	7 (38.9%)		
Radiotherapy (yes)	4 (3%)	1 (5.6%)	0.56	
Albumin	2.05±2.10 (S.E:0.18)	1.48±2.49 (S.E:0.60)	0.30	
Tumor Size	4.60±2.41	4.90±2.58	0.66	
Total lymph node excision	10.27±8.38	8.33±9.81 (S.E:2.31)	0.36	
Involved lymph node	Mean±SD	1.01±2.25 (S.E:0.21)	5.21±10.89 (S.E:2.91)	<0.001
	Yes	37 (27.6%)	5 (27.8%)	0.98
	No	97 (72.4%)	13 (72.2%)	
Differentiation	Well	81 (60.4%)	7 (38.9%)	0.001
	Moderate	24 (17.9%)	2 (11.1%)	
	Poor	5 (3.7%)	5 (27.8%)	
	Undifferentiation	24 (17.9%)	4 (22.2%)	
Margin involvement	Proximal	0	0	-
	Distal	0	0	-
	Radial	2 (1.5%)	0	0.60
Type of Surgery	Laparotomy	66 (49.3%)	14 (77.8%)	0.023
	Laparoscopy	68 (50.7%)	4 (22.2%)	
Tumor recurrence (yes)	0	2 (11.1%)	<0.001	
Tumor Metastasis (yes)	2 (1.5%)	3 (16.7%)	0.001	
Time of follow-up	36.78±23.94	21.17±14.99	0.008	

factor of tumor recurrence (Chi-square=6.74, $P=0.009$) and death (Chi-square=5.48, $P=0.008$) in rectal cancer.

The median survival times of colon and rectal cancers were 90 and 110 months, respectively (Figs 1 and 2).

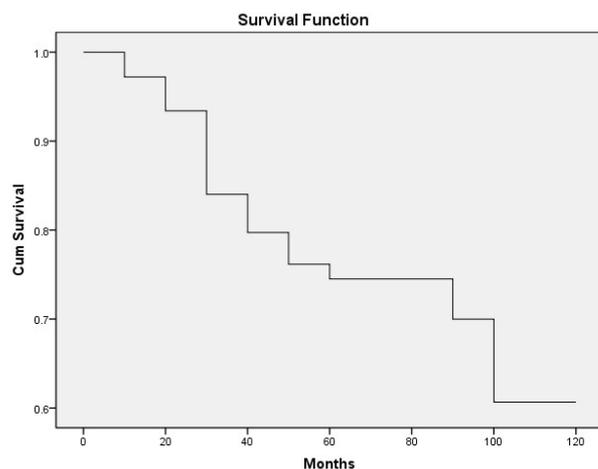
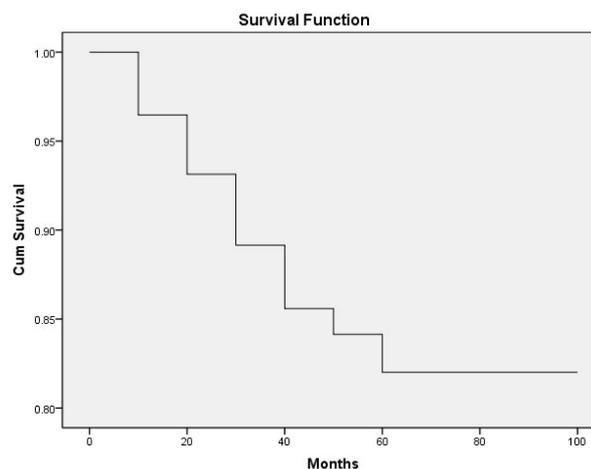
DISCUSSION

The present study was conducted to determine the prognostic factors for the recurrence and survival of patients with colon and rectal cancers. Based on the results, the average age of the patients with both malignancies was reported to be 57 years, indicating that the sixth decade of life has the highest prevalence rate for individuals. About one-quarter of the patients with colon cancer and one-fifth of the patients with rectal cancer experienced regional lymph node involvement, and with very little difference between the two, their radical margins were reported in about 2% of the cases. 8.3% of the patients

with rectal cancer and 1.3% of the patients with colon cancer experienced localized relapses. The results showed that the tumor size and number of involved lymph nodes were associated with a poor prognosis of colon cancer and considered as a risk factor for recurrence and metastasis. Other factors such as age, sex, marginal involvement, tumor location, cell differentiation, and metastasis were not associated with recurrence and metastasis. Also, the number of involved lymph nodes was associated with colon cancer-related deaths. In the case of rectal cancer, according to the present study, no risk factors for recurrence were found. But the interesting point is that the total number of lymph nodes removed during the operation had an inverse relationship with recurrence. This finding shows that removing more lymph nodes in the area indicates a better quality of surgery and its accuracy. The total number of lymph nodes removed has also been

Table 2: The clinical outcome of patients with rectal cancer

Factors		Alive patients	Dead patients	P value
Age		56.54±14.02	58.16±14.65	0.51
Sex	Male	81 (42.6%)	13 (34.2%)	0.33
	Female	109 (57.4%)	25 (65.8%)	
Radiotherapy (yes)		135 (71.1%)	29 (76.3%)	0.51
Albumin		4.32±0.78	4.28±0.68	0.84
Tumor Size		3.35±1.96	4.21±2.09	0.037
Total lymph node excision		6.07±5.95	4.76±6.17 (S.E:1.00)	0.22
Involved lymph node	Mean±SD	0.63±1.62 (S.E: 0.13)	0.76±1.43 (S.E: 0.26)	0.70
	Yes	33 (17.4%)	8 (21.1%)	
	No	157 (82.6%)	30 (78.9%)	
Differentiation	Well	103 (54.2%)	18 (47.4%)	0.29
	Moderate	33 (17.4%)	5 (13.2%)	
	Poor	10 (5.3%)	5 (13.2%)	
	Undifferentiation	44 (23.2%)	10 (26.3%)	
Margin involvement	Proximal	0	0	-
	Distal	2 (1.1%)	0	0.52
	Radial	4 (2.1%)	0	0.36
Type of Surgery	Laparotomy	76 (40%)	18 (47.4%)	0.40
	Laparoscopy	114 (60%)	20 (52.6%)	
Tumor recurrence (yes)		10 (5.3%)	9 (23.7%)	<0.001
Tumor Metastasis (yes)		15 (7.9%)	18 (47.4%)	<0.001
Time of follow-up		36.12±26.68	27.24±34.64	0.053

**Fig. 1:** Overall survival of rectal cancer.**Fig. 2:** Overall survival of colon cancer.

a predictor of rectal cancer-related deaths. Additionally, age and albumin level were prognostic factors for rectal cancer metastasis. After an average follow-up of 3 years, about 85% of the patients were alive.

Trivedi and colleagues conducted a study to determine the effective factors in the survival of patients with stage 2 colon cancer. They concluded that age was the only factor that was completely relevant to survival. Postoperative chemotherapy reduced the risk of death by up to 42% in their study, and the number of lymph nodes removed was relatively but not statistically significant.²⁰ In our study, age was not related to relapse but was related to metastasis of rectal cancer. Also, there was a significant relationship between the number of positive lymph nodes with relapse. Compton, in his review, stated that the tumor stage was the most accurate determinant of the prognosis for survival. The most promising factors in the recurrence of the disease in patients without metastasis were the quality of surgery, resection of the mesentery, and the proximity of the mass to the margin. He argued that other pathological factors such as tumor grade, histology, and vascular, neurological, and lymphatic invasion could be helpful in determining the risk of unpleasant complications of the disease.¹¹ In our study, the positive effects of margins did not have an effect on the recurrence. However, given the effect of total lymph node excision on rectal cancer recurrence and the impact of involved lymph nodes on colon cancer recurrence, it appears that proper surgical quality and complete lymph node dissociation are critical. Various factors have been introduced as prognostic factors in various studies. For example, Hao and colleagues reported histology grade, T stage, number of positive lymph nodes, the total number of excised lymph nodes, carcinoembryonic antigen (CEA), and neutrophil to lymphocyte ratio (NLR) as prognostic factors of colonic cancer. In their study, the histology grade, preoperative CEA, and NLR were determined as independent factors.³ Patel and his colleagues named male sex, alcohol use, and wound mass as risk factors for recurrent rectal cancer.⁸ Zhao and others described T stage, vascular invasion, and topical relapses as three important factors in determining the 5-year survival prognosis in patients with rectal cancer.¹³ Pacelli and colleagues expressed the availability of surgical facilities and radical mass removal

as positive prognostic factors for rectal cancer. They also acknowledged that increasing preoperative CEA, back pain, and adhesion of the mass to the pelvic wall based on a computed tomography (CT) scan were all significantly related to survival.

Also, preoperative chemoradiotherapy and radical removal of the tumor were independently associated with localized mass control.²¹ Parnaby and colleagues also concluded that LNR and extramural vascular invasion independently predicted overall survival and disease-free survival of colon cancer.¹⁶

In the study of Sinicrope and co-workers, the body mass index (BMI) of patients with colon cancer was associated with prognosis. They found that obesity was an independent factor in the prognosis and survival of colon cancer. Men with colon cancer and stage 2 and 3 of obesity ($BMI \geq 35 \text{ kg/m}^2$) had less survival than men of normal weight. Women with stage 1 of obesity ($BMI = 30 - 34 \text{ Kg/m}^2$) also had lower survival than normal women. Furthermore, weight gain ($BMI = 25 - 30 \text{ Kg/m}^2$) without obesity improved survival, and weight loss was associated with worsening survival.¹⁸ Our study also looked at the patient's nutritional status by reviewing the preoperative albumin level. Higher albumin levels were found to reduce the risk of rectal cancer metastasis.

CONCLUSION

As a result, it can be argued that in the current study, the recurrence of colon cancer had a direct relationship with mass size as well as the number of involved lymph nodes. In other words, the larger size of the mass and the increase in the number of involved lymph nodes around the mass can be associated with an increased chance of recurrence in colon cancer. Also, it has been shown that the removal of regional lymph nodes can play a role in protecting against the recurrence of rectal cancer.

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ETHICAL APPROVAL

There is nothing to be declared.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

- Arredondo J, Baixauli J, Beorlegui C, Arbea L, Rodríguez J, Sola JJ, et al. Prognosis factors for recurrence in patients with locally advanced rectal cancer preoperatively treated with chemoradiotherapy and adjuvant chemotherapy. *Dis Colon Rectum* 2013;56:416-21. doi: 10.1097/DCR.0b013e318274d9c6.
- Attaallah W, Gunal O, Manukyan M, Ozden G, Yegen C. Prognostic impact of the metastatic lymph node ratio on survival in rectal cancer. *Ann Coloproctol* 2013;29:100-5. doi:10.3393/ac.2013.29.3.100.
- Wuxiao ZJ, Zhou HY, Wang KF, Chen XQ, Hao XB, Lu YD, et al. A prognostic model to predict survival in stage III colon cancer patients based on histological grade, preoperative carcinoembryonic antigen level and the neutrophil lymphocyte ratio. *Asian Pac J Cancer Prev* 2015;16:747-51. doi:10.7314/apjcp.2015.16.2.747.
- Koelzer VH, Herrmann P, Zlobec I, Karamitopoulou E, Lugli A, Stein U. Heterogeneity analysis of metastasis associated in colon cancer 1 (MACC1) for survival prognosis of colorectal cancer patients: a retrospective cohort study. *BMC Cancer* 2015;15:160. doi:10.1186/s12885-015-1150-z.
- Ishihara S, Muroto K, Sasaki K, Yasuda K, Otani K, Nishikawa T, et al. Impact of Primary Tumor Location on Postoperative Recurrence and Subsequent Prognosis in Nonmetastatic Colon Cancers: A Multicenter Retrospective Study Using a Propensity Score Analysis. *Ann Surg* 2018;267:917-921. doi:10.1097/SLA.0000000000002206.
- Xu G, Zhang M, Zhu H, Xu J. A 15-gene signature for prediction of colon cancer recurrence and prognosis based on SVM. *Gene* 2017;604:33-40. doi:10.1016/j.gene.2016.12.016.
- Wray CM, Ziogas A, Hinojosa MW, Le H, Stamos MJ, Zell JA. Tumor subsite location within the colon is prognostic for survival after colon cancer diagnosis. *Dis Colon Rectum* 2009;52:1359-66. doi:10.1007/DCR.0b013e3181a7b7de.
- Patel SA, Chen YH, Hornick JL, Catalano P, Nowak JA, Zukerberg LR, et al. Early stage rectal cancer: clinical and pathologic prognostic markers of time to local recurrence and overall survival after resection. *Dis Colon Rectum* 2014;57:449-59. doi:10.1097/DCR.0b013e3182a70709
- Westberg K, Palmer G, Johansson H, Holm T, Martling A. Time to local recurrence as a prognostic factor in patients with rectal cancer. *Eur J Surg Oncol* 2015;41:659-66. doi:10.1016/j.ejso.2015.01.035.
- Asoglu O, Karanlik H, Muslumanoglu M, Igcı A, Emek E, Ozmen V, et al. Prognostic and predictive factors after surgical treatment for locally recurrent rectal cancer: a single institute experience. *Eur J Surg Oncol* 2007;33:1199-206. doi:10.1016/j.ejso.2007.02.026.
- Compton CC. Pathologic prognostic factors in the recurrence of rectal cancer. *Clin Colorectal Cancer* 2002;2:149-60. doi:10.3816/CCC.2002.n.020.
- Larsen SG, Wiig JN, Giercksky K-E. Hydronephrosis as a prognostic factor in pelvic recurrence from rectal and colon carcinomas. *Am J Surg* 2005;190:55-60. doi:10.1016/j.amjsurg.2004.07.043
- Zhou D, Ye M, Bai Y, Rong L, Hou Y. Prognostic value of lymph node ratio in survival of patients with locally advanced rectal cancer. *Can J Surg* 2015;58:237-44. doi:10.1503/cjs.001515
- Jeong S, Nam TK, Jeong JU, Kim SH, Kim K, Jang HS, et al. Postoperative carcinoembryonic antigen level has a prognostic value for distant metastasis and survival in rectal cancer patients who receive preoperative chemoradiotherapy and curative surgery: a retrospective multi-institutional analysis. *Clin Exp Metastasis* 2016;33:809-16. doi:10.1007/s10585-016-9818-6
- Cai Y, Li Z, Gu X, Fang Y, Xiang J, Chen Z. Prognostic factors associated with locally recurrent rectal cancer following primary surgery. *Oncol Lett* 2014;7:10-16. doi:10.3892/ol.2013.1640
- Parnaby C, Scott N, Ramsay G, MacKay C, Samuel L, Murray G, et al. Prognostic value of lymph node ratio and extramural vascular invasion on survival for patients undergoing curative colon cancer resection. *Br J Cancer* 2015;113:212-9. doi:10.1038/bjc.2015.211
- Petrelli F, Tomasello G, Borronovo K, Ghidini M, Turati L, Dallera P, et al. Prognostic survival associated with left-sided vs right-sided colon cancer: a systematic review and meta-analysis. *JAMA Oncol* 2017;3:211-19. doi:10.1001/jamaoncol.2016.4227
- Sinicrope FA, Foster NR, Sargent DJ, O'Connell MJ, Rankin C. Obesity is an independent prognostic variable in colon cancer survivors. *Clin Cancer Res* 2010;16:1884-93. doi: 10.1158/1078-0432.CCR-09-2636
- Fang YJ, Lu ZH, Wang F, Wu XJ, Li LR, Zhang LY, et al. Prognostic impact of ER β and MMP7 expression on overall survival in colon cancer. *Tumor Biol* 2010;31:651-8. doi: 10.1007/s13277-010-0082-0.
- Trivedi H, Chamarthy U, Dicarolo L, Herman J, Srkalovic G. Prognostic factors of overall survival for patients with stage II colon cancer. *Acta Med Acad* 2014;43:134. doi: 10.5644/ama2006-124.112
- Pacelli F, Tortorelli AP, Rosa F, Bossola M, Sanchez AM, Papa V, et al. Locally recurrent rectal cancer: prognostic factors and long-term outcomes of multimodal therapy. *Ann Surg Oncol* 2010;17:152-62. doi: 10.1245/s10434-009-0737-5