RESEARCH COMMUNICATION

Is Tumor Growth Faster with Obstructive Colonic Cancer?

Surawut Charoenkajonchai

Abstract

Background: It is generally known that long duration of untreated colonic cancer can lead to obstruction. Another contributing factor might be tumor growth rate. The present study was conducted to compare tumor growth rates related to lymph node metastasis of the obstructive and non-obstructive colonic cancers. Methods: 169 patients who underwent operations for colonic cancer were studied retrospectively. Patient and tumor characteristics as well as clinical outcomes were analyzed. Results: 94 patients (55.6%) presented with obstructed colonic cancers, and 75 (44.4%) with non-obstructed, 78.7% and 57.3%, respectively having a tumor size greater than 5 cm. On logistic regression analysis, both groups had similar lymph node metastasis rates (OR=1.6; 95% CI=0.8-3.2). Conclusion: No relations between obstruction and tumour size or lymph node metastasis were found. Thus, obstructions only occur because of other factors and do not contribute to tumor growth. Utilizing effective screening programs to determine obstructions is recommended.

Keywords: Obstructive colonic cancer - lymph node metastasis - tumor growth rate

Asian Pacific J Cancer Prev, **11**, 1581-1585

Introduction

Colorectal cancer is reported to be the fourth most common of cancer death in the world (Shibuya et al., 2002). In Thailand, it ranks as third in males (after liver and lung cancer), and fifth in females (after cervix, breast, liver and lung) (Khuhaprema and Srivatanakul, 2008). The rate of colorectal cancer in Thailand is increasing (Moore et al., 2008).

Surgery is the mainstay for treatment of colorectal cancer either for emergency or elective setting. Factors influencing mortality for colorectal cancer surgery include age, ASA status III-IV, proximal colon damage, peritonitis and perioperative renal failure (Tan and Sim, 2010). Obstructive colonic cancer can also influence mortality as a result of proximal colon damage and peritonitis. While it is reported that obstructive colonic cancer rate is as high as 8-29% in developed countries (Deans et al., 1994), in Thailand there have been no report about the obstructive rate of this cancer but it is assumed to be higher because of problems related to making public health accessible and the limitation of the screening program. Obstructive colonic cancer requires an urgent treatment, which results in high complication and mortality. It is also associated with poor long term outcome (Anderson et al., 1992; Biondo et al., 2005; Bass et al., 2009).

We can assume that obstructive colonic cancer has developed for a long period of time after its originating, and so has lymph node metastasis. Concerning this, the obstructive colonic cancer should have more lymph node metastasis than the non-obstructive cancer. Through our hospital's experiences, however, we found that the rate of lymph node metastasis in the obstructive colonic cancer cases was similar to that of the non-obstructive cases. This raised a question whether in fact the obstruction group experienced a rapid tumor growth rate. In early colorectal cancer, the estimated tumor-doubling time was around 26 months, and the growth speed was most affected by the depth of invasion of the initial lesions (Matsui et al., 2000). Another literature (Bolin, 1983) estimated 130 days of tumor-doubling time in 27 CRCs, and found rapid speed of growth in a poorly differentiated cancer. Through many literature reviews (Welin, 1963; Burnett and Greenbaum, 1981; Tada, 1984; Tsunoda et al., 1990; Hofstad and Vatn, 1997; Pickhardt, 2007), those who studied tumor growth, none of them compared growth patterns between obstructive and non-obstructive colonic cancer and paid attention in studying time interval before obstruction. Moreover, no study directly observed it prospectively without undermining ethical issues.

In this study, we asked a question whether or not patients presenting with an obstructive colonic cancer experienced a more rapid growth rate than those who were not. By using lymph node status, lymphovascular invasion and distant metastasis as indicators, we were able to compare growth rate relative to these indicators. We hypothesized that tumors grew at a more rapid rate in the obstructive group than in the non-obstructive group. If lymph node metastasis or lymphovascular invasion or metastasis spread wider in the non-obstructive group than in the obstructive group, it could be assumed that the latter was experiencing higher rate in tumor growth.

*General Surgical Unit, Department of Surgery, Chonburi Hospital, Chonburi, Thailand. *For correspondence : surawutch@gmail.com*

Materials and Methods

One hundred seventy patients who were diagnosed as colonic cancer underwent operations at Chonburi Hospital during the period from January 2005 to December 2008. One of them was not adenocarcinoma and was excluded from this study. Rectal cancer patients were not included in this study. Clinical records of the 169 patients were reviewed retrospectively. Patient and tumor characteristics, clinical data and treatment outcome were collected. Patient characteristics included gender, age, underlying diseases, presentation (obstruction, perforation, elective) and ASA status. Tumor characteristics included tumor location (ascending, transverse, descending and sigmoid colon), tumor size, lymph node metastasis, lymphovascular invasion status, distant metastasis and tumor behavior (well, moderately or poorly differentiated). Clinical data included degree of urgency (emergency, elective) and operation (Rt.hemicolectomy, etc.). Treatment outcomes included length of stay, septic complication and mortality.

Those in the obstructive group who underwent emergency operations were having either complete obstruction or impending perforation. The others in the same group underwent operations in the semi-elective setting. Those in the non-obstructive group who also underwent emergency operations were caused by peritonitis and found to be having perforated colonic cancers. Septic complication was defined by at least one of the following criteria: having fever more than 38°C, WBC>15000/mm^3, documented surgical site infection, UTI, pneumonia or any other organ infections. Death resulted from any cause during admission was considered as mortality. All these data were confidentially recorded in case report forms.

Statistics

The obstructive and non-obstructive groups were statistically compared for the aspects of patient characteristics and tumor characteristics. Chi-square tests were used to compare variables representing proportional data. T-tests were used to compare variables representing quantities. Multivariate analyses of the lymph node status were carried out using logistic regression model, and the evaluation of the differences between these two groups were performed with adjusting for three different variables, namely, T-staging, tumor size and tumor behavior. Lymphovascular invasion and distant metastasis status were also analyzed in a similar fashion. ANOVA was conducted to make comparisons between perforated, obstructed and elective groups, with respect to septic complication and mortality. Probability (p-value) < 0.05 was considered to be significant.

Results

Patient Characteristics

A total of 306 patients underwent operations for colorectal cancer resections. One hundred seventy of them were having colonic cancers, with one non-adenocarcinoma patient excluded. Of these remaining patients, 94 persons presented obstructions (55.6%), and 75 persons presented non-obstruction. There were 61 and 39 male patients in the obstructive group and the non-obstructive group (64.9% and 52%), and the average age was 62.9 and 60.9, respectively. The most underlying disease was cardiovascular and hypertension (49.7%), and nearly sixty percent (59.2%) of patients was in ASA status II.

Emergency operations were performed for 72 patients of the obstructive group (76.6%) and in 13 patients of the non-obstructive group (17.3%). For the latter, all of them were perforated colon cancer. The data is shown in table 1.

Tumour Characterisitcs

Tumour location was mostly found in sigmoid colon (54.2% in obstructive and 56% in non-obstructive group). The most common procedure performed in the obstructive group was sigmoid resection with end colostomy (38.2%). The obstructive group was significantly larger in size than the non-obstructive group. This showed in size > 5 cm. as it was found in 78.7% of the obstructive and in 57.3% of the non-obstructive group (p=0.003). Most tumor behavior was moderate differentiation (59.5% in obstructive and 62.6% in non-obstructive group). Nearly half of 169 patients were T4 disease (48.5%) but similar in both groups (53.1% and 42.6% ; p=0.23). Table 2 shows the tumor characteristics.

Lymphovascular Invasion, Metastasis and Staging

More lymph nodes were harvested in the obstructive group (21 vs. 17) but it was not statistically significant (p=0.33). Regarding the N-staging, N0:N1:N2 was

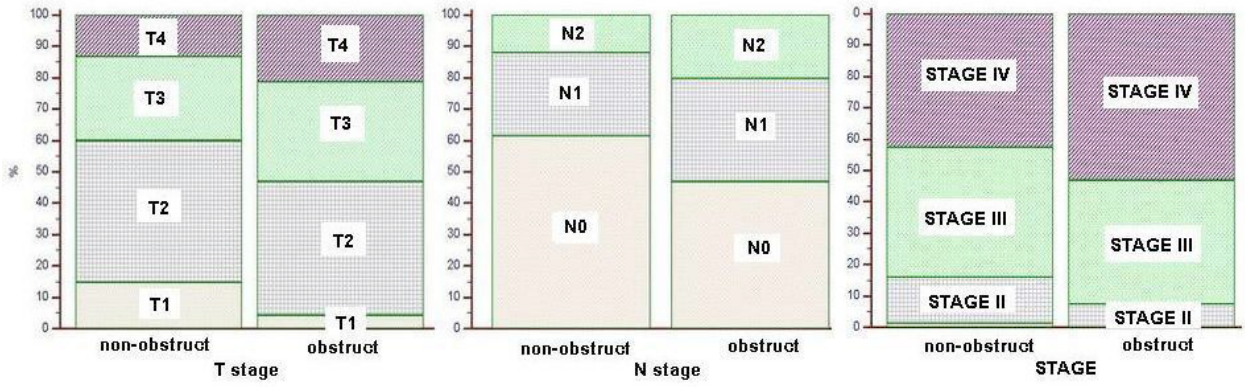

Figure 1. Tumor Stage Distribution of Obstructive and Non-Obstructive Colonic Cancer

Table 1. Patient Characteristics

		Obstructive (N=94)	Non-Obstructive (N=75)	p-value
Gender male		61 (64.9)	39 (52)	0.09
Age (range)		62.9 (21-89)	60.9 (27-84)	0.35
Co-Morbidity	none	43 (45.7)	29 (38.6)	0.36
	CVS/HT	47 (50.0)	37 (49.3)	
	Respiratory	4 (4.2)	6 (8)	
	DM	14 (14.8)	15 (20)	
	Renal	2 (2.1)	3 (4)	
ASA status	I	19 (20.2)	20 (26.6)	0.19
	II	54 (57.4)	46 (61.3)	
	III	21 (22.3)	9 (12)	
Emergency operation		72 (76.6)	13 (17.3)	0.00*

Numbers in parentheses were percentage unless otherwise specified; * statistically significant

Table 2. Tumor Characteristics

		Obstructive (N=94)	Non-Obstructive (N=75)	p-value
Tumor location	Right colon	18 (19.1)	15 (20)	0.94
	Transverse colon	12 (12.7)	10 (13.3)	
	Left colon	13 (13.8)	8 (10.6)	
	Sigmoid colon	51 (54.2)	42 (56)	
Tumor size	< 5 cm.	20 (21.2)	32 (42.6)	0.003*
	≥ 5 cm.	74 (78.7)	43 (57.3)	
Tumor behavior	well diff.	32 (34)	25 (33.3)	0.77
	moderately diff.	56 (59.5)	47 (62.6)	
	poorly diff.	6 (6.3)	3 (4)	
T stage	T1	0 (0)	1 (1.3)	0.23
	T2	7 (7.4)	11 (14.6)	
	T3	36 (38.2)	31 (41.3)	
	T4	50 (53.1)	32 (42.6)	
Lymph node	N0	44 (46.8)	46 (61.3)	0.14
	N1	31 (32.9)	20 (26.6)	
	N2	19 (20.2)	9 (12)	
Lymph node harvest (range)		21 (4-86)	17 (3-75)	0.33
Lymphovascular invasion		52 (55.3)	33 (44)	0.14
Distant metastasis		20 (21.3)	10 (13.3)	0.18
TNM stage	I	4 (4.2)	11 (14.6)	0.07
	II	40 (42.5)	34 (45.3)	
	III	30 (31.9)	20 (26.6)	
	IV	20 (21.2)	10 (13.3)	

Numbers in parentheses were percentage unless otherwise specified; * statistically significant

Table 3 Multivariate Logistic Regression Analysis of Lymph Node Status, Lymphovascular Invasion and Distant Metastasis Status

	Lymph node status		Lymphovascular invasion		Distant metastasis	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Obstruction						
Yes	1.6 (0.8-3.2)	0.16	1.5 (0.8-3.1)	0.25	1.5 (0.6-3.7)	0.38
T stage						
T1-2	0.1 (0.0-3.2)	0.16	0.2 (0.0-0.6)	0.01*	0.4 (0.1-2.0)	0.24
T3	0.5 (0.3-1.0)	0.06	0.4 (0.2-0.8)	0.01*	0.2 (0.1-0.5)	0.00*
T4 †	1		1		1	
Tumor size						
< 5 cm.	1.0 (0.5-2.1)	0.99	1.3 (0.6-2.9)	0.47	0.6 (0.2-1.7)	0.31
≥ 5 cm. †	1		1		1	
Tumor behavior						
well diff.	0.6 (0.3-1.2)	0.16	0.4 (0.2-0.8)	0.01*	1.2 (0.4-3.2)	0.78
moderate diff. †	1		1		1	
poorly diff.	2.1(0.4-11.3)	0.37	∞ (0.0-∞)	0.99	1.9 (0.5-8.1)	0.39

* statistic significant; † reference for its own variable

47:33:20 and 61:27:12 in the obstructive and the non-obstructive group respectively. The proportions were more aggressive in the obstructive than the non-obstructive group. However, this was not statistically significant

Table 4. Septic Complication, Mortality Outcome and Length of Stay

	Obstruction (N=94)	Perforation (N=13)	Elective (N=62)	p value
Sepsis	22 (23.4%)	6 (46.2%)	4 (6.5%)	0.001*
Death	6 (6.4%)	4 (30.8%)	2 (3.2%)	0.002*
Length of stay (range)	16.9 (7-68)	16.1 (5-26)	14.4 (5-67)	0.27

* statistic significant

(p=0.14). Similar interpretation could be drawn for the cases of lymphovascular invasion and metastasis. For the lymphovascular invasion, 55.3% of the obstructive and 44% of the non-obstructive group were lymphovascular invasion (p=0.14). For the metastasis, 21.3% of the obstructive and 13.3% of the non-obstructive group were metastasis (p=0.18). However, with respect to TNM staging, the proportion nearly reached significance. TNM stage I:II:II:IV was 4:43:32:21 and 15:45:27:13 in the obstructive and the non-obstructive group respectively (p=0.07). Figure 1 shows the distributions of T stage, N stage and TNM stage of the obstructive and the non-obstructive groups.

Multivariate Logistic Regression Analyses

Lymph node status, lymphovascular invasion and metastasis were analyzed using obstruction as an independent variable with adjustments for T stage, tumor size and tumor behavior. The data is shown in table 3. The obstructive group was more lymph node metastasis than the non-obstructive group. However it was not statistically significant (OR=1.6, 95%CI=0.8-3.2, p=0.16). The same pattern was also found in lymphovascular status (OR=1.5, 95%CI=0.8-3.1, p=0.25) and in distant metastasis (OR=1.5, 95%CI=0.6-3.7, p=0.38). The earlier T stage was lower in lymph node metastasis when it was compared with T4 stage but it did not fall within the significant level. When comparing the earlier T stage with T4 on the aspects of lymphovascular invasion and distant metastasis, it showed differences between them. The tumors whose sizes were smaller (<5 cm) were not different in lymph node metastasis than those whose size were larger (> 5 cm). Even the smaller had more lymphovascular invasion than the larger but it was not statistically significant (OR=1.4, p=0.47). Well differentiated tumor was less lymphovascular invasion than the moderately differentiated tumor (OR=0.4, p=0.01).

Septic Complications, Mortality and Length of Hospital Stay

The perforation group had the significant highest percentage in septic complication and mortality (46% and 30% respectively). The obstructive group was significant higher in septic complication and mortality than the elective group. Length of stay was higher in the obstructive group but it was not statistically significant (p=0.27) (Table 4).

Discussion

Most obstructing tumor had size > 5 cm. This simply means that the cancer lasted long before it was found and treated. However, through the statistical analyses as mentioned in the previous section, the obstructive group had about the same growth rate as the non-obstructive group when tumor growth was determined as the presentation of obstruction in relation with lymph node metastasis. If growth rate was evaluated in relation with lymphovascular invasion or distant metastasis, both groups also had similar growth patterns. This essentially means that the tumor was left last longer before it was found in the obstructive group. Since obstructive colon cancer has higher morbidity and mortality rates than non-obstructive colon cancer, the only effective strategy to rebuild the number of deaths is to encourage a good screening program. However, there is no existing program that can completely prevent obstruction to occur, even in developed countries whose screening programs are well implemented. One possible reason has to do with rapid tumor growth rate. Further study about factors contributing to the speed of tumor, especially for those obstructive cases that escaped the preventive program, is needed to expand our knowledge base. Nonetheless, a good screening program should be introduced intensively.

In conclusion, in this study, tumor growth rate was determined by the appearance of the obstruction in relation with the spread of tumor into lymph node or lymphovascular vessel or distant organ. There was no relation between the existence of tumor obstruction and the spread of tumor. Hence, obstructive and non-obstructive colonic cancer should have similar growth patterns. This implied that obstructions were not contributed by tumor growth rates but occurred because tumor had not been detected and treatment came too late.

References

Anderson JH, Hole D, McArdle CS (1992). Elective versus emergency surgery for patients with colorectal cancer. *Br J Surg*, **79**, 706-9.

Bass G, Fleming C, Conneely J, et al (2009). Emergency first presentation of colorectal cancer predicts significantly poorer outcomes: a review of 356 consecutive Irish patients. *Dis Colon Rectum*, **52**, 678-84.

Biondo S, Martí-Ragué J, Kreisler E, et al (2005). A prospective study of outcomes of emergency and elective surgeries for complicated colonic cancer. *Am J Surg*, **189**, 377-83.

Bolin S, Nilsson E, Sjödahl R (1983). Carcinoma of the colon and rectum--growth rate. *Ann Surg*, **198**, 151-8.

Burnett KR, Greenbaum EI (1981). Rapidly growing carcinoma of the colon. *Dis Colon Rectum*, **24**, 282-6.

Deans GT, Krukowski ZH, Irwin ST (1994). Malignant obstruction of the left colon. *Br J Surg*, **81**, 1270-6.

Hofstad B, Vatn M (1997). Growth rate of colon polyps and cancer. *Gastrointest Endosc Clin N Am*, **7**, 345-63.

Khuhaprema T, Srivatanakul P (2008). Colon and rectum cancer in Thailand: an overview. *Jpn J Clin Oncol*, **38**, 237-43.

Matsui T, Tsuda S, Yao K, et al (2000). Natural history of early colorectal cancer: evolution of a growth curve. *Dis Colon Rectum*, **43**, S18-22.

Moore MA, Attasara P, Khuhaprema T, et al (2009). Cancer epidemiology in mainland South-East Asia - past, present and future. *Asian Pac J Cancer Prev*, **10**, 67-80.

Pickhardt PJ (2007). The natural history of colorectal polyps and masses: rediscovered truths from the barium enema era. *AJR Am J Roentgenol*, **188**, 619-21.

Shibuya K, Mathers CD, Boschi-Pinto C, et al (2002). Global and regional estimates of cancer mortality and incidence by site: II. Results for the global burden of disease 2000. *BMC Cancer*, **2**, 37.

Tada M, Misaki F, Kawai K (1984). Growth rates of colorectal carcinoma and adenoma by roentgenologic follow-up observations. *Gastroenterol Jpn*, **19**, 550-5.

Tan K, Sim R (2010). Surgery for obstructed colorectal malignancy in an Asian population: predictors of morbidity and comparison between left- and right-sided cancers. *J Gastrointest Surg*, **14**, 295-302.

Tsunoda A, Shibusawa M, Takimoto M (1990). [Growth rate of experimental colonic cancer in rats]. *Nippon Geka Gakkai Zasshi*, **91**, 581-7.

Welin S, Youker J, Spratt JS (1963). The rates and patterns of growth of 375 tumors of the large intestine and rectum observed serially by double contrast enema study (Malmoe technique). *Am J Roentgenol Radium Ther Nucl Med*, **90**, 673-87.