Incidence of Primary Colorectal Cancer from Colonoscopy Examinations in Patients Presenting with Liver Mass

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Background: *An in-patient presented with atypical primary liver mass and was suspected of having liver metastasis. One method of investigation is colonoscopy; however, there are currently no clear guidelines to indicate when this procedure should be performed.*

Material and Method: *This was a retrospective review of 6 years' data from the surgical endoscopic unit in Rajavithi Hospital. The inclusion criteria were: (1) patient presented with liver mass, (2) radiological findings (mainly from CT scan or MRI) were not typical for hepatocellular carcinoma (HCC), intrahepatic cholagiocarcinoma (ICGC) and other primary liver tumors. The exclusion criteria were: (1) patients did not undergo the operation in Rajavithi Hospital, (2) there was loss of patient data during the follow-up period.*

Result: *A total of 1,532 cases underwent colonoscopy, of which 109 met the inclusion criteria. There were 24 cases of positive primary colorectal cancer and the incidence was 22% (95% CI 14.1-29.9), and 1 case of terminal ileum cancer. The final results after operation showed 40 cases of HCC, and 21 cases of intrahepatic cholangiocarcinma. Risk factors for testing positive for colorectal cancer were: presenting with GI symptoms; abnormal CEA levels; and positive family history of colorectal cancer.*

Conclusion: *To increase the incidence of positive results for colorectal cancer and reduce unnecessary colonoscopy in patients who present with liver mass, the factors which indicate colonoscopy should be patients who present with GI symptom, abnormal CEA level, and whose family history raises concern.*

Keywords: *Colonoscopy, Primary colorectal cancer, Liver mass, Incidence*

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For patients who present with liver mass which is suspected to be liver metastases, colonoscopy is an investigative procedure which is used to identify the primary site of the malignant metastases. Recently, a study from Germany showed a low incidence rate (14.7%) of synchronous liver metastasis[1]. Colonoscopy requires a complicated preparation such as daily diet change and the use of laxatives, and is not totally safe. Complications which can result from this procedure include colon perforation[2] and spleen avulsion[3]. Currently, there is no evidence database or clear guidelines for recommending the use of colonoscopy to rule out primary colorectal cancer in patients who present with liver mass suspected of being liver metastasis. The present study aimed to identify risk factors that could increase positive results from colonoscopy in patients presenting with liver mass.

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Material and Method

This was a retrospective review of the database in the surgical endoscopy unit of Rajavithi Hospital from January 2006-December 2011. All of the colonoscopies were performed by general or colorectal surgeons. Patients who met the inclusion criteria were evaluated for study.

The inclusion criteria were: (1) patient presented with liver mass; (2) radiological findings (mainly from CT scan or MRI) were not typical for hepatocellular carcinoma (HCC), intrahepatic cholagiocarcinoma (ICGC) or other primary liver tumors. The exclusion were: (1) patients did not undergo the operation in Rajavithi Hospital; (2) there was loss of patient data during the follow-up period. The present study was approved by the Institutional Ethical

Committee of Rajavithi Hospital.

Data collection

Demographic data recorded included GI symptom such as abdominal pain, bowel habit change and bleeding per rectum; radiological characteristic of liver mass; family history (colorectal cancer in first-degree relative); and CEA levels. Colonoscopic findings were recorded, as well as pathological results in cases where biopsy or postoperative surgical specimen removal from patients were performed.

Data were presented as mean $\pm$ SD and number (percent). Comparisons between independent groups were performed using the Pearson Chi-square or Fisher's exact test as appropriate and a p-value < 0.05 was considered statistically significant. Odds ratio (OR) with 95% confidence intervals (95% CI) was estimated for the effect of these factors on the outcome.

Results

From 2006-2011, a total of 1,532 patients underwent colonoscopy. There were no complications, and 109 patients met the inclusion criteria. There were 63 male patients (57.8%), and 46 female patients (42.2%) whose mean age was 61.36 years (31-89 years). Colonoscopy findings were normal for 72 patients (66.1%); 8 patients tested positive for polyps (7.3%); inflammatory bowel disease was found in 4 patients (3.7%); colorectal cancer was diagnosed in 24 patients (22.0%), (colon 19 patients, rectum 5 patients); and terminal ileum cancer was found in 1 patient (0.9%).

Final diagnoses other than colorectal cancer which were found by surgical specimen were as follows: 40 HCC, 21 intrahepatic cholangiocarcinoma, 3 gynaecologic cancer (1 CA ovary, 1 CA cervix, 1 CA uterus), 1 liver abscess, 1 liver cyst, 1 CA stomach, 1 CA ampulla, 1 lymphoma and 3 Adenocarcinoma of unknown primary site.

Ethnic and race factors were not relevant because all of the patients were Thai. Weight loss and BMI figures were not analyzed because of incomplete data.

The authors results showed that abnormal CEA levels (> 3.4 mg/ml), GI symptoms and family history were positive risk factors for the diagnosis of colorectal cancer from the colonoscopy procedure. Univariate analysis showed a stronger risk where there was a combination of 2 or more of these risk factors.

Discussion

The liver is the most common site of distant metastases from colorectal cancer with approximately 25%[4] of patients diagnosed with synchronous colorectal liver metastases (CLM) on presentation. On the other hand, 30%[5] of colorectal cancer is metastatic in all periods of the disease. A variety of modalities including laboratory tests, radiological examinations, endoscopy and laparoscopy are relevant in diagnosing patients with CRC hepatic metastases; however, colonoscopy is not a totally safe procedure, and risks of colon perforation and spleen avulsion have been reported. In order to decrease the number of unnecessary colonoscopy procedures, risk factors should be clearly defined in order to increase the number of positive results.

The authors studied 3 symptoms of the GI risk factor of colorectal cancer[6]: altered bowel habit, abdominal pain and bleeding per rectum, and the authors results agreed with those of Adelstein BA[7], i.e. bleeding per rectum and significant weight loss are associated with colorectal cancer. The present study, however, was limited by the small number of patients, and the authors had to use sub-group analysis of each symptom. In general, abdominal pain is a poor indicator for colonoscopy because the incidence of cancer in patients with this symptom is not different from the general population, except to the extent that these symptoms help to convince patients to undergo screening that may be indicated on the basis of age or family history. With regard to bleeding per rectum, there is no reliable way to determine whether this originates from an anal source or a colonic source and there is no dependable way to distinguish a distal from a proximal colonic source[8]. Generally, it is suggested that colonoscopy should be undergone by patients aged over 50; however, in younger patients, distal colon at least should be evaluated first[9]. In the present study, univariate analysis showed that the GI symptoms factor alone does not lead to a statistically significant increase in positive results from colonoscopy.

Carcinoembryonic antigen (CEA) is a glycoprotein that is found on the surface of CRC cells and can be secreted into the bloodstream[10]. Several studies have shown that elevated CEA is highly sensitive for the identification of hepatic metastases. Although some authors have argued that only a small number of patients benefit from surveillance of CEA levels, other investigators have concluded that CEA-based follow-up strategies are efficacious and cost-effective[11]. A study from the Mayo Clinic found that patient survival nearly doubled when hepatic metastases were identified on the basis of CEA

Table 1. Comparison of incidence by sex

	Cancer in colon or rectum	Other result
Male n (%)	14 (58.3)	49 (57.6)
Female n (%)	10 (41.7)	36 (42.4)
	24	85

Table 2. Demographic data

Factors	Colorectal cancer		Total (n = 109)	p-value
	Yes (n = 24)	No (n = 85)		
Age (years)				0.791
< 60	10 (41.7%)	38 (44.7%)	48 (44.0%)	
> 60	14 (58.3%)	47 (55.3%)	61 (56.0%)	
Mean ± SD	61.11 ± 12.09	62.25 ± 12.13	61.36 ± 12.05	
Min-Max	31-89	40-79	31-89	
Gender				0.952
Male	14 (58.3%)	49 (57.6%)	63 (57.8%)	
Female	10 (41.7%)	36 (42.4%)	46 (42.2%)	
GI symptoms				0.001*
Normal	12 (50.0%)	71 (83.5%)	83 (76.1%)	
Abnormal	12 (50.0%)	14 (16.5%)	26 (23.9%)	
CEA				0.006*
Normal	4 (16.7%)	41 (48.2%)	45 (41.3%)	
Abnormal	20 (83.3%)	44 (51.8%)	64 (58.7%)	
Family history				0.007*
Negative	22 (91.7%)	85 (100%)	107 (98.2%)	
Positive	2 (8.3%)	0 (0.0%)	2 (1.8%)	

Value were represented as number (%) and Mean ± SD. * significant at $p < 0.05$

Table 3. univariate incidence factors

Risk	Colorectal cancer		Total (n = 109)	OR (95% CI)	p-value
	No (n = 85)	Yes (n = 24)			
No risk	35 (41.2%)	3 (12.5%)	38 (34.9%)	Ref	
Only GI symptom	6 (7.1%)	1 (4.2%)	7 (6.4%)	1.94 (0.17-21.94)	0.591
Only CEA abnormal	36 (42.4%)	9 (37.5%)	45 (41.3%)	2.92 (0.73-11.67)	0.130
GI + CEA ± Family history	8 (45.8%)	11 (17.4%)	19 (17.4%)	16.04 (3.62-71.17)	< 0.001*

elevation rather than tumor-related symptoms[12]. The association of the abnormal-CEA-level risk factor with the incidence of colorectal cancer is significant. A study from Wu XZ[13] showed levels of CEA > 5 mg/ml carry a risk of synchronous liver metastasis of 85.2% sensitivity and 85.7% specificity. Meta-analysis from Tan E[14], showed that CEA > 5 mg/ml is a risk factor of metastasis or recurrence at odds ratio 15.5. In the present study, abnormal CEA levels show a significant association with colorectal cancer but univariate analysis shows that abnormal CEA alone is not a statistically significant risk factor.

With regard to the family history factor, the present study showed the same results as Dunlop MG[15], with the risk increasing with age and 10-fold at age 50 years, but due to limitations in sample size the authors could not use univariate analysis on this factor.

Univariate analysis showed that a combination

of 2 or more risks showed significant OR for identifying primary colorectal cancer; therefore, the authors recommend that the presence of at least 2 risk factors is a reasonable basis for advising patients who present with liver mass to undergo colonoscopy.

Conclusion

Factors which are likely to result in patients with liver mass gaining positive results from colonoscopy are abnormal CEA level, positive colorectal-cancer family history especially in a first-degree relative, and abnormal GI symptoms.

Potential conflicts of interest

None.

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อุบัติการณ์โรคมะเร็งลำไส้ใหญ่และทวารหนักในผู้ป่วยที่มีอาการนำด้วยก้อนที่ตับจากการตรวจส่องกล้องลำไส้ใหญ่

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ภูมิหลัง: *ในผู้ป่วยที่มีอาการแสดงหลักด้วยก้อนที่ตับนั้น มีส่วนหนึ่ง ที่ก้อนที่ตับนั้นไม่มีลักษณะทางรังสีวิทยาที่เข้าได้กับมะเร็งของตัวตับเอง และหรือมะเร็งทางเดินน้ำดีในตับและมะเร็งที่กระจายมาที่ตับอย่างชัดเจน ในการตรวจเพื่อหาสาเหตุหรือชนิดของก้อนที่ตับ วิธีหนึ่งคือการตรวจด้วยการส่องกล้องลำไส้ใหญ่ แต่ในปัจจุบันนั้นยังไม่มีหลักฐานหรือข้อบ่งชี้ที่ชัดเจนในการส่งตรวจด้วยการส่องกล้องลำไส้ใหญ่*

วัสดุและวิธีการ: *ศึกษาข้อมูลจากหน่วยส่องกล้องทางเดินอาหารแผนกศัลยกรรมทั่วไป โรงพยาบาลราชวิถีย้อนหลัง 6 ปี โดยมีเกณฑ์ในการเลือกข้อมูลในการศึกษาดังนี้ 1) ผู้ป่วยมีอาการแสดงหลักด้วยก้อนที่ตับ 2) ลักษณะทางรังสีวิทยาไม่เหมือนมะเร็งของตัวตับเอง (HCC) หรือมะเร็งทางเดินน้ำดีในตับ (intrahepatic cholangiocarcinoma) และเนื้องอกอื่นที่เกิดจากตัวตับเอง (ข้อมูลโดยส่วนใหญ่ โดยการทำเอกซเรย์คอมพิวเตอร์หรือการเอกซเรย์ด้วยคลื่นแม่เหล็กไฟฟ้า) เกณฑ์ในการคัดออก คือ 1) ผู้ป่วยไม่ได้รับการผ่าตัดรักษาที่โรงพยาบาลราชวิถี, 2) ไม่สามารถตรวจติดตามผู้ป่วยได้อย่างต่อเนื่อง และหรือข้อมูลระหว่างตรวจติดตามไม่ครบ*

ผลการศึกษา: *จำนวนผู้ป่วยที่เข้ารับการตรวจด้วยการส่องกล้องลำไส้ใหญ่ทั้งหมด 1,532 ราย จากจำนวนทั้งหมดมี 109 ราย ที่เข้ากับเกณฑ์ในการศึกษา และจากทั้งหมดพบมะเร็งลำไส้ใหญ่และทวารหนักทั้งหมด 24 ราย มะเร็งของลำไส้เล็กส่วนปลาย 1 ราย และผลสุดท้ายจากการศึกษาพบผู้ป่วยเป็นมะเร็งตับเอง 40 ราย มะเร็งทางเดินน้ำดีในตับ 21 ราย โดยปัจจัยที่ส่งผลให้พบมะเร็งลำไส้ใหญ่และทวารหนักจากการส่องกล้องลำไส้ใหญ่ คือ การที่มีอาการในทางเดินอาหารมีค่า CEA ผิดปกติ และการพบมีประวัติมะเร็งลำไส้ใหญ่และทวารหนักในครอบครัว*

สรุป: *เพื่อเพิ่มประโยชน์และโอกาสในการพบรอยโรคมะเร็งลำไส้ใหญ่และทวารหนัก และลดการตรวจด้วยการส่องกล้องลำไส้ใหญ่ที่ไม่จำเป็น ในกลุ่มผู้ป่วยที่มีอาการแสดงด้วยก้อนที่ตับ ปัจจัยที่ช่วยคือ การมีอาการทางเดินอาหาร การตรวจพบมีค่า CEA ที่ผิดปกติ และการมีประวัติมะเร็งลำไส้ใหญ่และทวารหนักในครอบครัว*