#### **Original** Article

# Abnormality of Appendix in **Incidental Appendectomy during Colorectal Cancer Surgery**

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#### Kev Words

Colorectal cancer; Colorectal surgery; Incidental appendectomy Purpose. Incidental appendectomy is a frequent but non-standard procedure during colorectal surgery. The purpose of this study was to evaluate the incidence of abnormal pathological findings of appendix in incidental appendectomy during colorectal cancer surgery and to determine its clinical significance.

Methods. A retrospective review of patients who were diagnosed with colorectal cancer and underwent oncological resection of the tumor together with incidental appendectomy at the department of colorectal surgery of our hospital between 2003 and 2012. The histological findings of 1,375 cases of incidental appendectomies during colorectal cancer surgery were analyzed and reviewed.

*Results.* This study included 1,375 patients with a mean age of  $61 \pm 12$ years (range 20-94). Among them, 58.8% were male, 6.91% (95 patients) had fecalith, 0.36% (5 patients) had neuroendocrine tumor, 0.15% (2 patients) had mucinous cystadenoma and 0.87% (12 patients) had synchronous metastatic colorectal cancer in the appendix. Abnormal pathologic alteration was found in 240 patines (17.45%) and a neoplasm was found in 19 patients (1.38%). No complication occurred from the incidental appendectomy.

*Conclusions.* Incidental appendectomy is a safe procedure and may be performed with colorectal cancer surgery to reduce the incidence of appendiceal neoplasm and prevent appendicitis in the future. Patient having colorectal carcinoma should undergo incidental appendectomy because the incidence of synchronous appendiceal neoplasm is not rare (1.38 percent). Metachronous neoplasm is a risk in the retained appendix in patients with colorectal cancer. Appendiceal fecaliths appear to play a role in the pathogenesis of acute appendicitis and are associated with complicated appendicitis. In conclusion, incidental appendectomy may be beneficial for patients undergoing colorectal cancer surgery.

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ncidental appendectomy is a frequent but non-standard procedure during colorectal cancer surgery. Whether or not to perform incidental appendectomy

during curative resection for colorectal cancer (CRC) is controversial and the relevant study is rare.

The appendix has a similar mucosal pattern to the

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colon and is derived embryologically from the large intestine, any neoplastic change of the colon and rectum could affect the appendix. Published studies reveal that patients with appendiceal cancer are frequently found to have synchronous or metachronous neoplasms elsewhere in the colon, with the incidence of 0.6-14% for synchronous cancer and 1-8% for metachronous cancer.<sup>1,2</sup> In addition, the incidence of synchronous primary appeniceal neoplasm and secondary (metastatic) appendiceal neoplasm in CRC patients was 0.3 and 1.0 percent, respectively.<sup>3</sup>

Incidental appendectomy was then suggested to eliminate potential future appendicitis or neoplasm because routine postoperative surveillance cannot assess the appendiceal mucosa.<sup>4</sup> Although there have been advances in both endoscopy and radiology in recent decades, the appendiceal mucosa remains inaccessible and the accuracy of preoperative diagnosis of appendiceal neoplasm is still poor. A study of surgically treated primary adenocarcinoma of the appendix revealed an interesting finding that no patient was the correct diagnosis made before surgery, and the diagnosis was considered in only 32% patient intraoperatively.<sup>5</sup>

Because of the difficulty in diagnosis of appendiceal tumors and the potential risk of forming synchronous and metachronous neoplasm of the appendix, the question of whether an incidental appendectomy should be performed for CRC patients has been raised.<sup>6</sup> In attempt to address the question, we need to understand the incidence of synchronous of appendiceal neoplasm in CRC patients. We hypothesized that patients with CRC might have the similar risk of synchronous and metachronous appendiceal tumor to that of the colon and rectum. The aim of this study is to evaluate the incidence of abnormal pathological findings of appendix in incidental appendectomy during colorectal surgery and to determine its clinical significance.

#### **Materials and Methods**

This retrospective study reviewed all consecutive patients who underwent oncologic resection of CRC

at the department of colorectal surgery of our hospital between January 2003 and December 2012. Data were obtained from the patient record documentation system.

The criteria of incidental appendectomy in our study were an uncomplicated primary elective operation, a stable condition, and a readily accessible appendix. Besides, there were additional criteria for incidental appendectomy according to (1) Age < 70 years old: Routine incidental appendectomy if patient agree; (2) Age > 70 years old: Not routine incidental appendectomy except patient request; (3) Patient ever underwent preoperative concurrent chemoradiation therapy for CRC. Patient consent was obtained perioperatively after thorough discussion to the patient family. All patients undergoing right hemicolectomy, total colectomy, subtotal colectomy and Hartmann's operation with end ileostomy were excluded because of the unavoidable appendix resection. Patients were also excluded if they had familial adenomatous polyposis syndrome or had a previous appendectomy, or if there had been direct invasion of CRC to the appendix during operation.

The study analyses include the location and histology of the primary tumor, the operation type and cancer staging. Macroscopic and microscopic features of the appendix were recorded. The presence of synchronous appendiceal tumors and/or metastasis was correlated with follow-up data to demonstrate the clinical significance of these findings.

#### Results

Between January 2003 and December 2012, 4373 consecutive patients underwent surgery for CRC at the department of colorectal surgery of our hospital. After reviewed, 1,375 (31.4%) consecutive CRC patients who underwent incidental appendectomy were included for analyzing in the study. Among them, 904 (65.75%) patients had rectal cancer surgery and 467 (33.96%) patients had left colon surgery (Distal transverse colon, Splenic flexure of colon, Descending and Sigmoid colon). Eleven (0.8%) patients had synchronous CRC surgery. Demographic data of patients are shown in Table 1. The preliminary results of the study revealed that the patients had a mean age of  $61 \pm 12$  years (range 20-94), 58.8% were male, 115 (8.36%) had left hemicolectomy, 407 (29.6%) had high anterior resection, 730 (53.09%) had low anterior resection, and 79 (5.74%) had abdominoperineal rectal resection.

The histological findings of the appendix from incidental appendectomy were presented in Table 2, which demonstrated that 77.96% (1,072 patients) of the patients presented normal appendix and 17.45% (240 patients) presented abnormality. Among the patients included in the study, 6.91% (95 patines) had fecalith, 6.84% (94 patients) had acute appendicitis or periappendicitis, 0.36% (5 patients) had neuroendocrine tumor, 0.15% (2 patients) had mucinous cystadenoma and 0.87% (12 patients) had synchronous metastatic CRC in the appendix or mesoappendix. Other less common abnormal findings included fatty change (0.22%), atrophy (4.36%), fibrous obliteration

**Table 1.** Demographic data of the patients included in this study (n = 1375)

study (II 1575)		
Demographic data	n	Percentage
Sex (male/female)	809/566	58.84/41.16
Operation method		
Abdominoperineal rectal resection	79	5.74
Low anterior resection	730	53.09
High anterior resection	407	29.6
Left hemicolectomy	115	8.36
Transverse colectomy	6	0.44
Colon segmental resection	6	0.44
Colostomy following Hartmann's	14	1.02
procedure		
Subtotal colectomy	18	1.31
Primary tumor location		
Rectum	904	65.75
Left colon	467	33.96
Synchronous colorectal cancer	11	0.8
Stage of primary tumor		
Carcinoma in situ	28	2.04
Ι	285	20.73
II	475	35.54
III	441	32.07
IV	146	10.62

Abbreviation: Left colon (Distal transverse colon, Splenic flexure of colon, Descending colon and Sigmoid colon).

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(0.51%), involuted appendix (1.53%) and Mucosa hyperplasia (0.29%).

Details of 19 (1.38%) patients with synchronous appendiceal neoplasms are shown in Tables 3 and 4. Among these patients, five patients (0.36%) had carinoid tumor in the appendix (Table 4). All these carcinoid tumors were less then 1 cm in size (focal, 0.2 cm, 0.2 cm, 0.5 cm and 1 cm). No distant metastasis of carcinoid tumors were found during follow-up for these patients.

There were no apparent appendiceal stump leaks or other complication specific to incidental appendectomy in the present study. The presence of synchronous appendiceal neoplasms or metastasis did not alter postoperative management. These patients should receive adjuvant or palliative chemotherapy because of nodal involvement or distant metastasis.

## Discussion

The appendix derives embryologically from the cecum and is histologically similar to the colorectum.<sup>9</sup> Any neoplastic pathology of the colon can occur in the appendix. Some authors have suggested that the presence of a benign adenoma of the appendix should be considered as a marker for future development of CRC and such patients should be screened and followed up.<sup>10</sup> The adenoma-carcinoma sequence for sequential development of cancer may be similar in ap-

**Table 2.** Pathology result of incidental appendectomies (n = 1375)

Pathology of appendix	n	Percentage
Normal appendix	1072	77.96
Fecalith	95	6.91
Acute appendicitis or periappendicitis	94	6.84
Neuroendocrine tumor	5	0.36
Metastasis of colorectal cancer	12	0.87
Mucinous cystadenoma	2	0.15
Fatty change	3	0.22
Atrophy	60	4.36
Fibrous obliteration	7	0.51
Involuted appendix	21	1.53
Mucosa hyperplasia	4	0.29

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Age (yr)/ Gender	Primary tumor	Type of surgery	Tumor histology	TNM stage	Appendix pathology
41 F	R	LAR	Mucinous adenocarcinoma	T4bN1aM1b	Pseudomucinous peritonei of the mesoappendix
39 F	S	HAR	Mucinous adenocarcinoma	T4N2bM1a	Metastatic adenocarcinoma on serosal aspect of appendix
69 F	R	LAR	MD adenocarcinoma	T3N1aM0	Mucinous cystadenoma
42 M	D	LH	MD adenocarcinoma	T4aN2bM1a	Metastatic adenocarcinoma in the serosal layer
52 F	Sp	Subtotal colectomy	MD adenocarcinoma	T4N0M1b	Metastatic adenocarcinoma in the mesoappendix
60 M	S	HAR	MD adenocarcinoma	T4N1M1a	Metastatic adenocarcinoma in the appendix
33 M	S	HAR	MD adenocarcinoma	T4N2M1a	Metastatic adenocarcinoma on serosal aspect of appendix
49 F	R	LAR	MD adenocarcinoma	T4N2aM0	Mucinous cystadenoma
75 F	S	Hartmann's procedure	MD adenocarcinoma	T4N2M1b	Metastatic adenocarcinoma in the appendix
78 F	R	LAR	MD adenocarcinoma	T4N0M1a	Metastatic adenocarcinoma in the appendix
57 F	Т	Transverse colectomy	MD adenocarcinoma	T3N1M1a	Metastatic adenocarcinoma in the appendix
74 M	R	Hartmann's procedure	MD adenocarcinoma	T3N2M1b	Metastatic adenocarcinoma in the mesoappendix
62 M	R	Hartmann's procedure	MD adenocarcinoma	T3N2bM1b	Metastatic adenocarcinoma in the appendix
79 M	R	LAR	MD adenocarcinoma	T3N2bM1a	Metastatic adenocarcinoma in the mesoappendix

 Table 3. Patients' characteristics, details of primary colorectal cancer, and pathological results of synchronous appendiceal neoplasm

Abbreviation: D (descending colon), F (female), HAR (high anterior resection), LAR (low anterior resection), LH (left hemicolectomy), M (male), MD (moderate differentiated), R (rectum), S (sigmoid colon), Sp (splenic flexure of colon), T (transverse colon), yr (year).

Patient No.	Age (yr)/Gender	Primary tumor	Tumor histology	TNM stage	Size and grade
54	45 F	Sigmoid colon	MD adenocarcinoma	T4bN1cM0	0.2 cm, Gr1
65	60 M	Descending colon	MD adenocarcinoma	T3N0M0	0.2 cm, Gr1
127	79 M	Rectum	MD adenocarcinoma	T3N0M0	1.0 cm, Gr1
208	65 F	Descending colon	MD adenocarcinoma	T1N0M0	Focal NE cell hyperplasia
251	62 M	Rectum	MD adenocarcinoma	T4aN1bM0	0.5 cm

Abbreviation: F (female), Gr (grade), M (male), MD (moderate differentiated), NE (neuroendocrine), yr (year).

pendix as in colon cancer.<sup>11</sup> Appendiceal neoplasms are thought to account for 0.4 to 1% of all gastrointestinal malignancies and are found in 0.7 to 1.7% of appendectomy specimens.<sup>12-14</sup> Little is known about the incidence of appendiceal neoplasm in CRC patients. To the best of our knowledge, there are two studies reported such incidence.<sup>3,4</sup> There are no obvious symptoms or signs of appendiceal tumors, and tumors are difficult to detect preoperatively. In a series published from the Mayo Clinic, no patient with an appendiceal tumor was correctly diagnosed preoperatively and even at operation only 32 percent were suspected.<sup>5</sup> The question of whether an incidental appendectomy should be performed in CRC patients has been raised due to the difficulty in diagnosis of appendiceal tumors and the certain risk of synchronous and meta-chronous neoplasm of the appendix.<sup>4,6</sup>

Khan et al. retrospectively reviewed 169 CRC patients who underwent CRC surgery and removal of the appendix. They reported a 4.1% of synchronous primary appendiceal neoplasm in these patients, and mucinous cystadenoma was the most common neoplasm.<sup>4</sup> Lohsiriwat et al. demonstrated that the incidence of synchronous primary appendiceal neoplasm and secondary (metastatic) appendiceal neoplasm in patients with resectable CRC is 0.3 and 1.0 percent, respectively.<sup>3</sup> In our study in Taiwan, we reported 0.51% (7 patines) of synchronous primary appendiceal neoplasm and 0.87% (12 patients) of secondary (metastatic) appendiceal neoplasm. The incidence of synchronous appendiceal neoplasm in our study (0.51%) is similar to the Lohsiriwat et al. (0.3%) in Thailand but much different from the Khan et al. (4.1%) in United Kingdom. One possible explanation for the low incidence of synchronous primary neoplasm of the appendix in CRC patients in the present study is that the incidence of appendiceal tumors in Asian population is different from that of Western population,<sup>20</sup> and thus the incidence of synchronous appendiceal neoplasms in CRC patients could vary among various ethnic and geographic background.<sup>3</sup> Some author reported 0.53 to 1.0% of CRC patients had metastatic lesions in the mesoappendix.<sup>3,6,17</sup> Our finding (0.87%) is fairly consistent with these previous studies. Furthermore, all appendices were macroscopically normal with no preoperative or perioperative suspect diagnosis of metastatic lesions in our study.

Among the synchronous primary appendiceal neoplasm in our study, 5 patients with carcinoid tumor (neuroendocrine tumor) were reported. The prevalence of appendiceal carcinoid is 0.3 to 0.9% in patients undergoing appendectomy.<sup>6,14,17</sup> In our study, the incidence of appendiceal carcinoid tumor (0.36%) is similar to that of previous study. Some authors suggested that most carcinoids less than 1 cm in size can be treated by simple appendectomy without any further procedure or investigation.<sup>18,19</sup> Appendiceal carcinoid tumors rarely cause metastatic disease and are most commonly an incidental localized lesion found at appendectomy or other abdominal procedure.<sup>20</sup> Patients with local disease are reported to have a good prognosis overall and a 5-year survival rate of 92 percent.<sup>21</sup> Of the five patients with carcinoid tumor in our study, no further right hemicolectomy was offered because the tumors are less than 1 cm in size and low grade in malignancy. Follow-up data of the five patients with carcinoid tumors reported no metastasis.

The unexpected finding in the present study was that 6.91% of the CRC patients had fecalith in the appendix. Some authors had reported the relationship and importance of fecaliths in the etiology of acute appendicitis.<sup>22,23</sup> The prevalence of fecaliths is higher in the developed countries than the developing countries. The low-fiber diets followed in developed countries lead to fecalith formation.<sup>23</sup> According to some clinical researches, appendix fecaliths are associated with earlier and higher rate of complicated appendicitis (perforation and abscess).<sup>24,25</sup> Besides, some authors reported that the relationship of low-fiber diet to risk of colorectal adenoma.<sup>26,27</sup> Many studies have reported the colorectal adenoma is risk factor to CRC 7,8 Based on the information above, we can say that CRC patients maybe have high incidence of facaliths because low-fiber diet in these patients is not rare. Facaliths are the most common cause of appendicular obstruction and may cause acute appendicitis. Early or incidental appendectomy in CRC patients may reduce the morbidity and mortality of complicated appendicitis in the future.<sup>22,24</sup>

The cost of an incidental appendectomy is extremely low compared with that in CRC surgery. A short extension of surgery would be encountered because it only takes 3-5 minutes to perform this additional procedure, however, low complication rate was reported.<sup>28,29</sup> The National Nosocomial Infection Surveillance System reported that the rate of surgical site infection for appendectomy was 1.0% to 3.5% and for colon operation was 3.6% to 12.8%, depending on clinical factors.<sup>30</sup> Some authors believed that this risk of surgical site infection of incidental appendectomy would be negligible in the setting of an open lower gastrointestinal procedure in patients who undergone mechanical bowel preparation.<sup>6</sup> There is at least a theoretical chance of appendiceal stump blow-out or leakage, but in our study there were no postoperative complication as a result of appendectomy. Besides, surgery for acute appendicitis after major abdominal operation can be very difficult because of adhesion or altered anatomy, leading to greater operative trauma as a larger incision and longer surgery.<sup>17</sup>

The limitations of this single-center study include study design and clinical decision. First, there could be a patient selection bias to perform incidental appendectomy because we did not have clear criteria for performing appendectomy for CRC patients at our institute, indicating the decision to perform incidental appendectomy was mainly made by the surgeon on his/her own clinical judgments. Second, we did not analyze the cost-effectiveness for incidental appendectomy in patients with CRC, but this concept was reported in one previous study.<sup>6</sup> Further cohort or prospective study is required.

## Conclusion

Base on this study, incidental appendectomy is a safe procedure and may be performed with colorectal cancer surgery to reduce the incidence of appendiceal neoplasm and prevent appendicitis in the future. In conclusion, incidental appendectomy may be beneficial for colorectal cancer patients undergoing surgery.

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<u>原 著</u>

## 附帶闌尾切除於大腸直腸癌症手術 之異常闌尾發現

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**目的** 附帶闌尾切除於大腸直腸手術一直以來是很常執行但非常規術式。本研究的目的 主要是藉由大腸直腸癌患者接受附帶闌尾切除之後,分析闌尾異常病理發現的發生率來 決定其臨床意義。

**方法** 回溯性收集自 2003 年至 2012 年被診斷大腸直腸癌並接受癌症切除手術合併附帶 闌尾切除的病人,我們共分析及回顧 1375 個闌尾病理切片結果。

**結果** 這篇研究總共收集 1375 位病人,平均年齡為 61 ± 12 歲 (20-94 歲)。在這些病人 當中我們發現,其中有 58.8% 為男性,有 6.91% (95 位) 有闌尾糞石,有 0.36% (5 位) 是 神經內分泌瘤,0.15% (2 位) 是黏液性囊腺瘤,0.87% (12 位) 是闌尾的大腸直腸癌同 時性轉移。總共有 240 位病人 (17.45%) 的闌尾為異常病理發現,這當中有 19 位病人 (1.38%) 為闌尾腫瘤 (Neoplasm)。在所有接受附帶闌尾切除的病人當中,並未發現有任 何相關併發症。

結論 附帶闌尾切除於大腸直腸癌手術當中是個安全的術式而且也許可以減少闌尾腫瘤的發生率及避免日後闌尾發炎。我們建議接受大腸直腸癌手術的病人應該同時接受附帶闌尾切除,因為同時性的闌尾腫瘤發生率並不是罕見 (1.38%)。異時性轉移腫瘤相對於保留闌尾的病人來說也是一個風險。闌尾糞石於急性闌尾炎中扮演致病因子之一,而且與發生複雜性闌尾炎有關。總結上述結果,附帶闌尾切除對於接受大腸直腸癌手術的病人可能是有利的。

關鍵詞 大腸直腸癌、大腸直腸手術、附帶闌尾切除。