Original Article

Rectal Carcinoid Tumor: Treatment and Long-Term Outcome in 30 Cases

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Key Words
Rectal carcinoid tumor;
Long-term outcome;
Polypectomy

Purpose. Rectal carcinoid tumors are rare; the best treatment of patients with such tumors remains uncertain. This study describes our treatment of 30 patients with rectal carcinoid tumors, evaluates their long-term outcomes, and discusses our findings vis-a-vis similar clinical studies. We suggest specific recommendations regarding the treatment of rectal carcinoid tumors.

Patients and Methods. Data were obtained retrospectively from a database of all colorectal malignancies at Kaohsiung Veterans General Hospital. From 1991 to 2010, 3,034 colorectal malignant tumors and 30 rectal carcinoid tumors were diagnosed. One-channel endoscopic polypectomy was performed on 25 patients, while the other 5 underwent radical surgery. We evaluated the rates of complete resection, complications associated with the procedure, local recurrence, and distant metastasis.

Results. Thirty patients (21 men and 9 women; mean age, 54.0 ± 13.7 years) were diagnosed with rectal carcinoid tumor. Tumors removed by polypectomy measured 2-15 mm (mean size, 6.6 ± 2.8 mm). No atypical endoscopic features were associated with these tumors. The rate of complete resection was 44%. Complications from the procedure, such as perforation or bleeding, were not found. Neither local recurrence nor distant metastasis was detected during follow-up examinations for an average of 36 months after polypectomy. The five patients who underwent radical surgery, local recurrence or distant metastasis was not detected during follow-up examinations at least 22 months after surgery.

Conclusion. Rectal carcinoid tumors rarely metastasize when they: (1) are less than 10 mm in diameter, (2) exhibit no atypical endoscopic features, (3) are confined to the submucosal layer, and (4) are not associated with lymphovascular invasion. Tumors that fit this profile are suitable for local excision by endoscopic resection.

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The term *carcinoid* is derived from the German word "*karzinoide*," first used by Oberndorfer in 1907 to describe tumors that are more indolent than typical adenocarcinomas. Carcinoid tumors in a wide range of organs have subsequently been identified, most commonly involving the lungs, bronchi, and gastrointestinal tracts.[1] Data from the surveillance, epidemiology, and end results (SEER) national cancer

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registry indicate that out of 169,073 colorectal cancer patients, only 1.5% had carcinoid tumor, and 73.7% of all carcinoid tumors developed in the rectum.[2]

Rectal carcinoid tumors are usually found incidentally during endoscopic examination. The typical endoscopic examination of rectal carcinoid tumors reveals smooth, round, sessile elevations covered with normal-appearing or yellow-discolored mucosa.[3] Other characteristics of rectal carcinoid tumors include a preponderance in males (1.6:1), small-sized tumors of 10 mm or less at detection (66.0%), a high incidence of submucosal invasion (76.3%) and hematogenous spread (58.2% of 287 metastases), an infrequent association with carcinoid syndrome (0.7%), and a relatively high 5-year survival rate after lesion removal (81.5%).[4]

Criteria predictive of the malignant potential of rectal carcinoid tumors include tumor size, endoscopic features, histological growth patterns, muscularis propria invasion, and lymphovascular invasion.[3-5] Among these parameters, the size of the primary tumor is considered the most simple and reliable. Metastasis occurs in less than 3% of tumors that are ≤ 10 mm in diameter and in 5-15% of tumors that are 11-20 mm in diameter; however, the frequency increases to 80% for those that are > 20 mm.[6-8] Recent guidelines on the management of rectal carcinoid tumors suggest that local resection is appropriate for tumors that are less than 11 mm and confined to the submucosa, as they are judged to have low metastatic potential.[27] In this study, we report our experience in treating 30 patients with rectal carcinoid tumors.

Patients and Methods

Between January 1991 and January 2010, 30 rectal carcinoid tumors were diagnosed histopathologically after endoscopic examination followed by one-channel endoscopic polypectomy or surgical excision at Kaohsiung Veterans General Hospital. We retrospectively reviewed the medical records of all these patients. Collected data included demographic information and detailed endoscopic and histopathological reports. We classified endoscopic findings as "atypical" according to Shim et al.: lesions with semi-pedunculated appearance, hyperemia, a central depression, erosion, and ulceration.[3]

The maximum size of each rectal carcinoid tumor was measured on freshly resected specimens. Tumors were examined histopathologically to evaluate the cut-margin involvement, depth of invasion, and presence of lymphovascular or perineural invasion. We defined complete resection of a specimen as no histopathological evidence of either lateral or vertical margin involvement. Lymph node metastasis was also examined in the 5 patients who were treated by colectomy.

The radical tumor resections were all by low anterior resections. Due to the retrospective nature of our study, we were unable to definitively determine why a certain method of surgical management was chosen.

The diagnostic methods used to follow patients after endoscopic excision or radical resection were noted (e.g., physical examination, endoscopy, chest radiography, abdominal and pelvic computed tomography, and ultrasonography). In all the patients, the diagnosis of recurrent or metastatic disease was made on the basis of either the results of a biopsy of the new lesion or radiographic findings.

Results

Over the 19-year period from 1991 to 2010, 30 patients at Kaohsiung Veterans General Hospital were diagnosed with rectal carcinoid tumor. The patients comprised 21 men and 9 women with a mean age of 54.0 ± 13.7 years (range, 30-80 years). The study population was thus predominantly male.

Twenty-five tumors removed by one-channel endoscopic polypectomy measured 2-15 mm in diameter, with an average size of 6.6 ± 2.8 mm. One tumor was 11-20 mm in diameter, but no tumor measured greater than 20 mm. There were no atypical endoscopic features associated with these tumors. The rate of complete resection was 44% (11/25). Complications from the procedure, such as perforation or bleeding, were not found.

According to histopathological evaluation, all tumors were located in the submucosal layer, and all

were classified as well-differentiated neuroendocrine tumors (carcinoid tumor). No lymphovascular or perineural invasion was observed in any of the tumors. In 14 patients, the resected specimen indicated cut-margin involvement. Because these 14 patients declined further surgical intervention, careful follow-up examinations were conducted instead. Neither local recurrences nor distant metastases were detected during follow-up examinations that were carried out on an average of 36 months after polypectomy (range, 1-96 months). The detailed characteristics of these 25 tumors are listed in Table 1.

Five patients underwent radical surgery involving low anterior resection with total mesorectal excision. The clinical and pathological features of these tumors are illustrated in Table 2. One patient had a tumor ≤ 10 mm in size, with invasion of the submucosa, without lymph node metastasis. There were no local recurrence and distant metastasis 22 months after surgery. Each of these 2 patients had a tumor in the size range of 11-20 mm. The invasion depth of these tumors was submucosal, with lymph node metastasis in 1 patient; neither local recurrence nor distant metastasis was found during the follow-up examination. The other 2 patients had tumors > 20 mm in size, with atypical endoscopic features. These tumors had invaded tissue to the depth of the muscularis propria, and lymph node metastasis was seen in one of the patients. However, local recurrences or distant metastases were not seen 32 months after surgery.

Discussion

Several features of rectal carcinoid tumors have been studied as possible predictors of patient outcomes. Shim et al. have reported that rectal carcinoid tumors develop atypical endoscopic features more

Table 1. Characteristics of tumors from 25 patients who underwent endoscopic polypectomy

	N (%)	Mean ± SD
Demographic		
Age(years)	25	50 ± 10
Range		30-71
Male	17 (68%)	
Clinical		
Distance from anal verge (cm)	25	6.7 ± 1.8
Range		2-10
Atypical endoscopic finding	0	
Pathological		
Tumor size (mm)	25	6.6 ± 2.8
Range		2-15
Cut margin free	11 (44%)	
Depth of tumor invasion		
Mucosa	0	
Submucosa	25 (100%)	
Muscularis	0	
Serosa	0	
Adjacent organs	0	
Lymphovascular invasion		
No	25 (100%)	
Yes	0	
Perineural invasion		
No	25 (100%)	
Yes	0	
Follow-up period (months)	25	36 ± 22
Range		1-96
Local recurrence		
No	25 (100%)	
Yes	0	
Distant metastasis		
No	25 (100%)	
Yes	0	

Table 2. Clinical and pathological features of tumors from patients who underwent radical surgery[a]

Patient[b]	Sex	Age	Tumor size (mm)	Atypical endoscopic findings	Invasion depth[c]	Lymph node involvement	Time from surgery to examination (months)
1	M	63	20	-	Sm	+	96
2	M	79	30	+	Mm	+	79
3	M	80	30	+	Mm	-	32
4	M	65	15	-	Sm	-	27
5	F	50	5	-	Sm	-	22

[a] All surgeries were low anterior resections.
[b] None of the 5 patients had surgical margin involvement, local recurrence, or distant metastasis.
[c] Sm, submucosa; Mm, muscularis propria.

frequently as the size of the tumor increases. They also report that ulceration may indicate a poor prognosis (invasion into the muscularis propria or metastasis to the liver or lymph nodes).[3] Fahy et al. suggest a composite score as the most accurate tool (carcinoid of the rectum risk stratification score, CaRRS). The features associated with a poor prognosis for patients with rectal carcinoid tumor include: large size, deep invasion, lymphovascular invasion, and elevated mitotic rate.[9] However, the size of the primary tumor alone was a simple and reliable factor for predicting the risk of metastasis.

Treatment for small (≤ 10 mm) rectal carcinoid tumors

Rectal carcinoid tumors are considered good candidates for local excision, including endoscopic or transanal resection, when they have the following profile: ≤ 10 mm in diameter, no atypical features, confined to the submucosal layer, rare lymphovascular invasion, and rare distant metastasis.[3,5] Various methods of endoscopic resection for rectal carcinoid tumors have been developed and are reportedly effective for complete tumor resection (Table 3).

Endoscopic resection such as one-channel or two-channel polypectomy is a simpler and less invasive procedure. Iishi et al. reported that the rate of complete removal of rectal carcinoid tumors with two-channel colonoscopy was significantly higher than with one-channel colonoscopy ($p < 0.05$).[11] Kobayashi et al. reported that two-channel colonoscopic polypectomy was indicated for rectal carcinoid tumors with a maximal diameter of 10 mm, no invasion of the muscularis propria, and no depression or ulceration in the lesion. High-frequency endoscopic ultrasonography (HFUS) can be used to evaluate the depth of tumor invasion and to determine whether rectal carcinoid tumors are good candidates for removal by endoscopic polypectomy.[12]

For removal by conventional endoscopic mucosal resection (EMR), the lesions were elevated by injecting saline (or other solute) into the underlying submucosal layer and then snared and resected using a high-frequency current.[13] Due to the submucosal nature of rectal carcinoid tumors, those resected by conventional EMR are more likely to have incomplete resection margins.[14,15] HFUS might be used to help overcome this problem. Another alternative to conventional EMR involves suctioning the area raised by solute injection into a transparent cap (EMR-C) and either cleaving the lesion directly or banding it, with subsequent snare resection and retrieval. While pilot studies suggest that these methods may be effective,[16-18] most of these reports include only a limited number of cases.

Mashimo et al. reported that for rectal carcinoid tumors up to 10 mm in diameter, endoscopic submucosal resection with a ligation device (ESMR-L) is superior to endoscopic polypectomy or conventional

Table 3. Reported results of endoscopic resection for rectal carcinoid tumor[a]

Author & year	Excision method[b]	Injection solute	Number of patients treated	Rate of complete resection (%)	Rate of local recurrence (%)
Iishi et al., 1996	Polypectomy (2-channel)	None	10	90	0
	Polypectomy (1-channel)	None	7	28.6	0
Imada et al., 1996	EMR-C	Glycerol	8	100	0
Charles et al., 1999	ESMR-L	None	5	100	0
Oshitani et al., 2000	EMR-C	Saline	6	85.7	0
Ono et al., 2003	ESMR-L	Saline	14	100	0
	Polypectomy or EMR	Saline or none	8	57.1	0
Nagai et al., 2004	EMR-C	Saline	8	100	0
	EMR	Saline	8	37.5	0
Kobayashi et al., 2005	Polypectomy (2-channel)	None or saline	41	82.9	2.6 (1/38)
Mashimo et al., 2007	ESMR-L	Saline	63	95.2	0
Present study 1991-2010	Polypectomy (1-channel)	None	25	44	0

[a] Rates of complications and distant metastases were 0 in all cases.
[b] EMR-C, endoscopic mucosal resection with a cap-fitted device; ESMR-L, endoscopic submucosal resection with a ligation device.

EMR in achieving complete resection. In their study, ESMR-L provided an overall high rate of complete resection (95.2%). Only 3 resected lesions out of 63 had involved margins after ESMR-L; these were considered incomplete resections on the basis of histopathology. These 3 patients chose not to undergo additional treatment, but careful follow-up examinations were conducted; no local recurrences or distant metastases were detected after ESMR-L.[10]

Several studies have demonstrated that successful endoscopic resection without local recurrence can be attained in up to 93% of cases by prior evaluation with HFUS.[19,20] Waxman et al. determined the following exclusion criteria for HFUS-assisted EMR: (1) lesion diameter of ≥ 20 mm, (2) associated superficial mucosal ulceration, (3) poor HFUS echo definition of the muscularis propria, and (4) failure to cleave from the muscularis propria upon submucosal catheterization.[20]

Complete resection of small carcinoid tumors of the rectum remains difficult with conventional polypectomy, as was performed at our hospital. All 25 tumors in our study were sessile and located in the submucosal layer of the rectal wall, making complete resection difficult. One patient in the present study underwent radical surgery even though the tumor was 5 mm in size (patient no. 5, Table 2). The reason for this was the failure of endoscopic polypectomy with submucosal injection to remove the tumor. In our study, the rate of complete resection was 44%, which is relatively low compared to results obtained with the new and innovative procedures previously described. Nevertheless, neither local recurrence nor distant metastasis was noted in our study. Possible reasons for this observation include: (1) electrocoagulation may have caused necrosis of the peripheral margins of the resected specimens; (2) the behavior of these carcinoid tumors was indolent; and (3) the follow-up period was too short; to record recurrences or metastases that may have occurred later.

Treatment for intermediate (11-20 mm) rectal carcinoid tumors

Treatment for intermediate-size rectal carcinoid tumors must be individualized, weighing the risk of a more extensive surgery against the risk of residual disease. Muscularis propria invasion increases the likelihood of residual disease, and is thus used to indicate the need for more aggressive surgery.[21,22] Shields et al. demonstrated that a tumor size greater than 10 mm and lymphovascular invasion were predictors of lymph node involvement ($p = 0.006$ and < 0.001, respectively); the presence of lymph node metastases and lymphovascular invasion were associated with subsequent development of distant metastases ($p = 0.033$ and 0.022, respectively). They found that up to one-third of tumors less than 20 mm in diameter exhibited lymph node metastases, with those greater than 10 mm being at particular risk.[23]

In our study, 3 patients had tumors with diameters between 11 mm and 20 mm. One patient underwent one-channel endoscopic polypectomy, and the other 2 patients had radical surgery with low anterior resection. Of these patients, only the one with a 20-mm tumor had subsequent lymph node metastasis. None of the 3 patients has had local recurrence or distant metastasis after regular follow-up.

Treatment for large (> 20 mm) rectal carcinoid tumors

The general consensus is that carcinoid tumors greater than 20 mm require surgery involving the excision of the associated lymphatic tissue because of a higher rate of both local recurrence and distant metastasis. In our study, 2 patients had tumors larger than 20 mm; both were treated with radical surgery. Both these tumors had invaded the muscularis propria, and one of the patients had lymph node metastasis. After receiving radical surgery, neither patient developed local recurrence or distant metastasis.

Conclusion

From our experience, we conclude that rectal carcinoid tumors rarely metastasize when they: (1) are < 10 mm in diameter, (2) exhibit no atypical endoscopic features, (3) are confined to the submucosal layer, and (4) are not associated with lymphovascular invasion. Tumors that fit this profile are suitable for local excision using methods such as endoscopic resection.

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原　著

直腸類癌：治療經驗與長期預後在 30 個病人

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目的　直腸類癌很少見；如何對這些病人提供最好的治療仍然不是很清楚。本篇研究的目的是對於 30 個直腸類癌病人提供我們的治療經驗與這些病人的長期預後，並且與其他臨床研究做比較。根據我們的治療經驗，具體提出關於治療直腸類癌的建議。

病人與方法　此篇是回溯性的研究文章，收集高雄榮民總醫院從 1991 年到 2010 年，共 3034 例大腸直腸惡性腫瘤，其中有 30 例是直腸類癌。25 個病人接受單通道內視鏡息肉切除術，而其他 5 位病人接受根治性手術。最後，對於腫瘤的完整切除率，與內視鏡切除術相關的併發症，局部復發率和遠處轉移率進行評估。

結果　一共有 30 個病人被診斷為直腸類癌。其中有 21 個男性和 9 名女性，平均年齡為 54.0 ± 13.7 歲。經由內視鏡切除的腫瘤大小介於 2 至 15 毫米，平均大小為 6.6 ± 2.8 毫米；而且沒有非典型內視鏡特徵。經由內視鏡切除的完整切除率是 44%。並沒有發生與內視鏡切除術相關的併發症，如穿孔或出血。接受內視鏡切除術的 25 個病人在平均追蹤 36 個月後並沒有發現局部復發或遠處轉移。即使是接受根治性手術的 5 個病人，在至少追蹤 22 個月後也沒有發現局部復發或遠處轉移。

結論　直腸類癌很少發生遠處轉移時，當他們：(1) 大小小於 10 毫米，(2) 沒有非典型內視鏡特徵，(3) 侵犯深度僅限於黏膜下層，(4) 沒有淋巴及血管侵犯。直腸類癌如符合上述四點特徵則適合經內視鏡局部切除術。

關鍵詞　直腸類癌、長期預後、息肉切除術。