

Clinical Spectrum and Endoscopic Treatment of Gastrointestinal Carcinoid Tumour

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ABSTRACT

Objective: To analyse the clinical spectrum and endoscopic treatment outcome of patients diagnosed with gastrointestinal carcinoid tumours.

Study Design: Case series.

Place and Duration of Study: The First Hospital of Putian City of Fujian Province, China from 2012 to 2019.

Methodology: Patients with gastrointestinal carcinoid tumours were searched on the gastrointestinal endoscopic database and the hospital medical records database. Patients who were evaluated and treated at other institutions or with insufficient clinical information were excluded. Data were extracted from the databases, including clinical presentation, tumour size and location, treatment, complications of treatment, and clinical and endoscopic follow-up.

Results: In 113 cases, 92 tumours were smaller than 1 cm, 16 tumours were between 1-2 cm, and 5 tumours were larger than 2 cm in size. Ninety-five (84.1%) tumours showed as nodules with smooth surface, and 4(3.5%) as neoplasms with malignant performance. The tumours were limited to the mucosa in 14 (12.4%) cases, invaded into the submucosa in 88 (77.9%) cases, and the muscularis propria in 6 cases (5.3%). Most of the tumours (87.6%) were located in the rectum. The Ki-67 index was more than 30% in cases with metastases. One hundred and eight (95.6%) gastrointestinal carcinoid tumour patients were treated with endoscopic resection including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), and 5 (4.4%) patients underwent surgical resection. All 108 patients including the 6 patients with positive margins had no relapse of carcinoid tumour on follow-up.

Conclusion: The rectum may be the most common location of gastrointestinal carcinoid tumours in Asian people. Most small tumours located in the stomach, colon, and rectum are nonfunctional, especially in rectum. Endoscopic excision including EMR and ESD is effective and safe for the treatment of small-sized gastrointestinal carcinoid tumours. Ki-67 index can be a good predictor for malignant potency of gastrointestinal carcinoid tumours.

Key Words: Gastrointestinal carcinoid tumours, Neuroendocrine tumour, Clinical features, Endoscopic treatment.

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INTRODUCTION

Carcinoid tumour is a special neuroendocrine tumour that may affect several systems. These tumours are most commonly found in the gastrointestinal tract and lungs. They are derived mainly from enterochromaffin or Kulchitsky's cells and have diverse pathologic findings depending on the site of origin and their hormone-secreting ability. According to the World Health Organisation recommendation, the carcinoid tumour should be synonymous with a well-differentiated neuroendocrine tumour.

Since most gastrointestinal carcinoid tumours are asymptomatic, they are easy to be missed. With the development of endoscopic technology, more and more gastrointestinal carcinoid tumours are diagnosed. Even though, the great advancement in the diagnosis and treatment of gastrointestinal carcinoid tumours in recent years, arguments remain in terms of the incidence rate, anatomic distribution, and prognosis of these tumours. Some researchers reported the rate varying from 1 to 4.5 per 100,000 per year, but other studies have found carcinoids in approximately 1% of necropsies.¹⁻⁵

In order to know better about these carcinoid tumours and the choice of treatment modalities, the aim of this study was to analyse the clinical spectrum and endoscopic treatment curative of patients diagnosed with gastrointestinal carcinoid tumours.

METHODOLOGY

By searching the gastrointestinal endoscopic database and Hospital Medical Records database of The First Hospital of Putian City of Fujian Province, China, from 2012 to 2019, 113 patients diagnosed with gastrointestinal carcinoid tumour were

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found and recruited for this study. The data were extracted from the databases, including patients' age, gender, clinical presentation, tumour size and location, treatment, complications of treatment, and clinical and endoscopic follow-up. Pathological features of the tumours were determined using pathology reports.

Quantitative data were expressed as mean \pm standard deviation and quantitative data were indicated as counts or percentages (%) and comparisons between resection groups were carried out by using χ^2 test, p-value <0.05 was regarded as significant. SPSS 26.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. The study was approved by the Healthcare System Human Research Committee.

Table I: Summary of results.

Item	Sort	n(%)
Symptom	Asymptomatic(+)	11(9.7%)
	Hematochezia(+)	6(5.3%)
	Abdominal Pain(+)	40(35.4%)
	Constipation(+)	35(31.0%)
	Diarrhoea(+)	37(32.7%)
	Abdominal Distension(+)	20(17.7%)
Immunohistochemistry	Got cases	67(59.3%)
	SYN(+)	65(97.0%)
	CGA(+)	53(79.1%)
	CD56(+)	56(83.6%)
The margins of the excision	(+)	6(5.3%)
	Endoscopic (EMR)	50(44.2%)
	Endoscopic (ESD)	58(51.3%)
Resection	Surgical	5(4.4%)
	Not occurred	102(90.3%)
	Bleeding	10(8.8%)
Complications	Perforation	1(0.9%)
	Smaller than 1 cm	92(81.4%)
	Between 1cm to 2 cm	16(14.2%)
Tumours size	Larger than 2 cm	5(4.4%)
	Polyps	14(12.4%)
	Nodule with smooth surface	95(84.1%)
Morphology	Neoplasm with malignant performance	4(3.5%)
	Limited to the mucosa	14(12.4%)
Depth	Submucosa	88(77.9%)
	The muscularis propria	6(5.3%)
	Through the muscularis	5(4.4%)

RESULTS

One hundred and thirteen patients diagnosed with gastrointestinal carcinoid tumours were included in this study, with 62 (54.9%) males and 51(45.1%) females. The mean age at diagnosis was 55.04 ± 12.796 , ranging from 20 years to 83 years. Eleven (9.7%) patients diagnosed under screening colonoscopy were asymptomatic; the others presented with hematochezia (6/113, 5.3%), abdominal pain (40/113, 35.4%), constipation (35/113, 31.0%), diarrhoea (37/113, 32.7%), and abdominal distension (20/113, 17.7%, Table I).

Of these patients, 92(81.4%) tumours were smaller than 1 cm, 16(14.2%) tumours were between 1-2 cm, and 5 tumours were larger than 2 cm. Fourteen (12.4%) tumours showed as polyps,

95(84.1%) tumours showed as nodule with smooth surface, and 4 tumours (3.5%, 1 each located in cardia and duodenum, and 2 in rectum) showed as neoplasm with malignant performance. The tumours were limited to the mucosa in 14 (12.4%) cases, invaded into the submucosa in 88 (77.9%) cases and the muscularis propria in 6(5.3%) cases, and five cases went through the muscularis. Ninety-nine (87.6%) tumours were located in the rectum, five were located in the body of the stomach, three in the duodenum, two in the sigmoid colon and one each in gastric cardia, gastric antrum, ileocecal junction, and descending colon.

Sixty-seven cases got the immunohistochemistry. Synaptophysin (Syn) was found to be positive in 65 (97.0%) cases, with chromogranin A (CgA) positive in 53(79.1%) cases. CD56 was positive in 56(83.6%) cases. The Ki-67 index was less than 2% in all 108 cases experienced endoscopic resection and was more than 5% in the 5 cases underwent surgical resection, even more than 30% in the 3 cases with metastases.

Of the 113 patients, 108 (95.6%) patients were treated with endoscopic resection including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), and 5(4.4%) patients who underwent surgical resection directly. All the 3 cases without an endoscopic excision had a tumour size larger than 2 cm, and 4 cases presented as malignant neoplasm. Of the 108 cases treated by endoscopic resection, 50 cases were treated by EMR, and 58 cases were treated with ESD. The complications occurred in 11 (10.7%) patients, including bleeding in 10 (9.2%) patients and perforation in 1(1.4%) patient. Bleeding occurred 3 to 5 days after the endoscopic resection and was cured by drugs and endoscopic intervention. The perforation was successfully closed under endoscopy. The margins of the excision were positive in 6(5.6%) patients, one patient received the subsequent surgical resection of the rectum. There was no significant difference in complication rate between ESD and EMR ($p=0.76$), but the positive margins were more frequently seen in EMR patients. All 108 patients including the 6 patients with positive margins had no relapse of carcinoid tumour on follow-up. Two patients (1 primary tumour located in the ileocecal junction and the other in the rectum) died of hepatic metastases 2 years after surgical resection. One patient had no further therapy with metastases into the peritoneal cavity after surgical resection.

DISCUSSION

This study reviewed an institutional experience of carcinoid tumours happened in the gastrointestinal tract, and found that most of the tumours were located in the rectum. The finding is in accordance with the record reported in Japan.⁶ On the contrary, other authors reported that most carcinoid tumours were in the small bowel in their study in United States.⁷ Racial disparities may be accounted for the different distribution in carcinoid tumours as in other solid tumours, and the rectum may be the most common location of carcinoid tumours in Asian people. Meanwhile, improved technology and diagnosis, as well as environmental exposure may also play a role in the different distribution.

In this study, gastrointestinal carcinoid tumours are happened more common in male and aged patients. Since smoking, drinking, and stress are more common in male patients, these may be related to the high incidence in male patients. For the high incidence in aged people, genetic variation and environmental factors may also play a role in the pathogenesis.

The most common symptom of these patients in this study is abdominal pain, following by diarrhoea, constipation, abdominal distention, and hematochezia. All of these symptoms lack specificity, the result is consistent with the report.⁸ All of the cases treated with endoscopic resection are smaller than 2cm, and none of the patients suffering from carcinoid syndrome, these suggest that the size of the tumour relates to the secretion of 5-hydroxytryptamine(5-HT).

According to the immunohistochemistry, the Ki-67 index was at a low level in small-sized gastrointestinal carcinoid tumours in this study, but high in cases which needed surgical resection, and higher in cases with metastases. This suggests that the Ki-67 index is important in predicting the outcomes in gastrointestinal carcinoid tumours, as reported in pulmonary carcinoid tumours.^{9,10}

Compared with surgical resection, endoscopic excision doesn't increase the recurrence rate for small-sized carcinoid tumours. All six patients with positive margins in the institution were free of local recurrence and metastases during follow-up. And, there is no difference in the complications between EMR and ESD. From these findings, it can be deduced that endoscopic excision including EMR and ESD is effective and safe for the treatment of gastrointestinal carcinoid tumours which are smaller than 2 cm in size. Positive margins are more frequently seen in EMR patients, and ESD is more recommendable for endoscopic treatment. In order to exclude the metastases, imaging methods including endoscopic ultrasonography, pulmonary and abdominopelvic computed tomography, rectal MRI, and octreotide imaging are all needed to be performed before endoscopic excision. Endoscopic follow-up is suggested after endoscopic surgery every 6 months for 1 year and then annually for 5 years. Abdominopelvic computed tomography is also recommended annually for 3 years for higher-risk tumours.

The smaller tumours especially smaller than 1cm in size have better prognoses, there is no relapse and metastases in the patients with such smaller tumours in the institution. The malignant performance means poor prognoses with a high metastases rate. The three patients with malignant performance both get metastases not long after surgical resection in the institute. The depth of invasion is the most risk factor for patients' prognoses, which is closely associated with metastases. The malignant performance is in accordance with deep invasion through the muscularis with a poor prognosis. The tumour size and lymph node status are important predictors of survival, as have been demonstrated by others.¹¹⁻¹³ By the way, the location of the primary tumour is closely related to the prognosis. The most common cause of carcinoid syndrome is a metastatic liver disease arising from a small bowel carcinoid tumour.^{14,15}

The major limitation of this study was using retrospective data collection.

CONCLUSION

The rectum may be the most common location of gastrointestinal carcinoid tumours in Asian people. Most small tumours located in the stomach, colon, and rectum are nonfunctional, especially in the rectum. Endoscopic excision including EMR and ESD is effective and safe for the treatment of small gastrointestinal carcinoid tumours. But carcinoid tumours have a malignant potential, and the metastases can occur years after diagnosis. The follow-up should continue for a lifetime. The Ki-67 index is important in predicting outcomes in gastrointestinal carcinoid tumours.

ETHICAL APPROVAL:

The study was approved by the Healthcare System Human Research Committee.

PATIENTS' CONSENT:

Informed consent was obtained from all patients.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

LX, YC, WC, SC, PX: Contributed to concept, design, literature search, clinical studies, data analysis manuscript preparation, and final approval.

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