Published in final edited form as:

J Surg Res. 2013 September ; 184(1): 183–188. doi:10.1016/j.jss.2013.05.107.

Clinicopathologic characteristics of colonic carcinoid tumors

Sara E. Murray, MD¹, Ricardo V. Lloyd, MD, PhD², Rebecca S. Sippel, MD, FACS¹, and Herbert Chen, MD, FACS¹

¹Section of Endocrine Surgery, Department of Surgery, University of Wisconsin, Madison, WI

²Department of Pathology and Laboratory Medicine, University of Wisconsin, Madison, WI

Abstract

Background—Extraappendiceal colonic carcinoids are uncommon neuroendocrine tumors with a poor prognosis compared to carcinoids of other gastrointestinal origins. Few studies have examined the clinicopathologic profile and behavior of this rare tumor.

Materials and Methods—A retrospective analysis was performed on patients with colonic carcinoid tumors evaluated at a single tertiary care center between 1996 and 2012. Collected data included patient and tumor characteristics, presentation, treatment, recurrence and survival. Results were integrated into a comprehensive review of the colonic carcinoid literature.

Results—In total, 114 patients with colorectal carcinoid tumors were identified, and 15 patients with extraappendiceal tumors were analyzed. The mean age was 58.6±3.0 years, and subjects were predominantly male (73.3%). The most common presenting complaint was abdominal pain (33.3%), although 26.7% of patients were asymptomatic. Cecal tumors were the most prevalent (73.3%), and the majority of patients underwent right hemicolectomy. Three patients with lesions <1 cm were treated endoscopically. The mean tumor diameter was 2.9±0.5 cm, with lymph node or distant metastasis present in 53.3% and 26.7%, respectively. All but 2 patients underwent a presumed curative resection. During a mean follow-up of 4.2±1.0 years, there was only one death (non-carcinoid specific). Eleven patients were alive without evidence of disease at last follow-up, and 3 patients were alive with disease, one of which initially had a presumed curative resection but recurred.

Conclusions—This case series further elucidates the clinicopathologic characteristics of colonic carcinoid tumors, which aids physicians in guiding the diagnosis and management of these rare tumors.

Introduction

Carcinoids are common neuroendocrine tumors of the gastrointestinal tract, although they are infrequently found within the non-appendiceal colon. Extraappendiceal colonic carcinoid tumors, including tumors located at the rectosigmoid junction but excluding those within the rectum, account for only 9.6% of all carcinoids and 14.1% of gastrointestinal carcinoid tumors.¹ While a decline in the proportion of colonic carcinoid tumors relative to all

© 2013 Elsevier Inc. All rights reserved.

Address for Correspondence: Herbert Chen, M.D., FACS, University of Wisconsin, Department of Surgery, Section of Endocrine Surgery, K3/705 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792, USA, Tel.: 608-263-1387, Fax: 608-263-7652, chen@surgery.wisc.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

carcinoids was observed on comparison between the early Surveillance, Epidemiology, and End Results (SEER) (1973–1991) and late SEER (1992–1999) subpopulations, sigmoid carcinoids analyzed individually exhibited a 137% proportional increase relative to all sigmoid tumors – one of the largest proportional increases at any anatomic site.¹

Colonic carcinoids exhibit one of the worst prognoses of all gastrointestinal carcinoid tumors. Prior studies from the 1970s to early 1990s reported dismal 5-year survival rates between 23% and 42%, although a more recent analysis of 477 carcinoids from the late SEER database reported 5-year survival rates for extraappendiceal colonic carcinoid tumors ranging from 59% for nonlocalized colonic carcinoid tumors to 87% for tumors at the rectosigmoid junction.^{1–4} It has been hypothesized that some poorly differentiated adenocarcinomas were misdiagnosed as carcinoid tumors in the past, leading to a skewed prognosis in earlier studies.⁵ Regardless, the poor prognosis of colonic carcinoid tumors is postulated to be a result of the large tumor diameter and high rates of nodal or distant metastatic disease at the time of diagnosis. It has also been suggested that colonic carcinoids exhibit a higher rate of undifferentiated histologic pattern with more aggressive clinical features than carcinoids at other sites.⁶

Due to the extreme rarity of this tumor, few studies have examined in detail the characteristics and behavior of colonic carcinoid tumors.^{2,3,7} The variations in site-specific incidence and the overall poor prognosis of colonic carcinoids demands further investigation. Therefore, the objective of this study was to better characterize the clinicopathologic profile of extraappendiceal colonic carcinoid tumors, and place these findings in the context of a comprehensive literature review of colonic carcinoid.

Materials and Methods

Patients were identified retrospectively using our institution's pathology database and linked to the corresponding medical record. Of 114 patients with colorectal carcinoids evaluated at our tertiary care center between January 1, 1996 and December 31, 2012, extraappendiceal tumors were identified in 15 patients. All patients with colonic carcinoid tumors were included, with the exception of those patients with appendiceal or rectal carcinoids. Tumors located at the rectosigmoid junction or the ileocecal valve with predominant involvement of the cecal side of the valve were included in the study sample. Patients with a carcinoid resection prior to presentation at our institution were excluded unless the detailed pathologic information from their initial procedure was available in our electronic medical records. In these cases, the pathology from the initial procedure was used for analysis.

The following information was extracted from the electronic medical records: patient demographics, past medical and surgical history, synchronous and metachronous second primary malignancies, clinical presentation, diagnostic modality, treatment method, pathology, adjuvant therapy, follow-up, recurrence, and survival. Characteristics of tumor pathology included tumor location, tumor diameter and depth of invasion, number of carcinoid lesions, margin status, lymph node or distant metastasis, lymphovascular invasion, perineural invasion, mitotic rate, Ki67 labeling index, and immunohistochemistry. Margin status was classified as positive, negative, or indeterminate (no mention in the pathology report of the margin status or an endoscopically removed specimen was in fragments and the margins could not be adequately assessed). Margins were considered positive if carcinoid was present less than 1 mm from the specimen edge. Tumor grade and staging were defined based on the American Joint Committee on Cancer criteria.⁸ It was assumed that patients without evidence of lymph node involvement on either pre-operative imaging or pathologic assessment were negative for lymph node metastases (N0). The length of follow-up was calculated from the date of initial tissue diagnosis to the most recent appointment in our

health care system, and length of survival was determined from the date of tissue diagnosis to the date of death.

Data were analyzed using Stata version 12 software (StataCorp, College Station, TX) and are expressed as mean with standard error of the mean (SEM). Comparisons of continuous variables were made using a paired sample T-test, whereas comparisons of categorical variables were compared using Fisher's exact test. Values of $p < 0.05$ were considered statistically significant. The institutional review board from the University of Wisconsin approved this study.

Results

Patient characteristics and clinical presentation

Of the 15 patients with extraappendiceal tumors analyzed, the mean age was 58.6 ± 3.0 years at diagnosis, and were predominantly male ($n=11$, 73.3%) and Caucasian ($n=13$, 86.7%). Additional patient demographics and presenting symptoms are listed in Table 1. The majority of patients were symptomatic prior to diagnosis, with abdominal pain being the most prevalent presenting symptom ($n=5$, 33.3%). Carcinoid syndrome was present in only 1 patient at diagnosis and was manifested by diarrhea with an elevated urinary 5-hydroxyindoleacetic acid.

Tissue diagnosis of carcinoid was obtained via endoscopy in 10 patients (66.7%), at the time of surgery in 4 patients (26.7%), and by liver biopsy of a metastatic lesion in 1 patient (6.7%). The indication for surgery in the 4 patients diagnosed intraoperatively was unrelated to the carcinoid. Two patients required an emergent laparotomy either for a cecal perforation or a bowel obstruction, whereas the other 2 patients underwent a colectomy for alternate indication including ulcerative colitis and a synchronous colon adenocarcinoma. Overall, three patients (20.0%) in the cohort had a synchronous second primary tumor at the time of carcinoid diagnosis, including rectal adenocarcinoma, colon adenocarcinoma, and transitional cell cancer of the bladder. No cases of metachronous cancers were observed.

Treatment

Specific tumor location within the colon is displayed in Table 1. Carcinoids were predominantly located in the cecum ($n=11$, 73.3%). Patients were managed with either endoscopic or surgical resection. The patients with rectosigmoid ($n=2$) or sigmoid ($n=1$) tumors underwent endoscopy with snare polypectomy. All of these tumors were < 1.0 cm in diameter. One of these patients required a repeat endoscopy for an indeterminate margin and had residual carcinoid on re-biopsy, although margins could not be assessed. On a third endoscopic evaluation, the colon appeared grossly normal and no additional biopsies were obtained.

Surgical management included right hemicolectomy ($n=11$) or subtotal colectomy ($n=1$). Rates of laparoscopic-assisted and open procedures are listed in Table 1. Four patients (26.7%) exhibited distant metastasis at diagnosis, all within the liver. Two of these patients underwent hepatic lobectomy or wedge resection, whereas the remaining 2 patients had unresectable hepatic disease. Therefore, overall 13 patients (86.7%) underwent a presumed curative procedure. Perioperative complications occurred in only 1 patient who developed an intra-abdominal abscess necessitating percutaneous drainage.

Adjuvant chemotherapy was administered in 3 patients, 2 of which received fluorouracil and leucovorin and 1 who participated in a phase II clinical trial with motesanib diphosphate, and is currently involved in a phase II trial with resveratrol due to disease progression.

Octreotide therapy was administered in the 2 patients with unresectable hepatic metastasis, one of which also received microwave ablative therapy post-operatively.

Pathologic characteristics

Complete pathologic and staging information is shown in Table 2. The mean tumor diameter was 2.9 ± 0.5 cm. Overall, 8 patients (53.3%) had lymph node involvement and 4 (26.7%) had distant metastasis at diagnosis. Of the 4 patients with submucosal tumors (T1a), only 1 exhibited nodal involvement. There was no evidence of distant metastasis in this group. Of patients with lesions invading the muscularis propria (T2 or higher) (n=11, 73.3%), 7 (63.6%) had involvement of regional lymph nodes, 4 (36.3%) had distant metastatic disease, and 3 (27.3%) had no evidence of regional or distant metastasis.

Nearly all patients had only one mucosal carcinoid lesion (n=13, 86.7%), whereas 3 patients had 2 lesions. Pathology markers and immunohistochemistry are listed in Table 3, although this information is not available for all patients. Of the 5 patients with lymphovascular or perineural invasion, 3 had distant metastatic disease. However, no statistical correlations were found between either the presence of regional or distant metastasis and tumor diameter, tumor invasion, lymphovascular invasion, perineural invasion, Ki67, or mitotic rate.

Survival

The mean length of follow-up in this series was 4.2 ± 1.0 years. One patient died within the follow-up period at 0.4 years after carcinoid diagnosis, although the cause of death was synchronous metastatic colon adenocarcinoma. Eleven patients were alive without evidence of disease at last follow-up, and 3 patients were alive with disease. The patients living with disease include the 2 patients with unresectable liver metastases at diagnosis, and one patient with a recurrence. This patient initially had an ascending colonic atypical carcinoid completely resected by right hemicolectomy but experienced a recurrence 0.6 years after surgery at the ileotransverse colostomy, gallbladder, omentum, and mesenteric lymph nodes. He subsequently underwent transverse colectomy, cholecystectomy, omentectomy, and lymphadenectomy. A follow-up computed tomography scan 1.7 years after his second resection demonstrated recurrence near the previously-resected lymph nodes. After that time the patient was lost to follow-up.

Discussion

Extraappendiceal colonic carcinoid tumors are rare malignancies accounting for only 1% of colonic neoplasms, and are uncommonly encountered by gastroenterologists and surgeons.⁶ Colonic carcinoids most often present with non-specific abdominal symptoms, but may be asymptomatic. They are most often located in the cecum and are frequently diagnosed at the late stages of IIIb or IV with lymph node involvement and distant metastases. They are typically treated with hemicolectomy and have high rates of disease-free survival for localized tumors. This study is one of only a few studies that provide a comprehensive clinicopathologic profile of extraappendiceal colonic carcinoid tumors.^{2,3,7} Our specific findings will be further discussed in the context of the known literature to provide a thorough review of the current understanding of the diagnosis, treatment, and prognosis of this rare tumor.

Colonic carcinoid tumors typically present in the seventh decade with nonspecific symptoms of abdominal pain, anorexia, unintentional weight loss, or hematochezia.^{3,7} Our findings were consistent with this data; however, we noted a higher rate of asymptomatic patients (26.7%) than reported previously.³ This may reflect the increasing use of screening colonoscopy resulting in the identification of clinically occult lesions at a greater frequency.

Carcinoid syndrome was observed in only 1 patient (6.7%) in this series, corresponding to prior observations that the majority of colonic carcinoids are nonfunctioning and carcinoid symptomatology is rare (<5%).⁹

Gender distribution demonstrates a slight female predominance of 57% to 60%, though this was not replicated in our series which may be a reflection of the small cohort size that was treated at a single tertiary care center.¹⁰ Regarding race, prior studies have demonstrated a white predominance (89%), although there is evidence that prevalence varies according to the specific location within the colon.² For example, analyses of the SEER data suggest that there may be a propensity for the development of sigmoid, descending, and rectosigmoid junction carcinoids in black patients, but cecal, ascending, and transverse carcinoids may be more likely in white patients.¹

Cecal carcinoids comprised the most frequent site of colonic carcinoids in our series at 73.3%, though this is significantly higher than rates reported previously (34.5% to 50.0%).¹⁻³ The predominance of right-sided carcinoid tumors may be due to a greater number of enterochromaffin cells in the right colon, or simply that tumors from the appendiceal base extend into the cecum.^{1,2}

The mean tumor size of colonic carcinoid tumors at presentation has historically been reported at approximately 5 cm.^{2,6} However, a 2009 study by Waisberg and colleagues reported a mean tumor size of 3.7 ± 1.2 cm, whereas our series reveals an even smaller mean of 2.9 ± 0.5 cm.⁷ If we were to exclude rectosigmoid tumors from our cohort (2 tumors <1.0 cm) to be consistent with prior studies, the mean tumor diameter remains small at 3.2 ± 0.5 cm. This highlights a recent trend described by Al Natour and colleagues in which the incidence of smaller and more superficial colonic carcinoid tumors is increasing.¹¹ It is thought to be a result of the expanding use of screening colonoscopy, leading to earlier detection of clinically occult colonic lesions.

While tumor size is often cited as the most important prognostic indicator for carcinoid tumors, the best indicators are in fact the evidence of invasive growth and the presence of regional or distant metastasis.¹ Colonic carcinoids exhibit one of the highest rates of nonlocalized disease at presentation of all carcinoid tumors.^{1,10} The overall rate of lymph node metastasis in our series was 53.5%, which is consistent with reported rates of 48% to 72%.^{1-3,7,10,11} Distant metastasis is present at the time of diagnosis in 25% to 31% of patients with colonic carcinoids, which was congruent with our observed rate of 26.7%.^{1,7,10} There was no correlation in our series between lymph node or distant metastasis and tumor size, tumor invasion, or markers of aggressive features such as lymphovascular or perineural invasion, or mitotic rate. However, previous studies with a larger number of subjects have noted associations.^{3,11} Analysis of the Connecticut Tumor Registry data found that 1 out of 6 tumors <2 cm was nonlocalized, compared to metastasis in two thirds of patients with tumors >2 cm.⁹ In addition, Al Natour and colleagues utilizing 929 patients from the SEER database analyzed predictors of lymph node metastasis based on tumor size and depth of invasion. They found that tumor size (stratifying tumors <1, 1 and <2, or ≥2 cm) and depth of invasion (intramucosal, submucosal, or muscularis propria) highly correlated with regional lymph node metastasis ($p < 0.001$, $p < 0.001$). Furthermore, patients with intramucosal tumors <1 cm had only a 4.0% rate of lymph node metastasis.¹¹

As previously stated, colonic carcinoid tumors exhibit one of the worst prognoses among all gastrointestinal carcinoids. It is postulated that this poor prognosis is due to delayed diagnosis resulting in high rates of nonlocalized disease at presentation. Given this propensity for metastatic spread, widely accepted consensus guidelines recommend a formal segmental colectomy with oncologic resection of the lymph drainage.^{12,13} Isolated hepatic

metastases should be resected if possible. Due to an increase in the diagnosis of small colonic carcinoid tumors that demonstrate a low propensity for nodal or distant metastasis, Al Natour and colleagues recently proposed that endoscopic resection might be appropriate for intramucosal tumors <1 cm.¹¹ In the 4 patients in our series with superficial tumors <1 cm, 1 (25%) had lymph node involvement. Clearly, further investigation is necessary to delineate the rate of nonlocalized disease in these small, superficial lesions, and the appropriateness of a localized endoscopic resection.

Although surgical resection is the only curative therapy for colonic carcinoid, additional treatment modalities are available for metastatic disease. Management may include somatostatin analogues, although carcinoid syndrome is rare in patients with colonic carcinoids, and there is currently no evidence to suggest the use of these agents in nonfunctioning tumors.¹² Two patients with progressive metastatic disease in our series received octreotide and experienced significant improvement in their symptoms. Interferon has been shown to upregulate expression of somatostatin and may act synergistically with somatostatin analogues to treat carcinoid syndrome.¹⁴ Cytotoxic agents may be used for tumors with high proliferative indices (Ki67 >5%) and patients with progressive disease. The combination of 5-fluorouracil, streptozotocin, and doxorubicin is most commonly used, though response rates are poor (<25%).^{12,14} Peptide receptor radionucleotide therapy using a variety of radiolabeled somatostatin analogues may also be considered in patients with metastatic carcinoid. A compound with promising results is ¹⁷⁷Lu-DOTA0, Tyr3octreotate, which resulted in a complete or partial tumor response in 23% of 188 patients with carcinoid tumors, though the number of colonic carcinoids treated was not specifically stated.¹⁵ Finally, targeted therapies to pathways implicated in the tumorigenesis of carcinoids are currently underway. Our lab has demonstrated that Notch-1 – a multifunctional transmembrane receptor that regulates cellular differentiation, development, proliferation, and survival – may act as a tumor suppressor in neuroendocrine tumors and is a potential therapeutic target.^{16–18} A phase II clinical trial is currently underway at our institution, evaluating the response of metastatic carcinoid to resveratrol, a naturally occurring phytoalexin and a potent Notch-1 activator.

Patients with carcinoid tumors are at an increased risk of incurring a secondary noncarcinoid malignancy compared to the general population. Associated tumors occur in 13% to 41% of patients with carcinoid tumors, and were observed in 20% of patients in our series.^{1,4,19–21} Common sites include the gastrointestinal tract, lung, urinary system, and prostate.^{4,21} The etiology for this increased risk is undefined, though it is hypothesized that secreted bioactive agents produce proliferative peptides that may enhance the development of other neoplasia.¹ Regardless, patients with a carcinoid tumor should undergo appropriate staging and surveillance of the gastrointestinal tract, lung, cervix and ovaries. At minimum, a full colonoscopy and contrast computed tomography (CT) scan of the chest, abdomen, and pelvis should be obtained at diagnosis.¹² Given the high incidence of gastrointestinal malignancies within six months before or after carcinoid diagnosis, Tichansky et al recommends a colonoscopy, upper endoscopy, and a small-bowel follow through at diagnosis and 6 months after diagnosis.²¹ Furthermore, the European Neuroendocrine Tumor Society recommends CT and colonoscopy follow-up through 10 years, with the frequency of surveillance based on the size of the initial carcinoid tumor.¹²

There are several limitations of this study, foremost of which is the retrospective nature. We were limited in our analysis by the comprehensiveness of the electronic medical record. Important characteristics, such as the length of symptoms prior to carcinoid diagnosis were not consistently documented and therefore could not be described. In addition, the small cohort size makes it difficult to elucidate associations between tumor and patient characteristics, treatment modalities, and prognosis. However, because of the rarity of

colonic carcinoids, the results of this study provide additional knowledge and expand the small body of current literature. Case series of these rare types of cancer must be aggregated and contextualized within other case series to help guide further treatment decisions. Lastly, due to the inconsistent and limited length of follow-up, a survival analysis was unable to be performed.

This single-institution case series adds to the small body of literature describing these rare colonic carcinoid tumors. Although colonic carcinoids are not highly prevalent in the general population, they typically present at late stages and have one of the worst prognostic profiles of all gastrointestinal carcinoid tumors. Additionally, there is evidence of an increasing incidence of tumors located within certain regions of the colon which is of unclear significance at this time. This case series further elucidates the clinicopathologic characteristics of colonic carcinoid tumors, which aids physicians in guiding the diagnosis and management of these rare tumors.

Acknowledgments

University of Wisconsin, Physician Scientist Training in Career Medicine grant, National Institutes of Health T32 CA009614-21.

References

1. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. *Cancer*. 2003; 97:934–959. [PubMed: 12569593]
2. Ballantyne GH, Savoca PE, Flannery JT, et al. Incidence and mortality of carcinoids of the colon. Data from the Connecticut Tumor Registry. *Cancer*. 1992; 69:2400–2405. [PubMed: 1568162]
3. Rosenberg JM, Welch JP. Carcinoid tumors of the colon: A study of 72 patients. *Am J Surg*. 1985; 149:775–779. [PubMed: 2409828]
4. Saha S, Hoda S, Godfrey R, et al. Carcinoid tumors of the gastrointestinal tract: a 44 year experience. *South Med J*. 1989; 82:1501–1505. [PubMed: 2595419]
5. Thomas RM, Sobin LH. Gastrointestinal cancer. *Cancer*. 1995; 75:154–70. [PubMed: 8000994]
6. Spread C, Berkel H, Jewell L, et al. Colon carcinoid tumors. A population-based study. *Dis Colon Rectum*. 1994; 37:482–491. [PubMed: 8181412]
7. Waisberg DR, Fava AS, Martins LC, et al. Colonic carcinoid tumors: a clinicopathologic study of 23 patients from a single institution. *Arq Gastroenterol*. 2009; 46:288–293. [PubMed: 20232008]
8. Edge, SB.; Byrd, DR.; Compton, CC., et al. *AJCC Cancer Staging Manual*. 7. New York, NY: Springer; 2010.
9. Modlin IM, Kidd M, Latich I, et al. Current status of gastrointestinal carcinoids. *Gastroenterology*. 2005; 128:1717–1751. [PubMed: 15887161]
10. Modlin IM, Sandor A. An analysis of 8305 cases of carcinoid tumors. *Cancer*. 1997; 79:818–829.
11. Al Natour RH, Saund MS, Sanchez, et al. Tumor size and depth predict rate of lymph node metastasis in colon carcinoids and can be used to select patients for endoscopic resection. *J Gastrointest Surg*. 2012; 16:595–602. [PubMed: 22143420]
12. Ramage JK, Goretzki PE, Manfredi R, et al. Consensus guidelines for the management of patients with digestive neuroendocrine tumours: well-differentiated colon and rectum tumour/carcinoma. *Neuroendocrinology*. 2008; 87:31–39. [PubMed: 18097130]
13. [Accessed on March 21, 2013] NCCN Clinical Practice Guidelines v.1.2012. Neuroendocrine Tumors. at: http://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf
14. Maroun J, Kocha W, Kvols L, et al. Guidelines for the diagnosis and management of carcinoid tumours. Part 1: The gastrointestinal tract. A statement from a Canadian National Carcinoid Expert Group. *Curr Oncol*. 2006; 13:67–76. [PubMed: 17576444]
15. Kwekkeboom DJ, de Herder WW, Kam BL, et al. Treatment with the radiolabeled somatostatin analog [¹⁷⁷Lu-DOTA⁰,Tyr³]octreotate: toxicity, efficacy, and survival. *J Clin Oncol*. 2008; 26:2124–2130. [PubMed: 18445841]

16. Kunnimalaiyaan M, Traeger K, Chen H. Conservation of the Notch1 signaling pathway in gastrointestinal carcinoid cells. *Am J Physiol Gastrointest.* 2005; 289:G636–G642.
17. Kunnimalaiyaan M, Chen H. Tumor suppressor role of Notch-1 signaling in neuroendocrine tumors. *Oncologist.* 2007; 12:535–542. [PubMed: 17522241]
18. Greenblatt DY, Cayo M, Ming, et al. Suberoyl bishydroxamic acid inhibits cellular proliferation by inducing cell cycle arrest in carcinoid cancer cells. *J Gastrointest Surg.* 2007; 11:1515–1520. [PubMed: 17874277]
19. Berge T, Linell F. Carcinoid tumors. Frequency in a defined population during a 12-year-period. *Acta Pathol Microbiol Scand.* 1976; 84:322–330.
20. Marshall JB, Bodnarchuk G. Carcinoid tumors of the gut. *J Clin Gastroenterol.* 1993; 16:123–129. [PubMed: 8463615]
21. Tichansky DS, Cagir BC, Borrazzo E, et al. Risk of second cancers in patients with colorectal carcinoids. *Dis Colon Rectum.* 2002; 45:91–97. [PubMed: 11786770]

Table 1

Patient and clinical characteristics

n	15
Age, mean $\pm$ SEM, yr	58.6 $\pm$ 3.0
Male, n (%)	11 (73.3)
Race, n (%)	
Caucasian	13 (86.7)
African American	1 (6.7)
Unspecified	1 (6.7)
Presenting symptoms, n (%)	
Abdominal pain	5 (33.3)
Diarrhea	4 (26.7)
Hematochezia	3 (20.0)
Nausea	1 (6.7)
Asymptomatic	4 (26.7)
Carcinoid syndrome, n (%)	1 (6.7)
Tumor location, n (%)	
Cecum	11 (73.3)
Ascending colon	1 (6.7)
Sigmoid colon	1 (6.7)
Rectosigmoid junction	2 (13.3)
Procedure, n (%)	
Endoscopic snare removal	3 (20.0)
Right hemicolectomy	11 (73.3)
Laparoscopic-assisted	3 (20.0)
Open	8 (53.3)
Subtotal colectomy (laparoscopic-assisted)	1 (6.7)
Patients with presumed curative treatment, n (%)	13 (86.7)

SEM = standard error of the mean

Percentages may not add to 100 due to rounding.

Table 2

Pathologic characteristics

Variable	n (%)
Tumor diameter, mean $\pm$ SEM, cm	2.9 $\pm$ 0.5
Primary tumor, n (%)	
T1a	4 (26.7)
T1b	0 (0)
T2	0 (0)
T3	10 (66.7)
T4	1 (6.7)
Lymph node involvement, n (%)	
N0	7 (46.7)
N1	8 (53.3)
Distant metastasis present, n (%)	4 (26.7)
Stage, n (%)	
Ia	3 (20.0)
IIa	0 (0)
IIb	3 (20.0)
IIIa	0 (0)
IIIb	5 (33.3)
IV	4 (26.7)

SEM = standard error of the mean

Percentages may not add to 100 due to rounding.

Table 3

Pathology markers and immunohistochemistry

Variable	Positive/total tested (%)
Lymphovascular invasion, n (%)	4/7 (57.1)
Perineural invasion, n (%)	3/7 (42.9)
Mitotic rate	
<2 per 10 hpf	4/6 (66.7)
2 per 10 hpf	1/6 (16.7)
“Very low” ^{**}	1/6 (16.7)
Ki67	
<3%	3/5 (60.0)
<5%	2/5 (40.0)
Chromogranin	5/6 (83.3)
Synaptophysin	5/6 (83.3)

* Tumor markers and immunohistochemistry were not available for all patients. Percentages reflect total positive values over the total number of patients receiving the test.

** The mitotic rate in this patient was reported as “very low” in the pathology report, without a specified value.

SEM = standard error of the mean

hpf = high power field