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Progression of Metastases and Symptom Improvement from Laparotomy in Midgut Carcinoid Tumors

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Abstract. A total of 121 consecutive patients with midgut carcinoid tumors underwent regular clinical control and 158 laparotomies for abdominal symptoms with 1 to 11 years (mean 5.2 years) of follow-up. Metastases were present in 93% of the patients at study inclusion and developed at initially uninvolved sites with an overall probability of 0.38. Patients without initial tumor spread developed mesenteric or liver metastases with the probability of 0.25 (mean delay 12 years), whereas those with mesenteric metastases exhibited a probability 0.56 to develop liver metastases (mean delay 6.1 years). Spread to extraabdominal sites in patients with mesenteric and liver metastases exhibited a probability of 0.22 (mean delay 4.3 years), and this spread was especially frequent (probability 0.60) in patients with only liver metastases at inclusion. Patients without the carcinoid syndrome (52%) mainly suffered from more or less episodic abdominal pain, nausea, and diarrhea. Marked mesenteric fibrosis detected at surgery ($n = 59$) generally was accompanied by symptoms of abdominal pain and weight loss, and it often required urgent intervention due to intestinal obstruction or ischemia. Complete or partial symptom alleviation was accomplished in 82% of the operated patients, and generally was most auspicious after primary acute or subacute procedures ($n = 54$). The complete or partial symptom improvements after surgery lasted for mean 5.3 years and tended to be longer after elective ($n = 50$) than acute operations. The findings substantiate encouraging results of laparotomy in a compromised cohort of patients with midgut carcinoid tumors. Because the patients also displayed a generally slow progression of metastases, liberal indications for laparotomy should prevail in symptomatic and possibly also asymptomatic individuals with midgut carcinoid tumors.

The midgut carcinoid is a rare tumor, with a reported clinical incidence of 0.5% to 1.5%, although a higher frequency of mainly asymptomatic lesions may be detected at autopsy [1–6]. Although these carcinoids tend to grow slowly, they are almost invariably malignant and preferentially spread to mesenteric lymph glands and liver, and eventually also to extraabdominal sites [1, 5–9]. The primary tumor is often inconspicuous and clinically silent, whereby a large proportion of the patients exhibit disseminated disease at diagnosis [1, 8, 9]. The presence of a carcinoid syndrome generally implies that the patient has liver metastases [1, 3, 5–9], although symptoms also occur at advanced disease stages owing to mesenteric metastases and fibrosis, which may cause obstruction and ischemia of the intestine [1, 5, 9–14]. Surgery is undertaken in patients with midgut carcinoids to remove the primary tumor, but it is also frequently required to alleviate symptoms related to the mesenteric involvement [4, 5, 7–9, 15–22]. A few patients are subjected to liver surgery, but this step seems to palliate the carcinoid syndrome only when unusually large and essentially solitary liver metastases are excised [3, 7–9, 16, 18, 21–31].

Acknowledging that management experience often is limited, it may be difficult to appreciate the indications for abdominal surgery in patients with midgut carcinoids, and this point may hold true especially when abdominal symptoms occur in patients with advanced tumors. Survival, however, is often considerable also in the presence of metastases, but it may be less encouraging mainly in patients with widely disseminated tumors [5]. To substantiate indications for surgery the dual purpose of the present study was to evaluate the probability of metastatic progression and the expectations on symptom responses to acute and elective laparotomy in a consecutively treated series of patients with advanced midgut carcinoid tumors.

Materials and Methods

The material consists of 121 patients with midgut carcinoid tumors being subjected to medical and surgical therapy at our hospital during 1980–1990. The patients comprise 53 women and 68 men with a median age of 61 years (range 26–83 years) at inclusion. The diagnosis was established through acute (42 patients) or elective (31 patients) laparotomy, or on basis of elevated 5-hydroxyindoleacetic acid (5-HIAA) values and percutaneous biopsy of liver or mesenteric metastases (48 patients). The midgut carcinoid tumors were histologically confirmed in all of them.

Follow-up encompassed 1 to 11 years (mean 5.2 years) during which all the patients underwent clinical assessment essentially every third month. These investigations included measurements of urinary 5-HIAA excretion (normal range 10–80 μmol/24 hr), and plasma chromogranin values (normal < 350 μg/L), as well as imaging with abdominal computed tomography (CT), ultrasonography, and octreotide scintigraphy during later parts of the follow-up.

During the study interval 81% of the patients underwent medical therapy encompassing cytostatics (9%), interferons

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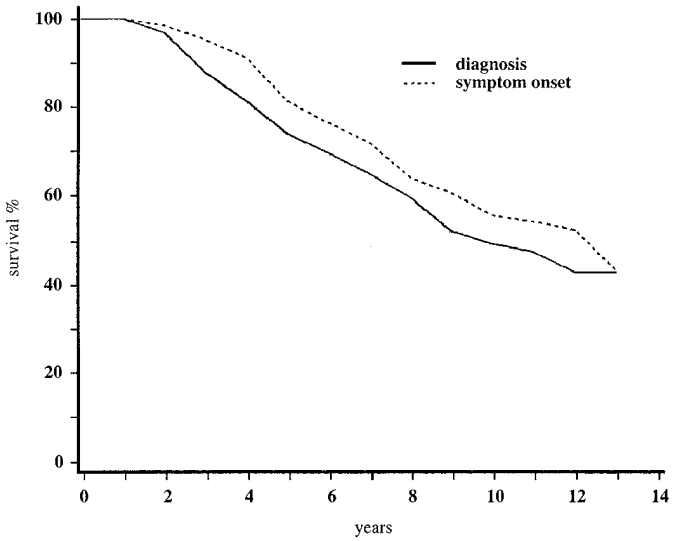

Fig. 1. Survival from symptom onset and diagnosis in 121 patients with midgut carcinoids.

Table 1. Patients (n = 121) with midgut carcinoid tumors demonstrating metastases at various locations at study entry and exit.

Metastases	Inclusion	Exit
None	7	11
Mesenteric	80	85
Peritoneal	23	39
Ovarian	2	4
Hepatic	62	80
Extraabdominal	2	16

(47%), and somatostatin analogs (3%), or various combination regimens (41%) for 1.0 to 8.2 years (mean 3.9 years). In addition 20 patients received hepatic artery gel foam injections. Altogether 52 patients succumbed during the study, and median survival from symptom debut and diagnosis was 12 and 9 years, respectively (Fig. 1). Carcinoid heart disease and heart failure seemed to be the cause of death in approximately 50% of the patients, and malnutrition and advanced mesentericointestinal involvement probably accounted for the death of another 40%. Other main contributory factors in this respect included extensive metastases, liver insufficiency, pulmonary infection, and uremia.

Metastases and Carcinoid Syndrome

Radiologic or surgical evidence of metastases was present in 93% of the patients at study inclusion (Table 1). Tumor spread to the intestinal mesentery was discernible in 80%, and these masses measured 4 to 15 cm in diameter in 39% of the patients. Significant retroperitoneal tumor extension, peritoneal carcinoidosis, and ovarian metastases were present in one-fourth of the patients. Liver metastases were demonstrable in 62% and were accompanied by palpable hepatomegaly in one-fourth of them. Fifteen individuals exhibited liver metastases without evidence of spread to other locations. Only two individuals had extraabdominal metastases (to lung and subcutaneous lymph nodes) at study entry. The carcinoid syndrome with flushing, diarrhea, urinary

Table 2. Frequency of symptoms at study inclusion in patients with (n = 58) or without (n = 63) carcinoid syndrome.

	Frequency (%)	
Symptoms	Carcinoid syndrome	Without syndrome
Diarrhea	100	43
Flush	100	15
Dyspnea, palpitation	38	6
Nausea/distension	26	39
Abdominal pain	41	81
Weight loss	36	37
Fever	21	3
Hepatomegaly/lower abdominal mass	50/0	0/21
Acute abdominal episode	5	52

5-HIAA excess, and sometimes also echocardiographic evidence of valvar fibrosis was present in 58 patients at inclusion (Table 2). In addition 25 individuals developed the syndrome a mean 4.5 years later (range 1.0–10.0 years). Median 5-HIAA values at study entry were 550 μmol/24 hr (range 85–2300 μmol/24 hr) in individuals with the carcinoid syndrome, and 50 μmol/24 hr (range $<$ 50 to 300 μmol/24 hr) in the others. The corresponding plasma chromogranin values were 3800 and 300 μg/L, respectively. Six patients with the carcinoid syndrome lacked evidence of hepatic tumor involvement, although all of them displayed voluminous mesenteric metastases extending retroperitoneally, and two had extraabdominal tumor spread. Conversely, 23 patients with liver metastases lacked the carcinoid syndrome despite the fact that 7 of them had substantial liver involvement.

Abdominal Symptoms

In addition to the invariable occurrence of diarrhea and flushing at study entry, patients with the carcinoid syndrome (n = 58) variably demonstrated dyspnea, palpitations, and palpable liver metastases; abdominal pain and weight loss were seen in less than half of them (Table 2). Acute abdominal symptoms requiring immediate clinical attendance were uncommon in these patients, but periods of recurrent fever occurred in about one-fifth of them. A few (14%) of the patients exhibiting the syndrome suffered from symptoms of cardiac insufficiency, hypoalbuminemia, and edema. Five patients with advanced heart failure underwent tricuspid valve replacement [31]. Patients without the complete carcinoid syndrome (n = 63), in addition to generally discrete and rare flushing, mainly suffered from abdominal pain (81%), diarrhea, nausea, and weight loss at study inclusion. Episodic gastrointestinal bleeding affected 5% of all the patients.

Irrespective of the presence or absence of carcinoid syndrome, patients with marked mesenteric fibrosis detected at surgery (n = 59) constituted a separate group with respect to abdominal symptoms, as essentially 90% of them suffered from acute abdominal pain requiring urgent clinical attendance. In addition most of them (58%) displayed substantial weight loss ($\geq$ 9 kg) and a palpable lower abdominal mass (56%); 39% of them had experienced cessation of diarrhea even leading to episodes of constipation.

Table 3. Operative procedures and findings in acute/subacute and elective laparotomies in patients with abdominal symptoms undergoing a primary or first reoperative procedure for midgut carcinoid tumors.

Parameter	Acute/subacute (n = 75)	Elective (n = 50)
Procedures (%)		
Mesenteric tumor dissection	44	23
Small intestinal resection	57	46
Colon resection	24	30
Entrapment release alone	6	2
Intestinal bypass	9	4
Resection ovarian/peritoneal metastases	3	2
Laparotomy alone	6	7
Resection of liver metastases	1	9
Cholecystectomy	2	3
Findings (%)		
Mesenteric metastases		
$<$ 4 cm	41	58
$\geq$ 4 cm	49	30
Marked mesenteric fibrosis	59	20
Intestinal ischemia[a]		
Minor	17	2
Extended	19	8
Peritoneal carcinoidosis	29	18
Duodenal/colonic entrapment	11/6	5/4
Significant ascites	21	16

[a]All patients with intestinal ischemia had marked mesenteric fibrosis.

Abdominal Surgery

Including 32 operations at other hospitals undertaken generally in close connection to referral, a total of 158 laparotomies were performed on 107 of the patients. Altogether 42 of them underwent up to four reoperations, and the interval between the primary operation and the first reoperation averaged 3.3 years. The 125 primary or first reoperative procedures performed because of abdominal symptoms constituted the material for evaluation of the effects of surgery. Both primary and reoperative intestinal procedures aimed at macroscopic radicality and included a search for multiple primary tumors in the intestine. When this step was impossible, alleviation of bowel entrapment, intestinal congestion, and ischemia was the principal intent, and more than 75% of the operations involved intestinal resection (Table 3). By dissection of proximal mesenteric vessels, it was generally possible to remove major parts of substantial mesenteric tumors without seriously compromising the intestinal vascular supply. Intestinal bypasses were avoided as far as possible but comprised the only alternative in some difficult reoperations; this measure occasionally was utilized more liberally prior to referral.

The abdominal explorations frequently revealed mesenteric metastases of substantial size (Table 3). Mesenteric fibrosis generally was most prominent in patients with the largest mesenteric tumors, and a substantial proportion of them showed congestion, venous stasis, and ischemia in the intestinal loops adhering to the mesenteric tumor. Intestinal entrapment and ischemia were more prevalent in the acute and subacute explorations. Duodenal entrapment by fibrosis was not uncommon and generally easily severed at surgery. Patients with entrapment of the right, the transverse, or occasionally the sigmoid colon, as well as those in whom removal of the mesenteric tumor compromised the circulation (generally of the right colon), underwent large bowel resection. Reoperative cases generally exhibited marked adhesions, which were particularly harsh in the area of previously resected tumors.

Despite the fact that most of the patients displayed hepatic metastases, various types of liver resection were performed in only a few patients with dominating lesions (Table 3). Most patients, however, had bilateral spread of numerous, unresectable liver metastases [7].

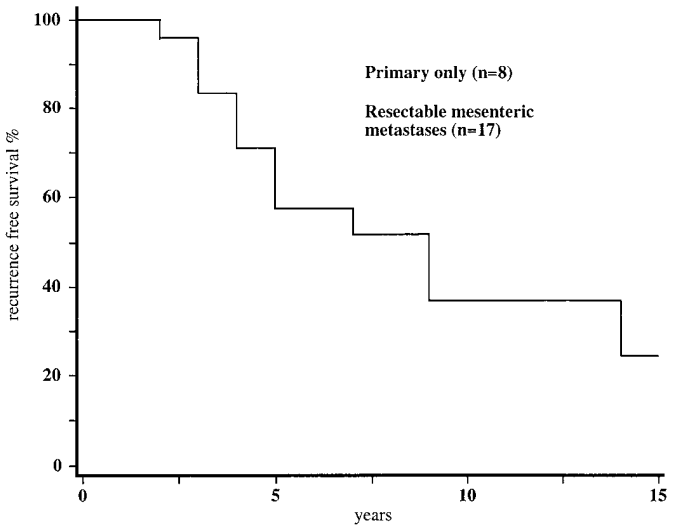

Fig. 2. Recurrence-free survival in patients without metastases at inclusion (n = 8) and in patients with only locoregional dissemination subjected to apparently curative surgery (n = 17).

Table 4. Probability of developing metastases to novel sites in patients subgrouped according to site of visualized metastases at study entry.

Metastases at entry	Novel sites: Mesentery	Liver	Extraabdominal	Total
None (n = 8)	0.25	0.13	0	0.25
Mesenteric (n = 37)	—	0.56	0.05	0.60
Only liver (n = 15)	0.27	—	0.60	0.60
Mesenteric and liver (n = 59)	—	—	0.22	0.22

Results

Metastasis Progression

Six of eight patients without metastases at inclusion and 3 of 17 individuals subjected to macroscopically radical tumor excisions displayed no signs of tumor spread at completion of the study period (Fig. 2). Of the others, 45 patients developed clinically discernible metastases to apparently uninvolved sites, which implies a total probability to develop such metastases of 0.38 during the investigated period (Table 4). Patients without signs of dissemination at study entry had the lowest probability to develop metastases (probability of 0.25), and when such occurred they were located in the mesentery and liver. Patients with mesenteric metastases at study entry were at high risk to develop liver metastases (probability 0.56), whereas spread to extraabdominal sites occurred rarely. In contrast, patients with liver metastases

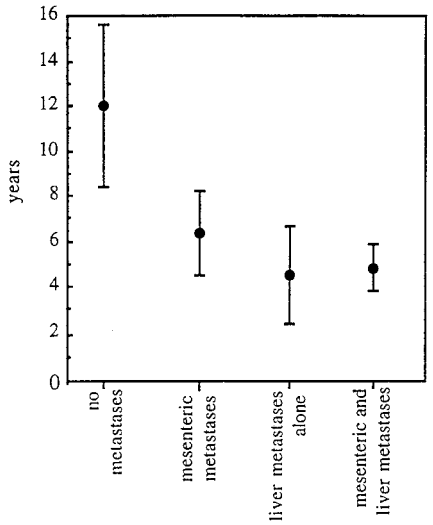

Fig. 3. Mean duration (± 90% confidence interval, years) until the demonstration of metastases to apparently uninvolved sites in patients subgrouped according to location of visualized metastases at study entry.

alone were at exceptional risk to develop spread to extraabdominal sites (probability 0.60), whereas mesenteric metastases developed less commonly (probability 0.27). Those with combined mesenteric and liver metastases at study entry less frequently developed spread to extraabdominal sites (probability 0.22). The time to develop novel metastases to any site averaged 12 years for those without secondary neoplasms at study entry, and the corresponding durations were 6.1 years for those with tumor in the mesentery and 4.3 years for those with liver involvement (with or without mesenteric metastases) (Fig. 3).

During the study period the two patients with extraabdominal metastases developed further spread to other distant sites, and such metastases occurred in another nine patients as well. At study end the extraabdominal metastases were confined to the skeleton (nine patients, including the cranium in six of them), lungs and mediastinum (seven patients), subcutaneous lymph glands (four patients), heart (two patients), and brain and orbita (one patient). Liver metastases generally increased significantly in size during the study period.

Symptom Response to Laparotomy

The elective operations were most often performed because of various combinations of recurrent abdominal pain, nausea, and distension, and occasionally to episodic vomiting (Table 5). There were small differences in this respect between the primary and first reoperative procedures. In contrast, the principal indications for acute and subacute operations mainly involved acute bowel obstruction for the primary procedures, whereas intermittent obstructions dominated among the reoperations.

When postoperative symptom improvement was evaluated, complete or partial alleviation occurred in 82% of the operations (Table 6). The outcome was the most auspicious in patients in whom symptoms of acute abdominal pain or ileus called for an acute or subacute primary operation. Less complete alleviation of mainly intermittent bowel obstruction was accomplished by reoperations. Elective operations, either as primary or reoperative procedures, were accompanied by essentially similar expectations on symptom improvement. The average duration of the favorable symptom responses were longer after primary than reoperative procedures (6 years versus 3 years), and this difference was similarly extensive for acute or subacute and elective procedures (Fig. 4).

The procedures comprising the third (eight patients) to fourth and fifth operations (two patients) were almost invariably undertaken because of recurrent intestinal obstruction and provided complete ($n = 6$) or partial ($n = 2$) symptom alleviation with a mean duration of 3 years.

Table 5. Principal or contributing indications for acute or elective abdominal surgery (primary operations and first reoperation) in patients with midgut carcinoid tumor.

Indication	Primary operation	First reoperation
Acute/subacute ($n = 75$)	$n = 54$	$n = 21$
Acute ileus	54	22
"Subileus," recurrent	31	73
Peritonitis	12	5
Elective ($n = 50$)	$n = 40$	$n = 10$
Recurrent abdominal pain	68	70
Weight loss	18	30
Distention/nausea	52	62
Diarrhea	65	40
Gastrointestinal bleeding	5	0

Table 6. Symptom response rates to primary operation and first reoperation in acute/subacute and elective procedures for midgut carcinoid tumor.

	Primary operation		First reoperation		
Response	Acute/subacute ($n = 54$)	Elective ($n = 40$)	Acute/subacute ($n = 21$)	Elective ($n = 10$)	All operations ($n = 125$)
Complete (%)	85	53	52	60	67
Partial[a] (%)	9	20	24	10	15
None (%)	6	27	24	30	18

[a]Arbitrarily determined as considerable but incomplete reversal of symptoms.

Complications to Laparotomy

Considering the substantial tumor burden in most of the patients, operative complications were relatively rare (Table 7). They tended to be more prevalent after acute than after elective operations and most commonly encompassed temporarily increased diarrhea. The postoperative (30 day) mortality was 3% for the 125 operations on symptomatic patients. Two deaths occurred within 2 months after re-repeated surgery in patients with chronic ileus and severe peritoneal adherence, and mortality in this particular subgroup consequently was significant (20%).

Discussion

Previous studies have documented disparity concerning symptomatology, incidence of metastases, and survival in patients with midgut carcinoids [1, 3, 5–7, 9, 16, 19, 32–39]. The disparity obviously relates to variable patient composition in different

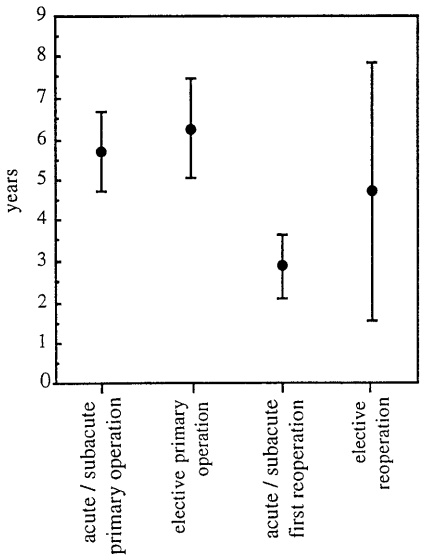

Fig. 4. Mean duration (± 90% confidence interval, years) of complete and partial symptom responses after primary operations (54 acute/subacute and 40 elective procedures), and first reoperations (21 acute/subacute and 10 elective procedures).

series, which would be expected to greatly influence symptoms and prognosis in a typical low-grade malignancy such as the carcinoid [40]. The present series apparently represents biased selection, as most of the individuals were recruited by referral for already disseminated malignancy. Despite the advanced disease, survival has been surprisingly favorable among our patients, which may reflect the benefits of the therapy, which included interferon, somatostatin analogs, and liver artery embolization; however, controlled studies are still lacking in this context [6–8, 11, 41–46]. It also cannot be excluded that it relates to increasing experience from combined medical and surgical treatment strategies, which has implied great alertness in dealing with abdominal symptoms and complications. Such complications nevertheless comprised a significant cause of tumor-related death in the current material. In our experience these symptoms tend to become of increasing concern with enhanced longevity of the patients and when features of the carcinoid syndrome are controlled medically [5, 7–9, 17–22, 47, 48].

Corroborating the difficulty of clinical recognition of midgut carcinoids, as many as 40% of our patients experienced considerable periods (mean 7.5 years) of prodromal symptoms before the disease was diagnosed [6, 19, 49–52]. Half of them had discrete flushing, diarrhea, palpitations, or intolerance for specific nourishment or alcohol before more evident features of the carcinoid tumor developed. In these patients the disease was often diagnosed by needle biopsy of radiologically recognized liver metastases. Another group of patients mainly endured increasing abdominal complaints and subsequently were diagnosed by laparotomy done to relieve partial or complete intestinal obstruction. Under these circumstances all small bowel tumors should be suspected to represent a midgut carcinoid, particularly in the presence of mesenteric metastases surrounded by fibrosis [1, 5, 7, 18–22].

Most of the patients entering the study without signs of tumor spread failed to display the development of metastases. However,

Table 7. Complications to acute/subacute and elective abdominal operations in patients with midgut carcinoid tumors.

	Percent	
Postoperative complications	Acute/subacute (n = 75)	Elective (n = 50)
Prolonged postoperative paralysis	8	3
Short bowel syndrome	6	0
Blind loop syndrome	7	4
Infection (abdominal/pneumonia)	3/5	3/0

corroborating the great tenacity of midgut carcinoids, more than 80% of patients subjected to grossly radical tumor excisions experienced recurrent disease during prolonged follow-up [5]. Altogether 93% of the patients had metastases when first seen in our hospital, which were located in regional lymph glands and the liver in 80% and 62%, respectively. A principal purpose of the present study consequently was to elucidate risks for disease progression with respect to tumor involvement of novel sites. It should be emphasized, however, that it generally was accompanied by progression of already established metastases, especially in the liver, and thus constitutes only one of the variables indicating advancement of the disease. Altogether 45 patients developed metastases to initially uninvolved sites during the study period. Patients with mesenteric involvement alone frequently endured liver metastases, but they rarely spread to extraabdominal sites (probability 0.05). Moreover, extraabdominal metastases developed occasionally in patients with mesenteric and liver metastases (probability 0.22), whereas they were exceptionally frequent (probability 0.60) in patients with discernible liver metastases alone. Because spread to distant sites is an unfavorable prognostic sign with midgut carcinoids [5], this possibility may be important to consider prior to operation in the less symptomatic patients. The development of metastases to apparently uninvolved sites generally required substantial periods of time, on average 4 to 12 years in subgroups of patients exhibiting different extent of tumor spread.

A carcinoid syndrome was initially present in 58 patients and developed in another 25 cases during the study period. Rare patients with the syndrome displayed no hepatic involvement but demonstrated substantial mesenteric/retroperitoneal spread. In contrast, a significant number of patients with even voluminous liver metastases did not exhibit the syndrome, which is consistent with the variable biologic properties of these tumors [53]. Patients with the carcinoid syndrome commonly had palpable liver metastases but less frequently prominent abdominal symptoms. In contrast, patients without a typical carcinoid syndrome often suffered from more or less acute abdominal symptoms. Indeed those with marked mesenteric fibrosis detected at surgery formed a specific subgroup in this context, as 90% of them experienced acute abdominal pain generally requiring urgent clinical attendance, and many exhibited severe weight loss.

The second principal purpose of the study was to evaluate whether patients with midgut carcinoid tumors could, even at advanced tumor stages, benefit symptomatically from laparotomy. It must be emphasized in this context that retrospective evaluation of symptom responses is difficult, and that the obtained figures should be regarded as estimates. Among 125 primary or first reoperative procedures being performed because of abdominal

symptoms, a history of postoperative symptom improvement was substantial, and altogether 82% of the patients demonstrated complete or partial symptom alleviation, which persisted for a mean 5.3 years. However, there seemed to be different expectations in this respect, as the outcome was most auspicious in patients with acute abdominal pain, weight loss, and subileus/ileus subjected to acute or subacute interventions. Patients with mesenteric fibrosis and ischemia were particularly relieved by surgery, and most of them (78%) remained free of preoperative symptoms during a mean 4.2 years of follow-up. Reoperations occasionally resulted in less complete alleviation of symptoms of intermittent bowel obstruction, and because of the presence of harsh fibrotic adhesions these operations were sometimes difficult. Diarrhea, nausea, and abdominal distension were less consistently or completely alleviated, emphasizing that particularly the diarrhea may have multifold causes in patients with midgut carcinoids [5]. The average symptom-free periods after operation were longer after acute or elective primary operations than after the reoperative procedures.

Our experience substantiates that patients with midgut carcinoids are at high risk to develop symptoms and complications related to the mesentericointestinal involvement of the disease. Despite suggestions that abdominal pain may occur as a consequence of the carcinoid syndrome [47, 53–56], we consider even moderate or episodic abdominal pain as indications mainly for threatening abdominal complications. It appears especially true if the pain is combined with signs of malnutrition, as such features seem to depend on the tumor mass itself only in end-stage carcinoid patients. In contrast, feeding-related or crampy abdominal pain, cessation of diarrhea, and weight loss often indicate intestinal obstruction or intestinal ischemia and call for operation. Also because obstruction and ischemia cannot be distinguished preoperatively, the patients should be liberally submitted to surgery with the aim of removing any compromised intestinal segment and if possible the mesenteric tumor [7, 18–22]. Consistent with the current demonstration of slowly progressing metastases and subjective benefits from abdominal surgery, the findings indirectly support removal of the mesentericointestinal tumor by elective operation even in "asymptomatic" patients with midgut carcinoid tumors [8].

Résumé

On a analysé les dossiers de 121 patients consécutifs ayant une tumeur carcinoïde de l'intestin moyen ayant eu un contrôle clinique régulier, parmi lesquels 158 ont eu une laparotomie pour des symptômes abdominaux. La suivie allait de 1 à 11 (moyenne: 5.2) ans. Des métastases ont été détectées chez 93% de ces patients au moment de l'inclusion de l'étude et se sont développées dans une site non affectée avec une probabilité globale de 0.38. La probabilité de développer des métastases mésentériques ou hépatiques chez les patients sans extension tumorale initiale était de 0.25 (délai moyen: 12 ans), alors que ceux avec déjà des métastases mésentériques ont développé des métastases hépatiques avec une probabilité de 0.56 (délai moyen: 6.1 ans). Les patients ayant déjà des métastases mésentériques et/ou hépatiques avaient une probabilité de développer des métastases extra-abdominales de 0.22 (délai moyen: 4.3 ans), alors que cette extension était particulièrement fréquente chez le patient ayant des métastases hépatiques seules au moment de l'inclusion de l'étude (probabilité de 0.60). Les patients sans syndrome carcinoïdien (52%) se plaignaient essentiellement de douleurs abdominales plus ou moins épisodiques, de nausées et de diarrhée. On a trouvé une fibrose mésentérique intense lors de l'exploration abdominale chirurgicale (n = 59) chez les patients se plaignant de douleurs et de perte de poids, et souvent nécessitant une intervention médicale en raison d'ischémie ou d'occlusion intestinale. Une amélioration des symptômes complète ou partielle a été obtenue chez 82% des patients après la chirurgie, et cette amélioration a été plus particulièrement évidente après un acte urgent, initial (n = 54). L'amélioration obtenue après chirurgie a duré une moyenne de 5.3 ans et avait une tendance d'être plus longue après la chirurgie élective (n = 50) plutôt qu'urgente. Ces données sont en faveur de la laparotomie dans un groupe déterminé de patients ayant une tumeur carcinoïde de l'intestin moyen. Etant donnée l'évolution généralement lente des métastases, les indications à la laparotomie doivent être larges chez le patient symtomatique et peut-être aussi chez certains patients asymptomatiques.

Resumen

Un total de 121 pacientes consecutivos con tumores carcinoides recibieron controles clínicos regulares y fueron sometidos a 158 laparotomías por síntomas abdominales con seguimiento de 1 a 11 (media, 5.2) años. Se presentaron metástasis en 93% de los pacientes en el momento de la inclusión en el estudio y se desarrollaron en ubicaciones inicialmente libres con una probabilidad global de 0.38. Las pacientes libres de extensión inicial del tumor, desarrollaron metástasis mesentéricas o hepáticas con una probabilidad de 0.25 (intervalo medio, 12 años), en tanto que aquellos con metástasis mesentéricas exhibieron una probabilidad de 0.56 de desarrollar metástasis hepáticas (intervalo medio, 61 años). La extensión a ubicaciones extra-abdominales en pacientes con metástasis mesentéricas y hepáticas exhibieron una probabilidad de 0.22 (intervalo medio, 4.3 años), en tanto que tal extensión fue especialmente frecuente (probabilidad 0.60) en pacientes con sólo metástasis hepáticas en el momento de la inclusión al estudio. Los pacientes libres de síndrome carcinoide (52%) exhibieron principalmente dolor abdominal más o menos episódico, náusea y diarrea. Cuando durante la cirugía se detectó fibrosis mesentérica marcada (n3D59), ésta generalmente se vio acompañada de síntomas de dolor abdominal y pérdida de peso y con frecuencia requirieron atención quirúrgica de urgencia por obstrucción o isquemia intestinales. Se logró el alivio completo o parcial de los síntomas en 82% de las operaciones y en general esto fue más favorable después de procedimientos primarios agudos/subagudos (n3D54). La mejoría total o parcial de los síntomas obtenida con la cirugía tuvo una duración media de 5.3 años, y demostró tendencia a ser más prolongada luego de operaciones electivas (n3D50) que de operaciones agudas. Los hallazgos corroboran resultados halagadores de la laparotomía en una cohorte de pacientes con tumores carcinoides del intestino medio. Puesto que los pacientes también exhibieron una más bien lenta progresión de las metástasis, se justifican indicaciones liberales para laparotomía en pacientes sintomáticos, y posiblemente también en los asintomáticos que porten tumores carcinoides del intestino medio.

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Invited Commentary

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Many surgeons faced with a patient with midgut carcinoid presenting with metastatic disease or with extensive mesenteric involvement would take a nihilistic approach and only reluctantly offer surgery as a form of therapy. They wait until the development of severe symptoms of obstruction or ischemia before contemplating laparotomy. This article by Makridis and colleagues demonstrates that the outcome of early, aggressive surgery in such patients, even those with extensive mesenteric spread, is often excellent, and that laparotomy should always be considered early in the management of such patients.

The authors present an impressive series of 121 consecutive patients undergoing laparotomy for midgut carcinoid. This malignant tumor is rare, yet they were able to achieve detailed follow-up on all their patients for 1 to 11 years (mean 5.2 years). It was interesting to note that most patients (93%) already had metastatic disease at the time of presentation, with 86% having mesenteric spread and 62% having liver metastases. Surgery was performed to remove the primary tumor, to alleviate the symptoms of mesenteric involvement, or as palliation of the carcinoid syndrome by resection of large, solitary liver metastases. The surgery performed was often extensive with dissection of proximal mesenteric vessels aiming to remove the bulk of mesenteric disease.

The results of their series are impressive. Although metastases were common at the time of presentation, the time course of the disease is often slow. For those without metastases at entry, the average time to develop metastases was 12 years, whereas for those who had metastases at entry the average time to develop further metastases at a different site following laparotomy was 6.1 years for those with mesenteric spread and 4.3 years for those with liver spread. In all, 82% of the laparotomies resulted in partial or complete improvement in symptoms that lasted for a mean 5.3 years. In fact, 78% of patients with mesenteric fibrosis became symptom-free after surgery.

The authors note that, although other workers state that abdominal pain may be part of the classic carcinoid syndrome, in their experience abdominal pain is generally related to obstructive or ischemic involvement of the gut by tumor. They advocate that in any patient with midgut carcinoid abdominal pain, even of moderate degree or episodic in nature, should be considered an indication for laparotomy.