

Surgery for Melanoma Metastatic to the Gastrointestinal Tract

Shefali Agrawal, MD, Tzy-Jyun Yao, PhD, and Daniel G. Coit, MD, FACS

Background: Gastrointestinal (GI) metastasis from melanoma has a dismal prognosis with few long-term survivors. We evaluated the role of operative intervention for melanoma metastases to the GI tract and attempted to identify prognostic factors to improve selection of patients for surgery.

Methods: Between 1977 and 1997, 68 of the 7965 patients with melanoma admitted to Memorial Sloan-Kettering Cancer Center underwent surgical exploration for melanoma metastatic to the GI tract. Characteristics of the primary tumor, regional lymph nodes, and metastatic pattern were reviewed. Data concerning the presenting signs and symptoms, laboratory values, operative findings, extent of surgical resection, recurrence pattern, and survival were analyzed.

Results: The most common presenting clinical features included anemia ($n = 41$; 60%) or abdominal pain ($n = 40$; 59%). The most frequently involved portion of the GI tract was the small bowel ($n = 62$; 91%), and the most common operative procedure was small bowel resection ($n = 54$; 79%). Postoperative mortality and morbidity were 2.9% ($n = 2$) and 8.8% ($n = 6$), respectively. Presenting symptoms were relieved in 90% of patients ($n = 61$). Median survival for all 68 patients following operative intervention was 8.2 months, with 18% survival at 5 years. By multivariate analysis, complete resection rendering the patient free of all identifiable disease ($n = 19$, median survival 14.9 months, 38% survival at 5 years) and a low preoperative serum lactate dehydrogenase (LDH) ($n = 28$, median survival 13.6 months, 35% survival at 5 years) were identified as independent favorable prognostic factors for survival.

Conclusions: Operative intervention for melanoma metastatic to the GI tract is recommended for palliative reasons and can be performed with low morbidity and mortality. It is associated with prolonged survival in patients rendered free of all identifiable disease following surgical resection and in those with a low preoperative serum LDH.

Key Words: Gastrointestinal tract—Melanoma—Surgery.

Although 44% to 52% of patients who die of disseminated melanoma have involvement of the gastrointestinal (GI) tract detected at autopsy,^{1,2} a clinical antemortem diagnosis is made in less than 5% of these patients.³ GI metastasis from melanoma has a dismal prognosis, with a median survival of 6–10 months after surgical resection.^{3–7} However, there are studies demonstrating good palliation of symptoms with acceptable morbidity and mortality following operation for melanoma metastatic to the GI tract. The following factors have been

identified as associated with improved survival: GI tract as the initial site of distant metastases⁸; complete resection of GI tract metastases^{7–9}; absence of small bowel involvement⁵; metastases at a single site in the GI tract⁴; absence of other visceral metastatic disease^{6,10}; adjuvant treatment⁶; and a disease-free interval of longer than 2 years between diagnosis of the primary melanoma and development of GI metastases.⁵

This retrospective study evaluates the role of surgical intervention in patients with melanoma metastatic to the GI tract and attempts to identify prognostic factors that may improve selection of patients for surgical resection.

PATIENTS AND METHODS

A review of the melanoma database revealed 7965 patients with melanoma admitted to Memorial Sloan-Kettering Cancer Center between 1977 and 1997. From this database we identified 68 patients who underwent

Received June 2, 1998; accepted January 6, 1999.
From the Department of Surgery (SA), Columbia University College of Physicians and Surgeons, New York, New York, and the Departments of Biostatistics (T-JY) and Surgery (DGC), Memorial Sloan-Kettering Cancer Center, New York, New York.

Presented at the 52nd Annual Meeting of the Society of Surgical Oncology, Orlando, Florida, March 4-7, 1999.

Address correspondence to: Daniel G. Coit, MD, Dept. of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021; Fax: 212-717-3400.

surgical exploration for melanoma metastatic to the GI tract. The characteristics of the primary tumor, regional lymph nodes, and the metastatic pattern before the diagnosis of GI tract metastases were reviewed. The presenting signs and symptoms, laboratory data, radiological and endoscopic studies, operative findings and procedure, subsequent follow-up, and recurrence patterns were analyzed. The patients were subdivided into two groups. Group 1 consisted of patients who underwent a curative resection rendering them free of identifiable disease at all sites; Group 2 was made up of patients who underwent laparotomy with residual disease in the GI tract or at other sites.

Statistical Analysis

Survival was defined as the time interval between operation for melanoma metastatic to the GI tract and death of the patient or the last follow-up. Age, sex, anatomical location of the primary tumor, stage at diagnosis, diagnosis of stage III prior to development of distant metastases, disease-free interval (DFI) prior to diagnosis of stage IV disease, single or multiple initial distant metastatic sites, GI tract as the only initial site of distant metastases, preoperative levels of serum lactate dehydrogenase (LDH), total protein and albumin, single metastasis to the GI tract, presence of residual disease after operation for GI metastases, and postoperative treatment were assessed as prognostic factors for survival. Univariate analysis was performed using the Kaplan-Meier method,¹¹ and the log-rank test was used to compare differences in survival distributions observed in subsets of patients.¹² The variables with $P \leq .1$ from the univariate analysis were chosen for multivariate analysis. Multivariate analysis was performed using the Cox proportional hazard regression model. All potential prognostic factors except serum LDH and total protein were analyzed as categorical variables in this model. Because this is an exploratory study in which prognostic factors were examined to generate a hypothesis for further studies, the probability of rejecting a true hypothesis (type I error) was not adjusted for as suggested by Hochberg and Hamhane.¹³

RESULTS

Demographics

Of the 68 patients who underwent surgical exploration for melanoma metastatic to the GI tract, 44 were men and 24 were women. The median age of the patients was 54 years (range, 26–79 years).

The site of the primary melanoma was the trunk in 23 patients (34%), the extremities in 22 patients (32%), the

head and neck in 6 patients (9%), the anal canal in 1 patient (2%), and occult in 16 patients (23%). The Clark level of the primary melanoma (excluding the 16 patients with occult primary tumors) was level II in 2 patients, level III in 8 patients, level IV in 11 patients, level V in 4 patients, and unknown in 27 patients. The Breslow thickness of the primary melanoma (excluding the 16 patients with occult primary tumors) was 0.76–1.50 mm in 8 patients, 1.51–4.00 mm in 17 patients, more than 4.00 mm in 6 patients, and unknown in 21 patients. The median Breslow thickness was 3.1 mm (range, 0.9–21.0 mm). Definitive surgical treatment of the primary lesion was performed in all patients.

Forty-five patients (66%) underwent regional lymph node dissection prior to diagnosis of GI metastases. Of the 26 patients who underwent therapeutic regional lymph node dissections, 25 patients had positive nodes, and of the 19 patients who underwent elective regional node dissections, 4 patients had positive nodes. Twenty-one patients progressed from stage I/II to stage IV, 37 patients were diagnosed with stage III prior to stage IV, and 10 patients presented with stage IV disease. The median time from the initial histologic diagnosis of melanoma to the development of GI tract metastases was 47.6 months (range, 0–383 months). The median time varied according to the stage of disease at the time of diagnosis: 73 months for Stage I and II ($n = 47$); 26 months for Stage III ($n = 11$); and 0 months (range, 0–40 months) for Stage IV ($n = 10$). Forty-four patients (65%) presented with a single initial distant metastatic site and 24 patients (35%) with two or more distant metastatic sites. GI tract involvement occurred as the first and only site of systemic disease in 24 patients (35%) and was the first site synchronous with other sites in 19 patients (28%). There was antecedent systemic disease prior to GI metastases in 25 patients (37%). In these 25 patients, systemic disease prior to GI metastases occurred in the lung in 14 patients; in the skin, subcutaneous tissue, or lymph nodes in 8 patients; in the liver in 2 patients; in the retroperitoneum in 2 patients; and in one patient each in the kidney, adrenal gland, spleen, gallbladder, and mediastinal lymph nodes.

Clinical Features

The common presenting signs and symptoms included anemia in 41 patients (60%), abdominal pain in 40 patients (59%), occult or apparent GI bleeding in 30 patients (44%), abdominal mass in 8 patients (12%) and weight loss greater than 5 kg in 6 patients (9%). The duration of symptoms prior to the diagnosis of GI metastases ranged from 0 to 24 months (median, 1 month). Preoperative diagnostic investigations included plain ra-

diographs, barium contrast studies, computed tomography, GI endoscopy, and angiography. Of the 61 patients who underwent computed tomography, contrast studies, or both, the diagnosis of GI metastases was confirmed in 53 patients (87%). Upper or lower GI endoscopy or enteroscopy was performed in 28 patients and was diagnostic in 10 patients (36%). The indication for operation was emergent in 19 patients (28%): for intestinal obstruction in 15 patients, GI perforation in 3 patients, and acute GI hemorrhage in 1 patient.

Operative Procedures

Thirty-one patients (46%) had metastases to a single site, and 37 patients (54%) had multiple site involvement of the GI tract. Small bowel was the most commonly involved portion of the GI tract, as observed in 62 patients (91%) with contiguous involvement of the mesentery in 15 (24%) and mesenteric lymph nodes in 17 (27%) of these patients. The jejunum was involved in 41 (66%), the ileum in 30 (49%), and the duodenum in 4 (6%) of patients. Other involved sites included the colon 14 (21%), the stomach 2 (3%), and the rectum 1 (1.5%).

Small bowel resection, the most common operative procedure, was performed in 54 patients (79%), followed by segmental colectomy in 11 patients (16%). Other procedures performed included pancreaticoduodenectomy ($n = 1$), wedge gastrectomy ($n = 2$), anterior resection of the rectum ($n = 1$), and enteric bypass ($n = 7$). Small bowel resection alone rendered 34 of the 54 patients (63%) in whom it was performed free of disease in the GI tract. Nineteen patients (28%) with complete resection of the GI metastases were rendered free of identifiable disease at all sites (Group 1); 26 patients (38%) underwent complete resection of the GI disease but had residual disease at other sites; 17 patients (25%) underwent partial resection of the GI disease; and 6 patients (9%) underwent laparotomy with no resection of the GI disease (Group 2). The sites of residual disease in

49 patients following operation for melanoma metastatic to the GI tract are shown in Table 1.

Postoperative complications in 6 patients (8.8%) included pulmonary embolism in 3 patients and hepatic failure, enterocutaneous fistula, and subphrenic abscess in 1 patient each. The two postoperative deaths (2.9%) resulted from pulmonary embolism and hepatic failure secondary to residual liver metastases on postoperative days 30 and 42, respectively. The median duration of hospital stay was 12.5 days (range, 5-42 days).

Following operation, presenting symptoms were relieved in 61 patients (90%). Of the remaining 7 patients (10%), 3 did not undergo any surgical resection or palliative procedure, and 4 had a continued fall in hematocrit. Forty-four patients (65%) received postoperative treatment in the form of chemotherapy ($n = 27$), immunotherapy ($n = 15$), and radiotherapy ($n = 3$), either singly or in combination.

Survival Distributions

Follow-up information was available for all patients. Median follow-up time for all 68 patients following operation for GI metastases was 7.6 months: 6.9 months for 50 patients dead of disease; 4.7 months for 6 patients alive with disease; and 54.6 months for 12 patients alive and free of disease at the time of analysis.

The median survival for all patients following operation for GI metastases was estimated to be 8.2 months (95% confidence interval = 6.9–11.4 months). The 1-, 2-, and 5-year survival rates for all patients operated for GI tract metastases were 35%, 23%, and 18%, respectively (Fig. 1). Univariate analysis demonstrated that the absence of residual disease at any site following surgery for GI tract metastases (especially the liver, lung, or brain), the GI tract as the only initial site of distant metastases, a single initial site of distant metastases, lower preoperative serum levels of LDH, and higher protein were strongly or moderately associated with better survival ($P \leq .1$) (Table 2). Four patients had residual disease in the brain; they died at 0.3, 1.0, 1.5, and 3.8 months following surgery for GI metastases. Because of the small number of patients, residual disease in the brain was not included in the multivariate analysis to avoid highly imprecise estimates.

The results of multivariate analysis indicated that most of the significant factors were related to each other. Among all factors, preoperative serum LDH ($P < .01$) and residual disease ($P = .03$) were independently associated with survival. Median survival for 19 patients with complete resection of GI tract metastases and no other evidence of disease (Group 1) was 14.9 months (range, 4.6–128.8 months), and for 49 patients with residual

TABLE 1. Sites of residual disease following operation for melanoma metastatic to the GI tract

Site	No. patients (%)
No residual disease	19 (28)
Skin, subcutaneous tissue, lymph nodes	15 (31)
GI tract	23 (47)
Extra-GI abdominal	26 (53)
Liver	13 (27)
Lung	16 (33)
Brain	4 (8)
Bone	4 (8)
Mediastinal lymph nodes	2 (4)

GI, gastrointestinal.

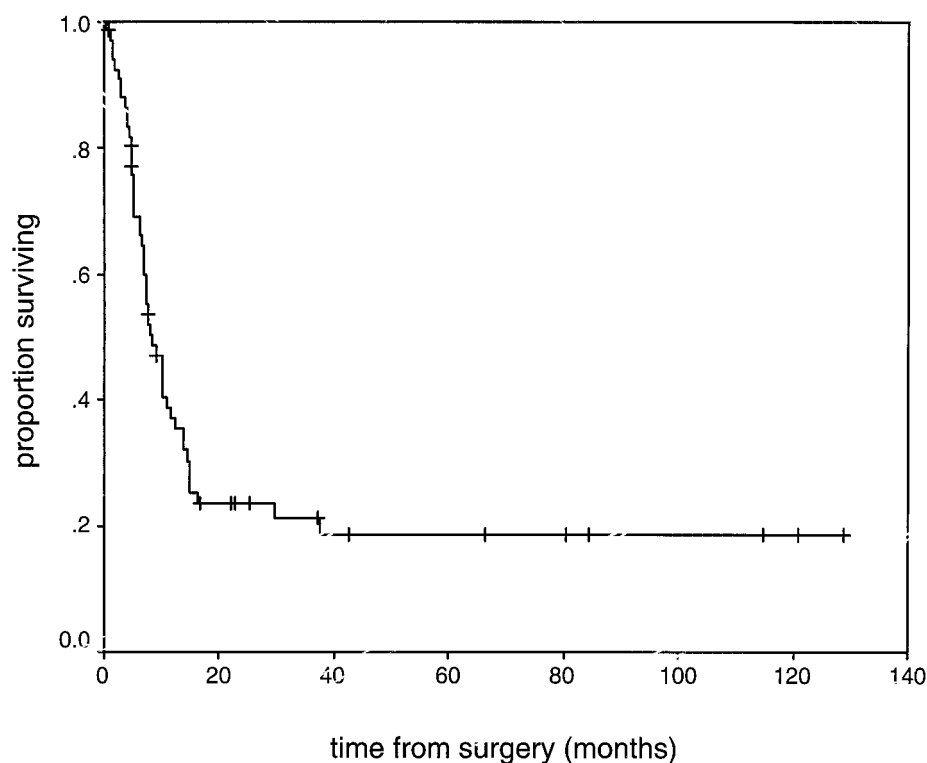


FIG. 1. Kaplan-Meier survival curve for 68 patients undergoing surgery for melanoma metastatic to the gastrointestinal tract.

disease in the GI tract or elsewhere (Group 2) it was 6.9 months (range, 0.3–114.7 months). The 1-, 2-, and 5-year survival rates for Group 1 were 67%, 45%, and 38%, respectively, and the 1-year survival rate for Group 2 was 22% (Fig. 2). Median survival for 28 patients with preoperative serum LDH levels <200 u/l was 13.6 months, compared to 6.5 months for 35 patients with LDH of 200 u/l or higher (LDH, serum proteins, and albumin levels were not known in 5 patients; Figure 3). The prognostic significance of LDH level in patients with/without residual disease is shown in Figure 4. The subset of patients with the most favorable prognosis were those rendered NED by surgery and with a preoperative LDH below 200 u/l.

Survival after operation for melanoma metastatic to the GI tract was not influenced by patient age or sex, anatomical location of the primary tumor, stage of the disease at diagnosis, diagnosis of stage III prior to development of distant metastases, disease-free interval (DFI) prior to stage IV, preoperative level of serum albumin, single metastases to the GI tract, or postoperative treatment. Median survival for 24 patients (35%) who received adjuvant immunotherapy as part of their treatment for systemic disease either before the development of GI metastases or following surgery for GI metastases was 7.3 months (range, 0.6–121.1 months); for

the remaining 44 patients (65%) who did not receive immunotherapy for systemic disease, it was 7.8 months (range, 0.3–128.8 months, $P = \text{NS}$). The number of patients in this series is too small to make any definitive comment about the impact of adjuvant chemotherapy or immunotherapy on the outcome.

Long-term Survival

Six patients survived for more than 5 years and are alive without evidence of disease at 67, 81, 121, and 129 months (Group 1) and 85 and 115 months (Group 2) after operation for melanoma metastatic to the GI tract. The 2 patients from Group 2 were rendered NED by nonsurgical treatment—chemotherapy and immunotherapy, respectively. The identifiable factors predictive of long-term survival in these 6 patients, 5 of whom had residual disease or recurrence, were that all of them were rendered free of disease by either surgical or nonsurgical means and their preoperative levels of serum LDH were 208 u/l or less.

Recurrence Patterns

Of the 19 patients from Group 1, 18 (95%) had a recurrence after a median of 5.5 months (range, 2–32 months), and 1 is alive without evidence of recurrence 129 months after resection of the GI metastases. Of the

TABLE 2. Univariate and multivariate survival analysis of patients who underwent operative intervention for melanoma metastatic to the GI tract

Factor		No. patients	Median survival (y)	Univariate analysis	Multivariate analysis
				P value	
Serum lactate dehydrogenase (u/l)	≥200	35	6.5	<.01	<.01
	<200	28	13.6		
Residual disease	No	19	14.9	<.01	.03
	Yes	49	6.9		
GI tract	No	26	7.3	.89	
	Yes	23	6.3		
Liver and/or lung	No	24	9.0	.03	
	Yes	25	5.0		
Brain	No	45	7.3	<.01	
	Yes	4	1.3		
Initial metastatic site	GI tract only	24	13.6	<.01	
	Others	44	6.5		
Number of initial metastatic sites	1	44	10.0	.06	
	≥2	24	6.5		
Serum proteins (g/dl)	≥6.5	32	11.4	.10	
	<6.5	31	7.3		
Serum albumin (g/dl)	≥4.0	22	13.6	.19	
	<4.0	41	6.9		
Site of primary melanoma	Trunk	23	7.2	.30	
	Extremity	22	10.9		
	Head/neck	6	8.7		
	Occult	16	7.6		
Disease-free interval prior to stage IV (mo)	≥24	36	10.0	.31	
	<24	32	7.4		
Metastases to GI tract	Single	31	10.0	.38	
	Multiple	37	7.2		
Sex	Male	44	10.0	.46	
	Female	24	7.3		
Diagnosis of stage III prior to stage IV	I/II	21	10.0	.56	
	III	37	7.6		
	IV	10	6.9		
Stage at diagnosis	I/II	47	9.0	.72	
	III	11	7.6		
	IV	10	6.9		
Postoperative treatment	No	24	10.0	.78	
	Yes	44	7.6		
Age	≥60	26	9.0	.94	
	<60	42	7.6		

GI, gastrointestinal.

16 patients who had a visceral recurrence, 8 recurred in the GI tract. Seven of these 8 patients were reoperated for their GI disease, but only 2 were rendered free of disease and remain alive without evidence of disease 57 and 113 months after their second GI resection. The 2 patients from Group 1 who had a nonvisceral recurrence died of progression of disease 15 and 38 months after resection of their GI metastases.

Thirteen patients underwent a second operation for melanoma metastatic to the GI tract (including the 7 patients discussed above) for curative and palliative reasons. Five patients were rendered NED and remain alive without evidence of disease at 4, 51, 57, 81, and 113 months after their second operation. The remaining 8

patients with residual disease following their second GI operation died of disease after a median of 3 months (range, 1-10 months).

DISCUSSION

Most authors recommend surgical intervention in patients with GI tract metastases from melanoma, despite a reported median survival of only 6–10 months, because it provides effective palliation with minimal morbidity and mortality (Table 3) and may be associated with prolonged survival in certain subsets of patients.^{3–10} Survival data from studies evaluating operative intervention

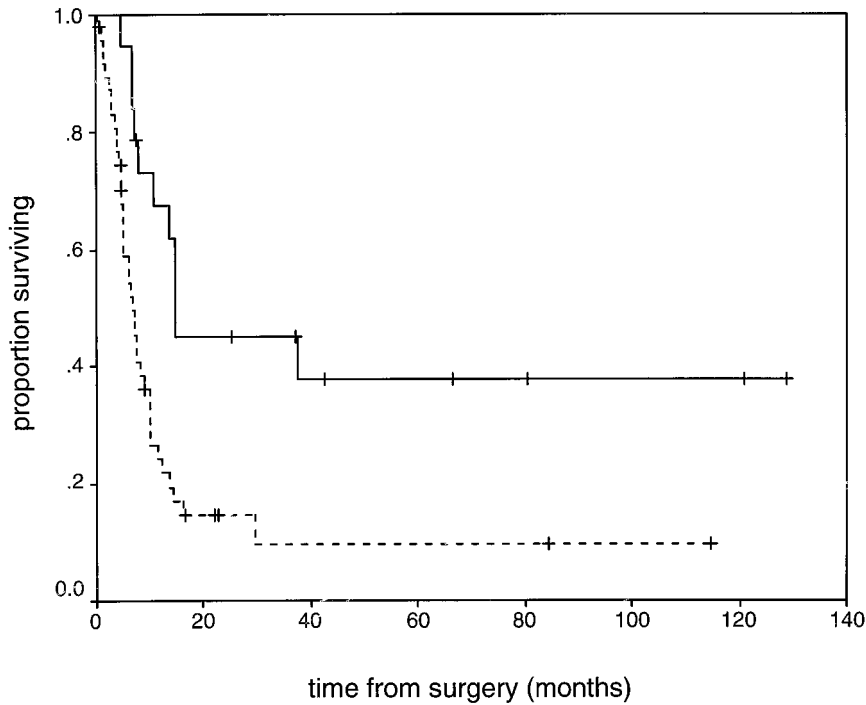


FIG. 2. Kaplan-Meier survival curve for 19 patients rendered free of disease (Group 1) and 49 patients with residual disease (Group 2). $P < .01$. Solid line, residual disease absent; broken line, residual disease present.

for melanoma metastatic to the GI tract are difficult to compare because of a variety of definitions of a curative resection, the subset associated with the most favorable prognosis. Some authors have defined curative resection

as complete resection of GI disease rendering the patient free of identifiable disease at all sites^{7,9} and others as removal of all disease from the abdomen with or without residual disease at other sites.⁸

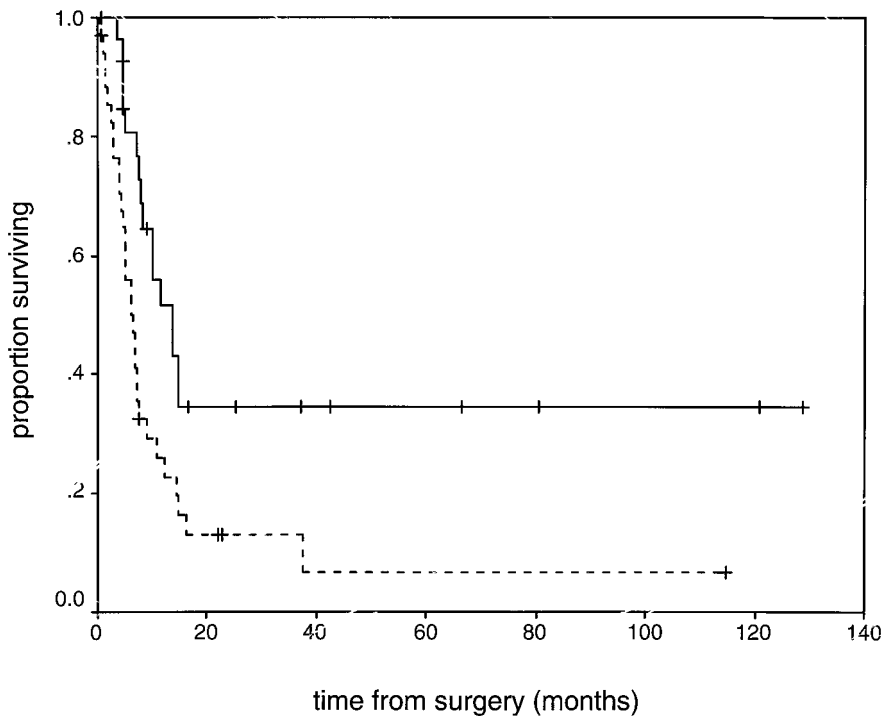


FIG. 3. Kaplan-Meier survival curve for 28 patients with LDH <200 u/L and 35 patients with LDH ≥ 200 u/L. $P < .01$. Solid line, LDH <200 u/L; broken line, LDH ≥ 200 u/L.

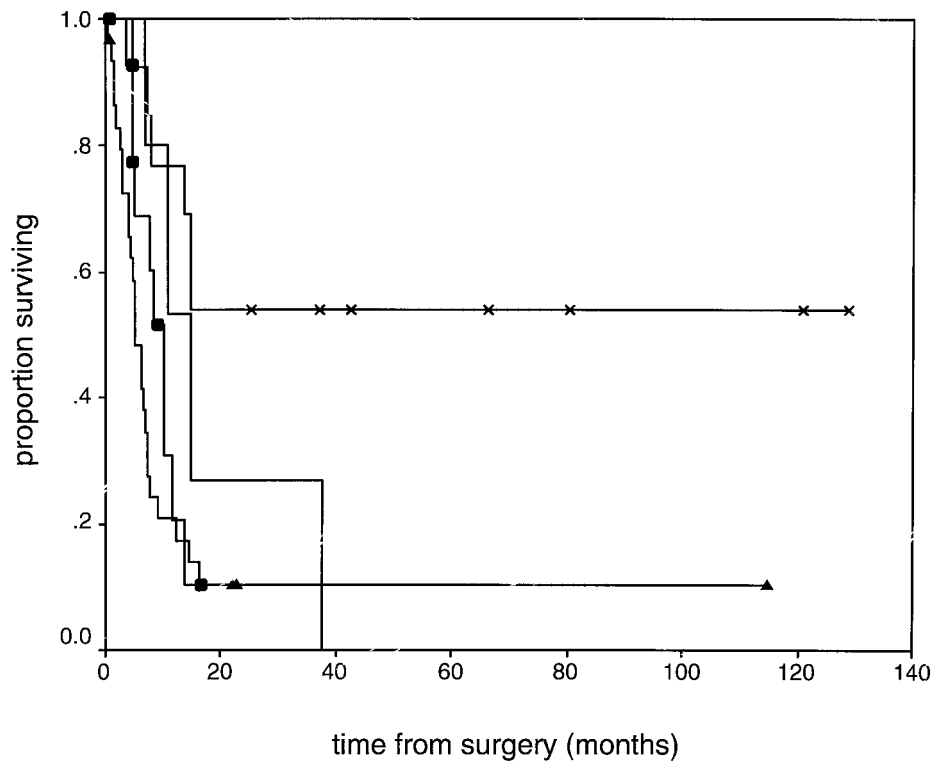


FIG. 4. Kaplan-Meier survival curve according to preoperative serum lactate dehydrogenase levels in patients rendered free of disease and patients with residual disease. X, residual disease absent, LDH < 200; solid line, residual disease absent, LDH \geq 200; ■, residual disease present, LDH < 200; ▲, residual disease present, LDH \geq 200.

Most patients in this study presented with abdominal pain related or unrelated to intestinal obstruction characteristically due to intermittent partial small bowel obstruction secondary to intussusception and anemia secondary to occult or apparent GI bleeding.^{7,8} The delay in diagnosis between the onset of symptoms and the diagnosis of GI metastases may be minimized by a thorough radiological and endoscopic investigation of melanoma patients with abdominal pain, anemia, or both. Luminal contrast studies or computed tomography (or both) yield a diagnosis in most patients, because these studies are complementary. Computed tomography detects intussusception, as well as mesenteric or omental implants, and luminal radiology—in particular, enteroclysis—helps identify small intraluminal masses that may be missed on

computed tomography.¹⁴ Upper or lower GI endoscopy was most helpful in excluding concurrent gastroduodenal or colonic metastases in patients with known small bowel metastases.

Nearly one-third of the patients presented with emergent complications of the GI tract, including intestinal obstruction, GI perforation, or acute hemorrhage requiring immediate surgical intervention.⁴ Jejunum and ileum, portions of the bowel most easily resected, also were the most frequently involved segments in the GI tract. Resection is recommended for reasons of palliation even though small bowel involvement has been reported to be associated with a shorter survival.^{5,7,8} Because 62 of the 68 patients in this series who underwent operation for melanoma metastatic to the GI tract had involvement of

TABLE 3. Survival and palliation after resection of melanoma metastases to the GI tract

Author	Year	No. patients	Palliation (%)	Morbidity (%)	Mortality (%)	Survival (%)			
						Median (mo)	1 y	2 y	5 y
Reintgen et al. ³	1984	38	90	15	0	8.5	—	15	15
Khadra et al. ⁶	1990	56	79	14	4	9.5	27	9	2
Ihde and Coit ⁴	1991	32	94	—	3	6.2	27	19	0
Caputy et al. ⁵	1991	41	81	32	5	9.5	44	—	9
Ricaniadis et al. ⁷	1995	48	73	29	11	5.7	25	13	7
Ollila et al. ⁸	1996	69	97	2	2	23	—	—	28
Present series	1997	68	90	9	3	8.2	35	23	18

the small bowel, it was not possible to evaluate small bowel involvement as a prognostic factor. Palliation of the preoperative symptoms in 90% of patients was similar to the 73% to 97% reported in other series.^{3-10,15} Extended palliation was observed in six patients who are alive without evidence of disease more than 5 years after resection of GI metastases, justifying extensive resection such as the pancreaticoduodenectomy performed in a patient alive for 121 months following operation for melanoma metastatic to the GI tract.⁷

There was no difference in survival in patients whose interval from diagnosis of the primary to the onset of GI metastasis was greater than 2 years versus those in whom it was less than 2 years, patients with diagnosis of stage III prior to stage IV versus those without a preceding stage III, patients with single versus multiple metastases to the GI tract, and patients who received postoperative treatment versus those who received no postoperative treatment. Although the DFI prior to distant metastasis to any site has been reported to be independently predictive of survival in melanoma patients,^{16,17} reviews of patients undergoing operative intervention for melanoma metastatic to the GI tract have been unable to confirm the importance of this variable.^{4,5,8} This suggests that once GI metastasis has occurred, survival may not be influenced by the patient's previous disease course. A single metastatic lesion has been reported to be a significant determinant of survival benefit in the surgical treatment of distant metastatic melanoma,¹⁷ with an earlier report on 32 patients from this institution noting a trend toward improved survival in the subset of patients undergoing surgery for a single GI metastasis which did not achieve statistical significance.⁴ However, in the present series, single or multiple metastases to the GI tract did not have an effect on patient outcome ($P = .38$). Median survival for 14 patients from Group 1 with isolated GI metastasis was 14.3 months and was 37.5 months for 5 patients with multiple GI metastases.

A single initial distant metastatic site or GI tract as a single initial metastatic site was associated with improved survival of patients undergoing surgery for melanoma metastases to the GI tract on univariate analysis but were not independent predictors of survival on multivariate analysis. This is in contrast to the study by Ollila et al., which reports the GI tract as the initial site of distant metastases to be an independent prognostic factor for long-term survival in patients operated for melanoma metastases to the GI tract.⁸

Multivariate analysis of the factors influencing survival after surgery for melanoma metastases to the GI tract demonstrated that surgical resection rendering the patient NED and a low preoperative serum LDH were

independent prognostic factors predictive of long-term survival. Median survival for 19 patients from Group 1 was 14.9 months; for 49 patients from Group 2 with residual disease in the GI tract or elsewhere, it was 6.9 months. This survival advantage in patients with distant metastatic melanoma who are rendered free of all identifiable disease by surgery has been reported in earlier studies.^{18,19} Ricaniadis et al., in their review of 48 patients operated for melanoma metastatic to the GI tract, report a median survival of 27.2 months for Group 1 patients and 5.1 months for patients with residual disease following surgery.⁷ Branum et al. also report significantly improved survival in patients with melanoma metastases to the GI tract who were rendered NED, with survival outcomes similar to the present series.⁹ Ollila et al. have defined a curative resection as one that removes all identifiable disease from the abdomen with or without documented nonresected sites of stage IV disease outside the GI tract and have reported a median survival of 48.9 months and a 5-year survival rate of 41% in this subgroup of patients.⁸ This is in contrast to our results, which demonstrate that the presence of residual disease, whether GI or extra-GI, has a significantly adverse impact on survival, with a 1-year survival of 22%. In the present series, median survival for 26 patients rendered free of disease in the GI tract but with residual disease elsewhere was 7.3 months, and for 23 patients with residual disease in the GI tract it was 6.3 months, as compared to a median survival of 14.9 months for 19 patients rendered free of disease at all sites. Patients with concurrent metastases in the liver, lung, or brain that were unresectable at the time of surgery (residual disease) for the GI metastases fared poorly. This is consistent with reports in literature of visceral sites of metastases such as liver, lung, brain, or bone being associated with the lowest survival rates in melanoma patients with distant metastases.^{16,19}

A low preoperative serum LDH was an independent positive predictor of survival in patients undergoing operative intervention for melanoma metastatic to the GI tract. Serum LDH level has been reported as an independent prognostic factor in several malignancies, including lymphoma,²⁰ germ cell tumors,²¹ Ewing sarcoma,²² osteosarcoma,²³ small cell lung cancer,²⁴ and mesothelioma,²⁵ and as an important predictor of survival in prostate cancer²⁶ and nasopharyngeal carcinoma.²⁷ A rise in the level of serum LDH does not necessarily indicate liver metastases but does correlate with tumor cell turnover (growth and necrosis) and tumor burden.^{24,28} An elevated serum LDH level has been reported to be one of the most significant independent adverse factors in studies evaluating prognostic factors for survival in patients

with disseminated melanoma.²⁸⁻³⁰ In this study the median survival for patients with preoperative LDH levels less than 200 u/l was 13.6 months versus 6.5 months for patients with LDH of 200 u/l or greater, which is comparable to the 11.5 and 6 months, respectively, reported by Eton et al.²⁹

In conclusion, surgical resection for melanoma metastatic to the GI tract is recommended for palliative reasons in symptomatic patients, providing significant improvement in quality of life with low operative morbidity and mortality. The impact of surgical resection on the natural history of metastatic melanoma is unknown. However, the fact that 38% of patients rendered disease-free after resection and 35% of patients with low LDH remain alive at 5 years suggests that an aggressive surgical approach towards these patients may be warranted in selected patients, even in the absence of symptoms.

REFERENCES

- de la Monte SM, Moore GW, Hutchins GM. Patterned distribution of metastases from malignant melanoma in humans. *Cancer Res* 1983;43:3427-33.
- Patel JK, Didolkar MS, Pickren JW, Moore RH. Metastatic pattern of malignant melanoma. A study of 216 autopsy cases. *Am J Surg* 1978;135:807-10.
- Reintgen DS, Thompson W, Garbutt J, Seigler HF. Radiologic, endoscopic and surgical considerations of melanoma metastatic to the gastrointestinal tract. *Surgery* 1984;95:635-9.
- Ihde JK, Coit DG. Melanoma metastatic to stomach, small bowel or colon. *Am J Surg* 1991;162:208-11.
- Caputy GG, Donohue JH, Goellner JR, Weaver AL. Metastatic melanoma of the gastrointestinal tract. *Arch Surg* 1991;126:1353-8.
- Khadra MH, Thompson JF, Milton GW, McCarthy WH. The justification of surgical treatment of metastatic melanoma of the gastrointestinal tract. *Surg Gynecol Obstet* 1990;171:413-6.
- Ricaniadis N, Konstadoulakis MM, Walsh D, Karakousis CP. Gastrointestinal metastases from malignant melanoma. *Surg Oncol* 1995;4:105-10.
- Ollila DW, Essner R, Wanek LA, Morton DL. Surgical resection for melanoma metastatic to the gastrointestinal tract. *Arch Surg* 1996;131:975-80.
- Branum GD, Seigler HF. Surgical intervention in the management of intestinal metastases from malignant melanoma. *Am J Surg* 1991;162:428-31.
- Jorge E, Harvey HA, Simmonds MA, Lipton A, Joehl RJ. Symptomatic malignant melanoma of the gastrointestinal tract: operative treatment and survival. *Ann Surg* 1986;199:328-31.
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457-81.
- Peto R, Pike MC, Armitage P. Design and analysis of randomized clinical trials requiring prolonged observations of each patient, II: analysis and examples. *Br J Cancer* 1977;35:1-39.
- Hochberg Y, Hamhane AC. Introduction. In: *Multiple comparison procedures*. New York: John Wiley & Sons, 1987:1-16.
- McDermott VG, Low VHS, Keogan MT, Lawrence JAL, Paulson EK. Malignant melanoma metastatic to the gastrointestinal tract. *Am J Radiol* 1996;166:809-13.
- Klaase JM, Kroon BBR. Surgery for melanoma metastatic to the gastrointestinal tract. *Br J Surg* 1990;77:60-1.
- Barth A, Wanek LA, Morton DL. Prognostic factors in 1,521 melanoma patients with distant metastases. *J Am Coll Surg* 1995;181:193-201.
- Karakousis CP, Velez A, Driscoll DL, Takita H. Metastectomy in malignant melanoma. *Surgery* 1994;115:295-302.
- Hena MA, Emrich LJ, Nambisan RN, Karakousis CP. Effect of surgical treatment on Stage IV melanoma. *Am J Surg* 1987;153:270-5.
- Overett TK, Shiu MH. Surgical treatment of distant metastatic melanoma. *Cancer* 1985;56:1222-30.
- Popat U, Przepiork D, Champlin R, et al. High-dose chemotherapy for relapsed and refractory diffuse large B-cell lymphoma: Mediastinal localization predicts for a favorable outcome. *J Clin Oncol* 1998;16:63-9.
- International Germ Cell Cancer Collaborative Group. International germ cell consensus classification: A prognostic factor-based staging system for metastatic germ cell cancers. *J Clin Oncol* 1997;15:594-603.
- Aparicio J, Munarriz B, Pastor M, et al. Long-term follow-up and prognostic factors in Ewing's sarcoma. A multivariate analysis of 116 patients from a single institution. *Oncology* 1998;55:20-6.
- Ferrari S, Bacci G, Picci P, et al. Long-term follow-up and post-relapse survival in patients with non-metastatic osteosarcoma of the extremity treated with neoadjuvant chemotherapy. *Ann Oncol* 1997;8:765-71.
- Maestu I, Pastor M, Gomez-Codina J, et al. Pretreatment prognostic factors for survival in small-cell lung cancer: A new prognostic index and validation of three known prognostic indices in 341 patients. *Ann Oncol* 1997;8:547-53.
- Herndon JE II, Green MR, Chahinian AP, Corson JM, Suzuki Y, Vogelzang NJ. Factors predictive of survival among 337 patients with mesothelioma treated between 1984 and 1994 by the Cancer and Leukemia Group B. *Chest* 1998;113:723-31.
- Furuya Y, Akimoto S, Akakura K, Igarashi T, Murakami S, Shimazaki J, Ito H. Response of prostate-specific antigen after androgen withdrawal and prognosis in men with metastatic prostate cancer. *Urol Int* 1998;60:28-32.
- Liaw CC, Wang CH, Huang JS, Kiu MC, Chen JS, Chang HK. Serum lactate dehydrogenase level in patients with nasopharyngeal carcinoma. *Acta Oncol* 1997;36:159-64.
- Sirott MN, Bajorin DF, Wong GYC, Tao Y, Chapman PB, Templeton MA, Houghton AN. Prognostic factors in patients with metastatic malignant melanoma. *Cancer* 1993;72:3091-8.
- Eton O, Legha SS, Moon TE, et al. Prognostic factors for survival of patients treated systemically for disseminated melanoma. *J Clin Oncol* 1998;16:1103-11.
- Keilholz U, Scheibenbogen C, Sommer M, Pritsch M, Geuke AM. Prognostic factors for response and survival in patients with metastatic melanoma receiving immunotherapy. *Melanoma Res* 1996;6:173-8.