

SMALL-BOWEL RESECTION FOR METASTATIC MELANOMA

Ibrahim F. Al-Sheneber, MD, FRCSC;* Sarkis H. Meterissian, MD, FRCSC;* Antoine Loutfi, MD, FRCSC;*
A. Kevin Watters, MD, FRCPC;† Henry R. Shibata, MD, FRCSC*

OBJECTIVE: To determine whether complete resection of small-bowel metastases from melanoma improves patient survival.

DESIGN: A computer-aided chart review.

SETTING: Hospitals associated with McGill University.

PATIENTS: Twenty patients (17 men, 3 women), identified from 1524 patients with melanoma, who underwent surgery to the small bowel for metastases. Patient age and clinical presentation, tumour site and stage were recorded.

INTERVENTION: Exploratory laparotomy with complete or partial resection of involved small bowel.

MAIN OUTCOME MEASURES: Operative morbidity, mortality and length of survival related to the extent of small-bowel resection.

RESULTS: Eleven patients had complete resection, 8 patients had partial resection and 1 patient had a palliative bypass only. Long-term survival (ranging from 2 to 10 years) was 36% in those who had complete resection and 0% in those who had partial resection; operative morbidity and mortality were 20% and 15% respectively.

CONCLUSION: Complete resection of small-bowel metastases in patients with metastatic melanoma can result in long-term survival.

OBJECTIF : Déterminer si l'ablation complète de métastases à l'intestin grêle provenant d'un mélanome améliore la survie du patient.

CONCEPTION : Examen de dossiers assisté par ordinateur.

CONTEXTE : Hôpitaux associés à l'Université McGill.

PATIENTS : Vingt patients (17 hommes, 3 femmes) identifiés parmi 1524 patients atteints de mélanome qui ont subi une intervention chirurgicale à l'intestin grêle à cause de métastases. On a consigné l'âge du patient et l'aspect clinique, le site de la tumeur et son stade.

INTERVENTION : Laparotomie exploratoire avec résection complète ou partielle de la partie atteinte de l'intestin grêle.

PRINCIPALES MESURES DES RÉSULTATS : Morbidité opératoire, mortalité et durée de la survie liées à l'ampleur de la résection de l'intestin grêle.

RÉSULTATS : Onze patients ont subi une résection complète, 8 ont subi une résection partielle et un autre a subi un pontage palliatif seulement. La survie à long terme (variant de 2 à 10 ans) s'est établie à 36 % chez les sujets qui ont subi une résection complète et à 0 % chez ceux qui ont subi une résection partielle. La morbidité et la mortalité opératoires se sont établies à 20 % et 15 %, respectivement.

CONCLUSION : La résection complète des métastases de l'intestin grêle chez les patients victimes d'un mélanome à métastases peut permettre une survie de longue durée.

*From the *Department of Surgery, Royal Victoria Hospital, McGill University, and the †Department of Pathology, McGill University, Montreal, Que.*

Accepted for publication Mar. 16, 1996

Correspondence and reprint requests to: Dr. Ibrahim F. Al-Sheneber, Room S10-18, Department of Surgery, Royal Victoria Hospital, 687 Pine Ave. W, Montreal QC H3A 1A1

Melanoma is an unpredictable tumour that may metastasize to any organ in the body. It has an unusual predilection for the gastrointestinal tract, particularly the small bowel, and is the most common cause of malignant intussusception in adults. Intestinal metastases are reported in 50% to 60% of cases in autopsy series but are diagnosed before death in only 1% to 4% of patients.¹

The role of surgery to achieve long-term survival in these patients is not well established and is generally viewed with scepticism. We present our experience with melanoma metastatic to the small bowel and identify the clinical, radiologic and pathological features. We studied the mortality and morbidity of surgical intervention to see if long-term survival could be achieved by complete resection of involved small bowel.

PATIENTS AND METHOD

Between 1970 and 1994, malignant melanoma was diagnosed in 1524 patients at McGill University-affiliated hospitals. A computer-aided chart review identified 20 patients (17 men, 3 women) who had surgical intervention for melanoma metastatic to the small bowel. Data on patient age and clinical presentation and tumour site, stage and diagnosis were collected. The TNM classification of the American Joint Committee on Cancer was used for staging of the primary lesion.² The surgical procedures were documented, and the available pathological slides were reviewed to confirm the original diagnosis. Postoperative outcome was analysed, and the Kaplan–Meier method was used to construct actuarial survival curves. The log-rank test was used to test significance of discrete variables on survival.

FINDINGS

At the time of the initial diagnosis the mean age of the 20 patients was 48.4 years (range from 26 to 78 years). At the time of intestinal involvement the mean age was 52.4 years (range from 28 to 84 years).

Two patients were found to have small-bowel metastases at the time their primary cutaneous lesions were identified. In the remaining 18 patients the mean time interval between diagnosis of the primary disease and the appearance of metastatic disease was 4.4 years (range from 1.8 to 14.7 years).

The primary lesions were stage I in 1 patient, stage II in 2 patients, stage III in 10 patients and stage IV in 7 patients. The sites of the primary lesions included the trunk in nine patients, the head and neck in six patients and the extremities in three patients; two patients presented with metastatic lymphadenopathy with unknown primary site. The sites of metastases in the stage IV patients included lung, liver, brain and distant subcutaneous sites. For the 17 patients in whom the Clark level of invasion³ of the melanoma was known, one tumour was level I, four were level II, six were level III and six were level IV.

Symptoms were variable and non-specific, but pain and vomiting were the most frequent, followed by rectal bleeding, fatigue and weight loss. The commonest clinical presentation was intestinal obstruction (10 patients), followed by gastrointestinal bleeding (7 patients). Obstruction was secondary to intussusception in seven patients and was associated with rectal bleeding in four of them. Four patients had peritonitis due to bowel perforation by the tumour. A palpable mass was detected on physical examination in four patients.

In six patients surgical exploration was based only on clinical findings and an abdominal series showing free air or complete small-bowel obstruction. Eight patients underwent an upper gastrointestinal series or enteroclysis: small-bowel dilatation, intraluminal filling defects and the spring-coil appearance characteristic of small-bowel intussusception were found. Computed tomography, done in two cases, demonstrated extraintestinal metastases and a mass representing the intussuscepted bowel. In two patients who presented with lower gastrointestinal bleeding of unknown etiology, surgical exploration was based on a positive angiogram in one patient and a positive nuclear scan in the other.

The most common site of involvement was the jejunum (80%), with 10 patients having isolated jejunal lesions and 6 patients having combined jejunal and ileal lesions. The lesions were almost invariably in the proximal segment of the jejunum and the distal segment of the ileum. Three patients had isolated ileal metastases, and one patient had a duodenal lesion. The lesions were multiple in 15 patients; both the mesentery and omentum were involved in 11 patients, whereas multiple segments of the small bowel were involved in 4 patients.

Complete resection was achieved in 11 patients (55%), 8 patients (40%) had partial resection with or without enteroenteric bypass and 1 patient (5%) underwent palliative gastrojejunostomy and biopsy for an unresectable duodenal lesion.

Three patients died in the 30-day postoperative period. One patient, who had undergone bowel resection for a perforated metastatic lesion, recovered but was re-explored 3 weeks later because of peritonitis, which proved to be due to another perforated metastatic lesion. A second pa-

tient, known to have liver metastases, underwent palliative resection but had ascites with peritonitis and died of septicemia 3 weeks after surgery. The third patient who had brain metastases improved symptomatically with radiotherapy but suffered unrelenting acute complete small-bowel obstruction and was operated on with palliative intent. He died postoperatively of disseminated malignant disease.

There were four complications: wound infection, pneumonia, prolonged paralytic ileus that resolved with nonoperative management and a postoperative anastomotic hemorrhage that was controlled by re-exploration.

Of the 11 patients who had complete resection, 4 (36%) were alive and disease-free at 2, 5, 8 and 10 years, respectively, after resection. All had stage III disease prior to the development of their intestinal metastases. All had multiple lesions. In this group there was only one postoperative complication, which was the anastomotic-site hemorrhage. The mean survival in the remaining patients in this group,

who died, was 19.5 months. Two of them were known to have lung and brain metastases prior to their intestinal disease. One patient was well and disease-free for 7 years after resection and died of disseminated prostatic cancer. The remaining four patients died with distant metastases (to liver in two patients and to brain in two patients) within 7 months of the small-bowel resection.

In the partial resection (and palliative bypass) group, all nine patients have died. Three patients died within 30 days of operation. For the remaining six patients, the mean postoperative survival time was 10.8 months (Fig. 1).

Analysis of actuarial survival figures showed a statistically significant difference ($p < 0.036$) according to type of resection performed, in favour of complete resection. When the patients were restratified according to the local extent of the disease, 9 patients had disease limited to the bowel wall and 11 patients had disease extending to the mesentery or omentum. However, there was no significant difference in

survival between these two groups (Fig. 2). Likewise the time interval between the primary cutaneous melanoma and the development of intestinal metastases did not significantly influence survival (Fig. 3).

DISCUSSION

The frequency of small-bowel metastases from melanoma in our study was 1.3%, similar to the 1.5% reported by Reintgen and colleagues¹ and the 1.4% reported by Gutman and associates.⁴ The most common site was the jejunum, a finding that is in agreement with other reports.^{1,5} The lesions are described in the literature as either polypoid pedunculated masses arising from the mucosa or well-circumscribed submucosal nodules.^{1,6,7} Occasionally they are amelanotic or composed of spindle cells and thus may be confused with poorly differentiated carcinoma or leiomyosarcoma. Immunohistochemical methods are employed to detect markers like S-100 protein, which will help to differentiate between these tumours.

The resectability rate of small-bowel metastases from melanoma varies from 26% to 88%^{1,5} in different series. Our rate was 55%. Complete resection resulted in four survivors and seven patients who died. Two of them had other visceral metastases preoperatively and four had metastases shortly after resection (within 7 months). It is likely that their metastases were present preoperatively but were not detected on routine clinical and radiologic examinations. The remaining patient lived for 7 years after resection and died of another primary cancer. It has been shown that complete resection gives superior survival for gastrointestinal metastases and metastases at other sites.^{6,8,9} Our results are in agreement with this. Our 5-year survival rate was 15%, and one

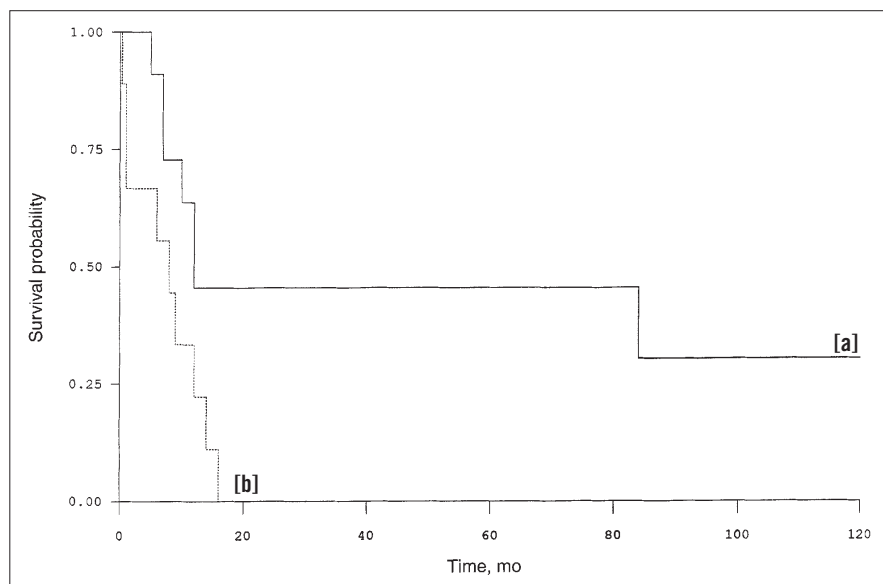


FIG. 1. Survival of patients with melanoma metastatic to small bowel, according to type of resection: complete (solid line [a]) or partial (dotted line [b]).

other patient was alive and disease-free 2 years after resection. Klaase and Kroon⁷ reported a 19% survival rate in 23 patients with gastrointestinal metastases and Caputy and associates¹⁰ reported a 9% survival in 41 patients.

After excluding the three perioperative deaths in our series, the mean and median survival rates were 2.5

years and 1 year respectively. It is hard to compare these results with those of previous reports because of different patient characteristics, but, generally speaking, the mean survival reported in the literature ranges from 1 to 2 years,^{1,5,11} the median survival time being less than 1 year.^{5,12}

(Since compiling these data we

have encountered another patient with small-bowel metastases from melanoma. This 26-year-old woman had a lower-extremity melanoma excised in 1988. Her first relapse was in the jejunum 4 years later. The involved bowel was resected, but she had another intra-abdominal recurrence 8 months later, which was also resected. She has been in good health for more than 2 years with no evidence of disease clinically or radiologically.)

The reports in the literature on the prognostic significance of relapse-free survival in malignant melanoma are conflicting. Roses and colleagues⁸ and Karakousis and associates¹³ have shown a better outcome with longer relapse-free survival in metastatic melanoma in general, but other reports^{7,10} of gastrointestinal relapse do not support this observation. In our study, the time interval between diagnosis of the primary melanoma and small-bowel metastases did not affect survival. Also, we found that extension of the disease to the mesentery or omentum did not affect survival, probably because it did not prohibit complete resectability. Unfortunately we could not find any other study that addressed this issue. The key determinants of survival are complete resection and the absence of other distant metastases. Because this is a retrospective study, the information on quality of life and relief of symptoms could not be accurately reported.

In summary, patients with a history of melanoma who present with gastrointestinal symptoms, especially obstruction or bleeding, should be investigated for intestinal metastases. Surgical intervention with complete resection of all visible tumour may be associated with long-term survival and should be attempted, since alternative therapeutic options are ineffective.

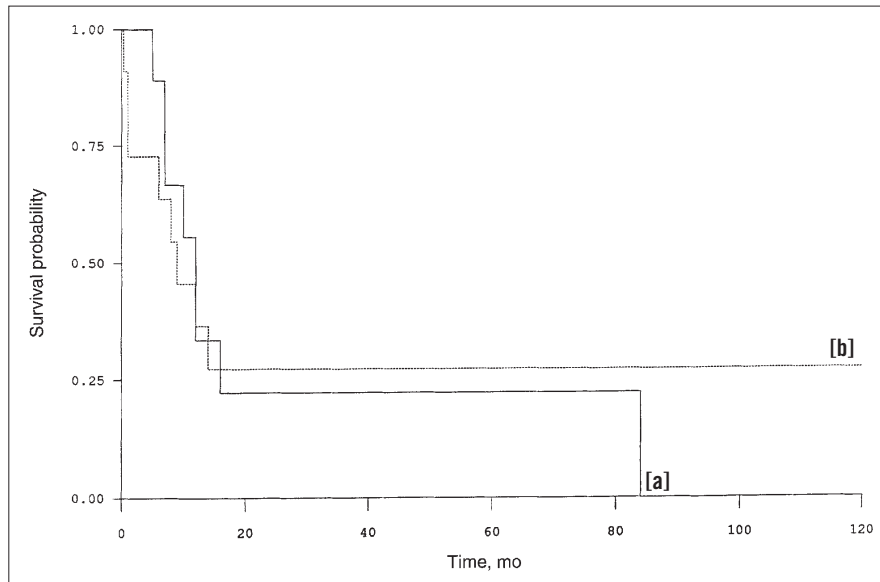


FIG. 2. Survival according to extent of metastatic disease: intestinal (solid line [a]) or extra-intestinal (dotted line [b]).

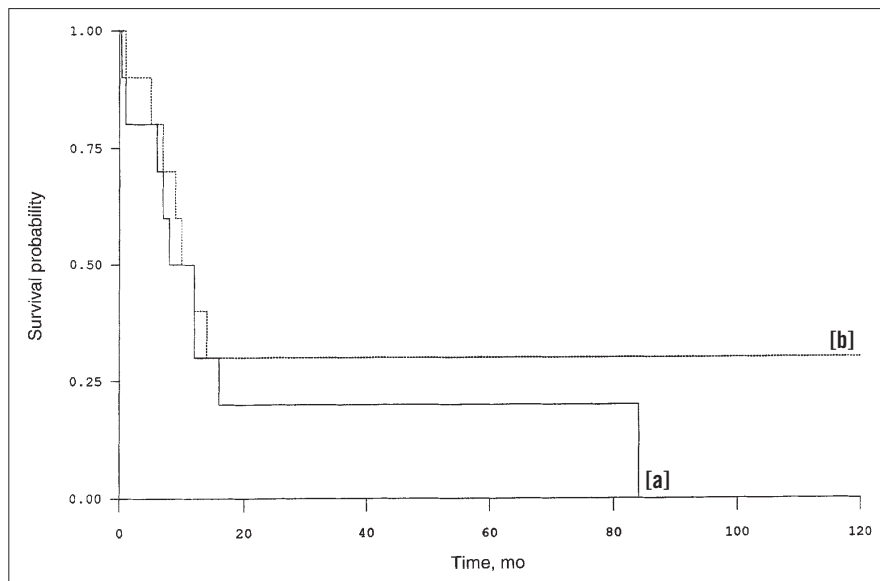


FIG. 3. Survival according to time from diagnosis of primary disease to intestinal metastatic disease: less than 3 years (solid line [a]) or 3 years or longer (dotted line [b]).

We thank Ms. Ita Smyth for typing the manuscript, and Mrs. Manuela Das Neves and Mrs. Virginia Raposo from the Tumour Registry of the Royal Victoria Hospital, Montreal, for their invaluable assistance.

References

1. Reintgen DS, Thompson W, Grabutt J et al: Radiologic, endoscopic and surgical considerations of malignant melanoma metastatic to the small intestine. *Surgery* 1984; 95: 635-639
2. American Joint Committee on Cancer: *Manual for Staging of Cancer*, 4th ed, J.B. Lippincott Company, Philadelphia, 1992
3. Clark WH Jr, From L, Bernardino EA et al: The histogenesis and biologic behavior of primary human malignant melanomas of the skin. *Cancer Res* 1969; 29: 705-715
4. Gutman M, Klausner JM, Inbar M et al: Surgical approach to malignant melanoma in the gastrointestinal tract. *J Surg Oncol* 1987; 36: 17-20
5. Khadra MH, Thompson JF, Milton GW et al: The justification for surgical treatment of metastatic melanoma of the gastrointestinal tract. *Surg Gynecol Obstet* 1990; 171: 413-416
6. Branum GD, Seigler HF: Role of surgical intervention in the management of intestinal metastases from malignant melanoma. *Am J Surg* 1991; 162: 428-431
7. Klaase JM, Kroon BB: Surgery for melanoma metastatic to the gastrointestinal tract. *Br J Surg* 1990; 77: 60-61
8. Roses DF, Karp NS, Oratz R et al: Survival with regional and distant metastases from cutaneous malignant melanoma. *Surg Gynecol Obstet* 1991; 172: 262-268
9. Overett TK, Shiu MH: Surgical treatment of distant metastatic melanoma: indications and results. *Cancer* 1985; 56: 1222-1230
10. Caputy GG, Donohue JH, Goellner JR et al: Metastatic melanoma of the gastrointestinal tract. Results of surgical management. *Arch Surg* 1991; 126: 1353-1358
11. Jorge E, Harrey HA, Simmonds MA et al: Symptomatic malignant melanoma of the gastrointestinal tract. *Ann Surg* 1984; 199: 328-331
12. Goodman PL, Karakousis CP: Symptomatic gastrointestinal metastases from malignant melanoma. *Cancer* 1981; 48: 1058-1059
13. Karakousis CP, Velez A, Driscoll DL et al: Metastectomy in malignant melanoma. *Surgery* 1994; 115: 295-302

SESAP VIII Questions

Questions SESAP VIII

ITEM 465

Which of the following statements about carotid endarterectomy is NOT true?

- (A) Patients with asymptomatic critical stenosis benefit from carotid endarterectomy
- (B) The risk of contralateral stroke is reduced after carotid endarterectomy
- (C) Operative mortality is less than 2%
- (D) It prolongs survival when compared with patients treated medically
- (E) It should be accompanied by antiplatelet medication

ITEM 474

The indications for carotid endarterectomy in a patient with a 75% diameter stenosis of the left internal carotid artery are established for all of the following EXCEPT

- (A) history of left amaurosis fugax
- (B) asymptomatic 60-year-old man
- (C) history of stroke with marked residual right arm paresis
- (D) preceding coronary artery bypass for tight stenosis of the left main coronary artery
- (E) history of aphasia lasting 20 minutes

For the question in item 465, select the one answer that is best of the five given, and for the incomplete statement in item 474, select the one completion that is best of the five given.

For the critique of Items 465 and 474 see page 220.

(Reproduced by permission from *SESAP '96-'98 Syllabus: Surgical Education and Self-Assessment Program*, Volume 2, 9th edition. For enrolment in the Surgical Education and Self-Assessment Program, please apply to the American College of Surgeons, 55 East Erie St., Chicago, IL 60611, USA.)