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Melanoma Recurrence Surveillance

Patient or Physician Based?

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Objective

The authors determined the roles of the physician and the patient in melanoma recurrence detection.

Methods

The University of Alabama Melanoma Registry, consisting of 1475 patients surgically treated for cutaneous melanoma from 1958 to 1984, was searched to find 195 evaluable cases of melanoma recurrence. Patients were grouped by the type of return visit. Group I returned on a previously determined date, whereas group II returned before the scheduled visit.

Results

Symptoms of recurrence were present in 90% of group I patients and 93% of group II and correlated with the site of recurrence in more than two thirds of cases. Recurrence sites were local, regional, and distant in 35%, 31%, and 29% of group I, respectively, and 42%, 25%, and 29% of group II. The median interval to recurrence was 24.2 months in group I and 37.7 months in group II ($p = 0.059$). Median overall survival was 57 months in group I and 62 months in Group II ($p = 0.210$).

Conclusions

Symptoms are present in 90% of the patients with recurrent melanoma and accurately predict the site of recurrence. Overall survival is not affected by the type of patient return visit.

The annual incidence of melanoma is rising such that the risk of developing melanoma is estimated to be 1:75 by the year 2000.[1,2] This alarming statistic is accompanied by a trend toward thinner and, thus, better prognosis melanomas. Currently, more than 80% of patients surgically treated for cutaneous melanoma are cured.[3]

Postoperative surveillance for malignancy is directed toward detection of recurrence, identification of new primary neoplasms, and patient reassurance. Controversy exists regarding follow-up of patients with more common malignancies such as breast carcinoma, because detection of asymptomatic recurrence adds little to overall survival in several reports.[4–8] The long-term, disease-free survival of patients with metastatic melanoma is low, even when the recurrence is resectable or treated with chemotherapy.[9,10]

Much is known about the pattern and timing of recurrence in cutaneous melanoma, but there is little reported about the most efficient method of detection.[11–16] The purpose of this study was to evaluate the patient's and physician's roles in the detection of recurrent melanoma and their influence on survival.

MATERIALS AND METHODS

The University of Alabama Melanoma Registry contains 1475 patients treated surgically with curative intent

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from 1958 to 1984 for primary cutaneous melanoma. The design of this registry has been previously reported.[12] Two hundred twenty patients with recurrent melanoma were identified.

For analysis, patients were grouped by the type of return visit. Group I returned at a previously determined date, whereas group II returned before the regularly scheduled visit. Recurrence was defined as local (within 5 cm of the original excision site), regional (nodal and/or in-transit), or distant.

One hundred ninety-five of the 220 patients with recurrences had sufficient follow-up data for analysis. As seen in Table 1, patients are distributed equally by gender, race, histology, and initial surgical treatment. Group II had a greater percentage of patients with intermediate thickness tumors (1.5–4.0 mm) than group I; however, this difference was not statistically significant. All patients were clinical stage I or II at the time of initial surgery.

Suggested postoperative surveillance procedures during this time period were periodic physical examination, chest x-ray, and serum liver function tests. Abnormalities were further investigated as indicated with ultrasound, computerized tomography, or bone scan. Physical examination was performed every 3 months for years 1 and 2, every 6 months for years 3 to 5, and yearly thereafter. Chest x-ray and blood chemistries were obtained every 6 months for years 1 to 3 and annually thereafter.

Patient charts were reviewed to define the site of first recurrence, type of presentation, and ultimate outcome. The site of recurrence was noted to be symptomatic or asymptomatic according to the recorded history in the chart and the site documented by objective means, i.e., physical examination or radiographs. Local and regional recurrences were treated surgically, whereas distant metastases were treated at the discretion of the primary physician.

Disease-free survival (interval to recurrence after treatment of the primary tumor), last follow-up date, and death were calculated from the date of primary diagnosis to eliminate lead-time bias. Survival curves were generated by the Kaplan-Meier method with a Mantel-Haenszel comparison for significant differences. Chi square analysis also was performed when appropriate.

Table 1. PATIENT AND TUMOR CHARACTERISTICS

	Group I (n = 128)	Group II (n = 67)	p Value
Gender			
Male	55.6%	51.4%	NS
Female	44.4%	48.6%	NS
Race			
White	99.3%	93%	NS
Black	0.7%	7%	NS
Thickness			
<0.75 mm	2.6%	3.8%	NS
0.75–1.5 mm	23.4%	20.5%	NS
1.5–4.0 mm	29.2%	47.4%	0.068
>4.0 mm	11.7%	6.4%	NS
Unknown	33%	22%	NS
Histology			
SSM	44%	52.5%	NS
NM	52%	42.4%	NS
LMM	2%	1.7%	NS
ALM	2%	3.4%	NS
Ulcerated	53.3%	55.7%	NS
Initial surgery			
WLE	86%	84.3%	NS
WLE and LND	14%	15.7%	NS

RESULTS

Recurrence was symptomatic in 90% of group I and 93% of group II patients, with an equal distribution of symptom sites between the two groups (Table 2). Local and regional recurrences were the most common initial sites of recurrence in both groups, accounting for two thirds of the cases. Symptoms correlated with physical or radiographic findings in 71% of group I and 85% of group II patients for local recurrence and 62% of group I and 74% of group II patients for regional recurrence; 62% of group I and 64% of group II patients had documented distant metastases corresponding to their presenting symptoms.

The disease-free survival, or interval to recurrence, was 24.2 months in group I and 37.4 months in group II ($p = 0.059$). This trend toward statistical difference primarily was attributable to the longer interval to discovery of distant metastases in group II (50.3 months) *versus* group I (28.1 months) ($p < 0.001$). The intervals were similar between group I and group II for local (26.2 *vs.* 23.5 months) and regional (21.6 *vs.* 28 months) recurrences.

Only 61 patients are alive, 36 in group I and 25 in group II, with a median follow-up of 78 months. Thirty-eight have no evidence of melanoma, 23 in group I and 15 in group II. Those patients alive with disease have distant metastases in 45%, local disease in 36%, regional disease in 4.5%, and multiple sites of disease in 14.5%.

Overall survival was not affected by the type of return visit (Table 3). Subset analysis of survival by recurrence site showed no difference in survival after local, regional, or distant recurrences between group I and group II. Within each group, there was a trend for longer survival in patients with local or regional recurrence when compared with distant metastases. Because only ten patients in group I and three patients in group II were asymptomatic, a meaningful subset analysis by the presence or absence of symptoms could not be performed. Analysis by

Table 2. SUBJECTIVE AND OBJECTIVE RECURRENCE SITES

	Group I		Group II	
	Symptom Site	Recurrence Site	Symptom Site	Recurrence Site
Local	37%	35%	39%	42%
Regional	26%	31%	22%	25%
Distant	24%	29%	28%	29%
Local and regional	2%	1%	3%	—
Multiple	1%	1%	—	2%
Not specified	—	3%	—	2%

tumor thickness was not possible because 33% of group I and 22% of group II had no values recorded.

Survival and disease control after treatment of local, regional, or distant recurrence was similar between the two groups. The percentage of patients alive and free of disease after recurrence treatment in group I was 31%, 13%, and 4% for local, regional, and distant recurrence, respectively, and 28%, 25%, and 5% for group II.

DISCUSSION

Patients treated for malignancy generally are followed at regular intervals to detect recurrences, identify new primary tumors, and provide reassurance that treatment has been successful. Patient visits for physical examinations and diagnostic evaluations are more frequent during periods when the incidence of recurrence is highest. Theoretically, this practice provides a survival advantage because surgical, chemotherapeutic, or radiation treatment is more effective when tumor burden is low and further disease progression is arrested. Although the majority of tumors recur in the first 3 years, long-term follow-up could be indefinite because melanoma continues to reappear for decades after treatment.

Patterns and timing of cutaneous melanoma recurrence have been reported.[11] The most common sites and time intervals are well documented and form the basis for postoperative surveillance recommendations. Recurrence risk is predicted accurately by a number of prognostic variables.[12-16] Applying these prognostic criteria, 80% of patients with melanoma will experience long-term, disease-free survival and thus, benefit only from new primary tumor identification and reassurance in a follow-up program.[3]

Previous studies of more common malignancies such as breast carcinoma have implied that intensive follow-up programs do not influence survival with detection of asymptomatic recurrences.[4-8] The rising incidence of melanoma means more patients will require postoperative monitoring.[1,2] Thus, a better definition of surveillance efficacy for recurrent melanoma is required. The roles of the patient, physician, and diagnostic studies need clarification to ensure high-quality medical care is delivered in a cost-effective manner.

More than 90% of patients with recurrent melanoma were symptomatic in this study, implying that patients initially discover recurrence. Retrospectively, we cannot determine the duration of symptoms; therefore, patients were grouped by the timing of the return visit. This assumed patients requesting an interval evaluation were symptomatic for a shorter duration than those waiting for a regularly scheduled visit. The validity of this assumption has not been proven, although a trend existed for a longer interval to recurrence for patients presenting at an unscheduled visit. When analyzed by recurrence site, the interval to recurrence diagnosis was similar for patients with a local or regional recurrence in either group (25 months). However, a significantly longer interval to discovery of distant metastases was noted in the group of patients presenting at unscheduled visits (50 months vs 28 months). Interpretation of this result must be tempered with the knowledge that only 34 patients from group I and 18 patients from group II were available for this analysis. Thus, this interval difference may be much smaller if evaluated in a larger group of patients.

Despite the overall delayed detection of recurrence in group II, no overall survival difference existed between the two methods of recurrence presentation. This is best explained by the lack of effective therapy for distant melanoma metastases; thus, earlier diagnosis of an ineffectively treated metastasis affords no survival advantage. Those patients with local or regional recurrence were diagnosed at similar intervals, and surgical treatment provided similar outcomes. Although our data confirm that melanoma recurrence usually is fatal, 43% of patients with local or regional recurrence in the scheduled group and 53% of patients with local or regional recurrence in the unscheduled group were alive and free of disease with a median follow-up of 78 months.

Totally patient-directed postoperative melanoma surveillance cannot be recommended from this study because symptoms may not always correlate with physical findings. Second, we can only evaluate survival in symptomatic melanoma recurrence because more than 90% of our patients had symptoms, leaving too few asymptomatic patients for evaluation. Therefore, a reasonable alternative is periodic physical examination to detect lo-

Table 3. SURVIVAL (MONTHS)

	Group I	Group II	p Value
Disease-free survival	24.2	37.4	0.059
Overall survival	57	62	0.210

cal recurrence, in-transit metastases, and lymphadenopathy that escape patient self-detection. This conclusion also has been reached by authors evaluating methods of follow-up of breast cancer.[4–8]

Advocating routine radiographic and laboratory studies to search for asymptomatic distant metastases is difficult to justify because treatment seldom provides a lasting survival benefit. Fewer than 10% of study patients, less than 1% of the entire registry, were alive and free of disease after diagnosis of distant recurrence, thereby supporting this view. This era of health-care reform requires consideration of the financial cost of follow-up. Although decisions about patient care cannot be completely directed by cost analysis, justification of expensive evaluations that infrequently discover treatable conditions is difficult. For example, the cost per patient for an intensive postoperative surveillance program over 5 years—consisting of 12 physician visits, 7 chest x-rays, and 7 sets of liver chemistries—would be $1193.50, based on current charges. The financial outlay for each of the 32,000 new patients diagnosed with melanoma each year would be significant and hard to advocate because less than 20% will recur and most with distant metastases will not benefit from treatment.

Intuition and common sense justifies careful and intensive postoperative surveillance for melanoma. Our observations suggest this may not be true. This small retrospective evaluation requires confirmation with larger studies, especially those containing a larger group of asymptomatic patients, before practice patterns can be safely changed. Complete abandonment of patients after surgical treatment of melanoma is incorrect because some are salvaged with wide excision of local recurrence or lymphadenectomy for regional recurrence. Patient symptoms often accurately predict recurrence; however, they are not infallible. Thus, a thorough periodic physical examination by an experienced physician must remain a part of the surveillance program. The intervals between physician visits could be safely lengthened without influencing overall survival if patients are educated to recognize the signs of local, in-transit, and regional recurrences, especially because these are the most common sites of recurrence and are readily detectable by the patient. The absence of effective therapy for distant melanoma metastases makes routine radiographic and biochemical analyses of questionable value. Hopefully, this study will stimulate further investigation and development of more effective strategies for postoperative melanoma recurrence surveillance.

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Discussion

DR. HIRAM C. POLK, JR. (Louisville, Kentucky): Dr. McDonald, Dr. Copeland, Ladies, and Gentlemen, the data on follow-up of melanoma patients is very, very sparse. Therefore, this paper is thought provoking, will be valuable, and will be referenced widely.

There are three main purposes for follow-up of the cancer patient. One is the quality assurance issue to determine if you are doing as good a job as you are supposed to. The second is to determine and detect treatable recurrence. And the third, which was not addressed in this paper and is fairly important in the melanoma patient is, of course, the detection of new primaries.

It looks as if at least 5% of patients who are cured of melanoma in their lifetime will develop a new primary melanoma. And, of course, early detection makes treatment very much more sensible.