may allow definitive identification of patients with subclinical regional lymph node metastases.

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Discussion

DR. EDWARD M. COPELAND, III (Gainesville, Florida): Dr. Souba, Dr. Tseng, and their colleagues have produced a very useful study to decide on surgical therapy for melanoma of the hands and feet: A one centimeter margin and no elective lymph node dissection for lesions less than 1.5 mm, and a 2 cm margin and an elective lymph node dissection for lesions greater than 1.5 mm in size. In their study, patients with thick melanomas had a 50% or greater incidence of regional lymph node metastasis. They favor sentinel lymph node biopsy. Based on their data, I would favor elective lymph node dissection because of the high rate of nodal metastasis and because, in my hands, a sentinel node is less often accurately identified by isosulfan blue or a radio tracer when the distance required to travel is from the tip of the extremity to either the axilla or to the groin.

Have the authors done the sentinel node technique for any of these reported cases? And, if so, with what degree of success?

In-transit metastases have been a problem described in some reported series with melanomas of the hands and feet. Did any of these patients develop in-transit metastasis? If so, what is the recommend treatment for in-transit metastasis at the MGH?

My last remaining question: In treating sub-ungual melanomas of the finger, is it safe to amputate only the distal digit?

DR. WILLIAM C. WOOD (Atlanta, Georgia): Dr. Griffen, Dr. Copeland, Fellows, and Guests. I want to think Dr. Tseng and Dr. Souba and their colleagues for the privilege of reviewing this very fine manuscript.

Although only 5% of patients with melanoma present in the distal extremity, this is one of the problematic areas in managing malignant melanoma, and your contribution is most helpful. You address two issues: margins and local control, and the candidates for sentinel node staging. And I have four questions.

The first is regarding local control. Even in the tumors greater than 1.5 mm in thickness, there were only three local failures. What was the thickness of those three lesions?

The second question is similar. I am very unhappy with thresholds in biology for two reasons. First, I do not think they are natural. Was there an absolute in your data where anything over 1.5 mm seemed to have a random likelihood of recurrence and of lymph node metastases? Is there a linear relationship to thickness, as you get thicker and thicker? Or even a geometric relationship, as has been suggested?

My other problem about thresholds is that once a threshold of 1.5 mm is published, in the clinic over the next few weeks we see a host of patients who all seem to have lesions that are either 1.4, 1.5, or 1.6 mm in thickness, which is somewhat problematic.

Third, did acral lentiginous lesions, as compared with subungual lesions, as compared with lesions of the dorsum of the hand or foot, have any apparent effect on outcome? Or was thickness the only determinant? Did you look at microsatellites, for example?

Also, you combined hand and foot. Did you see any difference between hands and feet that was apparent as a trend, at least?

That was my fourth question, and I wish to commend the authors for a very fine presentation, and I thank the Society for the privilege of commenting.

DR. KIRBY I. BLAND (Providence, Rhode Island): Vice President Griffen, Secretary Copeland, Members, and Guests of the Association. I, too, would like to congratulate Dr. Souba, Dr. Tseng, and their co-authors for bringing this important clinical review to the Association.

The authors observed in this retrospective analysis that cutaneous melanoma of the hands and feet, less than 1.5 mm thick-

ness, has a significantly reduced incidence of metastatic disease, and is effectively treated by local excision with 1 cm margins. Conversely, thicker lesions (*e.g.*, greater than 1.5 mm) predictably have a poor prognosis which is reflected in an increased incidence of regional, nodal and systemic disease.

In this relatively small series of 116 patients, Dr. Souba and Dr. Tseng have verified, as have others, that an increase in the vertical growth phase of the cutaneous melanoma, regardless of site, portends grave outcome relative to local, regional, and systemic recurrence. I thank the authors for forwarding me the manuscript in advance, and I recommend it to be reviewed by the membership. I have a number of questions for the authors which relate to the justification of their conclusions relative to management of the specific sites they have analyzed.

First, Dr. Tseng and Dr. Souba, your series has a large preponderance of female subjects in this database of 116 patients. Numerous epidemiologic studies have suggested recurrence and survival advantage for the female, regardless of age or site, indicating a biological advantage for this gender. Your database appears to be large enough to note outcome differences for the sexes; therefore, were there lower frequencies of local, regional, and systemic recurrences in females, and were their lesions thinner than their male counterpart?

The European trial conducted by Veronesi et al., suggested, in their large study of thin Stage I cutaneous melanoma, that a 1 cm margin is equivalent to a 3 cm margin relative to local-regional recurrence and the development of systemic disease. Further, the recent intergroup melanoma study reported by Dr. Balch et al., which many in this audience contributed to its results, recommended a 2 cm margin for lesions less than 1 mm thickness. This study defined the intermediate melanoma thickness as 1 to 4 mm. Results of the intergroup trial are difficult to explain, as there was a modest increase in survival in patients 60 years of age or younger for lesions between 1 and 2 mm thickness after elective lymph node dissection (ELND); however, patients with lesions greater than 2 mm but less than 4 mm were not benefited by ELND. Your data suggest that for hand and feet, lesions less than 1.5 mm thick all had negative nodes with ELND. This frequency was 14% histologically positive nodes for lesions greater than 1.5 mm thickness. We agree with your recommendation of using sentinel lymph node biopsy by lymphatic mapping. Our current approach is to use both vital dyes and radionuclide scintigraphy with a hand-held gamma camera to histologically evaluate the sentinel node and determine the necessity of node dissection.

With the low frequency of nodal metastases, 0%, for lesions less than 1.5 mm, are you currently recommending lymph node mapping only for the thicker lesion or do you consider all patients, regardless of tumor thickness, to be eligible for lymphatic mapping? This has special importance because of the difficulty getting proper technical distribution of dyes and radionuclides following injections of the digits or webspaces of the hand and feet and insure accurate mapping? Admittedly, lymph node mapping is much simpler with injections on the dorsum of the hands or feet, or on the palms and sole, when compared to these interdigital spaces.

My next question relates to local recurrence for the thin and thick lesions. If I follow your data correctly, regardless of melanoma thickness, the local recurrence frequency was quite low. Local failure for lesions greater than 1.5 mm was identical when excision was less than 2 cm and for wide local excisions of 2 cm.

Recognizing that your data represent relatively small numbers in each category, how do you justify 2 cm excisions to be beneficial over those of 1 cm, especially when closure can be quite difficult after excision of these lesions in the distal extremities? Failures appear to be a product of the biology of the tumor, not margins, as local recurrence was identical for wider margins of excision in these thick lesions.

Further, as you have indicated, these wider excisions necessitate larger operative procedures, including the need for skin grafting and full-thickness tissue coverage, thus incurring greater operative time and subsequent cost for the management of these difficult lesions.

Finally, a comment and a question. When one compares the histologic variants and their impact on outcome, it appears that there are no differences relative to local recurrence for subungual, acral lentiginous, or dorsal cutaneous melanoma variants under 1.5 mm. None had local failure. Further, there is very little variation in local recurrence for the 79 patients with thicker lesions as well. Presumably, all thick subungual lesions were managed with amputations and the local recurrence was zero, while dorsal and acral lesions had local recurrence rates of 3% to 6%.

Additionally, there appears to be no regional nodal or systemic recurrence deviations among any of the 79 patients with thick histologic subtypes. This observation underscores further the importance of proper microstaging of the primary lesion to insure consistent and reproducible local regional management. What impressed me in this particular portion of the analysis is that all patients with thick lesions had virtually identical regional systemic failures, which again is a function of the vertical growth phase of the tumor, not the histologic subtype or its location. It is in this group of patients with thick lesions that we would proceed with regional sentinel node lymphatic mapping because of the high risk for these thicker lesions to harbor micrometastatic disease.

Dr. Tseng and Dr. Souba, would you modify your operative approach for thin or thick lesions based on specific histologic subtype?

I enjoyed this paper, and I thank the authors for bringing this to the attention of the Association. I thank you for the privilege of the floor.

DR. HIRAM C. POLK, JR. (Louisville, Kentucky): Dr. Griffen, Dr. Copeland, Ladies, and Gentlemen. I think the Association owes a debt of gratitude to Dr. Souba and Dr. Tseng for bringing this up, because this group of patients is often lost by being lumped with other groups of patients.

First, 92% to 94% of melanomas are categorized perfectly as to risk by standard reference to thickness, location, gender, and age. That is easy enough. What they have done very nicely here is focus on a group of patients that is probably occult high risk to begin with because of the inclusion of a good number of acral lentiginous lesions. Also, there is no such thing as a thin subungual melanoma.

So by definition, there is a subgroup here that they have

identified very nicely. You could also notice a tendency, and I think it is a tendency of regional referral for more thick melanomas, that probably would be referred to them than would be referred to a number of places, because that is exactly the referral pattern that ought to exist.

The issue is we are all trying to look for the occult high-risk melanoma. The appearance of alpha interferon as a putative treatment for occult lymph node positive melanoma is really a fairly statistically significant positive observation. The difference is small, but it is real. And it is one of the few glints of hope we have had in a long time.

The issue is to try to take what is currently so fashionable, lympho-scintigraphy in the identification of the sentinel node, and use it to stratify patients who may benefit greatly from node dissection and additional treatment.

I have a question and a comment about the question. What is the cost of lympho-scintigraphy of the sentinel node biopsy?

The yield is going to be very small; the cost has to be correspondingly small, and I suspect it is not.

The second point I want to make is, obviously, the treatment of choice for the thick hand or foot melanoma is probably isolated regional perfusion, as was described by Creech and Krementz a long time ago. It is ideal treatment for these patients, and it addresses not just the local recurrence but the problem of regional nodal metastases as well. So I think you have brought up some points here that are very important.

The cost issues and the ultimate efficacy of lympho-scintigraphy need to be sorted out. I think you have done us all a favor by identifying a group of patients with hands and foot melanoma that are not commonly discussed and need special attention. Thank you very much.

DR. HAROLD J. WANEBO (Providence, Rhode Island): Mr. Chairman, Members, and Guests: The authors are to be congratulated on a presentation of a unique series of melanoma patients.

This small series epitomizes the aggressiveness of melanoma at a unique site. We consider scalp melanomas to be very high risk, primarily because of site, but certainly, these melanomas are equally high risk, primarily because of site.

According to the authors' data, at least in the thicker lesions, acral lentiginous melanomas are really no different from the other types. For example, superficial spreading melanomas on the dorsum of the hands or the foot is intriguing; if they are thicker than 1.5 mm, they are equivalent to acral lentigenous melanomas of equal thickness. I would have thought that acral lentiginous melanomas were a much higher risk.

I have some questions for the authors. Was there any relationship to survival? Actually, I do not think we saw any survival data. Are there some differences? Secondly, I know that the group at Massachusetts General Hospital has used isolation regional perfusion, very similar to what Dr. Polk asked. Were any of these patients treated by isolation perfusion? This would certainly address some of the issues, especially the effects on distant metastases, that are likely to occur in these patients.

We are mindful of the fact that among the thicker lesions, more than 50% have lymph node metastases, usually a harbinger of distant failures.

I was intrigued also by the very low local recurrence rate. I wondered if in-transit metastases were included in that aspect because this was one of the reasons that many of us thought perfusion might be better in that subgroup of patients. It would be interesting to see what that data shows.

Lastly, I am concerned about the technical questions of how to do sentinel node biopsies in these patients because of the distance from the extremity sites to the nodal drainage basis. I would be interested to see how this data is accomplished. In fact, I think I would agree with Dr. Copeland that if 50% of the thicker lesions are developing lymph node metastases, one should do a planned elective dissection for that group of patients. I think this is a stance we would take.

This is a very fascinating paper, and I enjoyed the privilege of being the discussant.

DR. JENNIFER TSENG (Closing Discussion): Thank you, Dr. Griffen, Dr. Copeland, and the discussants for the privilege of doing this discussion. And I would like to thank all the discussants for their very insightful and illuminating comments.

First, I will discuss some of Dr. Copeland's questions regarding the sentinel node mapping. We have been performing sentinel node mappings ever since Dr. Souba came to the Massachusetts General Hospital four years ago. During that time we have mapped about 15 patients with melanomas of the hands or feet. Virtually all of these, interestingly, have mapped either to the axilla or to the groin, suggesting to us that there is very little that would actually map to, for instance, the epitrochlear nodes or to the popliteal nodes. We have not had any difficulty identifying the sentinel node in these patients.

Regarding in-transit melanomas, we had no isolated in-transit metastases in our series. There were a small number of patients who had in-transit metastases in association with systemic disease. At the Massachusetts General Hospital, we generally treat isolated in-transit metastases with lymph perfusion, although now there are several gene therapy studies that for which patients are eligible.

As for node dissections, although the incidence of regional node disease, as Dr. Copeland pointed out, is very high in these patients with thicker lesions, about 50%, there were still 50% of patients that did not have positive nodes. Given the safety and, we think, accuracy of lymphatic mapping, we do map all patients with lesions greater than or equal to 1 mm, and we believe that we avoid unnecessary lymphadenectomies in these patients.

To respond to Dr. Copeland's final comment about subungual melanomas of the hand, yes, we do believe in a distal lesion that it is safe to amputate at the distal phalanx, and the numbers of patients that we have in our study bear this out.

Dr. Wood commented on local control of melanomas greater than or equal to 1.5 mm of thickness. Our failures in these patients, the three local failures, were all thick lesions. They were all greater than 2.5 mm. So the lesions that are 1.5 mm are definitely not as dangerous as lesions that are 3 mm or 4 mm, which addresses his next question about thresholds.

We, too, are uncomfortable with absolutes or thresholds in these kinds of diseases. In our study we found there is a continuum of thickness; that there is more of a linear relationship than an absolute cutoff. With that in mind, we still find it useful to try to find groups and to divide melanomas into groups that

could be useful for surgeons. One and a half millimeters appeared to be an appropriate cutoff.

In terms of histology, as several of the discussants pointed out, we did not find real differences if thickness was eliminated. We did not find real differences between pathologic subtypes. There were some nodular melanomas that were very thick, and those appeared to do worse. But, again, that went along with thickness.

We did find that microsatellites and ulceration were negative prognostic factors, independent of thickness, as has been suggested by a number other studies.

As for the differences between the melanomas of the hands and feet, the feet actually tended to have thicker lesions and therefore had worse prognoses.

Addressing some of Dr. Bland's questions, we did not find significant differences between our female patients and our male patients. However, we did have a preponderance of female patients, so it might be that when we have more data we can make further comments about sex differences.

Regarding lymph node mapping at the Massachusetts General Hospital, again, we map people that are 1 mm or greater with the caveat that if somebody has very negative characteristics, significant ulceration, we would consider mapping even slightly less than that. It, too, is a continuum.

Responding to a technical question, we also use technetium only; we do not use the blue dye in our institution.

In response to a query by Dr. Bland, thickness was the principal determinant of badness in our melanomas. The numbers are somewhat small, but we found that histology did not seem to be as important independent of thickness.

Regarding Dr. Polk's comments about cost, in this era I think it is incredibly important to look at cost of surgical procedures. We do not have precise cost data available, but lymphatic mapping is an outpatient procedure done under local anesthesia. We believe, given the fairly high incidence of occult nodal disease in these patients and the high percentage of patients with melanomas of the foot that are in the hospital for several days, that intra-operative localization of the sentinel node will be cost effective because it will eliminate the need for unnecessary lymph node dissections.

We are preparing a study of our mapping, and we will take cost into account in part because of Dr. Polk's comments.

I would like to discuss Dr. Wanebo's comments on survival. In our study, we addressed surgical therapy primarily. We did look at outcome, and our average follow-up was about 17 months. The majority of patients that developed regional metastases or systemic disease did die of their disease.

Regarding the learning curve in sentinel mapping, there are about 200 patients that we have mapped at the Massachusetts General Hospital, and we were able to see, just in the three and a half years that we have been doing this, a very severe learning curve because it is difficult initially to find the sentinel node, but with more experience it can become quite simple.

Finally, I would like to address an important question from Dr. Bland. Our data do suggest that narrower margins (for instance, less than 2 cm) may be just as effective, even for thicker lesions. Currently, our numbers are too small to be certain.

I would like to thank the Southern Surgical Association for the privilege of closing our paper.