

Clinical Science

Association of sentinel lymph node diameter with melanoma metastasis



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Abstract

BACKGROUND: Lymph nodes are an important part of the immune system and the size of the lymph node reflects local immunologic activity. The purpose of this study was to examine the association between sentinel lymph node (SLN) size and the presence of nodal metastasis in patients with melanoma.

METHODS: Retrospective review of a prospectively maintained database of patients undergoing SLN biopsy for cutaneous melanoma between February 1995 and January 2013. The maximum pathologic diameter and the volume of the largest node was used. A nodal diameter of 1.5 cm, included in 2 interquartile ranges of both positive and negative SLNs, was used as the cutoff for multivariate regression.

RESULTS: Of 1,017 SLN biopsies, 826 (81%) had complete size measurements and were included in the analysis. Patients with a positive SLN were younger (median 50 vs 53 years, $P = .032$), had deeper primary lesions (2 vs 1.4 mm, $P < .001$), and had larger SLN volume (.8 vs .6 cc, $P = .009$) or maximum diameter (1.9 vs. 1.6 cm, $P = .03$). Sex, pathologic ulceration, mitosis, and the type or location of the primary was not statistically different. On multivariate analysis; age, depth of primary, and both SLN volume and maximum diameter remained significant. An SLN greater than 1.5 cm in maximum diameter has a 60% increased odds ratio of being positive after adjusting for age, sex, and depth of primary lesion ($P = .046$).

CONCLUSIONS: Larger SLN maximum diameter is associated with nodal positivity independent of age, sex, depth of primary lesion, and location of SLN biopsy. The etiology and significance of larger SLNs warrant further analysis.

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The incidence of melanoma is increasing throughout the United States and in many parts of the world with some reports suggesting it is the fastest growing cancer in men, and the 2nd fastest growing cancer in women.^{1,2} The global economic impact of the disease is substantial.³ While efforts aimed at earlier detection and the development of

new effective treatments have helped reduce the overall mortality, there still remains a need for improved methods of predicting which patients benefit most from specific interventions.⁴ Sentinel lymph node (SLN) biopsy is considered standard of care for selected patients based on the risk associated features of the primary lesion such as size, depth, regression, ulceration, mitotic rate, and lymphovascular invasion of the primary tumor.⁵⁻⁷ In addition, the SLN status is an important indicator of the risk of metastasis to additional lymph nodes in the regional basin and beyond. It provides important staging information, is a crucial prognostic indicator of survival and assists in determining subsequent steps in patient care.⁷⁻⁹

It has been hypothesized that lymph nodes act as gatekeepers of the immune system, and that increased lymph node size is an indication of greater regional immunogenic activity.¹⁰⁻¹² In cancer patients, lymphadenopathy (either clinical or radiographically), is often associated with an increased likelihood of lymph node metastasis.¹³ The response evaluation criteria in solid tumors (RECIST) guideline states the cutoff for a pathologically enlarged lymph node to be 1.5 cm in dimension.¹⁴ Despite these general rules regarding size of lymph nodes, there are limited data evaluating the actual size of the SLN and its relationship with the presence or absence of nodal metastasis.

The SLN status is critical for staging, prognosis, and has an enormous impact in determining the next steps in treatment, management, and expected outcome.^{15,16} Immunologic activity and inflammation influence nodal size. It is also assumed that the immune system plays an important role in cancer development and prevention. The size of the SLN may carry additional meaningfulness, as it may reflect the immunogenicity of melanoma, represent a surrogate for aggressiveness of the tumor, or even reflect an ineffective or nonspecific immune response. If the size of the SLN carries significant prognostic information, perhaps it could play a role in the algorithm in management of melanoma after tumor excision. This may be especially important for patients with a small melanoma less than 1 mm, where controversy exists as to when an SLN biopsy is warranted.^{17,18} SLN size and its association with nodal involvement could be helpful combined with other predictive variables to assist in decision-making for performing an SLN biopsy. In light of this background, the purpose of this study was to determine if there is a relationship between size of the SLN and melanoma metastasis in the regional basin.

Methods

A retrospective review of an institutional prospectively maintained institutional review board approved database of patients undergoing SLN biopsy for cutaneous melanoma between 1995 and 2013 was reviewed. Patient selection included melanoma patients at the University of Colorado who underwent an SLN biopsy at our institution. This

included many patients who underwent initial excision of the primary tumor at an outside hospital, who were subsequently then referred to the institution. In general, an SLN biopsy was recommended based on National Comprehensive Cancer Network recommendations. Exclusion criteria were those patients who did not undergo an SLN biopsy, those with previous procedures or resections in the nodal basin in question, and those that did not have size/volume measurements in our records.

Key variables were extracted including the patients' age, sex, melanoma characteristics (including type of melanoma, site of melanoma, depth of primary lesion, location of primary lesion, presence of ulceration, mitosis, lymphovascular invasion, regression), number of SLNs, and length/width/height measurements of the largest SLN excised. Volume of the lymph node was calculated by approximating the volume of an ellipsoid, which is $V = 4/3\pi abc$, where a = radius of the width, b = radius of the length, and c = radius of the height. See Fig. 1. The key outcome that we looked at was the presence of cancer in any (one or more) of the SLNs biopsied. The pathology department at the University of Colorado evaluated and reported on all lymph nodes. The length, width, and height measurements were taken after the lymph nodes had been fixed in formalin but before being placed in cassettes for cutting.

Statistical analysis was completed using STATA 13 (StataCorp. 2014. Stata Statistical Software: Release 13; StataCorp LP, College Station, TX). Descriptive statistics were reported as a median with corresponding interquartile range unless otherwise specified. A univariate and multivariate logistic regression analysis was completed using SLN metastasis (yes/no) as the binary outcome. Independent variables used for the adjusted multivariate analysis included age, sex, depth of primary tumor, and location of lymph node biopsy.

Results

There were a total of 826 patients included in our study who underwent an SLN biopsy during the study period. We found 677 (82%) patients had a negative SLN compared with 149 (18%) with a positive SLN on biopsy. The median age for the negative and positive SLN groups were 53(43 to 61) and 50 (38 to 59) respectively. This was a statistically significant difference ($P = .032$). There was no significant difference in sex between the groups. Further details of melanoma type and location can be found in Table 1.

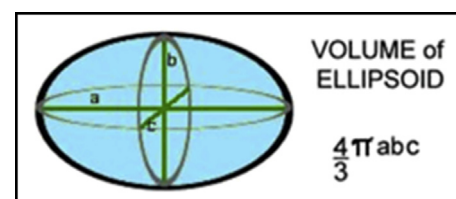


Figure 1 Formula for calculating the volume of an ellipsoid.

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