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Review

Utility of sentinel node biopsy in patients with high-risk cutaneous squamous cell carcinoma

J.E. Allen [a,*], L.B. Stolle [b]

[a] Department of Plastic Surgery, Aarhus University Hospital, Aarhus, Denmark
[b] Department of Plastic Surgery, Odense University Hospital, Odense, Denmark

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Abstract

Background: Currently there is no consensual agreement on the standard use of Sentinel Lymph Node Biopsy (SLNB) in staging of high-risk patients.
Objective: The objective was to define the predictive value and role of SLNB combined with the different high-risk factors to determine which patients could benefit from SLNB.
Method: We conducted a review of the literature on cutaneous squamous cell carcinoma (SCC) and SLNB published in the year 2000 until May 2012. 173 patients with SCC tumors and SLNB were found. Risk factors were listed along with lymph node status. Sensitivity, specificity and negative predictive value (NPV) were calculated for the cumulative results for each risk factor.
Results: Sensitivity for the total cohort was 79%, specificity was 100% and negative predictive value was 96%. The sensitivity, specificity and NPV were 78.26%, 100% and 95.14%, respectively, for tumor size >2 cm. Sensitivity, specificity and NPV for a tumor localized at a high-risk area were 72.63%, 100% and 96.74%, respectively. Specificity was 100% as was NPV for immunosuppression.
Conclusion: SLNB has a high NPV and low false negative rate and carries a low risk of complications. SLNB may prove to enhance the survival or aid the prognosis of high-risk cSCC. Further, detailed investigations and longer follow-up times are needed to define the right group of patients that could benefit from this procedure.

Keywords: Cutaneous squamous cell carcinoma; Sentinel lymph node biopsy; High-risk factors; Review

Introduction/background

Cutaneous squamous cell carcinoma is overall the second most common skin cancer worldwide and the incidence is rising. The prognosis is generally favorable with an overall metastatic rate of 5% and the disease is generally curable with surgical therapy.[1] However, a small subset of cutaneous squamous cell carcinoma is characterized by aggressive behavior, increased risk of metastasis and lower survival. Risk factors for metastasis include tumor size, localization, Clark level IV and above, poorly differentiated histological subtype, immunosuppression, and perineural invasion.[2] Patients with lymph node metastasis have a 5-year survival ranging from 26 to 34%[1]

The utility of sentinel lymph node biopsy (SLNB) in staging of melanoma is well established as an independent prognostic factor for survival and has proved to prolong the disease-free survival.[3–5] It has yet not shown to improve the overall survival but SLNB is still widely accepted as a minimally invasive procedure with high accuracy for detection of nodal metastases and as a diagnostic tool. Several authors have examined the utility of SLNB as a method for staging patients with non-melanoma skin cancer who are at high risk for metastasis.[1,2,6] These studies suggested that it might be useful in patients with high-risk

* Corresponding author. Department of Plastic Surgery, Aarhus University Hospital, Noerrebrogade 44, 8000 Aarhus, Denmark. Tel.: +45 29256829.
E-mail address: julieeallen@hotmail.com (J.E. Allen).

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cutaneous squamous cell carcinoma. Cherpalis et al. suggest that patients with lymph node metastasis may be cured by lymph node dissection and radiotherapy and SLNB would therefore be an important staging tool and in planning the right treatment for patients with high-risk cSCC.

There is no consensual agreement on the standard of staging practice for the high-risk patients or any consensus on which patients could benefit from the procedure.

We performed a review of the literature on high-risk cutaneous squamous cell carcinoma and SLNB to define the predictive value and role of SLNB combined with the different high-risk factors. We sought to determine the characteristics of cutaneous squamous cell carcinoma that predict a positive sentinel lymph node/metastasis. This could obviate a full lymphadenectomy in SN negative patients and ensure early intervention for the patient with occult metastases.

Method

We conducted a review of the literature on cutaneous squamous cell carcinoma and sentinel lymph node biopsy published in year 2000 until May 2012. The search was limited to English literature. PubMed was searched using the following search words: *immunosuppression, squamous cell carcinoma or skin squamous carcinoma or cutaneous squamous cell carcinoma, and lymph node dissection or sentinel lymph node*. A search in PubMed, Embase and Cochrane databases was conducted using the following Mesh terms: *Sentinel lymph node biopsy or sentinel lymph node excision, immunosuppression or immune-compromised host or organ transplantation and squamous cell carcinoma*.

Studies regarding anogenital, lung, esophageal, oral, or burn wound squamous cell carcinoma were excluded.

77 articles were screened and reference lists were reviewed to include other relevant articles. 103 articles were reviewed and studies were only included if SLNB was performed and the article contained information about the patient and pathology of the tumor. 13 cohort studies and 7 case reports, altogether 173 patients with SCC tumors and sentinel lymph node biopsy.

The patients were pooled and listed for the following risk factors and their SLNB result; tumor size >2 cm, localization in head and/or neck, Clark level, immunosuppression, perineural invasion, ulceration and histological subtype (low, moderate or high differentiation), the last being known to be a high-risk factor, why we only included the low differentiated of the three.

The diagnosis of cSCC was verified on histological examination of the tumor. All patients in our study underwent preoperative lymphoscintigraphy using technetium-labeled tracer and a hand-held probe was used peroperatively to locate the sentinel node. The sentinel nodes were stained with conventional hemotoxylin-eosion staining.

Sensitivity, specificity and negative predictive value (NPV) were calculated for the cumulative results for each risk factor. Sensitivity, measuring the proportion of actual positive SLNB and correctly identified as such and specificity, measuring the proportion of negative SLNB which is correctly identified as such. NPV describes the performance of the procedure and defines the proportion of subjects with a negative SLNB who are correctly diagnosed. Recurrence in the SLNB-negative biopsied nodal basins was defined as false negative and used to estimate the SLNB failure rate. The accuracy of the sentinel lymph node could not be assessed since completion of lymph node dissection was not preformed following negative SLNB.

Results

173 patients were included in the study altogether. Sensitivity for the total cohort was 79%, specificity was 100% and negative predictive value was 96.1%. Please see Table 1. 3.5% were false negative SN. 121 patients out of the 173 were described as having a tumor size >2 cm. There were five false negative SLNB where the patients initially had negative nodal status, but within a mean of 11.5 months developed nodal metastasis. The high-risk areas included ear, nose, lip, head and neck and the total number of patients meeting these criteria was 100. There were three false negatives in this group. The histological subtype was divided into high level of differentiation,

Table 1
The cumulative results of SLNB for high-risk cSCC.

Risk factors	Sensitivity	Specificity	NPV	*n*	False neg. rate	Follow-up months	References
Tumor >2 cm	78.26%	100%	95.15%	121	4%	32.2 (1–81)	1,3–5,10,13,14,16–19,21,22,24–27
High risk areas	72.73%	100%	96.74%	100	3%	38.9 (2–72)	1,3–5,13,14,17,19,21,24–26
Low differentiation	66.64	100%	88.24	42	9.5%	36.8 (4–72)	1,3,4,10,13,14,17,19,21,24
>Level IV	76.47%	100%	95.12%	95	4.2%	35.2 (1–72)	3–5,13,14,16–19,21,22,25,27
Immunosuppression	–	100%	100%	6	0	19.3 (4–44)	1,12,21,26
Perineural invasion	50.00%	100%	88.89%	10	10%	36.0 (1–72)	1,10,13,21,26
Ulceration	75.00%	100%	85.74%	10	10%	24.3 (6–72)	3,13,14,16,18,22,27

n = number of patients, false neg. rate = false negative rate.
NPV = negative predictive value = number of true negative/(number of false negative + number of true negative).
Sensitivity = number of true positive/(number of true positive + number of false negative).
Specificity = number of true negative/(number of true negative + number of false positive).