
Factors associated with large cutaneous squamous cell carcinomas

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Background: Large cutaneous squamous cell carcinoma (SCC) is associated with a higher risk of disfigurement, local recurrence, and metastasis; however, little is known about factors associated with tumor size at diagnosis.

Objectives: We sought to evaluate factors associated with SCC size, including diagnostic/treatment delay and patient and tumor characteristics.

Methods: We studied a stratified sample of 308 patients with SCC recently treated at a dermatologic referral center in Italy. Medical records were reviewed and telephone interviews conducted. Multiple logistic regression was used to examine factors associated with SCC size.

Results: With univariate analyses, among both invasive and in situ cases, SCC greater than 2 cm was significantly associated with male gender, tumors arising in chronic lesions, and tumors located on not easily visible sites. Long delay before surgical removal was significantly associated with large SCC size only for invasive SCC ($P < .001$). Among patients with invasive SCC, when controlling for age and gender, multivariate analysis showed a significantly higher likelihood of SCC greater than 2 cm with a total delay longer than 18 months before surgical removal (odds ratio = 4.18; 95% confidence interval 2.45-7.13) and for tumors arising in chronic lesions (odds ratio = 6.42; 95% confidence interval 3.13-13.2).

Limitations: The study was cross-sectional and based on a single center.

Conclusions: Long total delay in removal significantly increased the likelihood of invasive SCC greater than 2 cm. Our findings highlight the importance of early detection and treatment to prevent large invasive SCCs, which are associated with a higher risk of disfigurement, recurrence, and metastasis. Particular attention should be paid to chronic skin lesions and not easily visible body sites during physician- and patient-performed examinations. (*J Am Acad Dermatol* 2010;63:404-11.)

Key words: cutaneous squamous cell carcinoma; delay; lesion size; skin cancer.

Cutaneous squamous cell carcinoma (SCC) is the second most frequent skin cancer, and it is associated with relevant morbidity and

Abbreviations used:

CI: confidence interval
OR: odds ratio
SCC: squamous cell carcinoma

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costs.^{1,2} In the majority of cases, cutaneous SCCs cause only local disease. However, advanced disease can result in significant tissue destruction and facial disfigurement, requiring major plastic surgery with potentially serious psychologic and functional consequences, and negative effects on the patients' quality of life.^{3,4} In addition to local infiltration and tissue destruction, some higher-risk SCCs can also metastasize.^{5,6} Among patients with operable, metastatic cutaneous SCC of the head and neck, the 5-year

disease-free survival is 70% to 75%, despite treatment.⁷ Factors associated with a higher risk of local recurrences and metastases include lesion diameter greater than 2 cm, SCC arising on chronically diseased skin, and immunosuppression.^{1,5,6} Preventing the occurrence of larger SCCs can be important for reducing the risks of disfigurement, local recurrences, and metastases, with a potentially positive impact on morbidity, mortality, and costs. There are extremely limited data on factors associated with larger lesions among patients with SCC. Studies on factors associated with the extent of tumor invasion at diagnosis, examining also diagnostic and treatment delay, have regarded mainly cutaneous melanoma.⁸⁻¹² Only one previous study included 48 cases of cutaneous SCC in addition to other keratinocyte carcinomas,¹³ showing that anatomic site, histology, age, gender, and patient self-reported delay were associated with defect size. These findings are, however, referred to the total sample of keratinocyte carcinomas, with SCCs representing a relatively small subgroup. The objective of our study was to evaluate factors associated with larger SCCs, including delay in diagnosis and treatment, and patient and tumor characteristics.

METHODS

The study is part of a wider project on the diagnostic and treatment patterns regarding SCC. As previously described,¹⁴ we reviewed medical records of patients recently treated for SCC, extracting clinical and pathology data, and combined them with patient telephone interviews. Among the 2179 patients with SCC treated between June 2004 and February 2006 at our hospital, a dermatologic referral center for central and southern Italy, 1895 patients had the necessary baseline information and fulfilled the inclusion criteria, ie, age 18 years or older and histologically confirmed cutaneous SCC within the last 24 months. Exclusion criteria were: genital and oral SCC, keratoacanthoma, organ transplantation recipients, recurrent SCC, and physical/cognitive impairment preventing completion of the interview. We aimed at including a stratified sample of 340 patients. In particular, patients were stratified by SCC size; all 91 patients with cutaneous SCC greater than 2 cm in diameter, defined as "large SCC," and fulfilling the

inclusion criteria were eligible. Oversampling of this subgroup was aimed at ensuring a sufficient number of patients at higher risk. Among them, 69 patients completed the interviews, whereas 22 (24.2%) could not be interviewed as a result of refusal (n = 9), physical/cognitive impairment (n = 8), inability to contact the patient (n = 4), and death (n = 1).

Concerning all other patients with lesions less than or equal to 2 cm, we contacted a sample of 287 patients. Consecutive patients were contacted by telephone, starting every interviewing session with patients operated on during a different month among the 21 months covered by the survey. The first patients who could be reached, were willing to participate, and fulfilled the inclusion criteria were interviewed. Among patients with lesions less than or equal to 2 cm, 246 patients completed

the interviews, whereas 41 (14.3%) could not be interviewed as a result of refusal (n = 9), physical/cognitive impairment (n = 7), incomplete interviews (n = 3), and inability to contact the patient (n = 22). We excluded 4 patients with recurrent SCC and 3 organ transplantation recipients. Hence, the analyses are based on a total of 308 patients, including 238 SCCs less than or equal to 2 cm and 69 larger SCCs, with both groups spanning the 2-year study period.

Clinical and pathology information and date of surgical SCC removal were obtained from medical records. The remaining variables were obtained through patient interviews. For 27 patients operated on for more than one SCC within the last 24 months, the largest lesion was considered the index lesion (mean SCC number per patient was 1.2 [SD = 0.4]). Measurements were taken of the major diameter of the lesion.

The questionnaire was developed based on a literature review^{9,10,15-17} and included sociodemographic information and skin cancer history. For example, patients were asked: (1) Who noticed the lesion the first time? Answers: I noticed it myself; a relative or friend; a dermatologist; a general practitioner; another doctor; others (please specify); (2) When did you (or the person/doctor who first noticed the lesion) notice the lesion the first time? Approximate date; (3) Was the lesion noticed during a visit that included a routine skin examination?; (4) Was the lesion noticed during a medical visit for an

CAPSULE SUMMARY

- Total delay longer than 18 months before surgical removal was associated with invasive squamous cell carcinoma (SCC) lesions greater than 2 cm.
- SCCs arising in chronic skin lesions and those located on not easily visible sites were associated with larger SCC size at diagnosis.
- Considering that large SCCs have a higher risk of disfigurement, recurrence, and metastasis, early treatment is essential.

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