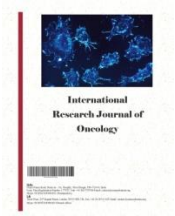

International Research Journal of Oncology

2(2): 107-113, 2019; Article no.IRJO.51568

The Management and Treatment of Skin Cancer – Are We Doing It Right?

J. O'Connor[1*], X. Du[2], B. Adabavazeh[2] and S. Hoque[2]

[1]King's College London, Guy's Campus, Great Maze Pond, London, SE1 1UL, United Kingdom.
[2]University Hospital Lewisham, Lewisham High Street, London, SE18 6LH, United Kingdom.

Authors' contributions

This work was carried out in collaboration among all authors. Authors SH and XD designed the study. Author JO performed the data collection, statistical analysis and wrote the first draft of the manuscript. Author BA reviewed analysis and amended the first draft. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. Guy-Armel Bounda, Department of Clinical Pharmacy, School of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University, China.
Reviewers:
(1) Francesca Gorini, National Research Council, Italy.
(2) D. Ramachandrareddy, Vinayakamission University, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/51568

Short Research Article

Received 28 July 2019
Accepted 30 September 2019
Published 09 October 2019

ABSTRACT

Objective: This study aims to identify whether the University Hospital of Lewisham is managing patients according to the published guidelines and to create local guidelines for the identification and management of squamous cell carcinomas.
Design: This was a retrospective cross-sectional standards audit of patients diagnosed with squamous cell carcinoma at the University Hospital of Lewisham. A total of twenty patients were chosen at random for this study (out of a total of 79) by the specialist registrar dermatologist using a random number generator. Patients were divided into low-risk, high-risk and not recorded risks of squamous cell carcinoma. The number of follow-ups and the duration of follow-ups per patient was recorded.
Main Outcomes and Measures: To determine whether high-risk and low-risk squamous cell carcinomas are being managed in line with up to date guidelines. This is measured by the number of follow-ups, the duration in months of follow up and the time between each follow-up appointment and appropriate definitive treatment.
Results: This study had a mean age of 75 at diagnosis of squamous cell carcinoma (range 55-92); 12 of these patients were male and 8 of these patients were female. 100% of patients received

**Corresponding author: E-mail: johanna.oconnor@nhs.net;*

appropriate definitive treatment. When comparing high-risk and low-risk squamous cell carcinoma patients using an unpaired t-test there was no statistical significance (p=>0.05) in the length of follow up, the frequency of follow-ups or the time between each follow-up appointment. Only 60% of patients followed up were provided education on self-examination.

Conclusions and Relevance: Management of patients diagnosed with squamous cell carcinomas at the University Hospital of Lewisham did not differ between high and low risk squamous cell carcinoma patients and therefore the department could reduce follow up appointments for patients with low risk squamous cell carcinomas.

Keywords: Squamous cell carcinoma; management; treatment; cancer; skin.

1. INTRODUCTION

Squamous cell carcinoma (SCC) is a malignant tumour of keratinocytes in the outer layer of the skin and is the second most common form of skin cancer after basal cell carcinoma. The overall prognosis for SCC's is good as >95% of the patient's present without metastases. However, in those that do, the five-year survival rate is poor with as little as 25% surviving after five-years [1]. There are several known causes of SCC's. The most common cause is ultraviolet (UV) radiation exposure which is found naturally in sunlight and artificially in tanning beds [2]. In particular, UVB radiation causes mutations in the p53 tumour suppressor gene which is an important step in tumour progression [3]. Certain skin types are more susceptible to UV radiation than others. A scale by Thomas B. Fitzpatrick was developed in 1975 based on a person's skin colour and ability to tan. Those that had less epidermal melanin and greater susceptibility to burning rather than tanning (Fitzpatrick Type 1) had the greatest cancer risk compared to those with high levels of melanin who never burn in sun exposure (Fitzpatrick Type 6) [4,5].

People who are immunocompromised are also at an increased risk of developing an SCC. Certain medications used for immunosuppression such as calcineurin inhibitors (cyclosporine and tacrolimus), azathioprine, mycophenolic acid and prednisolone increase patients risk of developing SCC's [6]. Thus, cutaneous SCC's are the most common cancer in organ transplant patients [7].

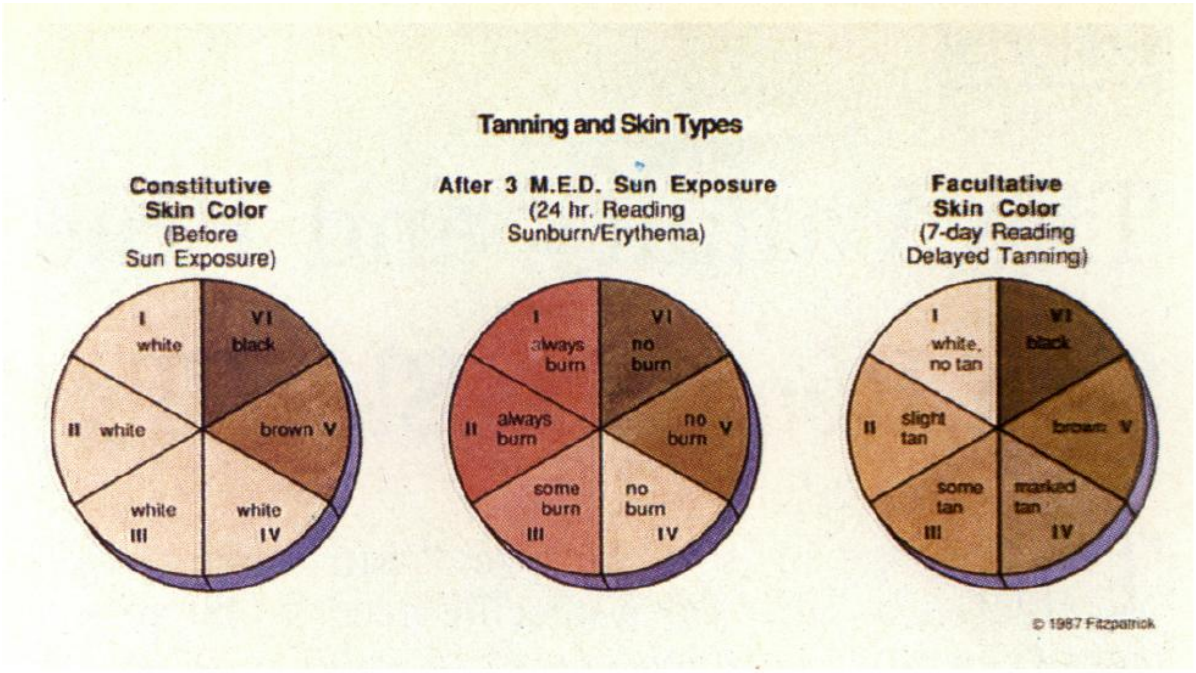

Fig. 1. Fitzpatrick scale of skin types, a scale before sun exposure, whether the skin type burns or tans and the resulting skin colour produced [4]

Other risk factors include chronic inflammation, such as those seen in chronic ulcers, burns, and scars. As well as, ionizing radiation therapy, arsenic exposure, human papillomavirus (HPV), polycyclic hydrocarbons and genetic disorders such as albinism and xeroderma pigmentosa.

It is important to identify high-risk SCC's which require more aggressive management amongst low-risk SCC's which make up the majority of presentations. Guidelines by the British Association of Dermatologists (BAD) in 2009 list several risk factors for high-risk SCC's [6]. These include site, size, depth/invasion, histology, immunosuppression and previous treatment (more details are provided in Table 1). The Scottish Intercollegiate Guidelines Network published guidelines in 2014 which include similar criteria to the BAD guidelines of 2009 (for more details, see Table 2).

The BAD and SIGN guidelines (above) are made up in part by the 7th edition tumour-node-metastasis (TNM) cancer staging system derived by the American Joint Committee on Cancer (AJCC) in 2010. However, in 2017 the AJCC released the 8th edition of their TNM cancer staging system which has significant changes [8]. The AJCC suggests that clinicians must now state the maximum clinical dimensions of every potential invasive skin cancer and that the anatomical site and tumour differentiation no longer influences SCC staging [9]. The updated staging also reflects epidemiological research demonstrating perineural invasion as a strong indicator of metastasis risk. These changes are likely to be incorporated into updated guidelines by the BAD and SIGN, although no new guidelines have been released yet.

The current TNM cancer staging system is divided into three categories, tumour, node and metastasis. Once a tumour has been biopsied it can be classified based on its thickness and ulceration status (whether the skin over the tumour looks broken). The 'T' category is from T0 (no tumour) to T4 (tumour thickness >0.4mm) and can be either of an 'a' or 'b' category, i.e. non-ulcerated or ulcerated respectively. The 'N' category is determined by metastatic spread to regional lymph nodes and whether there is a presence of in-transit satellite and/or microsatellite metastases. The level of node staging is from N0 (no regional metastases) to N3 (four or more tumour involved nodes and/or two or more nodes with the presence of in-transit satellite or microsatellite metastases). The 'M' category indicates whether the tumour has distant metastases and imaging is essential. Distant metastases range from M0 (no evidence of distant metastasis) to M1 (evidence of distance metastasis). It is further categorised

Table 1. Risk factors for high-risk squamous cell carcinomas as described by the British association of dermatologists [10]

Risk factors	Description
Site	In order of metastatic potential: lip, ear, non-exposed areas (e.g. perineum), areas of radiation or thermal injury
Diameter	Tumours greater than 2 cm
Depth and level of invasion	Tumours greater than 4mm in depth or beyond the subcutaneous tissue
Histological differentiation and subtype	Broders grades 3 and 4 (poorly differentiated)
Host immune suppression	
Previous treatment	

Table 2. Risk factors for high-risk squamous cell carcinomas as described by the Scottish intercollegiate guidelines network [1]

Risk factors	Description
Site	The ear is the highest risk tumour site in patients followed by scalp, neck, nose and lip
Diameter	Horizontal diameter >20 mm
Depth and level of invasion	Tumours greater than 4mm in depth or beyond subcutaneous tissue, very high-risk tumour if depth >6 mm. Perineural invasion. Lymphovascular invasion.
Histological differentiation and subtype	Desmoplastic subtype and poorly differentiated tumours
Host immune suppression	
Previous treatment	

from 'a' to 'd' based on the site (e.g. soft tissues, lung, non-central-nervous-system sites and central nervous system) as well as by lactate dehydrogenase (LDH) levels, with 0 being not elevated and 1 being elevated. Thus, cancer staged as T4a N3 M1a(1) describes a tumour which has a thickness of >0.4 mm and has not ulcerated, has spread to four or more regional lymph nodes and has metastasised to either skin, soft tissue or a regional lymph node with a raised LDH. For more information on the staging system please refer to the original cancer staging manual (AJCC).

While there have been changes to the guidelines determining the metastatic potential of SCC's, management of low-risk SCC's and high- risk SCC's remains the same. The gold-standard treatment for SCC's is surgical excision with Mohs' micrographic surgery deemed more suitable for high-risk SCC's. Low-risk SCC's are susceptible to a wider range of treatments which include curettage, cautery, cryotherapy and radiotherapy [11,1]. After treatment, SIGN guidelines suggest follow up for high-risk SCC's should be offered every three to six months, over 24 months. For some high-risk SCC patients (as determined clinically by dermatologists) may require a final appoint-ment at three years. The BAD guidelines are more conservative and suggest follow up for high-risk SCC's to be between 2-5 years 11. However, follow up for low-risk SCC's requires only one appointment in which patient education in self-examination and skin cancer prevention should be addressed (if it hasn't already been done).

This study aimed to determine the clinical management of SCC's in the University Hospital of Lewisham and to create guidelines for the trust.

2. METHODS

The inclusion criteria for this audit were all patients diagnosed with an SCC in 2014 who were managed at the University Hospital of Lewisham (UHL). The total number of patients who met these criteria were 79, of these patients, 20 were selected at random by the specialist registrar using a random-number generator and data was collected from both paper and electronic documents. Data included: patient age, gender, referral date, details of SCC, whether the risk was recorded, the number of appointments, the date, and type of treatment, the histopathological report, and documentation of whether self-examination education was provided. Grading of SCC's in this study was performed based on the BAD and SIGN guidelines as well as the 7th edition TNM cancer staging system by the AJCC. Patients were determined to have undefined SCC's when insufficient data was provided in paper / electronic documents.

Written informed consent was not required as patient data has not been used in this article.

Lewisham and Greenwich Trusts and the University Hospital of Lewisham approved this audit.

3. RESULTS AND DISCUSSION

Of the 20 patients audited, 13 patients had high-risk SCC's, 5 patients had low-risk SCC's and 2 patients had undefined SCC's. The mean age at diagnosis of SCC's in these patients was 75 with a range from 55-92. Overall, the average number of follow-ups for patient's post-treatment was 10.9. The average number of months patients were seen in follow up dermatology clinics was 20 and the average time between appointments was 2.6 months. In patients defined as high-risk, the average number of follow up appointments post-treatment was 13, the average time between appointments was 3 months and the average number of months seen in follow up by the dermatology clinic was 24 months. The average number follow-ups for low-risk patients' post-treatment was 10.6. The average number of months low-risk patients were seen in the dermatology clinic was 30 and the average time between appointments was 2 months. An unpaired t-test showed an insignificant difference ($p=0.97$) when comparing high-risk patients and low-risk patients for the average number of follow-ups, the average number of months patients were seen post-treatment and the average time between appointments. A comparison between high-risk and low-risk SCC patients can be seen in Fig. 2.

In all the patients reviewed not a single patient had the risk of their SCC documented. Written records suggested that 12 out of 20 patients (60%) were provided self-examination and instruction sheets, and 0 out of 5 low-risk patients were reviewed once after treatment as per guideline recommendations.

All patients received appropriate definitive treatment in the form of surgical excision, curettage or Moh's surgery.

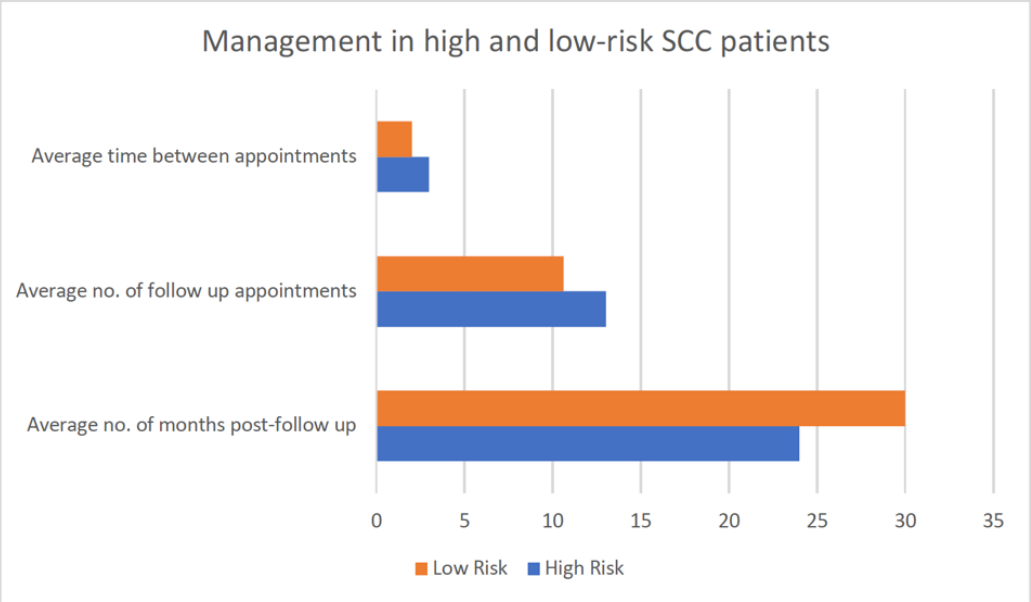

Fig. 2. A comparison in the management of high and low-risk squamous cell carcinomas (SCC's)

An unpaired t-test for each category was insignificant (p=>0.05)

Pathological stage (AJCC8)	High risk site? (ears, lip, non sun-exposed) Y/N	>20mm and >4mm depth? Y/N	Moderate or poor differentiation? Y/N	High risk individual e.g. immunmo-suppression? Y/N	SCC Risk (High if Y to any on checklist to left or AJCC8 T3 and above)

Follow-up guidance:

Risk of metachronous SCC	Lifelong follow up ~4-6-monthly
Low-risk SCC **EXCISED**	Discharge
Low-risk SCC **CURETTED**	1 follow-up review in 4-6 months
High-risk SCC **EXCISED or MOH's* or RADIOTHERAPY**	4-6 months for 2 years
	*High-risk Moh's SCC reviewed by Moh's Unit at 3 month point initially.

Fig. 3. A proforma for identifying high-risk squamous cell carcinomas based on the British association of dermatology guidelines (2009) and the Scottish intercollegiate guidelines network (2014) as well as the American Joint Committee on Cancer (2017) guidelines on cancer staging. SCC: Squamous cell carcinoma; AJCC8: American Joint Committee on Cancer 8th edition

4. DISCUSSION AND CONCLUSION

In the United Kingdom, at least 260,000 skin cancers are treated every year and identifying, managing and treating skin cancer accounts for approximately 50% of dermatologist's workload [11]. Guidelines for the management of SCC's by BAD and SIGN require clinicians to identify the risk of SCC's. It was therefore surprising to find that the risk of a patients SCC was not documented for any of the patients reviewed in this study. The BAD and SIGN guidelines for the

management and treatment of SCC's depends heavily on identifying the risk of metastatic potential to ensure that patients at high-risk are followed up and treated more aggressively than those at low-risk. Treatment for low-risk SCC's includes surgical excision (the gold standard) as well as other methods such as curettage and cryotherapy. Treatment for high-risk SCC's requires radiotherapy or surgical excision and Mohs micrographic surgery is an effective treatment [12,13].

After appropriate treatment, patients are followed up by the dermatology clinic depending on their risk of metastasis. For high-risk SCC's patients follow up should be for at least 24 months with the time between each appointment being 3-6 months. In UHL, high-risk SCC patients were being managed in line with guidelines set out by the BAD and SIGN. However, the management of low-risk SCC patients was similar to high-risk patients with no statistical significance in the number of follow-ups or the length of follow-ups post-treatment. Identifying and documenting patients as being low-risk at diagnosis may have assisted in highlighting patients who would not need such close follow-up. This means that extra resources are being used unnecessarily in low-risk patients as they require a maximum of one follow-up. Of those that are followed up only 60% of appointments were documented to include patient education on self-examination, an important tool in catching reoccurrence in patients early. Given the resource challenges, it is particularly critical to ensure that patients are triaged appropriately and clinic space is allocated according to clinical needs.

At a time when the National Health Service (NHS) is short of 177 dermatologists (in England alone), we must try to use our resources carefully, especially as Health Education England is simultaneously reducing specialty training posts [14]. The findings of this study prompted the update of the multi-disciplinary team skin cancer proforma to assess and record SCC risk, which is reflective of previous guidelines and the AJCC 8th edition of TNM cancer staging, Fig. 3. While the SIGN and BAD guidelines are yet to be updated, both sets of criteria (BAD, SIGN and AJCC 8th edition) have been used in this guideline in an attempt to catch all high-risk SCC's.

This proforma may be useful in other trusts within the U.K. to help multi-disciplinary skin cancer teams stratify SCC risk and arrange patient follow-up accordingly. This proforma can also be easily adapted once new guidelines have been produced. A further audit in five years will be necessary to determine whether the proforma was useful in improving management and reducing unnecessary follow-ups in low-risk SCC patients at UHL

CONSENT

As per international standard written participant consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard informed and written ethical permission has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/51568