Surgical Treatments of Non-Melnaoma Skin Cancers: A Review

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Citation

M Amjadi, B Coventry, J Greenwood. *Surgical Treatments of Non-Melnaoma Skin Cancers: A Review*. The Internet Journal of Plastic Surgery. 2010 Volume 7 Number 2.

Abstract

Background Non-melanoma skin cancers (NMSC) are the most common cancers diagnosed in Australia*. The most common forms of NMSC are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). The continuing rise in the incidence of NMSC will translate to greater need for surgical interventions. Objective*
This article aims to review the current literature regarding excisional surgical treatments of NMSC.
Data sources A review of all literature using databases of Pubmed and Medline searching for keywords of 'skin' or 'cancer' or 'surgery' was carried out.
Review methods All the titles and abstracts of all articles found were searched and relevant articles were selected. A further review of all the references mentioned in the selected studies was carried out and all relevant articles were added to the database. Results Although early or superficial NMSC can be effectively treated with topical agents[ii] [iii], there are numerous factors that call for surgical management[iv]. Broadly 'surgical' approaches include surgical excision, curettage, electro-desiccation, cryosurgery, and Mohs micrographic surgery (MMS). Surgical excision, curettage, and MMS are treatments that have the advantage of including histological evaluation. Conclusions Surgical management of NMSC remains the most reliable and the most convenient method of treatment of simple NMSC. The operator needs to remain mindful of the limitations of this modality. The surgeons who maintain an interest in this field should remain abreast of the developments in diagnostic technologies as well topical and non-excisional treatment modalities which are in use by our colleagues in dermatology. AIHW & AACR 2004. Cancer in Australia 2001. AIHW cat. no. CAN 23. Canberra: AIHW (Cancer Series no. 28)[ii] Goette, DK. Topical chemotherapy with 5-fluorouracil. A review. J. Am. Acad. Dermatol. 1981; 4:633[iii] Love WE; Bernhard JD; Bordeaux JS; Topical imiquimod or fluorouracil therapy for basal and squamous cell carcinoma: a systematic review; Arch. Dermatol. 2009; 145: 1431-8[iv] Silverman MK; Kopf AW; Grin CM; Bart RS; Levenstein MJ; Recurrence rates of treated basal cell carcinomas. Part 1: Overview; J. Dermatol. Surg. Oncol. 1991; 17: 713-8

In 2001, there were an estimated 256,000 Australians treated for BCC and a further 118,000 were treated for SCC [1] using surgical treatments. These cancers are usually diagnosed and treated outside hospitals by general practitioners and dermatologists and in skin cancer clinics [2], but they are not legally notifiable and are not routinely registered by all states and cancer registries. Moreover, many BCC and SCC are treated using cryotherapy, and are not reported histologically, signifying that the incidence of these cancers is perhaps two-fold higher or more. Operator preference, patient preference, need for histological diagnosis, site of lesion, desire to control spread, cosmetic considerations, and failure of prior non-surgical therapy are all features that call for surgical management. Successful surgical excision of the tumour is often determined by complete histological excision of the neoplastic lesion together with a margin of clinically normal surrounding tissue. The peripheral and deep surgical margins of the excised tissue can be examined histologically using formalin fixed postoperative vertical sections or intra-operative frozen section histology may be used if immediate results are required. Wider surgical margins may be used for diffuse primary, incompletely excised, or recurrent lesions.

A review of all literature using databases of Pubmed and Medline, searching for keywords of 'skin' or 'cancer' or 'surgery' was carried out. All the titles and abstracts of articles found were searched and relevant articles were selected. A further review of all the references mentioned in the selected studies was carried out and all relevant articles were added to the database. All selected articles were reviewed and categorised into groups based on the technique

or the technology being investigated.

MOHS MICROGRAPHIC SURGERY

MMS is a technique that aims to optimise control of the tumour margins. Under local anaesthesia, the tumour, together with a small rim of clinically normal tissue, is excised and microscopically evaluated. Histological findings from the surgical margins are correlated with the use of a diagram (Mohs map) [3]. If microscopic margins are positive, their locations are noted on the Mohs map and wider re-excision of that part of the involved margin is performed until all margins are negative [4].

MMS is associated with the highest rate of complete clearance of any treatment modality for many high-risk skin cancers, including basal cell carcinoma (BCC) [5]. MMS results in reported five-year cure rates of about 98 to 99% for primary BCC and 95% for more difficult recurrent BCC [6].

There are, however, some significant limitations to MMS. MMS was compared to standard surgical excision in a prospective trial in which 612 patients with BCC on the face (408 primary and 204 recurrent lesions) were randomly assigned to MMS or standard surgical excision [7]. This study suggested that the ultimate cure rates were similar with standard excision and Mohs excision. MMS is also significantly more expensive than standard surgical excision, and it has been shown not to be cost effective for broad clinical usage [8]. A typical MMS procedure lasts two to four hours and more complicated cases take longer. Reconstruction following MMS adds at least another hour to the procedure. A significant amount of the total time is spent with histological preparation and analysis; during this time, patients are temporarily bandaged, and are likely to need repeated administration of local anaesthetics during the length of the procedure. Sedation anaesthesia is used in some centres for some lesions, which may add to the overall cost. Moh's procedures are useful for selected cases, notably for body regions where wider excision is limited or cosmetically challenging, especially for difficult facial lesions, or for recurrent tumours.

SURGICAL EXCISION

Surgical excision is the other highly effective treatment modality for primary NMSC. Complete removal of 95 to 99% can be expected for 'low-risk' lesions using excision with margins of 2 to 5mm [9]. A lesion is defined as low-risk if it is less than 1.5cm in diameter, has not previously been treated, is not in a difficult to treat area, and is nodular or cystic [12 13].

Incomplete excision, where one or more surgical margins contain malignant tissue, has been reported to occur in 4 to 7% of cases [10]. Reliable interpretation of a histology report requires an understanding of how a surgical specimen is examined. Standard vertical section processing of the excised lesion allows the pathologist to examine representative areas of the margin, and it has been estimated that at best about 44% of the entire margin is typically examined, which may in part explain why tumours that were reported as 'completely or fully excised' occasionally recur [11]. Approximately 40% of incomplete primary BCC excisions have a single horizontal subclinical outgrowth over only 1–30 degrees of their periphery [12]. Detection of this is not always possible using standard sectioning. A survey of 11 pathologists in the United States found considerable variation in the routine processing of elliptical skin excisions [13]. Five used a single cross-section along the short and long axes, three took bread loaf sections across the short axis and three used a cross bread loaf (single section in long axis, multiple across the short axis). None routinely used peripheral sections, but four considered using them on larger excisions. The various methods of transverse sectioning provided efficient examination of the centre of the specimen, but incomplete examination of the margin. Complete sectioning of the entire excised tissue block is impractical and costly. Routine bread loaf sections are taken at no closer than 2mm intervals, providing examination of less than 1% of the margin [14]. This problem is compounded by a lack of uniformity in the use of the term 'close to the margin'. In the above-mentioned survey three pathologists used the term to describe tumour within 0.1mm, two less than 0.5mm and three greater than 1mm from the edge of the specimen [21]. Three studies accepted any histological margin greater than zero in examined sections, and had a high incomplete excision rate. It is likely many of these tumours would have appeared to be 'narrowly excised'. The resulting high recurrence rate demonstrates the increasing probability of undetected 'incomplete excision', as the histological margin becomes much smaller than the sectioning interval (approximately 2mm with conventional histological processing). The Royal College of Pathologists [15] has recommended that routine histological reporting should include the size of the minimum peripheral and deep margins in millimetres. This removes the ambiguity of the term 'close margins' used alone. An alternative is to routinely perform peripheral sections. Neither method has

become part of routine practice, which limits the accuracy of margin assessment. There has been no specific recommendation issued from the Royal Australasian College of Pathologists in this regard as yet, and the general consensus is to follow the recommendations of the Royal College of Pathologists as stet above. The current recommendations in Australia, based on now National Health and Medical Research Council (NHMRC) guidelines which have been recently rescinded due to technicalities but still recommended by the Australian Cancer Council, mention that 'The measured tumour margins should be included in the report particularly when the tumour extends closer to a border. Measured tumour depth may also be included in the report particularly in biopsies taken prior to radiotherapy. The presence of perineural vascular or lymphatic tumour invasion should also be included in the report. The validation of tumour clearance margins is partially dependent on the number of tissue blocks and sections examined when the conventional technique of bread loafing the excisional specimen is used. Using this technique infiltrative morphoeic and microlobular subtypes may have undetected extensions to surgical margins.' [16]

'Incomplete excision' typically reflects tumour spread beyond clinical observable margins. Sparse data exist on the correct recommended deep surgical margin. Studies using intra-operative histological examination of resection margins suggest that the excision of small (less than 20mm) 'well-defined' lesions with a 3mm peripheral margin will clear the tumour in 85% of cases. A 4 to 5mm peripheral margin will increase the peripheral clearance rate to approximately 95%, indicating that approximately 5% of well-defined NMSC extend over 4mm beyond their clinical margins. A larger margin is required for histologically aggressive subtypes of skin cancers with 13 to 15mm margins required for more than 95% clearance [17] . Two studies in particular have examined the histological presence of tumour within a 5mm margin of the clinically apparent tumour edge [18] . The mean histological margin was larger than the surgical margin (by 0.7mm), implying the true histological edge was usually beyond the marked clinically observable tumour edge. If an allowance for tissue shrinkage is added, as performed in the later study, the difference between these margins increases to 1.9mm.

Comparison of the two studies mentioned above suggests there is considerable variability in what clinicians identify as the tumour edge [25 27] . For example, peritumour inflammation was often mistaken for tumour, such that the true histological edge was effectively mistakenly overestimated during clinical marking. It is likely this difference largely accounts for the lower clinical surgical margin required in the earlier series to achieve 95% tumour clearance. Both studies imply a mean tissue sacrifice of more than 4mm to achieve 5% incomplete excision rate with postoperative margin assessment. Other relevant factors associated with incomplete excision include operator experience [19] , and anatomical site. Surgical excision of skin cancers on the head, which is the most common site for BCC, is less effective with increasing tumour size. The incomplete excision rate is approximately double for most head and neck skin cancers [20] , which indicates the usual margins should be increased by about 1mm in these body areas. The higher incomplete excision rate has been explained on the basis of selection of narrower margins for head and neck skin cancers and more extensive subclinical spread. The central facial area is a cosmetically important region and has little tissue, so surgeons may tend to use narrower margins with the resultant higher incomplete excision rate. There is also evidence for more extensive subclinical tumour spread. In 12,054 BCC excisions determined by histology and location, sent to a single dermatopathology laboratory, morphoeic BCC were much more common on the head and neck than the rest of the body [21] . The five-year cure rate for lesions less than 6mm in diameter in the head and neck region was 97%, as compared to a rate of 92% for lesions greater than 6mm in diameter in the same region [22] . Histological subtype of the tumour also influences the rate of recurrence after surgical treatment, with more aggressive subtypes associated with higher rates of recurrence [23] . Simple nodular BCC may have a more aggressive infiltrative component that is not clinically apparent. Clinical assessment of the tumour margin is more difficult for infiltrative, sclerosing, morphoeic and micronodular BCC. In a study of 1039 consecutive BCC submitted to a pathology laboratory, micronodular, infiltrative and morphoeic tumours were more than threefold as likely to be incompletely excised than nodular or superficial tumours [24] . Mixed tumours occurred in 38% of excisions and behaved like the more aggressive subcomponent. Unfortunately, the presence of an infiltrative or sclerosing component is not always identifiable preoperatively.

Various prospective and retrospective reviews of incompletely excised BCC suggest that not all tumours will recur. A completely excised tumour is not usually expected to recur. Tumour recurrence after histological clearance implies incomplete histological examination, local

metastasis, skip lesions, surgical seeding, or a new primary tumour. Most studies show that if a primary BCC and its microscopic contiguous extensions are completely excised as determined by complete peripheral and deep margin examination or thorough transverse sectioning with well clear margins, then recurrence occurs in less than 2% of excisions. Studies using approximately 2 to 5 years of follow-up have reported recurrence rates following incomplete excision of 30% to 41% [25] . Re-excision of incompletely excised lesions revealed the presence of residual tumour in 45% to 54% of cases when the tissue was examined using standard tissue sampling [26] . It has been suggested that some incompletely excised lesions may demonstrate a more aggressive histological subtype when the lesion recurs, especially on the central face [27] . The risk of recurrence appears highest in those lesions where both lateral and deep margins are involved and the incomplete excision is performed to remove recurrent lesions. There is good evidence to support a policy of re-treatment of incompletely excised lesions especially when they involve critical mid-facial sites, where the deep surgical margin is involved, the surgical defect has been repaired using skin flaps or skin grafts, and where histology shows an aggressive histological subtype [28] . Clinically, lesions on mid-face, those larger than 2 cm, long lasting or recurrent lesions are considered as aggressive. Histologically, lesions demonstrating features of morphoeic, infiltrative, or micronodular BCC; mixed tumours such as basisquamous tumours or so called ‘collision tumours’ of mixed NMSC and melanoma; and lesions with perineural, perichondrial, or perioseal involvement are considered to be aggressive. Patients with incompletely excised primary BCC should undergo surgical excision shortly after the initial procedure to confirm the presence of clear margins [42] . Such procedures result in improved cure rates and decrease the need for more complex excision of recurrent tumours. A recurrence rate of less than 2% has been reported 5 years following subsequent histologically complete excision of an incompletely excised primary BCC in two different series [29] . In practical terms, margins are often clearer to determine when scars are fresh and have not been obscured or have become ill-defined through maturation, in order to successfully re-excise close or tumour involved excision edges.

When tissue conservation is required, some form of histological margin examination should be performed prior to surgery. Clinical assessment results in the correct diagnosis of 59–90% of BCC [28] . Histological examination is a more reliable method of subcategorisation, but is often not performed prior to definitive treatment. A study reported preoperative biopsy prior to only 15% of definitive excisions [30] . It is important to recognize that excision of a BCC with a recommended 4 mm margin does not ensure both adequate excision and minimum tissue sacrifice. If the tumour border is carefully determined preoperatively and the recommended 4mm margin is added, then postoperative margin assessment will reveal that 75% of excisions could have been performed with a margin that was 2mm smaller; however, 5% of excisions will still be inadequate. A lower incomplete excision rate can be achieved but only at the expense of additional healthy tissue. Perhaps if surgical re-excision might prove difficult, then a wider initial margin may be appropriate. This is applicable for closures involving flap repairs or grafts. Such measures may also save the cost of further excisional surgery.

Surgical management of NMSC remains the most reliable and the most convenient method of treatment of simple NMSC. The operator needs to remain mindful of the limitations of this modality, and be aware of the range of treatment options, including non-invasive methods, which are currently available. The surgeons who maintain an interest in this field should remain abreast of the developments in diagnostic technologies as well topical and non-excisional treatment modalities which are in use by our colleagues in dermatology.

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