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Revision of margins under frozen section in oral cancer: a retrospective study of involved margins in pT1 and pT2 oral cancers

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Abstract

Operative assessment of the resection margins by frozen section is routine in many hospitals, but the usefulness of the technique relies on its sensitivity, specificity, sampling errors, and errors associated with relocation of involved margins. Its usefulness is indicated by assessment of overall survival and locoregional recurrence in patients whose margins were initially involved but were successfully revised after frozen section compared with those of the patients whose initially-involved margins were not revised. Patients with consecutive primary pT1, pT2 oral squamous cell carcinoma in whom initial resection resulted in involved margins were selected from the patients treated during the period January 2010 to December 2011 at a tertiary cancer hospital in India. The outcome of patients whose revision of margins after frozen section was successful was compared with that of patients who had "false negative" results after frozen section. Sixty-eight patients had involved margins after initial resection, of whom 42 (62%) had successful revision after frozen section (clear margins group). The remaining 26 patients (38%) had "false negative" results on frozen section, and had no further revision (invaded margins group). Local recurrence was more common in the invaded margins group, although not significantly so in this short retrospective series (p=0.08). The risk of death was greater in patients with local recurrence, hazard ratio (HR) 4.74 (95% CI 1.79 to 12.61, p=0.002). However, overall survival (p=0.73), incidence of locoregional recurrence (p=0.59) and neck recurrence (p=1.0), did not differ significantly between the groups.

Keywords: Margin revision; Frozen section; Oral cancer; pT1; pT2

Introduction

In the Indian subcontinent nearly half of all cancers are in the head and neck, and of these a third are oral cancer.[1] This is attributed to various forms of tobacco consumption such as bidi smoking, pan, gutka, and other chewable forms, and the patients often have associated oral submucous fibrosis with extensive field changes in the oral cavity.[2]

The airway, the degree of mouth opening, and the accessibility of the tumour are often challenging for the surgeon, who wants to achieve consistently clear margins. Invaded margins are 1.7 times more likely to be encountered in oral carcinoma than in other cancers of the head and neck,[3] so surgeons often rely on operative frozen section examination to confirm whether or not the margins are clear. This is one of the most important factors responsible for disease-free survival, and involved margins are associated with early recurrence.[4] Untreated involved margins always recur.[5]

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According to various authors, the incidence of close margins is up to 42%, and of involved margins is 1%-22%.[4–12] Lee[13] suggested that all these margins should be treated by reoperation.

The use of operative assessment of margins by frozen section may be beneficial, as an optimally-orientated resection specimen can make finding the site of an involved margin simple, and so preclude a second operation. Although assessment of margins by frozen section is accurate "false negative" results are possible, so the usefulness of frozen section depends on the error involved in "false negative" results, error in relocation of the involved margin by the surgeon, and the possible sampling error during processing of the specimen when the closest margin may not be sampled by the pathologist.

Most of the revised margins do not contain tumour. Perhaps an entirely different site was sampled, or there was inadequate clearance of the margins and the edge of the tumour might have been sampled by the pathologist in the second instance. Kerawala and Ong showed that an error of 1 cm was present in 23/71 (32%) of cases when they revisited the site of the tumour.[14] There is therefore a question about the further management of these patients - whether they should be given adjuvant treatment assuming that residual disease was present, or whether their margins should be classified as clear.

Patients with unrevised involved margins are usually treated by adjuvant chemoradiotherapy, whereas those whose margins were revised after being initially involved might not be. In this paper we retrospectively compare the outcome of patients with involved margins that were successfully revised after frozen section with that of patients whose involved margins were not revised.

Patients and Methods

We organised a retrospective study at a tertiary cancer hospital of patients treated surgically for oral cancer between January 2010 and December 2011 (IRB approval no IEC/2014/42).

A total of 563 patients were considered for the study. Patients with non-squamous cell carcinoma; residual, recurrent, or second primary tumours; carcinoma of the lip; and those with locally advanced disease (stage pT3 and pT4), were excluded. The selected group comprised 68 patients with primary pT1 and pT2 oral squamous cell carcinomas the margins of which were involved after initial resection. Specimens with microscopic tumour at the margins, together with those in which there was tumour within 1 mm of the cut margin, were considered to have involved margins. The median (range) follow up period was 24 (12–34) months.

The patients were divided into two groups, the first of which comprised patients with involved margins that were further revised under operative frozen section control until tumour-free margins were obtained (clear margins group). The second comprised patients who were said to have involved margins on the final histopathological report. These patients had had "false negative" reports for tumour at the margins at the operative frozen section examination, and final histological examination showed microscopic tumour at the margins that were not revised further (invaded margins group).

We use frozen section for assessment of margins routinely. Specimens are orientated and tagged by the surgeon before pathological examination. A minimum of five margins, which included four mucosal margins and one deep margin, were evaluated by frozen section in each case. Revision if tumour was found on frozen section was followed by a 5 mm excision of the respective margin, and the surgeon marked the surface of the margin away from the tumour for sampling by the pathologists.

Statistical analysis

Univariate analysis was used for categorical data using either Fisher's exact test or the chi square test as appropriate. Student's *t* test was used to assess the significance of differences in continuous data between groups. Variables associated with survival ($p < 0.10$) on bivariate analysis were further tested in a multiple Cox's regression model that adjusted for potential risk factors. The analyses were made with the help of SPSS software (version 17.0 for Windows, SPSS, Chicago, IL, USA). The tests were two-tailed, and probabilities of less than 0.05 were accepted as significant.

Results

Forty-two patients (62%) had successful revisions under frozen section control (clear margins group) and the remaining 26 (38%) had "false negative" results and were not revised further (invaded margins group) Their clinical details and results are shown in Table 1.

There was an overall significant association of stage of the disease with death ($p = 0.015$; chi square test for trend) (Table 2). The Kaplan-Meier survival analysis showed similar mortality in both groups by 24 months (range 12 months to 34 months) ($p = 0.65$; log rank test) (Fig. 1).

Discussion

Resection is the treatment of choice for oral cancer and, of all the prognostic factors, invasion of the margins is the most important in patients with early stage disease. Close margins are common, however, particularly in resections in the oral cavity. Byers et al[15] reported clear margins in only 67% of their 216 cases.

We retrospectively studied data from a tertiary cancer hospital to obtain information about the clinical usefulness of operative examination of frozen sections, and evaluated pT1 and pT2 oral cancers (in which the number of margins