Treatment and follow-up of oral dysplasia: a systematic review and meta-analysis

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CRD summary
This review examined the treatment and follow-up of patients with oral dysplasia and concluded that surgical excision decreased, but did not eliminate, the risk of malignant transformation. This appears to have been a well-conducted review, but given the scarcity of evidence on treatment effectiveness and the limitations with the included diverse studies, these findings should be interpreted with caution.

Authors' objectives
To examine treatment and follow-up in patients with oral dysplasia.

Searching
MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to June 2008. Search terms were reported and the reference lists of retrieved articles and relevant reviews, and personal reference lists were searched manually.

Study selection
Observational cohort and case-control studies of patients with a histologically confirmed diagnosis of oral dysplasia, who were followed-up for at least one year, were eligible for inclusion. Eligible studies had to report one of the following outcomes: rate of development to oral cancer (malignant transformation) and the time interval or duration to malignant transformation. Where full publications were not available, abstracts were eligible for inclusion, but the original authors had to be contacted. Studies of patients diagnosed with dysplasia, who also had synchronous cancer at diagnosis or identified within three months, were excluded.

Included studies were conducted in European countries, Taiwan, Japan, USA, and India. The majority of studies were conducted in a hospital setting and enrolled patients between 1963 and 2001. Where reported, the mean or median age of patients ranged from over 35 to 60.8 years, but these figures included patients with all oral leukoplakia lesions, not just those with confirmed dysplasia. Some patients were smokers and one study reported on alcohol consumption. Outcomes were assessed through medical records, biopsy, or questionnaires. Some patients underwent surgical excision, while others underwent non-surgical treatment, such as cryotherapy or laser therapy.

Two reviewers independently screened studies for inclusion.

Assessment of study quality
Two reviewers independently assessed the included studies, using modified criteria that were agreed before assessment and included items on blinding of outcome assessment, follow-up data, and attempts to address confounding variables. Disagreements were resolved by a third reviewer.

Data extraction
One reviewer and one statistician extracted malignant transformation rates to calculate percentages. A third reviewer checked the data extraction.

Prevalence rates of malignant transformation, and data on the effect of variables, such as dysplasia grade and clinical risk factors, were also extracted, but are not reported here.

Methods of synthesis
Malignancy transformation rate percentages were combined by treatment modality (surgical excision versus non-surgical excision) and adjusted for dysplasia grade (mild and moderate dysplasia versus severe dysplasia and carcinoma in situ).
Statistical heterogeneity was assessed through a visual inspection of a forest plot and 95% confidence intervals. A funnel plot was used to assess publication bias.

**Results of the review**

Six prospective and eight retrospective studies (n=992 patients; 341 surgical and 651 non-surgical) were included in the review. Sample sizes ranged from 13 to 166 patients, with most studies having less than 100 patients. None of these studies were blinded, only three reported that there was no sampling method bias, and seven reported an adequate follow-up rate (over 80%). The mean length of follow-up ranged from 1.5 to 9.3 years.

Patients who were treated surgically reported statistically significant lower malignancy transformation rates (5.4%) compared with patients who were treated non-surgically (14.6%), and this difference remained statistically significant after adjusting for malignancy grade (p=0.003). There was evidence of significant heterogeneity between studies and there was evidence of publication bias on visual inspection of the funnel plot.

**Authors’ conclusions**

Surgical excision decreased the risk of malignant transformation, but did not eliminate it.

**CRD commentary**

The review question was broad and did not specifically focus on treatment effectiveness. The supporting inclusion criteria for patients, outcomes, and study design were appropriate. An adequate search of the literature was undertaken, but it was unclear whether there were any language restrictions, which means that language bias cannot be ruled out. There was evidence of publication bias. The authors undertook each stage of the review in duplicate, thereby reducing the potential for reviewer error and bias. There was evidence of statistical heterogeneity, and the authors acknowledged the clinical and methodological heterogeneity among studies. The average percentages from pooled data from such clinically and statistically diverse studies might not be reliable.

In general, this appears to have been a well-conducted review, but given the scarcity of evidence on treatment effectiveness, the poor quality of the included non-randomised studies, and the heterogeneity, these findings should be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** The authors stated that even when treated by surgical excision, oral dysplasia appeared to have a significant transformation rate to oral cancer over a period of years and patients should be kept under surveillance for up to 20 years.

**Research:** The authors stated that further research was needed to evaluate the follow-up protocols for efficacy and cost-effectiveness, particularly to determine the surveillance duration and frequency. Further research was also needed to identify less invasive and more effective treatments, and to identify better prognostic markers for the transition from dysplasia to malignancy.

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