A META-ANALYSIS OF SURGICAL OUTCOMES OF INFRANOTCH T4B AND T4A ORAL CANCERS
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## SYNOPSIS

<table>
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<th>Title</th>
<th>A meta-analysis of surgical outcomes of infranotch T4b and T4a oral cancers</th>
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<tbody>
<tr>
<td>Short Title</td>
<td>Infranotch T4b vs T4a in OSCC</td>
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<td>Phase</td>
<td>NA</td>
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<td>Methodology</td>
<td>Systematic review and Meta-Analysis</td>
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<td>Study Duration</td>
<td>1 months</td>
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<td>Study Centre(s)</td>
<td>Single institute – All India Institute of Medical Sciences, Raipur</td>
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**Objectives**

**Primary:** To determine the overall surgical outcomes of infranotch T4b oral cancers.

**Secondary:** To analyse the difference in surgical outcomes between T4b and T4a oral cancers.

| Time frame | 2000 to 2022 |

**Main Inclusion Criteria and Exclusion**

1.1 Inclusion Criteria:

1.1.1 Treatment naïve oral T4b disease

1.1.2 Original articles published in peer reviewed journals

1.1.3 Study must report at least one risk factor - OS, DFS, DSS, or LC

1.2 Exclusion Criteria:

1.2.1 Non-human studies

1.2.2 Neoadjuvant chemotherapy / Radiation therapy prior to surgery

1.2.3 Any previous oncological treatment

1.2.4 Recurrent or second primary tumours

1.2.5 Not reported – post operative outcomes
### Infranotch T4b Vs T4a OSCC Meta-analysis

| 1.2.6 | Review articles, meeting abstracts, case reports, editorial letters, as well as other forms of publication |
| 1.2.7 | Incomplete data or insufficient information |
| 1.2.8 | Overlapping study populations, shared dataset |

#### PICO

| **Population** | Patients who having OSCC with T4a and infranotch T4b disease undergoing surgical resection of primary disease |
| **Intervention** | Primary resection of OSCC |
| **Comparison** | To determine the overall surgical outcomes of infranotch T4b oral cancers. To analyse the difference in surgical outcomes between T4b and T4a oral cancers |
| **Outcomes** | The overall surgical outcomes following T4b and to compare its outcomes with T4a cases Systematic analysis of difference in surgical outcomes between T4b and T4a oral cancer |

#### Database

PubMed, PMC, SCOPUS, and Cochrane

#### Search strategy


Boolean operators (NOT, AND, OR) will also be used in succession

#### Statistical Methodology

- Article quality shall be determined by ROBINS tool on RevMan v.5.4 (Cochrane collaboration, Copenhagen, Denmark)
- Higgin’s I² - Heterogeneity of the included studies
- tau-squared test, degree of freedom (df) and chi squared test
3. **TITLE**

A meta-analysis of surgical outcomes of infranotch T4b and T4a oral cancers

4. **BACKGROUND AND RATIONALE**

Oral cancer poses a significant burden worldwide. According to the latest Globocan data, 3.7 lakh new oral cancer cases are diagnosed yearly (1). T4b oral cancers are defined as masticator space involvement, encasement of the carotid artery, skull-base and pterygoid plate involvement. T4b cancers are not uncommon in routine practice (2). According to 2023 National Comprehensive Cancer Network (NCCN) guidelines, the management of T4b oral cancers is clubbed along with the management of unresectable nodal disease and those unfit for surgery (3). It suggests treatment with radiation therapy (RT) with or without chemotherapy (CT), and the intent of treatment is based on the patient's performance status. Sixteen years back, Liao and colleagues from Taiwan showed that select patients with masticator space involvement performed well following surgery and adjuvant RT / CT RT (4). This outcome was comparable with T4a cancers in his cohort. This seminal article led to changes in American Joint Committee on Cancer (AJCC) oral cancer staging (5). In the same paper, Liao proposed further compartmentalisation of infratemporal fossa (ITF) into infranotch and supranotch. Surprisingly, the subset of infranotch T4b cases in his series outlived T4a oral cancers. Following his description of surgery for oral cancer with masticator space involvement, there was an increase in publications suggesting equivalent surgical outcomes for T4b with T4a. This led us to conduct this meta-analysis to determine the overall surgical outcomes following T4b and to compare its outcomes with T4a cases.
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5. **AIM**
To conduct the meta-analysis to determine the overall surgical outcomes following T4b and to compare its outcomes with T4a cases.

6. **OBJECTIVES**
   6.1. **Primary**
       6.1.1. To determine the overall surgical outcomes of infranotch T4b oral cancers
   6.2. **Secondary**
       6.2.1. To analyse the difference in surgical outcomes between T4b and T4a oral cancers metastasis

7. **POPULATION AND SETTING**
The inclusion and exclusion criteria are as follows:

   8.1 **Inclusion Criteria:**
       8.1.1. Treatment naïve oral T4b disease
       8.1.2. Original articles published in peer reviewed journals
       8.1.3. Study must report at least one risk factor - OS, DFS, DSS, or LC
   8.2 **Exclusion Criteria:**
       8.2.1. Non-human studies
       8.2.2. Neoadjuvant chemotherapy / Radiation therapy prior to surgery
       8.2.3. Any previous oncological treatment
       8.2.4. Recurrent or second primary tumours
       8.2.5. Not reported – post operative outcomes
       8.2.6. Review articles, meeting abstracts, case reports, editorial letters, as well as other forms of publication
       8.2.7. Incomplete data or insufficient information
       8.2.8. Overlapping study populations, shared dataset

8. **INTERVENTION**
Not applicable
9. **STUDY DESIGN**

Meta-Analysis

10. **STUDY PROCEDURES**

All the data shall be retrieved from three database - PubMed, EMBASE, and Cochrane.


Boolean operators (NOT, AND, OR) will also be used in succession.

The searched articles shall be independently screened by two authors.

The screened articles shall be analyzed with full text documents for eligibility by two authors, any dispute regarding the eligibility shall be resolved by the third author.

All included articles were independently screened. The following study characteristics were recorded: author, year of publication, country, sample size, type of study, Level of evidence, NOS, Risk of Bias, number of T4b cases, number of T4a cases, 2-year and 5-year overall survival, disease-free survival, disease-specific survival, and local control of the included studies were recorded and compiled.

The extracted data will be cross checked by another author.

The quality of the study will be assessed, the data variables shall be analysed using predetermined statistical tests.

A strict adherence to 2009 PRISMA guidelines shall be followed. A PROSPERO registration shall be obtained for the meta-analysis.

11. **STATISTICAL CONSIDERATIONS**

- Article quality shall be determined by ROBINS tool on RevMan v.5.4 (Cochrane collaboration, Copenhagen, Denmark)
- Higgin’s $I^2$- Heterogeneity of the included studies
- tau-squared test, degree of freedom (df) and chi squared test
- A p-value for heterogeneity (Ph) < 0.1 and $I^2 > 50\%$ indicated significant heterogeneity.
Infranotch T4b Vs T4a OSCC Meta-analysis

- Therefore, the Random effects model (DerSimonian Laird method) for heterogenous articles shall be applied
- Potential publication bias will be measured using fail-safe method. A p-value < 0.05 was considered as statistically significant
- Jamovi software V 2.3.26 will be used along with Revman 5.4 for statistical analysis

12. FEASIBILITY

Oral cancer poses a significant burden worldwide. T4b oral cancers are defined as masticator space involvement, encasement of the carotid artery, skull-base, and pterygoid plate involvement. T4b cancers are not uncommon in routine practice. A preliminary data search on PubMed database yields 140 articles pertaining to surgical outcomes of OSCC with T4a vs infra notch T4b disease.

13. SIGNIFICANCE

Everyone desires to adequately address the primary disease in OSCC, which enables better overall outcomes for our patients, which increases overall survival and disease-free survival. Although many studies have reported overall survival and disease-free survival, the number of samples in a single study was small and less persuasive.

Since the initial publication from Liao et al., (4) following his description of surgery for oral cancer with masticator space involvement, there are various publications suggesting equivalent surgical outcomes for T4b with T4a. We comprehensively searched the literature for surgical outcomes of OSCC with T4a vs infra-notch T4b disease and conducted a meta-analysis.

14. BIBLIOGRAPHY


