

The Incidence of Primary Synchronous Parotid tumors: A Systematic review and Meta-Analysis

Srivatsa Surya Vasudevan, MD, MS¹; Estephania Candelo, MD, MSc¹; Jeffrey R. Janus, MD, FACS¹
¹ Department of Otorhinolaryngology and Head and Neck Surgery, Mayo Clinic Florida, Jacksonville, FL, USA.

ABSTRACT

Introduction

While historically being associated with Warthin's tumors, synchronous primary parotid tumors can occur across many histopathologic diagnoses and be either homogenous (same histology) or heterogenous (different histology) in nature. This study focuses on determining the synchronous occurrence of parotid tumors and identifying the most prevalent combinations of tumor types.

Methods

A systematic search of studies from PubMed/MEDLINE, Embase, Science Direct, Scopus, EBSCO, Cochrane Library from inception to 2022 was conducted by two independent reviewers. The search strategy involved looking for articles with keywords related to "synchronous" and "parotid tumor". A random-effect meta-analysis was performed to determine the pooled incidence and odds ratio (OR) of parotid tumor synchronicity.

Results

In total, 25 studies met the inclusion criteria out of 740 articles, totaling 20,373 parotid tumor patients. Out of which, 486 cases of primary parotid synchronous tumors were identified. The mean age was 59.9 (SD ± 5.4) years with Male:Female ratio of 3.3:1. Synchronous homogenous tumors were reported in 418 (86.1%) patients; synchronous heterogenous parotid tumors are reported in 68 (13.9%) patients. Among the homogenous synchronous tumors, Warthin tumor is the most commonly reported tumor in 386 (92.3%) cases, followed by pleomorphic adenoma in 10 (2.3%) cases. The overall pooled incidence of primary synchronous parotid tumor was 3.4% (95% CI, 2.2%-5.2%). The incidence of synchronous benign-only tumors was 6% (95% CI, 4%-8.8%) and the incidence of synchronous malignant-only tumor is 0.4% (95% CI, 0.01%-15.8%). The incidence and risk of synchronous homogenous tumor was higher than that synchronous heterogenous tumor (OR=5.06, 2.67-9.61, p-value = <0.0001, I² = 53.9%).

Conclusions

This is the largest study to determine the rate of synchronicity of parotid tumors. The occurrence of certain subtypes of parotid tumors which simultaneously may help surgeons with clinical/surgical decision making with respect to this patient population.

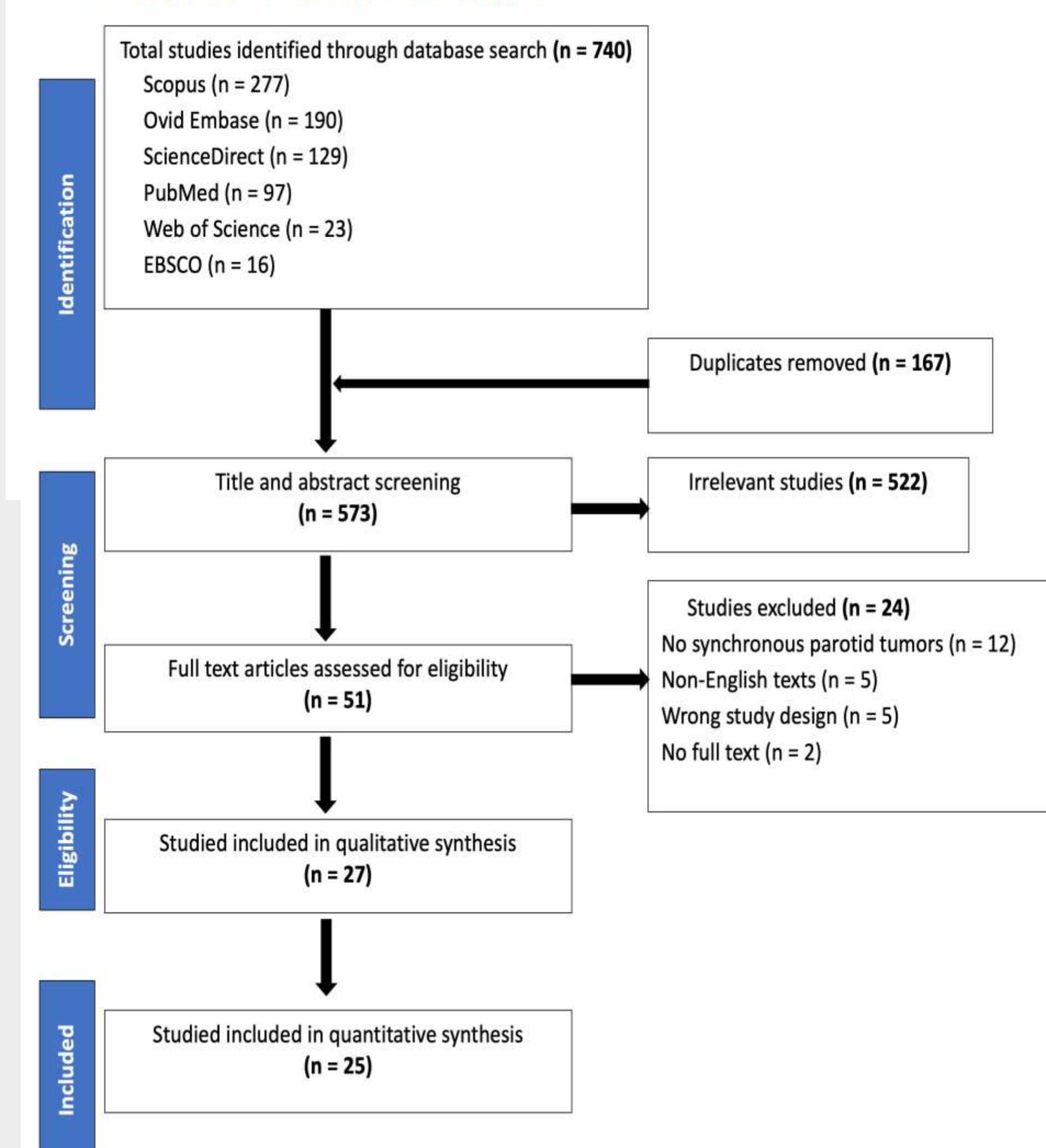
AIM

- To determine the overall incidence and likelihood of having primary synchronous parotid tumor.
- To explore the incidences of histologically homogenous and heterogenous parotid tumor combinations.

METHODS AND MATERIALS

- Selection Criteria:** Studies were included if they focused on primary parotid tumors, encompassed patients with either unilateral or bilateral tumors, studies with more than 10 cases, or were observational studies related to primary synchronous parotid tumors. Exclusion criteria consisted of studies addressing secondary metastasis to the parotid, review articles, letter to the editor, and non-English language texts.
- Data Extraction and Analysis:** Two independent reviewers extracted the data from selected studies. Discrepancies were resolved through discussion and consensus or by consulting a third reviewer.
- Quality Assessment:** Newcastle-Ottawa Scale (NOS) for Cohort and Case-control was used to evaluate the risk of bias of cohort studies. Meanwhile, the quality of case series was determined using the Institute of Health Economics (IHE) Quality Appraisal Checklist, assessing both internal and external validity^{1,2}.
- Statistical Analysis:** A meta-analysis was employed to determine the pooled incidence of primary synchronous tumors. Random effect analysis was used to calculate the overall incidence of primary synchronous parotid tumor. Forest plots visually represented the incidence rates from each study and the overall pooled incidence rate. Additionally, a subgroup analysis was conducted to study the incidence of various synchronous tumor subtypes. All statistical analyses were performed with the significance level set at p<0.05. Primary meta-analysis was performed using Comprehensive Meta-analysis software version (CMA) version 4 and Egger's regression and Begg & Mazumdar's rank correlation were performed using Meta-

FIGURE 1. PRISMA Flowchart



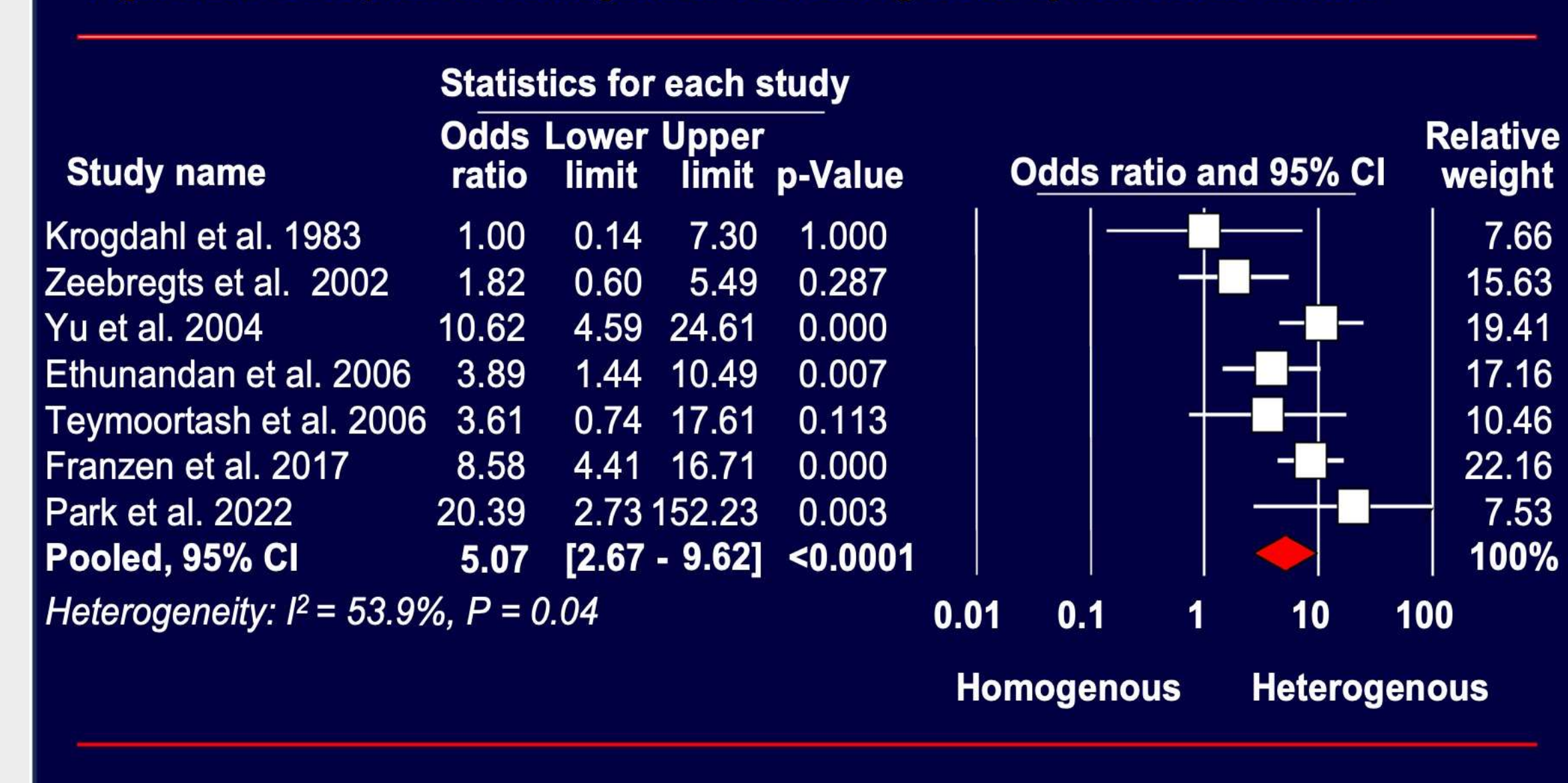
- Of the 20,373 analyzed parotid tumors, 486 were identified as primary synchronous parotid tumors (Figure 1).
- Across 25 studies, the overall incidence of these tumors stood at 3,480 per 100,000 (95% CI: 2,285 - 5,267), with heterogeneity index (I² = 94.6%).

Table 1. Subgroup analysis of primary synchronous subtypes

Outcomes	Number of studies	Number of observations	Number of events	Incidence per 100,000	(95% CI)	I ² (%)
Overall Incidence	25	20373	486	3480	2285 - 5267	94.6
Histological differences						
Synchronous Homogenous tumors	19	9104	418	4728	3256 - 6820	92
Synchronous Heterogenous tumors	13	16267	64	817	335 - 1978	91.7
Nature of the tumor						
Benign-only synchronous	18	9060	318	6065	4095 - 8896	89.6
Malignant-only synchronous	3	3125	21	471	12 - 15857	94.8
Laterality of the tumor						
Unilateral	20	18771	289	2346	1380 - 3961	94.2
Bilateral	18	8782	170	2252	1456 - 3467	85.5

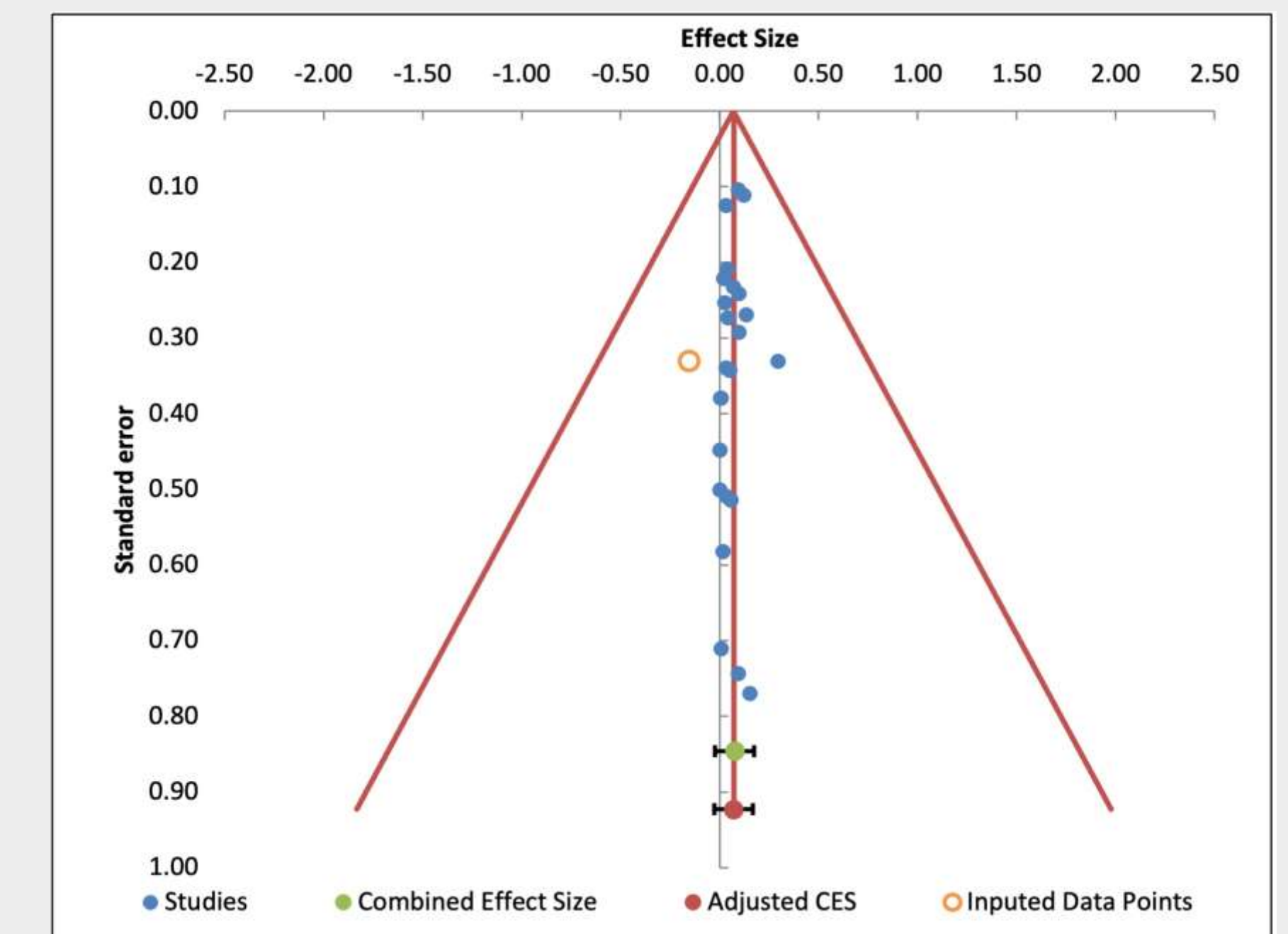
- Regarding the nature of the tumor, benign tumors, covered in 18 studies, had an incidence of 6,065 per 100,000 (95% CI: 4,095 - 8,896). In contrast, malignant tumors, reported an incidence of 471 per 100,000 (95% CI: 12 - 15,857) (Table .1)

Figure 2. Forest plot for Homogenous vs Heterogenous synchronous tumors



- Distinguishing histological differences, synchronous homogenous tumors had an incidence of 4,728 per 100,000 (95% CI: 3,256 - 6,820). Synchronous heterogenous tumors, documented in 13 studies, showed an incidence of 817 per 100,000 (95% CI: 335 - 1,978). The incidence of synchronous homogenous tumors was significantly higher than that of synchronous heterogenous tumors, with an odds ratio (OR) of 5.06 (95% CI: 2.67-9.61, P-value < 0.0001, I² = 53.9%) (Figure 2)
- Lastly, in terms of laterality, unilateral tumors, from 20 studies, showed an incidence of 2,346 per 100,000 (95% CI: 1,380 - 3,961), while bilateral tumors, from 18 studies, exhibited an incidence of 2,252 per 100,000 (95% CI: 1,456 - 3,467).

Figure 3. Funnel plot for publication bias



- Among homogeneous synchronous tumors, Warthin tumors were the most common, occurring in 92% of cases. For heterogeneous tumors, the combination of Warthin tumor with pleomorphic adenoma was the predominant occurrence, representing 39.7%.
- Publication bias:** The Egger's regression indicates no publication bias (p=0.266), a finding supported by Begg & Mazumdar's rank correlation (p=0.296). The symmetrical funnel plot further corroborates the absence of bias (Figure 3).

DISCUSSION

- Our meta-analysis focused on the occurrence of synchronous tumors depending on the nature of the tumor and histological classification.
- Although most of the studies were cohort, 28% of our studies were case series and performing sensitivity analysis on each study removed proved not one study removal caused change in the overall incidence effect.
- Further studies need to be focused on the somatic and familial risk factors associated with synchronous tumor occurrences in parotid.

CONCLUSIONS

This is the first review to evaluate the incidences of primary synchronous parotid tumors comprehensively. From our systematic review, we determined the overall incidence of primary synchronous parotid tumor to be 3,480 cases per 100,000 parotid tumor population. We also found that homogenous tumors are 5 times more likely to occur in comparison to heterogenous tumors.

REFERENCES

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