ORAL CANCER IN HUNGARY: EPIDEMIOLOGICAL TRENDS, DIAGNOSTIC BEHAVIOR, AND CLINICAL CHALLENGES

Summary of the PhD thesis
by

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PUBLICATIONS PROVIDING THE BASIS OF THE THESIS

1. Sonkodi I, Nagy J, **Novák P**, Braunitzer G, Virág K, Boda K, et al. A retrospective screening and epidemiological study of oncological and other diseases in the oral and maxillofacial region at the University of Szeged, Department of Oral Medicine (1960-2014). *Fogorv Sz* 2016;109(3):94-101

SJR rank: Q4 (medicine/miscellaneous, 2016)

IF: N/A

2. **Novák P**, Szabó RM, Braunitzer G, Vereb I, Bágyi K, Nagy Á, et al. Diagnostic confidence and oral cancer screening: insights from a nationwide cross-sectional study in Hungary. *Int Dent J* 2025; In press.

SJR rank: Q1 (dentistry/miscellaneous, 2024)

IF: 3.2

3. **Novák P**, Sükösd F, Hamar S, Németh I, Tiszlavicz L, Szalay I, et al. Metachronous clear cell carcinoma of the tongue and kidney: a diagnostically challenging coincidence. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012;114(4):e25-30.10.1016/j.oooo.2012.01.028

SJR rank: Q2 (pathology and forensic medicine, 2012)

IF: 1.495

ABBREVIATIONS

CD10	Cluster of Differentiation 10
DNA	Deoxyribonucleic Acid
EMA	Epithelial Membrane Antigen
HCCC	Hyalinizing Clear Cell Carcinoma
IARC	International Agency for Research on Cancer
IF	Impact Factor
LOH	Loss of Heterozygosity
OR	Odds Ratio
RCC	Renal Cell Carcinoma
SJR	SCImago Journal Rank
VHL	von Hippel–Lindau (gene)
WHO	World Health Organization

I. INTRODUCTION

Oral cancer represents a serious and growing public health burden globally, and Hungary is among the most affected countries in Europe. Despite the anatomical accessibility of the oral cavity, late-stage diagnoses are common, significantly reducing survival rates. In Hungary, lifestyle factors such as smoking and alcohol use, contribute to the persistently high mortality.

Early detection through regular screening is both feasible and cost-effective. However, screening practices are inconsistently implemented across healthcare settings. Existing literature suggests that knowledge alone does not guarantee diagnostic activity: healthcare professionals must also feel confident in their diagnostic skills to act.

The thesis explores this wider topic from three aspects: first, through a retrospective epidemiological study analyzing long-term trends in oral and maxillofacial tumors based on over five decades of data from the University of Szeged; second, by examining the diagnostic behavior, confidence, and knowledge levels of Hungarian healthcare professionals and students in a nationwide cross-sectional survey; and third, by presenting a diagnostically complex case underscoring the role of molecular diagnostics in differential diagnosis.

II. OBJECTIVES

The present thesis is based on three published studies that address different aspects of oral cancer diagnosis and detection. The specific objectives of each study were as follows:

1.Retrospective Epidemiological Study

To analyze long-term trends in the incidence and pathology of oral and maxillofacial tumors using data collected over more than five decades (1960–2014) at the University of Szeged. The aim was to assess changes in lesion frequency and distribution, and to draw implications for opportunistic screening strategies.

2.Nationwide Cross-Sectional Survey

To investigate how Hungarian dentists, physicians, and clinical-grade medical and dental students engage in oral cancer screening and patient education. Special focus was placed on identifying the roles of diagnostic self-confidence, objective knowledge, and perceived sufficiency of training in shaping professional behavior.

3.Clinical Case Study

To document and resolve a diagnostically challenging case involving clear cell carcinomas of the tongue and kidney occurring in the same patient. The objective was to determine whether the lingual tumor represented a metastasis or a new primary malignancy, using histopathological, immunohistochemical, and molecular genetic analyses.

III. METHODS

III.1. Retrospective Epidemiological Study

A descriptive retrospective analysis was conducted using patient data collected between 1960 and 2014 at the University of Szeged's Department of Oral Medicine. During this period, 338,200 new patients were registered, and diagnoses of oral and maxillofacial tumors were systematically recorded. Beginning in 1968, all cases with premalignant or malignant lesions were documented using a structured, coded data sheet suitable for digital processing. Lesions were classified according to WHO and IARC criteria. Linear regression was used to assess incidence trends of benign, precancerous, and malignant lesions over time, with special attention to decade-by-decade changes and screening-related implications.

III.2. Nationwide Cross-Sectional Survey

A nationwide questionnaire-based cross-sectional study was carried out among Hungarian dentists, physicians, and clinical-grade medical and dental students. Data collection took place between April 2022 and December 2023. The survey included 18 items addressing demographic information, oral cancer knowledge, diagnostic self-confidence, regularity of screening and preventive advice, as well as preferred educational formats. Clinical-grade students were defined as those in years 4–6 (medicine) and

3–5 (dentistry). Responses were analyzed using binomial and multinomial logistic regression to explore how factors like confidence, perceived knowledge sufficiency, and group affiliation predicted screening and advisory behaviors.

III.3. Clinical Case Study

This study presents a diagnostically complex case involving a 63-year-old woman with a prior history of renal clear cell carcinoma who developed a painless nodular lesion on the tongue. Following surgical excision, both the renal and lingual tumors underwent histopathological evaluation. A comprehensive immunohistochemical panel was applied, testing for markers including CD10, RCC antigen, pancytokeratin, EMA, and vimentin. Molecular pathology involved DNA extraction from formalin-fixed tissue, microsatellite-based LOH analysis, and sequencing of the VHL gene. These tests aimed to clarify whether the lingual tumor represented a metastasis or an independent primary malignancy.

IV. RESULTS

IV.1. Retrospective Epidemiological Study

The retrospective analysis included clinical records of 338,200 new patients seen at the University of Szeged, Department of Oral Medicine, between 1960 and 2014. Among these, 20,065 cases of oral tumors were identified, including 9,482 benign, 5,438 precancerous, and 5,145 malignant lesions. Additionally, 14,446 patients were diagnosed with other oral mucosal diseases.

The proportion of precancerous and malignant cases combined equaled 3.1% of all new patient cases. Data analysis revealed a continuous and significant rise in the incidence of all lesion types over the decades. Benign tumors increased fifteen-fold, precancerous lesions thirty-fold, and malignant tumors twenty-five-fold. The steepest increases were observed between the 1970s and 1990s, with peak incidence occurring between 1986 and 2002. During this period, tumor-related diagnoses accounted for over 10%—and in certain years nearly 30%—of all new clinical cases.

These findings provide compelling evidence of a growing burden of oral oncology in Southern Hungary and highlight the crucial role of opportunistic screening and early detection. The consistency and scale of the data support the long-standing importance of this regional

stomato-oncological center and suggest that population-level interventions may be warranted in high-risk areas.

IV.2. Nationwide Cross-Sectional Survey

A total of 803 participants completed the survey, including 184 physicians, 164 dentists, 127 medical students, and 328 dental students. Respondents were asked to report their screening practices, assess their own diagnostic confidence and knowledge levels, and list key risk factors and clinical signs of oral cancer.

Across all groups, the average number of correctly identified clinical signs and risk factors was moderate, typically around three per category. Most participants correctly recognized smoking and alcohol use as primary risk factors, but knowledge of less obvious factors such as chronic irritation or viral infections was more limited. Clinical signs such as ulceration and exophytic growth were better known, though overall accuracy varied by group.

The results showed a clear gradient in both diagnostic confidence and screening behavior: dentists and dental students reported higher levels of both, while physicians and medical students were significantly less active and less confident in these areas. Logistic regression confirmed that diagnostic self-confidence and perceived knowledge sufficiency were the strongest predictors of regular screening and advisory behavior, far exceeding the predictive power of objective knowledge alone.

Despite recognizing their own limitations, relatively few participants expressed a strong interest in further education on oral cancer. Among those who did, online learning formats and written information materials were strongly preferred, while in-person seminars and workshops were less favored.

These findings highlight a disconnect between awareness of a knowledge gap and motivation to seek further training. They also point to the need for education strategies that not only increase knowledge but also build confidence and practical screening skills among health professionals.

IV.3. Clinical Case Study

The third study involved the clinical investigation of a 63-year-old female patient who presented with a painless nodular lesion on the right side of her tongue, seven years after undergoing nephrectomy for renal clear cell carcinoma. Given the patient's oncological history and the lesion's histological appearance, a possible lingual metastasis was initially considered.

Following surgical excision, histopathological analysis revealed a tumor composed of clear cells with minimal nuclear atypia and a background of hyalinized stroma. Immunohistochemical staining showed positivity for pancytokeratin and EMA but negativity for CD10, RCC antigen, and vimentin—markers typically associated with renal clear cell carcinoma. This profile was more

consistent with hyalinizing clear cell carcinoma (HCCC) of the minor salivary glands.

To strengthen the differential diagnosis, molecular analysis was conducted on both tumors. LOH analysis identified allelic imbalance upstream of the VHL gene in the renal tumor but not in the lingual lesion. Sequencing of the VHL gene revealed no mutations in either sample.

These combined clinical, histological, immunohistochemical, and molecular findings supported the diagnosis of a second primary tumor—a rare metachronous HCCC of the tongue rather than a metastasis. The patient underwent regular follow-up and showed no evidence of recurrence or metastasis for three years post-treatment.

This case underscores the importance of an integrated diagnostic approach, especially when evaluating clear cell neoplasms in patients with complex oncological histories. It also adds to the limited body of literature documenting metachronous presentations of morphologically similar but etiologically distinct tumors.

V. CONCLUSIONS

Based on the presented studies, we draw the following conclusions, which we consider as the new scientific findings of the thesis:

From the analysis of long-term institutional data (Sonkodi et al., 2016), it was established that the incidence of premalignant and malignant oral lesions has significantly increased over the past five decades in the Southern Hungarian region. This trend highlights the need for structured secondary prevention strategies and justifies the implementation of opportunistic screening, particularly in high-risk populations.

From the results of the national cross-sectional survey (Novák et al., 2025), it was demonstrated that diagnostic self-confidence is a stronger predictor of oral cancer screening and preventive advisory behavior than objective knowledge. The findings show that while most healthcare professionals and students acknowledge their knowledge deficits, relatively few express interest in further education. Moreover, preferred educational formats (e.g., online courses) may be poorly suited to strengthening the diagnostic competence needed for effective screening. These results support the need for educational interventions that go beyond knowledge transmission and specifically aim to enhance clinical confidence and decision-making capacity.

From the case study on clear cell carcinoma of the tongue (Novák et al., 2012), it was confirmed—through histopathological, immunohistochemical, and molecular genetic methods—that the oral lesion represented a primary tumor, not a metastasis from the previously treated renal carcinoma. To the authors' knowledge, this was the first reported case in the English-language literature of two histologically similar but independent clear cell carcinomas occurring metachronously in the kidney and the tongue. This case illustrates the diagnostic complexity of rare salivary gland neoplasms and underscores the importance of multidisciplinary diagnostic approaches in patients with prior oncological histories.

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