

# The clinical and epidemiological analysis of lip carcinoma in Holy Cross District in Poland

## Obraz epidemiologiczno-kliniczny raka wargi w regionie świętokrzyskim

### Wkład autorów:

A – Study Design  
B – Data Collection  
C – Statistical Analysis  
D – Manuscript Preparation  
E – Literature Search  
F – Funds Collection

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### ABSTRACT:

**Objective:** Lip carcinoma, as classified according to TNM system, is one of localizations of oral carcinoma. However it differs in numerous factors from other head and neck cancer.

**Material:** 342 patients with diagnosed lip carcinoma, collected from 2001 to 2012, who in majority came from one of Poland's region – Holy Cross District. Among them 312 were treated primarily with surgery or with surgery + Rtg. Therapy.

**Methods:** In retrospective survey the factors of age, sex and localization of lip carcinoma were taken into analysis. Apart of that in the subgroup who underwent surgery, the local and clinical staging, histopathology and selected patho-morphological factors were also presented.

**Results:** In the analyzed group (n=342) the sex ratio was 6 : 1 in favor of men, with average age of 69,5 years, and the most common location (93,4%) of tumor was the lower lip. The majority of treated patients (n=312) have started therapy at the lower (T1+T2) local stage (93,9%), and in 97,4% squamous cell carcinoma was finally diagnosed.

**Discussion:** Clinico-epidemiological characteristics of presented material is similar to data found in the literature. It must be stressed out that presented results might be comparable only with the data where TNM criteria of the lip are followed.

### KEYWORDS:

lip carcinoma, epidemiology, clinical characteristics

### STRESZCZENIE:

**Wstęp:** Rak wargi, będący według kryteriów TNM jedną z lokalizacji raka jamy ustnej, posiada szereg cech odróżniających go od innych nowotworów głowy i szyi, zarówno epidemiologicznie, jak i w obrazie klinicznym.

**Materiał:** Grupa 342 chorych z rozpoznaniem rakiem wargi, zebrana w latach 2001–2012, pochodziła w większości z jednego regionu Polski – województwa świętokrzyskiego. Wśród 312 pacjentów z tej grupy przeprowadzono leczenie chirurgicznie, bądź w skojarzeniu z terapią rentgenowską.

**Metoda:** Analiza retrospektywna uwzględniała: wiek, płeć chorych, umiejscowienie guza w obrębie wargi, a w grupie poddanej leczeniu chirurgicznemu – stopień zaawansowania miejscowego, klinicznego, typ histopatologiczny oraz wybrane cechy patomorfologiczne guza.

**Wyniki:** W analizowanym materiale (n =342) przeważali mężczyźni w stosunku 6:1, przy średniej wieku 69,5 lat. Najczęstszym umiejscowieniem raka (93,4%) była warga dolna. Większość leczonych chorych (n=312) rozpoczęła terapię we wczesnym (T1+T2) zaawansowaniu miejscowym (93,9%), a w 97,4% ustalono rozpoznanie *Carcinoma planoepitheliale*.

**Dyskusja:** Charakterystyka epidemiologiczno-kliniczna przedstawionego materiału jest podobna do doniesień w literaturze. Wymaga podkreślenia, że wyniki można odnosić jedynie do publikacji, gdzie ścisłe kryteria lokalizacyjne TNM raka wargi były zachowane.

**SŁOWA KLUCZOWE:** rak wargi, epidemiologia, charakterystyka kliniczna

## INTRODUCTION

Carcinoma of the lip, classified according to the TNM system as one of various locations of carcinoma within the oral cavity, differs from other tumours of this area in aetiology, clinical picture, and treatment outcomes. For example – the most important carcinogenic factor for this type of cancer, i.e. UVB exposure, does not play any role for other locations of cancer found. Lip carcinoma, due to its location that is easy to spot and, in most cases, due to its slow growth, is usually diagnosed at early stages. The observed probability of 5-year total survival of 75-95% is higher than the values observed for other cancers within the area of the oral cavity [12].

In several epidemiological summaries, the summation of data concerning the lip carcinoma, which has better prognosis and constitutes approximately 30% of all oral cancers, with the data concerning the carcinoma of the tongue or the floor of the oral cavity, leads to distortion in the published treatment outcomes. Moreover, in the TNM system the „lip” is described as a distinct location of the oral cancer, and this location is limited in

this system to the vermillion, which is often not taken into account in the studies discussing this type of cancer. In the classic anatomical description the lips constitute the part of the face that determines the borders of the rima oris.

## AIM OF THE STUDY

The aim of the study was to present an epidemiological-clinical analysis of a group of patients that included 342 cases with lip carcinoma, diagnosed between 2001 and 2012 at the Department of Otolaryngology and Head and Neck Surgery of the Holy Cross Cancer Centre (Pol. Świętokrzyskie Centrum Onkologii – ŚCO). The majority of the patients were also treated at this centre. Data concerning the patients' age and gender, as well as the location of the cancer within the lip were analysed for all patients (n=342), whereas the data concerning the local and clinical grade, growth type and tumour histopathology were analysed only for the group who underwent primary treatment – surgery or surgery with supplementary radiation therapy, at the ŚCO (n=312).



Fig. 1. Lip carcinoma cases diagnosed in particular years, according to the National Cancer Registry (Pol. Krajowego Rejestru Nowotworów (KRN) and the data from the Holy Cross Cancer Centre (ŚCO).

**Tab. 1.** The comparison of lip carcinoma cases registered in Holy Cross District (according to the National Cancer Registry) with the number of cases diagnosed in Holy Cross Cancer Center from 2001 to 2012.

YEARS	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	OGÓŁEM
Registered (according to the National Cancer Registry)	44	44	35	20	18	31	16	24	26	24	30	18	330
Diagnosed at ŚCO	36	38	28	29	19	31	18	26	29	31	31	27	342

## MATERIAL

The study material comprised patients with lip carcinoma who were diagnosed and treated according to a uniform scheme by the same team. During the analysed period of 12 years, almost all patients from the Holy Cross district were diagnosed and treated at our centre, and small disparities in particular years between the data published by the National Cancer Registry and the data that were gathered by us could be the result of minor migration of the patients. The analysis of such a large group of patients with lip carcinoma from one district was considered worthy of publication and analysis.

Therefore, it can be ascertained that the presented material depicts the epidemiological and clinical status of lip carcinoma in the Holy Cross District. A general epidemiological-clinical analysis was performed on the group of 342 patients in whom the diagnosis of lip carcinoma was made at the ŚCO. Within that group, a detailed analysis that included local stage, local metastases and final histopathological diagnosis, was performed only for patients (n=312) in whom primary surgical treatment was performed. The remaining patients (n=30) were not taken into account in the analysis, as they were either excluded because they had been disquali-

fied from causal treatment, had not expressed consent to it, had chosen another centre for their treatment, or had been referred to ŚCO for treatment due to local recurrence or metastases to cervical lymph nodes, and, therefore, underwent secondary treatment.

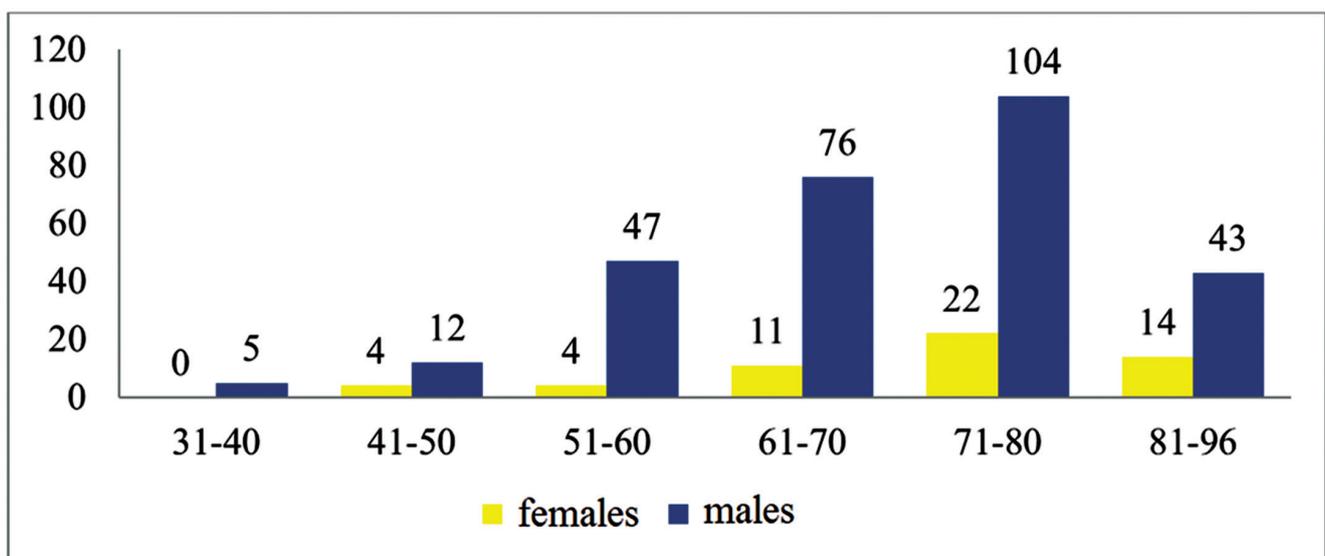
## METHOD

The study was retrospective in nature, and it was based on the records of the ŚCO, and the summative data in the Excel software did not include any personal information. Bioethical Committee expressed consent to this study.

Descriptive statistics for qualitative data included the summary of numerical and percentage values. The intervals for values and mean values were calculated for quantitative data.

## OUTCOMES

Male patients comprised as much as 83.9% of all patients in the analysed group (total n=42), and the lower lip was the

**Fig. 2.** The number of patients in each age group of males and females, in 10-year intervals, for the whole diagnosed group of patients with lip carcinoma between 2001 and 2012 (n=342).

**Tab. II.** Sex and age characteristics in particular locations, for the whole group (n = 342) of lip carcinoma cases diagnosed from 2001 to 2012 in Holy Cross Cancer Center.

Lip cancer location	FEMALES	MALES	TOTAL (K + M)
	n (%) mean age (x) age (min–max)	n (%) mean age (x) age (min–max)	n (%) mean age (x) age (min–max)
lower lip	52 94,5% 74,1 46–96	268 93,4% 69,0 33–91	320 93,6% 69,8 33–96
upper lip	2 3,6% 58,5 49–68	4 1,4% 60,0 45–74	6 1,8% 59,5 45–74
oral commissure	1 1,8% 66,0 66	15 5,3% 67,3 53–89	16 4,7% 67,1 53–89
total	55 100,0% 73,4 46–96	287 100,0% 68,8 33–91	342 100,0% 69,5 33–96

most commonly observed location of primary lip carcinoma focus (93.6%). High value of the mean value calculated for the patients' age (73.4 years for females and 68.8 years for males) should be underlined, and peak incidence in both subgroups was observed in the 8th decade.

In the group subjected to treatment (n=312), early local stages (T1 + T2) prevailed statistically significantly (chi squared  $p < 0.0001$ ) – T1 (64.7%) and T2 (29.2%). The values for T3 and T4 were 4.5% and 1.6%, respectively. Due to the fact that lower lip carcinoma cases prevailed (n=291), and smaller numbers of upper lip carcinoma (n=5) and oral commissure (n=16) were observed, the former location determines the outcomes for the whole group of treated patients.

Neither were any metastatic lymph nodes at N3 stage observed, nor any distant metastases (M1) were observed in the whole analysed material. It came as a surprise that in all 6 cases of N2 lymph nodes there was no relationship between the regional grade and the local grade (T1: T2: T3: T4 = 2: 2: 2: 0), and all these cases were observed within the lower lip. In the subgroups of upper lip carcinoma and carcinoma of the oral commissure, no local metastases to lymph nodes were observed. The summary presented in Tab. IV indicates that high clinical grades (III and IV grade) comprised only 9.3% (29/312) of the cases, which is significantly different for lip carcinoma and distinct from carcinomas located in other areas of the oral cavity.

Among 312 cases after surgical treatment, squamous cell carcinoma (Lat. carcinoma planoepitheliale) was diagnosed in 97.4% of the cases (304/312). In three cases, basal cell carcinoma

**Tab. III.** The local staging in different locations of lip carcinoma (n = 312)

LOCATION	LOWER LIP	UPPER LIP	ORAL COMMISSURE	TOTAL
Local stage				
T1	198	3	1	202 (64,7%)
T2	78	2	11	91 (29,2%)
T3	12	0	2	14 (4,5%)
T4	3	0	2	5 (1,6%)
Total	291	5	16	312 (100,0%)

**Tab. IV.** Staging of the local and regional metastases of lip carcinoma (n=312)

NODAL STAGE	N0	N1	N2	TOTAL
Zaawansowanie miejscowe				
T1	200	0	2	202 (64,7%)
T2	83	6	2	91 (29,2%)
T3	10	2	2	14 (4,5%)
T4	5	0	0	5 (1,6%)
Total	298	8	6	312 (100%)

was diagnosed in 3 cases, and 5 single cases of sebaceous carcinoma, metatypical carcinoma, adenoid cystic carcinoma, fusocellular malignant neoplasm and microcystic adnexial carcinoma were observed.

Statistically significant  $\chi^2$  relationship ( $p = 0.02$ ) between low local „T” stage values and high „G1” differentiation of the neoplasm, was observed. In pathological reports, perineural

**Tab. V.** The Histological differentiation of squamous cell carcinoma, depending on the local stage of lip carcinoma (n = 312)

LOCAL STAGE	T1	T2	T3	T4	IN TOTAL
The stage of cancer differentiation according to Broders					
in situ (Bowen's disease)	2	0	0	0	2 (0,6%)
G1	103	39	5	1	148 (47,4%)
G2	75	46	8	3	132 (42,3%)
G3	4	1	1	1	7 (2,2%)
Not applicable	20	5	0	0	25 (8,0%)
Total:	202 (64,7%)	91 (29,2%)	14 (4,5%)	5 (1,6%)	312 (100,0%)

invasion was observed in 19 cases out of 312 (6,1%), and intravascular infiltration was observed in only one case, along with perineural invasion.

According to the assessment made by the histopathologist, the size of the tumour was within a broad range between 5 mm and 83 mm ( $x = 17$  mm), in the majority of cases, i.e. in 59.2% of the cases (185/312), it did not exceed 20 mm. The margins differed from 1 to 10 mm ( $x = 5$  mm), in the majority of cases, i.e. 37.2% (116/312) did not exceed 3 mm. A detailed analysis of infiltration to surrounding tissues was not performed, as this element was not included in the evaluation of the surgical specimen in the reports prepared by the histopathologist. Ulceration (according to the clinical assessment or the histopathologist's report) was observed in 78.5% of lip carcinoma cases (245/312). The analysis of radicality of resection according to the histopathologist's assessment is to be presented in a separate paper together with the acquired treatment outcomes.

## DISCUSSION

The International Statistical Classification of Diseases and Related Health Problems (ICD-10) classification by the WHO defines the lips as the structure that comprises the surfaces of the lip vermilion, skin and oral mucosa, within the borders of descriptive anatomy (C00.0 – C00.9). Moreover, „the lip” constitutes an integral part of the „oral cavity”. Such a description of the lip is contradictory with the current TNM classification from 2010, common for AJCC (American Joint Cancer Committee) and UICC (Union Internationale Contre le Cancer), in which the lip is defined as the lip vermilion from the vermilion-skin border to the tangent line of both lips with the mouth closed ([www.seer.cancer.gov](http://www.seer.cancer.gov)) [8, 23]. Within the lip, following areas are distinguished in the TNM system as distinct locations: the lower lip, the upper lip, and oral commissure. In the presented study, the location of the tumour in strict accordance with the TNM criteria constituted the basis for classifying the

patients into the study group, i.e. comprising malignant epithelial neoplasms, that develop primarily within the vermilion of both lips and the oral commissure. In comparison to the data available in literature, the analysed group of 312 patients diagnosed and treated at a single centre, is one of the larger ones [3, 10, 18, 19, 26]. The largest study, with which the own material was compared, discussed the group (n=1252) presented by Zitsch et al. (1995) gathered over 47 years but, in some cases, not corresponding strictly to the up-to-date TNM criteria [26]. Out of the Polish articles, the largest material of lip cancer cases, however, limited to the lower lip, was presented by Szuta et al. (n=306) [24]. Other Polish studies concerning lip carcinoma include the studies by Sołtan et al. (n=284), Jaworska et al. (n=47), or Kaźmierczak et al. (n=21) [14, 15, 21].

Unfortunately, several summaries concerning lip carcinoma do not take into account the accepted TNM criteria, which limit the „lip” location only to the vermilion, or present the data as a part of material together with the data concerning the cancer of the oral cavity [1, 4, 7, 16, 25]. Such summaries, particularly if they apply to prognosis, are of extremely limited value and could not have been taken into account in comparison to own material. One of numerous examples could be the study by Kruger et al. taking into account the time period of 10 years in western Australia that presented the treatment outcomes of an impressive group of patients with lip carcinoma (n=1129) but together with tongue carcinoma (n=392) [16].

Male patients prevailed in the analysed material (8.9%), which is in accordance with similar summaries (from 80.7% to 90.4%) [3, 6, 9, 13, 18, 22, 27]. The age of patients with the peak of incidence in the 7th-8th decade of life for both sexes (mean value for M+F= 69.5 years, M = 68.8 years; F = 73.4 years) is also similar to what was found in the majority of studies [3, 11, 13, 17, 28]. However, there are some summaries in which the mean age of the patients was lower – 58.8 years (Souza et al.) or 62.0 years (Veness et al.) [22, 27]. One should take into account that patients' age influences the estimated probability

of survival that is determined in elderly patients by biological factors or other disorders [6]. When analysing the age structure of patients with lip carcinoma, a tendency for an increase in incidence over the age of 50 – in each decade was observed, and the highest value was noted in patients over the age of 80 (see Fig. 2). A similar relationship, with the highest incidence in the 7th and 8th decade, was observed by several other authors [16,17,28].

The primary focus of carcinoma was most commonly located within the lower lip (93.2%), which is similar to what was observed in other studies [1, 3, 13, 22, 26, 27]. The percentage of this location of lip carcinoma in the material gathered by Casal et al. was as high as 99.5% [3].

Cases in which the local stage was T1 + T2 in own material comprised in total 93.9% of the whole group. Also, several other studies confirm the prevalence of low local and clinical lip carcinoma grades [3, 20, 28].

Squamous cell carcinoma cases comprised as much as 97.4% of all cases, and well-differentiated cases (G1) comprised almost half (47.4%) of the total number of cases. This observation is also similar to the observations made in other studies [2, 3, 18, 22, 27]. In the summaries cited in literature, the pattern of SCC in diagnostic pathology was usually over 90% [2, 3, 26].

In the studies, in which lip carcinoma was diagnosed in a reliable manner with strict accordance to the TNM rules, with exclusion of the cases within the external anatomical surface of the lip, the pattern of basal cell carcinoma within the vermilion was approximately 5% [3, 26] – in our material it was found in only 3 out of 312 cases [0.9%]. Similarly, only in 2 out of 312 cases [0.6%] carcinoma was diagnosed as the „in

situ” stage. When it comes to this index, significantly more (3.4%) intraepithelial foci of lip carcinoma were observed in only one study [13]. With strict accordance to the TNM criteria, only cases that were confirmed malignant epithelial carcinomas within the vermilion in histopathology were included in the analysis. In the prepared literature review, such neoplasms were casuistic findings. And so, single cases were reported as „verrucous carcinoma”, adenocarcinoma, „unspecified carcinoma”, lymphoepithelioma, angiosarcoma, leiomyosarcoma, adenoid cystic carcinoma, or Merkel cell carcinoma or [3, 5, 17,26].

Ulceration was observed in 78.5% (245/312) of lip carcinoma cases in own material. In studies, in which this feature was included, similar percentage was observed (Gutierrez-Pascual et al. – 64. 6%, Fernandez-Angel et al.– 72.5%) [9, 13].

## CONCLUSIONS

In the analysed material of patients with lip carcinoma, male patients were noted almost 6 times more frequently than female patients, and the neoplasm was most commonly observed within the lower lip. The majority of patients commenced their treatment at early local stages (T1 + T2) (93.9%), and squamous cell carcinoma comprised 97.4% of all cases diagnosed in histopathology. The acquired epidemiological and clinical picture of lip carcinoma is similar to the one observed in literature.

Epidemiological-clinical analyses for patients with lip carcinoma should be compared only with groups gathered according to the TNM criteria established for this location and they should not be put together with the outcomes concerning another region, i.e. the „oral cavity”.

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