ANALYSIS OF THICKNESS AND DEPTH OF INVASION AS PROGNOSTIC FACTORS IN SQUAMOUS CELL CARCINOMAS OF TONGUE AND/OR FLOOR OF MOUTH DIAGNOSED AT THE BRAZILIAN NATIONAL CANCER INTITUTE BETWEEN 1999 AND 2006

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BACKGROUND

Oral and oropharyngeal cancer is the 11th most common cancer in the world, with two-thirds of the cases occurring in developing countries. More than 90% of oral cancer cases are squamous cell carcinoma (SCC). Pathological parameters of SCC may better reflect the prognosis, especially in relation to thickness and depth of invasion. Thickness is represented macroscopically, from the normal mucosa level to the deepest point of tumor invasion. The depth of the tumor is obtained microscopically, having as initial reference the basal layer of the epithelium to the deepest point of the tumor invasion.

OBJECTIVE

To evaluate the prognostic of tumor thickness and depth of invasion in patients with SCC of the tongue and/or floor of mouth diagnosed between 1999-2006.

METHODS

Study population: Records from 90 patients diagnosed with SCC of the tongue and/or floor of mouth diagnosed between 1999 and 2006 at the Brazilian National Cancer Institute were collected database.

Histopathological analysis: It was performed regarding the degree of differentiation (WHO) (EL–NAGGAR et al., 2017) and evaluation histopathological of the risk (BRANDWEIN-GENSLER et al., 2005)

Digitized slides: The slides were digitized on the APERIO® digital scanning platform and the images were stored in a management system and database.

Thickness and depth invasion analysis: Thickness was evaluate by macroscopic analyzed using the value 4 mm as a parameter (GANLY et al., 2013) as well depth invasion which was analyzed after the slides were digitized on the APERIOR digital scanning platform with the value 4 mm as a parameter (HUANG et al., 2009).

Statistic analysis: It was performed, analyzed and submitted to bivariate (X^2 and Mann Whitney) and survival (Kaplan-Meier and Log rank) analysis.

RESULTS

Profile of study population: Total of 90 patients were included in the study. White (60.5%), males (85.6%), aged between 41-60 years (50%), alcohol-drinkers (87.8%) and smokers (86.7%) were most affected. Predominated tongue tumors (55.1%), clinical stage II (44.4%) and treated with surgery (100%). Nine were identified cases of disease progression, 19 cases of recurrence. 44 came to death, of these 28 patients had confirmed death from cancer (Table 1).

Histopathological analysis: Moderately-differentiated tumors (82.4%) according to the histopathological grading of WHO with standard type invasion 4 (76.9%), perineural invasion of small nerves (58.2%) and lymphocytic infiltrate type II (47.3%) were predominat. The intermediate score of the risk was predominant (58.6%) (Table 2).

Thickness and depth invasion analysis: Predominated tumors with thickness >4mm (90.2%) and value 12.9 mm of mean. Depth of invasion >4 mm (87.0%) with 10.3 mm of mean was predominant (Table 4).

Statistical analysis: Association was observed between initial clinical stage and male (p=0.037), alcohol-drinkers (p=0.019) and not having adjuvant treatment. Thickness was significantly associated with moderately differentiating tumors (p= 0.013) and perineural invasion of small nerver (p=0.008). Depth of invasion and moderately differentiating tumors (p=0.013), perineural invasion of small nerves (p=0.005), intermediate risk score (p=0.019) were significantly associated. Association between thickness and depth of invasion (p<0.0001).

Table 1: Sociodemographic, clinical-pathological features of patients (No=90)

VARIABLE	CATEGORY	No. (%)
Gender	Male	77 (85.6%)
	Female	13 (14.4%)
Race	White	52 (85.6%)
	Brown	23 (26.7%)
	Balck	11 (12.8%)
Age	≤40 years	9 (10.0%)
	41-60 years	45 (50.0%)
	>60 years	36 (40.0%)
Smokers	Yes and ex	78 (86.7%)
	No	12 (13.3%)
Alcohol-drinkers	Yes and ex	79 (87.8%)
	No	11 (12.2%)
Tumor location	Tongue	49 (55.1%)
	Floor of mouth	22 (24.7%)
	Tongue and floor of mouth	18 (20.2%)
Inicial treatment	Sugery	90 (100%)
Adjuvant treatment	Yes	44 (48.9%)
	No	46 (51.1%)
Clinical stage	I	13 (14.4%)
	II	40 (44.4%)
	III	28 (31.1%)
	IV	9 (10.0%)
Disease progression	Yes	9 (10.0%)
	No	81 (90.0%)
Recurrence	Yes	19 (21.1%)
	No	71 (78.9%)
Second primary tumor	Yes	16 (17.8%)
	No	74 (82.2%)
Death	Yes	44 (48.4%)
	No	47 (51.6%)
Death from cancer	Yes	28 (63.6%)
	No	16 (36.4%)

Table 2: Histopathological analysis of patients (No=91)

VARIABLE	CATEGORY	No (%)
WHO grading	Well differentiated	6 (6.6%)
	Moderately diferentiated	75 (82.4%)
	Poorly diferentiated	10 (11.0%)
Invasion pattern	Type 1, 2 ou 3	20 (22.0%)
	Type 4	70 (76.9%)
	Type 5	1 (1.1%)
Invasion perineural	Without invasion	37 (40.7%)
	Small nerver	53 (58.2%)
	Large nerves	1 (1.1%)
Lymphocytic infiltrate	Type 1	42 (46.2%)
	Type 2	43 (47.3%)
	Type 3	6 (6.6%)
Escore of the risk	Low	6 (6.9%)
	Intermediate	51 (58.6%)
	High	30 (34.5%)

Table 3: Analysis of the thickness and depth invasion (No= 92)

	Thickness	Depth invasion
CATEGORY	No (%)	No (%)
>4	83 (90.2%)	80 (87.0%)
≤4	9 (9.8%)	12 (13.0%)

Table 4: Distribution of socio-demograph variables according to clinical staging (No = 90)

VARIABLE	CATEGORY	CLINICAL Initial(I +II) No, (%)	STAGING Advanced (III+ IV) No, (%)	p
Gender	Male	42 (46.7%)	35 (38.9%)	0.037
	Female	11 (12.2%)	2 (2.2%)	
Alcohol-drinkers	Yes	43 (47.8%)	36 (40.0%)	0.019
	No	10 (11.1%)	1 (1.1%)	
Adjuvant treatment	Yes	19 (21.1%)	25 (27.8%)	0.003
	No	34 (37.8%)	12 (13.3%)	

Survival analysis: Overall survival (OS) median was 73.59 months. Patients aged 41-60 years (p=0.030), with moderately differentiating tumors (p= 0.015), disease progression (p<0.0001), without recurrence (p=0.009) and died by cancer (p=0.003) had a lower OS. Already disease-free survival (DFs) was 56.16 months. Group who died (p<0.0001), with disease progression (p<0.0001), scare or absent inflammatory infiltrate (p=0.026), had a lower DFS.
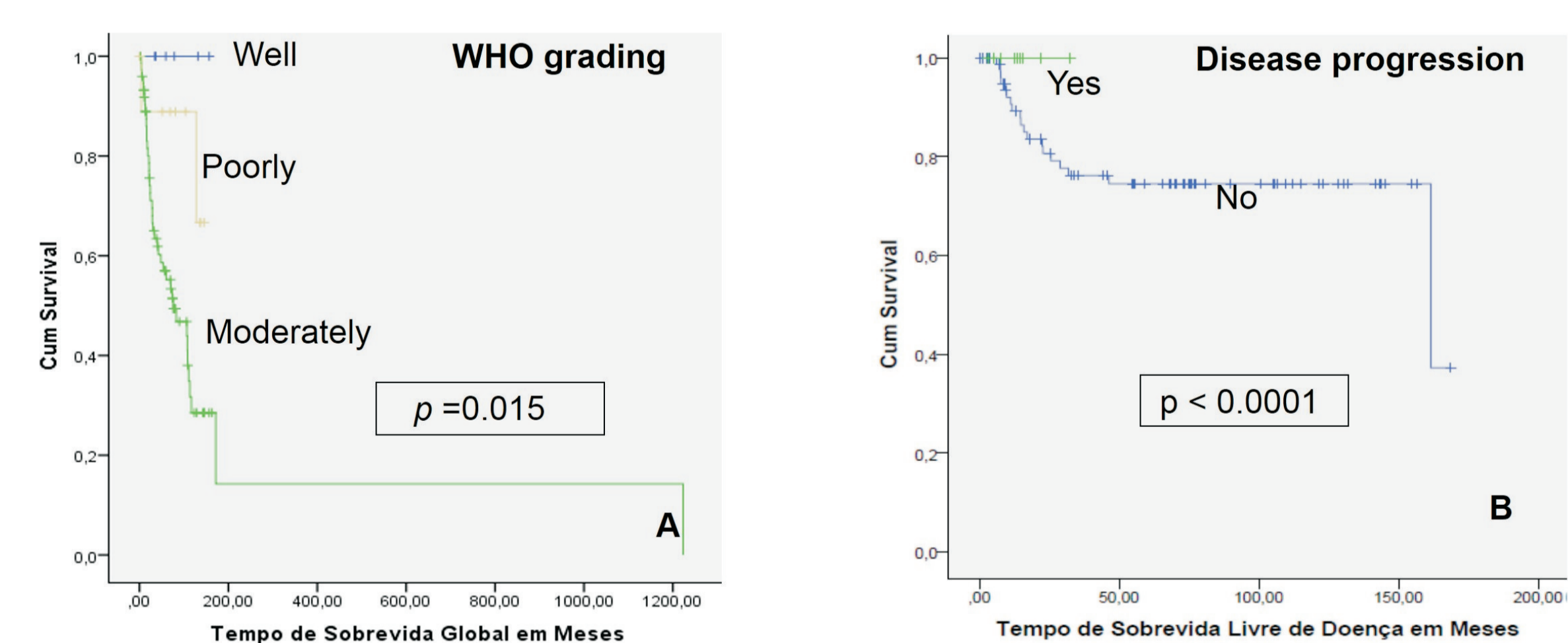
Graphic 1: Kaplan-Meier curves. A - Overall survival B- Disease-free survival

CONCLUSIONS

• The profile of patients with OSCC analyzed doesn't differ from literature for developing countries.

• Thickness and depth of invasion are important prognostic factors, showing the aggressiveness behavior of oral SCC.

REFERÊNCIAS BIBLIOGRÁFICAS

GANLY, I. et al., Long-term regional control and survival in patients with "low-risk", early stage oral tongue cancer managed by partial glossectomy and neck dissection without postoperative radiation: the importance of tumor thickness. Cancer, 119(15): 1168 -1176, 2012.

HUANG SH et al., O'SULLIVAN B. Predictive value of tumor thickness for cervical lymph-node involvement in squamous cell carcinoma of the oral cavity: a meta-analysis of reported studies. Cancer 115:1489–1497, 2009.

EL-NAGGAR AK, et al., WHO Classification of Head and Neck Tumors (4th edition). IARC Lyon, 2017.

BRANDWEIN-GENSLER, M. et al. Oral squamous cell carcinoma: histologic risk assessment, but not margin status, is strongly predictive of local disease-free and overall survival. Am J Surg, 29(2): 167-178, 2005.

Projeto Gráfico: Setor de Edição e Informação Técnico-Científica / INCA

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