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Differences in Oral Squamous Cell Carcinoma From Colombia and Spain: A Retrospective Cohort Study

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ABSTRACT

Objective: To compare the clinicopathological characteristics and survival of two cohorts of patients with oral squamous cell carcinoma (OSCC) from Spain and Colombia.

Methods: Clinicopathological and survival variables of patients with OSCC from six maxillofacial surgery departments in Spain and Colombia were retrospectively reviewed. Variables were compared according to country of origin.

Results: We included 649 patients, 359 from Spain and 290 from Colombia. The Colombian cohort was younger, drank more alcohol, had less comorbidities, and reported a greater mean number of days both from symptoms to diagnosis and from then to treatment, which was ~2.5 times longer in the Colombian cohort. Colombian patients were diagnosed at a more advanced stage. The treatment of choice was resective surgery. In the Colombian cohort, more patients received radio and chemotherapy together with surgery. Second primary tumors and recurrences were more frequent in the Colombian sample (7.2% vs. 2.8%; $p = 0.008$) and in the Spanish cohort (32% vs. 23.1%; $p = 0.012$), respectively. Overall survival was similar between the two samples (HR = 1.15; 95% CI = 0.93–1.42; $p = 0.195$) and disease-specific survival was worse in the Colombian one (HR = 1.30; 95% CI = 1.03–1.65; $p = 0.027$).

Conclusions: There were epidemiological differences between patients with OSCC in both cohorts and a longer delay in diagnosis and treatment in the Colombian sample.

1 | Introduction

According to GLOBOCAN, the global incidence of lip and oral cavity cancer has decreased in 2022. The latest results show that this cancer currently ranks 16th among the different types of cancer. In 2022, 389,846 new cases occurred and 188,438 patients died (Bray et al. 2024). Oral squamous cell carcinoma (OSCC) is the most common lip and oral cavity cancer, accounting for 90%

of malignant head and neck tumors (Montero and Patel 2015). OSCC is a malignant tumor of epithelial origin with a high capacity for invasion, destruction, and dissemination to adjacent structures. Five-year survival has improved in recent times, with published studies showing 5-year overall survival (OS) ranging from 50% to 70% (Nocini et al. 2022; Chamoli et al. 2021).

Different risk factors play a role in the development of OSCC, such as genetics and habits like tobacco and alcohol consumption. The joint consumption of tobacco and alcohol has a synergistic effect that increases the risk of developing OSCC (Chamoli et al. 2021; Caponio, Silva et al. 2024). There are also studies that have linked OSCC to oral microbiota dysbiosis (Zhong et al. 2021; Lorenzo-Pouso et al. 2022; Mauceri, Coppini et al. 2022), an unhealthy diet, and different comorbidities such as diabetes and hypertension (Zotti et al. 2020; Ramos-Garcia et al. 2021; Seo et al. 2020).

Differences in survival among patients may be due to differences in risk factors, access to healthcare for diagnosis and treatment, therapies received, and post-surgical management (Chow 2020; Xu et al. 2024). Therefore, the distinct lifestyles of each population, such as the type of habits, diet, as well as their health and socioeconomic status may influence the incidence and survival of OSCC (Tay et al. 2020; Gaur et al. 2011). The American Joint Committee on Cancer (AJCC) established treatment criteria and guidelines to standardize cancer care. The implementation of these protocols depends on the organization and type of healthcare system, which is different among countries (Mattavelli et al. 2020; Zanoni, Patel et al. 2019). The healthcare system in Spain is public, primary and specialized care is provided in health centers and hospitals belonging to the National Health System (Bernal-Delgado et al. 2018). In other countries, however, this can be regulated by private or community insurance. In Colombia, there are service companies in charge of managing the resources and the care network, depending on these companies for the selection of the intervention (Sanabria-Quiroga 2020). These differences in healthcare systems may influence the diagnosis, treatment, and follow-up of patients with OSCC, which may have an impact on the life expectancy and quality of life of OSCC patients (Bran Piedrahita et al. 2020). Although there is an extensive publication record on classical prognostic factors, to the best of our knowledge, no study has been conducted that addresses differences in survival and clinicopathologic features between samples of patients with OSCC in these countries. Furthermore, there are few studies on the epidemiology of OSCC in South America, and most of them have been performed in Brazil (Abrahao et al. 2020; Kowalski et al. 2020).

In this scenario, the aim of this study is to compare epidemiological variables, time from first symptoms to diagnosis and then to treatment, clinicopathological variables, and rates of OS, disease-specific survival (DSS), and recurrence-free survival (RFS) over time between two cohorts of patients with OSCC from Spain and Colombia.

2 | Materials and Methods

This study was conducted and reported following the Strengthening the Reporting of Observational Studies in Epidemiology statement (von Elm et al. 2008).

A retrospective review of the medical records of OSCC patients from six maxillofacial surgery departments in Spain and Colombia was performed. The study was approved by the Ethics Committees of each center with the following approval reference numbers: Hospital Universitario Ramón y Cajal and Hospital Universitario Puerta del Hierro (IRB n° 26/04/2022 ACTA 432), Hospital Universitario Central de Asturias (IRB n° 2023.042), Hospital Internacional de Colombia (IRB n° 215 of 02/03/2022), Clínica FOSCAL (IRB n° 05765/022), and Hospital Universitario Erasmo Meoz (IRB n° 2021-36-018048-2). The information was collected from the databases of each hospital. Only those patients with OSCC diagnosed between January 2010 and December 2015 at the aforementioned centers were included.

Data were included for patients who (1) were older than 18 years at the time of OSCC diagnosis; (2) had a clinical and histological diagnosis of primary OSCC; and (3) suffered OSCC in the following locations according to ICD-10: C00, C02, C03, C04, C05, and C06 (Sankaranarayanan et al. 2015). Patients were not included if they (1) had a histologic diagnosis other than OSCC; (2) had an OSCC on the base of the tongue (C01); (3) had previously treated malignant neoplasm in the head and neck region; and (4) patients who died during the first month after OSCC treatment.

The following epidemiological data were collected: age at diagnosis, sex, tobacco and alcohol consumption, number of cigarettes per year, number of alcoholic drinks per year, time from symptoms onset to diagnosis, time from diagnosis to treatment, comorbidities, and usual drug use. The staging system was updated to AJCC version 8th. Information on the exact location of OSCC, degree of differentiation, and type of treatment was also collected. Follow-up of patients was reviewed, collecting second primary tumors and recurrences.

Survival outcomes were established as (1) OS, calculated from the day of surgery to the day of last follow-up or death for any reason; (2) DSS, calculated from the date of surgery to the date of death from OSCC or to last follow-up; and (3) RFS, estimated from the date of surgery to the date of recurrence or to last follow-up.

2.1 | Statistical Analysis

Categorical data were shown as relative numbers and percentages, while continuous variables were shown as means and standard deviations (SD). Categorical variables were compared using the Chi-square test. The Shapiro–Wilk test was used to determine the normal distribution of quantitative variables. Since most of the variables conformed to a normal distribution, the t-test was used to analyze the association between categorical and numerical variables.

Univariate analysis was performed to determine the unique prognostic value of the patients' country of origin of the samples. For this purpose, the Kaplan–Meier curve with the Log-rank test was used to estimate the hazard ratio (HR) and 95% confidence interval (95% CI) for time-dependent outcomes (OS, DSS,

and RFS). Survival rates at 12, 36, 60, 90 and 120 months were also calculated.

Statistical analysis was performed with SPSS version 29.0 (SPSS Inc.) for Windows. The Python package KaplanMeierFitter was used to calculate survival rates at 12, 36, 60, 90, and 120 months.

To assess the impact that COVID-19 may have had on the survival of patients with OSCC, analyses and survival curves (OS, DSS, and RFS) were also performed by truncating the data in March 2020, when the pandemic was declared. In this case, follow-up was calculated to account for the onset of the pandemic, with the last follow-up set for February 29, 2020, and the living status was modified accordingly in those patients who had not died by that date.

3 | Results

3.1 | Demographic Characteristics

A total of 649 patients with OSCC were included, 359 from Spain and 290 from Colombia. The epidemiological characteristics of the two samples can be seen in Table 1. It was observed that the Spanish cohort was significantly older than the Colombian one [66.55 (SD = 13.82) vs. 64.09 (SD = 14.50) years; $p = 0.027$]. The male/female ratio was 1.6:1 in the Spanish sample and 1.3:1 in the Colombian sample ($p = 0.142$). In the Colombian cohort, there was a higher number of alcohol-drinking patients (41.8% vs. 32.9%). In addition, the consumption of alcohol units was twice as high in the Colombian cohort as in the Spanish cohort ($p < 0.001$). Significant differences were also observed in smoking history. The number of

TABLE 1 | Epidemiologic variables of patients with OSCC and statistical differences between the samples (number of observations, counts, and (%) either mean and standard deviation (SD)). *p*-values refer to independent *t*-tests or Chi-square tests.

Variable	Spanish sample $N = 359$	Colombian sample $N = 290$	*p*
Age	66.55 (13.82)	64.09 (14.50)	0.027
Sex			0.142
Male	221 (61.6%)	162 (55.9%)	
Female	138 (38.4%)	128 (44.1%)	
Cigarettes per year	3288.52 (3702.72)	3600.43 (2317.26)	0.414
Smoking history			< 0.001
Never smoked	166 (48.2%)	184 (64.5%)	
Current smoker ≤ 15 years	89 (25.9%)	23 (8.1%)	
Current smoker > 15 years	18 (5.2%)	62 (21.8%)	
Ex-smoker ≤ 15 years	58 (16.9%)	4 (1.4%)	
Former smoker > 15 years	13 (3.8%)	12 (4.2%)	
Units of alcohol per year	1143.5 (1043.8)	2572.1 (1769.6)	< 0.001
History alcohol			0.003
Never use	227 (65.4%)	162 (57.2%)	
Current use	114 (32.9%)	121 (41.8%)	
Former user	6 (1.7%)	0 (0%)	
Smoking and alcoholism history			< 0.001
Never smoked and never drinker of alcohol	144 (40.1%)	130 (44.8%)	
Smoker and alcohol drinker	96 (26.7%)	69 (23.8%)	
Alcohol drinker only	21 (5.8%)	50 (17.2%)	
Smoker only	77 (21.4%)	31 (10.7%)	
Number of diseases	1.64 (1.45)	0.62 (0.87)	< 0.001
Number of drugs	1.96 (1.01)	1.64 (0.84)	0.001
Time from symptoms to diagnosis (days)	55.15 (48.10)	140.27 (91.51)	< 0.001
Time from diagnosis to treatment (days)	70.03 (38.82)	176.48 (110.03)	< 0.001

patients who had never smoked was higher in the Colombian sample (64.5% vs. 48.2%), but the percentage of smokers at the time of diagnosis was similar, with no differences in the number of cigarettes consumed per year. The median (min/max) values for cigarettes consumed per year in the Colombian sample was 3650 (365–7300) versus 2555 (8–14,600) in the Spanish sample. And the units of alcohol per year were 2190 (365–11,825) in the Colombian sample and 780 (1–7000) in the Spanish sample. It should be noted that 26.7% of the Spanish cohort and 23.8% of the Colombian one reported smoking and drinking. When analyzing the number of systemic diseases, the mean was significantly higher in the Spanish sample [1.64 (1.45) vs. 0.62 (0.87); $p < 0.001$], and consequently the number of drugs received [1.96 (1.01) vs. 1.64 (0.84); $p = 0.001$]. Of interest, patients with OSCC in the Spanish sample reported a shorter mean number of days both from symptoms to diagnosis and then to treatment, which was ~2.5 times longer in the Colombian one ($p < 0.001$).

3.2 | Clinical and Histopathological Features

The results showed that the tongue (C02) was the most frequently affected area in both samples, with similar trends in the Spanish and Colombian samples (33% vs. 33.3%). The next most affected location was the floor of the mouth (C04) also with similar percentages in both samples (19% vs. 20.9%). The clinical manifestation of OSCC at the time of diagnosis included, in most cases, an ulcer (44.4% in the Colombian sample vs. 40.9% in the Spanish cohort) or an enlargement (38.9% vs. 40.6%), with no differences between samples. Statistically significant differences were observed for staging at the time of diagnosis, with Stage III being the most frequent in the Colombian sample (40.3%) followed by Stage I (24.5%); however, in the Spanish sample, OSCC was diagnosed more frequently in Stages I (29.7%), II (26.4%), and IVa (25%). There were differences in OSCC size (T), although T1 and T2 were the most common in both samples. Regarding lymph node involvement, differences could also be observed. In the Spanish cohort, a higher percentage of patients were N0 (66.1% vs. 38%, $p < 0.001$). Metastases (M) were more frequent in the Colombian one (5% vs. 1%, $p = 0.002$). The degree of differentiation was similar in the two samples, with well-differentiated (41.6% vs. 42.6%) and moderately differentiated (44.9% vs. 46.2%) OSCCs being the most frequent. The results are shown in Table 2.

3.3 | Treatment of OSCC, Relapses, and Second Primary Tumors

The results can be found in Table 3. Differences were found in the primary treatment of OSCC. In both samples, the treatments of choice were resective surgery alone (60.4% in the Spanish sample vs. 40.3% in the Colombian sample) and surgery followed by post-operative radiotherapy (29% in the Spanish sample vs. 31.7% in the Colombian sample). However, protocols were different, including additional chemotherapy. The occurrence of second primary tumors was higher in the Colombia cohort than in the Spanish cohort (7.2% vs. 2.8%,

TABLE 2 | Clinical and histological characteristics of patients with OSCC and statistical differences between the samples (number of observations, counts, and (%) either mean and standard deviation (SD)). *p*-values refer to independent *t*-tests or Chi-square tests.

Variable	Spanish sample $N = 359$	Colombian sample $N = 290$	*p*
Site (ICD)			0.624
Lip C00	35 (9.7%)	29 (10.4%)	
Tongue C02	118 (33%)	94 (33.3%)	
Floor of the mouth C04	68 (19%)	59 (20.9%)	
Gingiva C03	50 (14%)	37 (13.1%)	
Palate C05	55 (15.4%)	48 (17%)	
Others C06	32 (8.9%)	15 (5.3%)	
Clinical appearance			0.912
Plaque	30 (8.5%)	26 (9.1%)	
Ulcer	158 (44.4%)	117 (40.9%)	
Enlargement	138 (38.9%)	116 (40.6%)	
Erosion	21 (5.9%)	19 (6.6%)	
Others	8 (2.3%)	8 (2.8%)	
Clinical stage			<0.001
Stage I	105 (29.7%)	71 (24.5%)	
Stage II	93 (26.4%)	33 (11.5%)	
Stage III	60 (17%)	117 (40.3%)	
Stage IVa	88 (25%)	53 (18.3%)	
Stage IVb	2 (0.6%)	2 (0.7%)	
Stage IVc	4 (1.1%)	2 (0.7%)	
T			<0.001
T1	121 (34.4%)	133 (46%)	
T2	146 (41.5%)	90 (31%)	
T3	31 (8.8%)	66 (23%)	
T4	54 (15.3%)	0 (0.0%)	
N			<0.001
N0	233 (66.1%)	110 (38%)	
N1	61 (17.3%)	112 (38.6%)	
N2	34 (9.7%)	56 (19.3%)	
N2a	3 (0.9%)	5 (1.7%)	
N2b	11 (3.1%)	0 (0%)	
N2c	8 (2.3%)	2 (0.7%)	
N3	0 (0%)	3 (1%)	
N3a	0 (0%)	2 (0.7%)	
N3b	2 (0.6%)	0 (0%)	

(Continues)

TABLE 2 | (Continued)

Variable	Spanish sample $N=359$	Colombian sample $N=290$	p
M			0.002
Metastasis	3 (1%)	14 (5%)	
No metastasis	349 (99%)	276 (95%)	
Histological differentiation			0.683
G1 Well differentiated	148 (41.6%)	122 (42.6%)	
G2 Moderate	160 (44.9%)	132 (46.2%)	
G3 Poor	48 (13.5%)	32 (11.2%)	

$p=0.008$). On the other hand, the percentage of patients with relapses was higher in the Spanish sample (32% vs. 23.1%, $p=0.014$). The most common location of recurrence was the tongue in both cohorts.

3.4 | Survival

Mean follow-up time was similar for the Spanish and the Colombian samples (respectively, 66.7 SD = 38.1 vs. 65.5 SD = 37, median and range of 71 (1–150) vs. 66.5 (1–145)). OS did not show statistically significant differences between the two cohorts (HR = 1.15; 95% CI = 0.93–1.42; $p=0.195$). However, DSS was significantly worse in the Colombian samples (HR = 1.30; 95% CI: 1.03–1.65; $p=0.027$). Patients in the Spanish sample presented worse RFS than in the Colombian sample (HR = 1.45; 95% CI: 1.07–1.9; $p=0.016$). Figure 1 shows the survival curves for OS, DSS, and RFS for both samples.

As commented, survival was also calculated until March 2020 to take into account the impact of the COVID-19 pandemic on patient survival. In this case, mean follow-up time was similar for the Spanish and Colombian samples (respectively, 52.2 SD = 31 vs. 55.1 SD = 29.7, median and range 49.6 (1–123) vs. 55.2 (1–123)). This analysis showed that OS did not show statistically significant differences between the two cohorts (Spain vs. Colombia, HR = 1.18; 95% CI = 0.90–1.54; $p=0.228$). When considering follow-up prior to COVID-19, DSS showed no differences (Spain vs. Colombia, HR = 0.94; 95% CI: 0.69–1.28; $p=0.707$). Similar to when considering the entire follow-up, patients in the Spanish sample presented worse RFS than those in the Colombian sample (HR = 1.7; 95% CI: 1.2–2.4; $p=0.003$). Figure 1 shows the survival curves for OS, DSS, and RFS for both samples considering the entire follow-up period, while Figure 2 includes the Kaplan–Meier curves with adjusted follow-up and taking into account life status for the last follow-up on February 29, 2020.

When calculating survival rates considering the entire follow-up at 12, 36, 60, 90, and 120 months (Table 4), the OS rate was statistically significantly higher in the Colombian sample at 12 and 36 months but worse at 90 and 120 months. With respect to DSS, survival was significantly better in the Spanish sample at 90 and 120 months. Finally, the RFS showed fewer statistically significant events in the Colombian sample at 36, 60, and 90 months.

Taking into account the COVID-19 pandemic follow-up adjustment (follow-up truncated on February 29, 2020) (Table 5), OS rates were higher in the Colombian samples only at 12 and 36 months, and were similar to the Spanish sample at 60 and 90 months. Regarding DSS, there were no statistically significant differences at any time point comparison. RFS rates were similar to the results when total follow-up was considered, and fewer events were recorded in the Colombian sample at 36, 60, and 90 months.

4 | Discussion

In this study, we compared the epidemiological and clinicopathological characteristics, treatment, and survival rates of two samples of patients with OSCC from Spain and Colombia. This study shows that there are important differences in several aspects related to the OSCC between these two cohorts.

Risk factors associated with OSCC onset are multiple, including smoking and alcohol, genetic predisposition, diet, and poor oral hygiene (Li et al. 2024; Caponio, Silva et al. 2024; Singh et al. 2014). Alcohol consumption is considered an independent risk factor, but when consumed together with tobacco they act synergistically increasing the risk of developing OSCC (Marziliano et al. 2020; Hashibe et al. 2007). In this study, if we consider the number of patients currently smoking, we observe similarities in both cohorts (31.1% vs. 29.9%). Regarding alcohol history, we observed a higher frequency of alcohol consumption and higher doses of alcohol consumed in the Colombian cohort. Alcohol, in addition to increasing the risk of OSCC, has also been associated with the development of second primary tumors and treatment failure (Marziliano et al. 2020; Ali et al. 2017; Caponio, Zhurakivska et al. 2024). Indeed, in the Colombian cohort, which had more alcohol drinkers, the number of second primary tumors was higher than in the Spanish cohort.

We observed that a high percentage of patients were neither smokers nor drinkers (percentages above 40% in both cohorts). As other studies have noted, there is an emerging group of patients in whom classic risk factors are not identified. In some studies, the presence of OSCC has been observed in young non-drinking and non-smoking patients with poor survival that has been associated with an altered immune system (Fiedler et al. 2023; Tran et al. 2023; Harada et al. 2023; Valero et al. 2022). The retrospective design of this study did not allow us to evaluate possible alterations in the immune system. In any case, although there is a significant number of cases not associated with classical risk factors, efforts to reduce classic OSCC risk factors should continue. In Spain, there are campaigns promoted by the Ministry of Health to reduce tobacco consumption and primary care centers are offering help to those who want to quit smoking (Villalbi et al. 2019). Similarly, in Colombia, efforts have also been made by the Ministry of Social Protection, but they do not have the same scope in primary healthcare as in Spain (Uang et al. 2017).

TABLE 3 | Treatment protocols and evidence of relapse or second primary disease and statistical differences between the samples (number of observations, counts, and (%) either mean and standard deviation (SD)). *p*-values refer to independent *t*-tests or Chi-square tests.

Variable	Spanish sample $N = 359$	Colombian sample $N = 290$	*p*
Primary treatment			< 0.001
Surgery	217 (60.4%)	117 (40.3%)	
Surgery and pre–post radiotherapy	0 (0%)	1 (0.3%)	
Surgery and postradiotherapy	104 (29%)	92 (31.7%)	
Surgery and prechemotherapy	0 (0%)	8 (2.9%)	
Surgery and postchemotherapy	7 (2%)	2 (0.7%)	
Surgery with postradio and postchemotherapy	31 (8.6%)	63 (21.7%)	
Surgery with postradio and pre–postchemotherapy	0 (0%)	7 (2.4%)	
Radiotherapy			< 0.001
No	224 (62.4%)	127 (43.8%)	
Yes, preoperative	0 (0%)	0 (0%)	
Yes, postoperative	135 (37.6%)	162 (55.9%)	
Both	0 (0%)	1 (0.3%)	
Chemotherapy			< 0.001
No	321 (89.4%)	210 (72.4%)	
Yes, preoperative	0 (0%)	8 (2.8%)	
Yes, postoperative	38 (10.6%)	65 (22.4%)	
Both	0 (0%)	7 (2.4%)	
Second primary tumors			< 0.001
Yes	10 (2.8%)	21 (7.2%)	
No	349 (97.2%)	269 (92.8%)	
Recurrence			0.014
Yes	115 (32%)	67 (23.1%)	
No	244 (68%)	223 (76.9%)	
Recurrence site			0.115
Lips	11 (9.5%)	6 (9%)	
Tongue	35 (30.1%)	23 (34.3%)	
Palate	18 (15.5%)	18 (26.9%)	
Buccal mucosa	25 (21.6%)	9 (13.4%)	
Alveolar ridge	8 (6.9%)	7 (10.4%)	
Others	19 (16.4%)	4 (6%)	

The results of the present study showed that the diagnostic delay as well as the delay from diagnosis to treatment was greater in the Colombian sample, being 2.5 times longer in the Colombian cohort. Some studies have found no significant correlation between diagnostic delay and OS, DSS, and recurrence rates (Barrett et al. 2021; Thomas et al. 2021). In our case, we also observed no differences in OS between the two samples, but DSS was higher in the Spanish sample. However, Seoane et al. (Seoane-Romero et al. 2012) did not observe an association between late diagnosis and DSS, justifying the poor survival to the biological and proliferative characteristics of OSCC. Early diagnosis of OSCC leads to the diagnosis of smaller tumors requiring only surgical treatment. In addition, OSCC diagnosed at early stages do not have lymph nodes or distant metastases, which avoids adjuvant treatments. This will avoid receiving more aggressive treatments that reduce the patient's quality of life (Lima et al. 2021; Freire et al. 2021). In the present study, the Colombian sample, who had a longer diagnostic delay, presented tumors with a more advanced stage. And although surgical treatment was

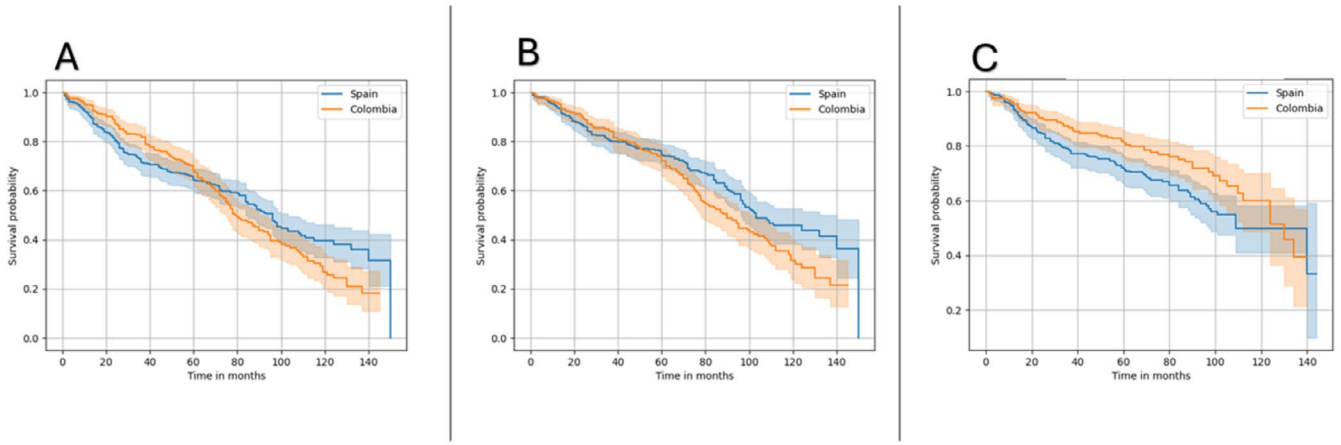

FIGURE 1 | Kaplan–Meier survival curves over time (months) considering all follow-ups: (A) overall survival (OS); (B) disease-specific survival (DSS); and (C) relapse-free survival (RFS) by sample country origin (Spain and Colombia).

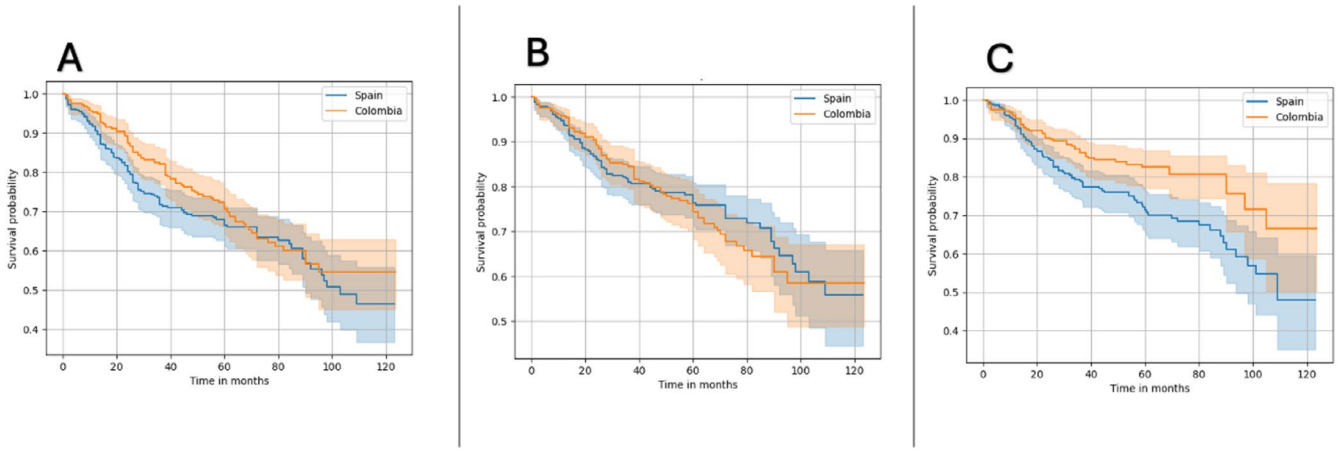

FIGURE 2 | Kaplan–Meier survival curves over time (months) to February 29, 2020: (A) overall survival (OS); (B) disease-specific survival (DSS); and (C) relapse-free survival (RFS) by sample country origin (Spain and Colombia).

the most common, there was a significant group of patients (21.7%) who received surgery with additional postradio- and postchemotherapy. Therefore, it could be that late diagnosis leads to more advanced and more complex tumors to treat. In any case, not only does the staging influences the treatment and survival of OSCC but also its histopathological grading. In our case, the histological differentiation of the included OSCC cases was similar between these two samples.

The causes of delay in diagnosis or treatment depend on different reasons, such as access to health services and socioeconomic status (Ramadan et al. 2023; Mauceri, Bazzano et al. 2022; Rich et al. 2023). Access to health services will depend on the origin of the patients. In Spain, patients with OSCC usually go first to their primary care physician or dentist, who refers the patient to the corresponding maxillofacial surgery service. In Spain, if the reason for consultation is oncological, the referral is urgent, as evidenced by the time that elapses from complaint to diagnosis in the Spanish sample, with an average of less than 2 months. Once the case has been diagnosed, surgical treatment of OSCC in Spain is also carried out quickly, in many cases not exceeding 1 month. All treatments are covered by the health system, and complementary tests and treatments should not be approved. In Colombia, the first consultation is made in general medicine. The general practitioner makes a referral to oncology services. This referral will depend on the type of social security affiliation to which the patient belongs and on the type of company providing services. Therefore, the company providing services will be in charge of administering the economic funds, managing the medical care, and accepting all the treatments to be performed, from the appointments with the specialists to the necessary complementary tests. This may delay the diagnosis and treatment. On the other hand, not all regional hospitals in Colombia have an oncology service, and therefore it is necessary to refer the patients to tertiary care hospitals (Sanabria-Quiroga 2020). So, in most cases, the waiting time for administrative and bureaucratic authorizations is the cause of long waiting times and delays in treatment in Colombia (Xie et al. 2024). Thus, the healthcare system of each country may affect the speed of care for patients with OSCC. The delay in diagnosis and, therefore, the OSCC diagnosis at more advanced stages could be due to barriers to access to health services for economic and/or administrative reasons.

Treatment protocols for OSCC are established by the AJCC and the Union for International Cancer Control to standardize

TABLE 4 | Survival rates for overall survival (OS), disease-specific survival (DSS), and relapse-free survival (RFS) by country (Spain and Colombia) at 12, 36, 60, 90, and 120 months. Rates are followed by (95% confidence intervarls, CI). *p*-value refers to the Chi-square test at a specific timepoint.

Variable	Spanish sample rate (95% CI)	Colombian sample rate (95% CI)	*p*
OS			
At 12 months	0.91 (0.87–0.93)	0.95 (0.92–0.97)	0.031
At 36 months	0.71 (0.66–0.76)	0.82 (0.77–0.86)	0.001
At 60 months	0.64 (0.59–0.69)	0.68 (0.62–0.73)	0.39
At 90 months	0.52 (0.46–0.57)	0.44 (0.37–0.50)	0.012
At 120 months	0.39 (0.33–0.46)	0.27 (0.20–0.34)	0.011
DSS			
At 12 months	0.94 (0.91–0.96)	0.96 (0.93–0.98)	0.29
At 36 months	0.80 (0.76–0.84)	0.84 (0.79–0.88)	0.21
At 60 months	0.74 (0.69–0.79)	0.72 (0.66–0.77)	0.49
At 90 months	0.60 (0.53–0.65)	0.48 (0.42–0.55)	0.016
At 120 months	0.46 (0.38–0.53)	0.31 (0.24–0.39)	0.009
RFS			
At 12 months	0.93 (0.90–0.95)	0.95 (0.92–0.97)	0.27
At 36 months	0.79 (0.74–0.83)	0.86 (0.82–0.90)	0.013
At 60 months	0.72 (0.66–0.76)	0.81 (0.75–0.86)	0.011
At 90 months	0.61 (0.54–0.67)	0.72 (0.64–0.78)	0.03
At 120 months	0.50 (0.41–0.58)	0.60 (0.49–0.70)	0.13

TABLE 5 | Survival rates for overall survival (OS), disease-specific survival (DSS), and relapse-free survival (RFS) by country (Spain and Colombia) at 12, 36, 60, and 90 months (last follow-up February 29, 2020). Rates are followed by (95% confidence intervarls, CI). *p*-value refers to the Chi-square test at a specific timepoint.

Variable	Spanish sample rate (95% CI)	Colombian sample rate (95% CI)	*p*
OS			
At 12 months	0.90 (0.87–0.93)	0.95 (0.92–0.97)	0.020
At 36 months	0.71 (0.66–0.76)	0.81 (0.76–0.86)	0.002
At 60 months	0.66 (0.61–0.71)	0.70 (0.64–0.75)	0.176
At 90 months	0.56 (0.49–0.63)	0.56 (0.48–0.64)	0.99
DSS			
At 12 months	0.93 (0.90–0.95)	0.95 (0.92–0.97)	0.307
At 36 months	0.81 (0.76–0.84)	0.84 (0.79–0.88)	0.266
At 60 months	0.76 (0.71–0.80)	0.74 (0.68–0.79)	0.592
At 90 months	0.66 (0.58–0.73)	0.60 (0.51–0.68)	0.356
RFS			
At 12 months	0.93 (0.89–0.95)	0.95 (0.91–0.97)	0.293
At 36 months	0.78 (0.74–0.83)	0.86 (0.81–0.89)	0.022
At 60 months	0.71 (0.65–0.76)	0.82 (0.76–0.86)	0.003
At 90 months	0.61 (0.52–0.68)	0.75 (0.65–0.82)	0.016

treatments based on available evidence to improve patient survival and quality of life (Moeckelmann et al. 2018). There are problems in adopting protocols with universality due to limited or insufficient resources, unavailable/limited technology, or healthcare systems. Access barriers and insufficient coverage depend on the medical policies and laws in each country, resulting in treatments not being the same in some areas, hospitals, and/or countries (Sanabria-Quiroga 2020; Xie et al. 2024; Baykul et al. 2010; Zanoni, Montero et al. 2019). Resective surgery accompanied by neo/adjuvant therapies such as radiochemotherapy (in advanced cases or close surgical margins) are the treatment of choice in patients with OSCC (Ghani et al. 2019). In the Spanish sample, the most frequent staging of OSCC was Stage I (29.7%), however, in the Colombian sample, the most frequent staging was Stage III (40.3%). In the Spanish sample, 66% of patients had no lymph node involvement, but in the Colombian sample, only 38% of patients with OSCC had no lymph node involvement. This may have resulted in a significant number of patients in the Colombian cohort being treated with additional radio and chemotherapy. However, the most common treatment in both samples was surgery alone (60.4% in the Spanish sample and 40.3% in the Colombian sample). There is a Cochrane review on the use of chemotherapy in the treatment of OSCC in

complex and advanced cases (Parmar et al. 2021). This review found that chemotherapy is beneficial when used in specific circumstances in conjunction with locoregional treatment, with no clear survival benefit. It was evidenced how concurrent chemoradiotherapy, compared to radiotherapy alone, is associated with more than 20% improvement in OS. This may be one of the reasons why there is no difference in OS between both samples, although the OSCC in the Colombian sample was more advanced.

Currently, the 5-year OS of OSCC ranges from 59% to 70%. GLOBOCAN's current results show higher survival-specific rates in countries close to Spain and Colombia, such as France (71.2%) and Brazil (74.1%) at 5 years (Bray et al. 2024). In the present study, the OS at 5 years was 64% in the Spanish sample and 68% in the Colombian sample, figures similar to those reported by other studies (Zanoni, Silva et al. 2019; Kowalski et al. 2020). However, 5-year DSS was 74% in Spain and 72% in Colombia. These small discrepancies between OS and DSS may be due to the fact that the Spanish cohort was slightly older and had significantly more systemic diseases that may have influenced a lower OS in the Spanish sample. Patients may have died of causes other than cancer. There are studies that have observed how having other diseases can have an impact on OSCC survival, reducing it (Seoane-Romero et al. 2012; Davies et al. 2023). On the other hand, higher staging worsens the prognosis and decreases survival (Zanoni, Patel et al. 2019). In the Colombian sample, there were more patients with OSCC who had higher stages, which could influence a lower DSS. It is worth noting that OS and DSS at 10 years were higher in the Spanish cohort than in the Colombian cohort (39% vs. 27% and 46% vs. 31%, respectively). Thus, OSCC survival may be influenced by multiple factors, such as patient age, stage of OSCC, comorbidities, lifestyle, persistence of risk factors (smoking and alcohol), and long-term follow-up.

It is important to note that the COVID-19 pandemic may have influenced the results of this study. The pandemic may have resulted in less close follow-up of patients with already treated OSCC, as revisions were spaced out or even canceled (da Cunha et al. 2021; Petti 2024; Neamtiu et al. 2022). Therefore, it is possible that on many occasions recurrences or second primaries were not diagnosed early and treated effectively, decreasing patient survival. On the other hand, if the patient was PCR positive for COVID-19 or suspected (by clinical profile), COVID-19 was considered the primary cause of death, while other diseases (including cancer) could have been considered contributory causes of death (Petti 2024; Henley et al. 2022). Due to these causes, survival rates through March 2020 were also calculated. Some differences were observed when performing these analyses. OS and DSS previously higher in the Spanish sample compared to the Colombian sample at 90 and 120 months, showed no differences at 90 months when follow-up was truncated. It was also observed a decrease in OS and DSS survival at 90 months if the entire follow-up was considered with respect to the follow-up until March 2020 in both countries. In the case of Spain, this result is in line with what Petti showed in his study (Petti 2024), as although this study showed a negative excess mortality in Europe for oral and pharyngeal cancer in 2020–2021 with respect to 2011–2019, it reports that specifically in Spain and Poland there was an excess mortality thus decreasing survival. We believe that it is important to show both results since it is impossible to know what was the real reason for which patients died during the COVID-19 pandemic.

We are aware that our study has some limitations. It is a retrospective study in nature, which may bias the results and does not allow relationships to be established. In addition, samples were selected from maxillofacial surgery services of six hospitals (three in Colombia and three in Spain), all located in different cities, but this is not representative of all patients with OSCC in Colombia and Spain. Another limitation is the impact that the COVID-19 pandemic could have had on the survival of OSCC patients in this study if full follow-up is considered.

As strengths, we believe that this study reflects the diagnostic and treatment delay in certain areas and shows that work should be done to ensure that all patients with OSCC have equal access to proper diagnosis and treatment. It also shows the epidemiological results of OSCC in a previously unstudied area, Colombia.

The results of the present study showed epidemiological differences between two samples of patients with OSCC from Colombia and Spain. There were differences in the risk factors, and the time to diagnosis and treatment was 2.5 times longer in the Colombian cohort. This may have led to a higher staging of OSCC in the latter sample. If the complete follow-up is considered, OS results were similar between both cohorts, but DSS was higher in the Spanish sample. We believe it is essential that all OSCC patients have proper access to a public healthcare system so that they can receive correct diagnosis and treatment. Further studies should be performed to clarify which factors influence survival in patients with OSCC.

Author Contributions

Ana María Rochel-Rochel: conceptualization, writing – original draft, methodology, formal analysis, data curation. **Julio Acero-Sanz:** writing – original draft, data curation. **Juan Carlos de Vicente:** data curation, writing – original draft. **Vito Carlo Alberto Caponio:** writing – original draft, formal analysis, software, data curation, methodology. **Cristina Cárdenas-Serres:** writing – review and editing, data curation. **Catalina Cáceres Ramírez:** data curation, writing – review and editing. **Silvia Juliana Villabona Flórez:** writing – review and editing, data curation. **Viviana Jiménez Andrade:** data curation, writing – review and editing. **Diego Gómez Abreu:** data curation, writing – review and editing. **Francy Archilla Flórez:** writing – review and editing, data curation. **Rosa María López-Pintor:** conceptualization, writing – original draft, methodology, formal analysis, resources, supervision, project administration.

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The authors have nothing to report.

Ethics Statement

The study was approved by the Ethics Committees of each center with the following approval reference numbers: Hospital Universitario Ramón y Cajal and Hospital Universitario Puerta del Hierro (IRB n° 26/04/2022 ACTA 432), Hospital Universitario Central de Asturias (IRB n° 2023.042), Hospital Internacional de Colombia (IRB n° 215 of 02/03/2022), Clínica FOSCAL (IRB n° 05765/022), and Hospital Universitario Erasmo Meoz (IRB n° 2021-36-018048-2).

Consent

Whenever applicable, this was registered.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data are available upon reasonable request to the corresponding author.

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