Histological grading of oral squamous cell carcinoma patients in Ibadan using Bryne's and Broders' Grading Systems- a comparative study

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Abstract

Background: Several histological grading systems for oral squamous cell carcinoma (OSCC) have been used previously to guide treatment and prognostication, amongst which are the Broders and the Bryne's methods. The Bryne's invasive tumour front (ITF) protocol has been adjudged to have good prognostic significance. We compared the use of Bryne's ITF system and Broders' grading system in grading OSCC at our centre in relation to clinico-demographic profile of patients.

Methods: Thirty two formalin fixed paraffin embedded (FFPE) tissue samples of histologically diagnosed OSCC patients at the University College Hospital (UCH) Ibadan were selected, demographic data and site of lesions were retrieved from the medical records of the patients. The haematoxylin and eosin (H&E) slides of the 32 cases were prepared and evaluated using Bryne's ITF system and Broders classification.

Results: Using Bryne's system, 28% of the cases had a high malignancy score while 72% had a low malignancy score. The high malignancy score lesions were most commonly seen in the palate (15.5%). Also Broders classification showed that 31.3% of cases were well differentiated tumours, 50% were moderately differentiated while 18.7% were poorly differentiated.

Conclusion: Either the Bryne's system or Broders classification can be used to grade OSCC with similar results being obtained.

Résumé

Contexte: Plusieurs systèmes de classement pour l'administration orale de carcinome spinocellulaire (CCCO) ont été précédemment utilisés pour guider le traitement et le pronostic. Un indice de prédiction du pronostic du carcinome épidermoïde oral (CCCO) en a servi d'histoire.

L'avant-tumeur invasive (ITF) de Bryne est dite avoir une pronostique importante supérieure aux autres systèmes de classification traditionnels. Nous avons évalué l'applicabilité du système de l'ITF de Bryne dans le classement CCCO dans notre centre par rapport aux profils clinico-démographiques des patients.

Méthodes: Trente-deux fixes formol paraffine intégré (FFPE) des échantillons de tissu histologiquement diagnostiqués des patient au centre hospitalier universitaire d'Ibadan remplissant les critères d'inclusion ont été choisis, les données démographiques et la localisation des lésions ont été extraites des dossiers médicaux des patients. Les diapositives de l'hématoxyline et de l'éosine (H & E) des 32 cas ont été préparées et évalués à l'aide du système de l'ITF de Bryne (Bryne et al. 1992).

Résultats: Environ 28% des cas avaient un score élevé de malignité, tandis que 72% avaient un faible résultat de malignité. Les résultats élevés de lésions de malignité ont été le plus fréquemment observés dans la bouche (15,5%). Les hommes ont une fréquence plus élevée de résultats de lésions de malignité (55,5%) que chez les femmes (44,4%). Il n'y avait pas de relation statistiquement importante entre le résultat de malignité de la Bryne que ce soit sur l'âge, sur le sexe ou sur la localisation de la lésion.

Conclusion: (ITF) Le système de classement de la malignité de la Bryne était le meilleur pour garder histologie de la CCCO, mais n'avait aucun lien avec les indices clinico-démographique.

Introduction

Oral squamous cell carcinoma (OSCC) is the most common malignant neoplasm occurring in the oral cavity. It is defined as a malignant epithelial neoplasm exhibiting squamous differentiation, as characterised by the formation of keratin and or presence of intercellular bridges [1]. It is a major health problem resulting in high morbidity and mortality. Globally, an estimated 263,900 new cases and 128,000 deaths from oral cancer (including lip cancer) occurred in 2008, with the highest oral cancer rates reported from Melanesia, South-Central Asia, Central and Eastern Europe [2].

Several grading systems for OSCC have been used previously to guide treatment and prognostication [3]. These include the following amongst many systems: Tumour Node Metastasis

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(TNM) system [3], Broders classification [4], Anneroth's classification [5] and Bryne's Invasive Tumour Front (ITF) malignancy grading system for OSCC [6]. Broders grading system was introduced in 1926 and it has been in use for many years. Tumours are graded as well differentiated, moderately differentiated and poorly differentiated based on the degree of differentiation and keratinization of tumour cells [4]. Anneroth in 1987, suggested that a new system of grading was needed due to the poor association between existing systems and patient survival [5]. In their study, they found an association between tumour grades and cure rate using a modification of existing systems [5].

Bryne *et al.* reported in 1989 that several studies have shown that invasive tumour front grading is a significantly better predictor of prognosis and a valuable supplement to clinical staging and suggested that it should be introduced into clinical practice [6]. They recognized that the cells in malignant lesions were heterogeneous with the cells at the deep invasive margin being less differentiated than those in the superficial layer [6-8]. Thus, Bryne *et al.* modified Anneroth's system in the grading of OSCC [6]. In Bryne's system, only the cells at the deep invasive margin of the tumours were graded [6-8]. This system was modified in 1992, and its usefulness in the histological grading of OSCC as well as its prognostic value has been attested to by studies from various countries [7-9]. This study therefore compared the use of Bryne's ITF system and Broders system in grading OSCC at our centre in relation to clinico-demographic profile of patients.

Materials and method

This was a retrospective study on the evaluation of Bryne's histological grading of malignancy in patients with histologically diagnosed OSCC. A list of all patients diagnosed of OSCC from January 2005 to December 2010 was obtained from the surgical day book of the Oral Pathology Department, University College Hospital, Ibadan. The socio-demographic data and paraffin blocks of patients were retrieved from the records, cases for which the paraffin blocks were not found or the socio-demographic information was incomplete were excluded from further use. New haematoxylin and eosin (H&E) slides were prepared while the inclusion criteria for this study were the availability of representative sections showing full thickness lesions with deep invasive areas and sections showing tumour-connective tissue interface. Thus, thirty two

of these were eligible for further analysis in this study. Ethical clearance for the study was obtained from the joint University of Ibadan /University College Hospital ethical review committee

Broders classification was used to categorise OSCC into well differentiated squamous cell carcinoma (WDSCC), moderately differentiated squamous cell carcinoma (MDSCC) and poorly differentiated squamous cell carcinoma (PDSCC) [4]. Bryne's histopathological malignancy grading system for OSCC was also applied to grade the tumours [7, 8]. This system consists of 4 morphological characteristics: degree of keratinization, nuclear polymorphism, invasive pattern and lymphoplasmocytic infiltration. Total average scores of histological malignancy grading were obtained by summing the scores attributed to each morphological parameter and then dividing by the number of parameters used. A range of 1.0-2.5 was considered as low malignancy score and 2.6-4.0 ranges as high score (Table 1). Histological assessments were independently carried out by two oral pathologists, AOA and AOA. In cases where opinion of the two authors differed, the disagreement was resolved after a joint review and a consensus on each case was reached with a third reviewer, BFA [10]. The ages of the cases were grouped into $\leq$ 45 years, 46-64 years and $\geq$ 65 years. [11]. A comparative analysis of the Bryne's system and the Broders classification was done.

For the purpose of this study, the oral cavity was defined as extending from the vermilion border of the lips to a plane between the junction of the hard and soft palate superiorly and the circumvallate papillae of the tongue inferiorly. This region includes the buccal mucosa, upper and lower alveolar ridges, floor of the mouth, retromolar trigone, hard palate, and anterior two thirds of the tongue [12].

All data were analyzed using the SPSS version 16.0. Chi square test was used to test association between categorical variables at 95% level of confidence (i.e. P <0.05) while the student t test was used to compare the mean of quantitative variables,

Results

A total of 32 OSCC cases were evaluated using Bryne's and Broders system. Patients' ages ranged from 30 to 106 years. The mean age of cases was 61.6 ±18.5 years. Subjects 45 years and below were 6 (18.7%) while the highest frequency of OSCC was seen in cases $\geq$ 65years, 17 (53.1%). About 65.6% (21) of cases were males giving a male to female

Table 1: Histological malignancy staging system according to Bryne *et al.* (1992)

| Morphological features | Histological Score | | | |
	1	2	3	4
Keratinization degree	Highly keratinized (> 50% of cells)	Moderately keratinized (20-50% of cells	Minimal keratinization (5-20% of cells)	No keratinization ke (0-5% of cells)
Nuclear Pleomorphism	Nuclear Pleomorphism (>75% of mature cells)	Nuclear Pleomorphism Moderately abundant (50-75% of mature cells	Abundant nuclear Pleomorphism (25-50% of mature cells)	Extreme nuclear Pleomorphism (0-25% of mature cells)
Pattern of invasion	Well defined margins	Solid strings and /or inlets	Small cell groups n<15	Cellular diffuse dissociation and Characterized in small and /or Isolated cell groups
Lymphoplasmocytic infiltrate	High	Moderate	Discrete	Absent

ratio of 1.9:1. There was no statistically significant difference between age; gender and occurrence of OSCC ($\div^2 = 1.636$, df = 2, p =0.441). OSCC was seen most frequently in the palate with 11 (34.4%) cases, followed by the mandibular gingivae 7 (21.9%), while the least cases were diagnosed on the lower lip 1 (3.1%).

Table 2: Age group and gender distribution of Bryne's Score

| Age group (years) | Malignancy score | | Total |
	Low	High	
≤45	4 (12.5%)	2 (6.2%)	6 (18.7%)
46-64	6 (18.8%)	3 (9.4%)	9 (28.2%)
≥65	13 (40.6%)	4 (12.5%)	17 (53.1%)
Total	23 (71.9%)	9 (28.1%)	32 (100%)
Sex			
Male	16 (50.0%)	5 (15.6%)	21 (65.6%)
Female	7 (21.9%)	4 (12.5%)	11 (34.4%)
Total	23 (71.9%)	9 (28.1%)	32 (100%)

The overall mean malignancy score in the present study was 2.48 ±0.54, 23 (72%) subjects had low malignancy score, while 9 (28%) subjects had a high malignancy score. The age group ≥ 65 years had the highest malignancy scores (Table 2). However, there was no statistically significant relationship between malignancy scores and age of patient ($\div^2 = 0.379$, df = 2, p = 0.827). Males had higher malignancy scores compared to females but was not statistically significant ($\div^2 = 0.56$, df = 1, p = 0.45) (Table 2).

For site distribution, the highest frequency of high malignancy scores was seen in the palate and mandibular gingivae while the palate also recorded the highest frequency of low scores. There was no statistically significant relationship between malignancy scores and site of lesions ($\div^2 = 4.79$, df = 1, p = 0.57).

Table 3: Comparative analysis of Broders classification and Bryne's score

| Degree of differentiation | Bryne's score | | Total |
	Low (1.00-2.50)	High (2.60-4.00)	
WDSCC (1)	10	0	10 (31.3%)
MDSCC (11)	13	3	16 (50%)
PDSCC (111)	0	6	6 (18.7%)
Total	23 (71.9%)	9 (28.1%)	32 (100%)
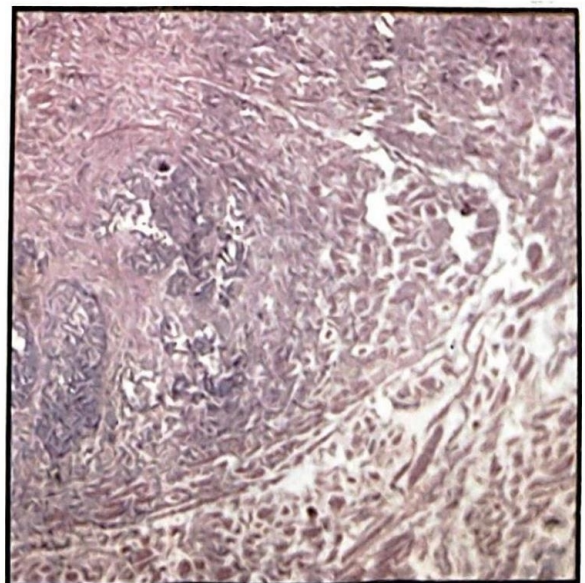
Magnification X 50

Fig. 1: Photomicrograph showing moderately differentiated OSCC exhibiting infiltration of muscle fibres with pushing well delineated border

For Broders classification of the 32 cases analysed, 10 (31.3%) cases were WDSCC, 16 (50%) MDSCC and six (18.7%) were PDSCC. The ability of Broders and Bryne's grading systems to categorize OSCC with same prognostic implication was statistically significant ($\div^2$ = 19.942, df = 2, p $\leq$0.001) (Table 3).

Discussion

WHO has recommended the use of cell differentiation along with other morphologic criteria such as the pattern of invasion and lymphocytic infiltration in the grading of malignant neoplasms [13]. We evaluated OSCC patients using Bryne's malignancy grading system and the Broders system since histological grading of tumours is more useful in treatment planning and prognosis prediction compared to clinical assessment by the TNM system. One of the reasons for this is the fact that histological changes often precede clinical changes [14].

To the best of our knowledge, there are only a few studies that have related the clinicopathological profile of OSCC patients to the Bryne's invasive tumour front malignancy grading system [11]. In our study, high malignancy score SCC were more prevalent in patients 65 years and above. This is similar to results obtained from a study by Kantola et al. who recorded high malignancy grade lesions in stage I and stage II tongue SCC patients above 65 years of age relative to the other age groups [11]. Also, males had a slightly higher percentage of tumours with high malignancy score with 5 cases (55.5%) compared to 4 in females (44.4%) while the palate recorded the highest frequency of high malignancy score. However, age, gender and site may play little or no role in the histological differentiation of tumours.

In this study, high malignancy scores were seen in all six poorly differentiated tumours which is similar to the finding of Bryne et al. [6] where high malignancy scores were seen in all poorly differentiated tumours. Therefore it can be concluded that a high malignancy score also suggests a poorly differentiated tumour [6].

In this study, the ability of Bryne's system to classify OSCC considered as poorly differentiated by Broders, as lesions with high malignancy scores was statistically significant, likewise its capability to group those categorized by Broders into well differentiated tumours, as lesions with low malignancy scores. This was similar to the findings by Munoz-Guerra et al. in their study [14]. Using Broders classification, MDSCC formed the most predominant type with 50% of cases. This is similar

to the report by some authors [14, 15], but at variance with others [16, 17]. At present, Broders classification is still widely used despite its shortcomings. It is based on the tumour cell population whereas that of Bryne's system features in addition to the tumour cells, the grading of the relationship between the tumour and the surrounding connective tissue. The Bryne's ITF is the most reproducible but the least used histological grading system [10].

Conclusion

We submit that although the Bryne's malignancy grading system had no relationship with clinico-demographic indices, it is a useful adjunct in predicting the biological behaviour of OSCC in our environment and either the Bryne's system or the Broders can be used to grade OSCC with similar results being obtained. However, an evaluation of more cases of OSCC would be necessary to further confirm or disprove the significance of the ITF system.

References

1. Pindborg JJ, Reichart P, Smith CJ and van der Waal.I. World Health Organization: histological typing of cancer and precancer of the oral mucosa. 2nd edition .Berlin: Springer-Verlag, 1997 p 21-22.
2. Jemal A, Bray F, Center MM, *et al.* Global Cancer Statistics. CA Cancer J Clin 2011; 61:69–90.
3. Bhargava A, Saigal S and Chalishazar M. Histopathological grading systems in oral squamous cell carcinoma: a review. J Int Oral Health 2010; 2:4.
4. Broders AC. Carcinoma. Grading and practical application. Arch Pathol. 1926; 2: 376-381.
5. Anneroth G, Batsakis J and Luna M. Review of the literature and a recommended system of malignancy grading in oral squamous cell carcinomas. Scand J Dent Res 1987; 95:229-249.
6. Bryne M, Stromme H, Lilleng R, *et al.* New malignancy grading is a better prognostic indicator than Broders' grading in oral squamous cell carcinoma. J Oral Pathol Med 1989; 18:432-437.
7. Bryne M, Koppang HS, Lilleng R and Kjaerheim A. Malignancy grading of the deep invasive margins of oral squamous cell carcinomas has high prognostic value. J Pathol 1992; 166: 375-381.
8. Bryne M. Is the invasive front of an oral carcinoma the most important area for prognostication? Oral Dis 1998; 4: 70-77.

9. Yazdi, I and Khalili, M. Grading of Oral Cancer: "Comparison of different systems with respect to lymph node metastasis in tongue SCC." Arch Iranian Med 1999; 2:1-5.

10. Doshi NP, Shah SA, Patel KB *et al.* Histological grading of oral cancer: a comparison of different systems and their relation to lymph node metastasis. Natl J Comm Med 2011; 2: 1.

11. Kantola S, Parikka M, Jokinen K *et al.* Prognostic factors in tongue cancer – relative importance of demographic, clinical and histopathological factors. Br J Cancer 2000; 83:5: 614–619.

12. Campbell WJ and de la Torre J. Head and neck cancer-squamous cell carcinoma-eMedicine Specialities 2008. http/www.emedicine.com/plasticsurgery/topic,accessed20/07/2010, 14:26:46.

13. Barnes L, Eveson JW, Reichert P *et al.* World Health Organization classification of tumours. Pathology and genetics of head and neck tumours. Lyon. IARC Press. 2005 p 164-178.

14. Muñoz-Guerra MF, Capote Moreno AL, Gómez Marazuela EM *et al.* Early stage oral cancer: prognosis with regard to histological grading, intratumoural lymphangiogenesis, and the expression of vascular endothelial growth factor-C (VEGF-C). Rev Esp Cirug Oral y Maxilofac .2006; 28:1:25-40.

15. Jerjes W, Upile T, Petrie A *et al.* Clinico-pathological parameters, recurrence, locoregional and distant metastasis in 115 T1-T2 oral squamous cell carcinoma patients. Head Neck Oncol. 2010; 210:9-12.

16. Effiom OA, Adeyemo WL, Omitola OG *et al.* Oral squamous cell carcinoma: a clinicopathologic review of 233 cases in Lagos, Nigeria. J Oral Maxillofac Surg. 2008; 66 (8): 1595-1599.

17. Odukoya O, Mosadomi A, Sawyer DR *et al.* Squamous cell carcinoma of the oral cavity. A clinico-pathological study of 106 Nigerian cases. J Maxillofac Surg. 1986; 14:267-269.