

Can preoperative computed tomography predict tissue origin of primary maxillary cancer?

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Abstract

Based on the histopathologic origin, malignant maxillary neoplasms may share some clinical characteristics but have different biological behavior, treatments, and prognoses. The aim of the present study was to explore the association between CT characteristics and tissue origin of primary maxillary cancer (MC). A retrospective review of CT findings was performed in patients diagnosed with MC between January 1, 2005 and December 31, 2013. Univariate and multivariable logistic regression analyses were performed to determine the association between tissue of origin and CT characteristics, with adjustment for possible confounding factors. A total of 164 patients (70 male, 94 female, age: 46.8 ± 18.3 years) were included. Patients were divided into epithelial (n = 88) and nonepithelial (n = 76), or odontogenic (n = 15) and nonodontogenic (n = 149) groups. After adjusting for age, sex, smoking status, alcohol use, tumor size, and stage in the multivariable logistic regression model, the lesions with cortical bowing were found more likely to be epithelial (odds ratio [OR] = 7.0, 95% confidence interval [CI], 1.4–36.1) than nonepithelial origin, while lesions with cervical lymphadenopathy were more associated with a nonodontogenic origin (OR = 12.6, 95% CI, 1.1–140.0) rather than odontogenic. Among epithelial cancers, lesions with cortical bowing were 14 times more likely to be salivary gland-type (OR = 13.8, 95% CI, 1.3–141.5). CT characteristics of cortical bowing and cervical lymphadenopathy might be suggestive of tissue origin in MC. Larger prospective studies are warranted to further examine the association.

Abbreviations: CI = confidence interval, CT = computed tomography, FOV = field of view, MC = malignant cancer, MET = malignant epithelial tumor, MNET = malignant nonepithelial tumor, MNOT = malignant nonodontogenic tumor, MOT = malignant odontogenic tumor, MRI = magnetic resonance imaging, OR = odds ratio, WHO = World Health Organization.

Keywords: computed tomography, epithelial, maxilla, neoplasm, odontogenic

1. Introduction

Primary cancers infrequently affect the jawbones, and most tumors affecting the jawbones show a predilection for the mandible and especially its posterior portion. The maxillary cancers (MCs) occur rarely but involve a wide range of primary malignant entities,^[1,2] originating from mucosal epithelium, seromucinous glands, soft tissues, bone, cartilage, neural/neuroectodermal tissue, or the odontogenic apparatus.^[3] MCs may share clinical characteristics but have different treatments and prognoses, based on the histopathologic origin.^[4] Cancers

originating from different tissue demonstrate differed biological behaviors as well, including the tendency to neural infiltration, and lymph node and distant metastasis. Accurate preoperative discrimination of tissue origin would benefit in accurate preoperative assessment and treatment planning.

Imaging plays a key role in preoperative evaluation, and determination of surgical approach and radiation therapy. Intraoral dental radiographs and panoramic radiographs are usually the first means to identify a suspected lesion.^[5] However, due to the anatomical complexity of maxillary area, cross-sectional imaging modalities such as computed tomography (CT) have become essential.^[6] CT covers both topography and fine structure of the lesion, and provides clear delineation of the anatomic extent and bone changes, with widely clinical availability and relatively low price.^[3] To our knowledge, no large studies have examined the ability of CT in discriminating MC with different tissue of origin. Given the clinical benefits of preoperative evaluation of tissue origin, we conducted the present study to identify the CT characteristics most useful for differentiating MC with different tissue of origin. Rather than providing an exhaustive review of all pathological entities, we divided the lesions into the clinically useful categories as follows: epithelial and nonepithelial or odontogenic and nonodontogenic. The term “odontogenic” indicates that the tumor is composed of cellular constituent whose primary purpose is to form teeth or tooth-related structures.

2. Materials and methods

2.1. Patient selection

A retrospective review of CT images was performed in patients with previously untreated primary MC between January 1, 2005 and December 31, 2013. All lesions were histopathologically

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confirmed from biopsy or surgery. We classified the lesions into malignant epithelial tumor (MET) and nonepithelial (MNET) groups, or malignant odontogenic tumor (MOT) and non-odontogenic (MNOT) groups according to the classification published by the World Health Organization (WHO) in 2005.^[2] Patients who had smoked at least 100 cigarettes in their lifetime were defined as “ever smokers,” and patients who had smoked fewer than 100 cigarettes in their lifetime were categorized as “never smokers.” “Ever drinkers” were defined as patients who had drunk at least 1 alcohol beverage per week for at least 1 year during their lifetime, and patients who had never had such a pattern of drinking were considered “never drinkers.”^[7] Patients were excluded in any of the following conditions: with artifacts on CT images interfering the diagnosis; with a previously diagnosed head and neck cancer and local therapy in head and neck region; underwent treatment of the maxillary lesion (surgery or chemoradiation) before CT scan. Our institutional review board approved this retrospective study.

2.2. CT acquisition and imaging interpretation

CT was performed within 7 days before biopsy or surgery, with a 64-channel helical CT system (Philips Brilliance, Philips Medical Systems, Best, The Netherlands). The scanning parameters were as follows: 120 to 140 kV, 200 to 300 mA, 23 cm field of view, 256 × 256 matrix, and 5-mm section thickness. A dose of 1.5 mL/kg body weight of iopamidol (Iopamiro 320, Bracco, Milan, Italy) or iopromide (Ultravist 300, Schering, Germany) was intravenously administered with a power injector at a rate of 2.5 mL/s.

CT findings were interpreted by consensus on a PACS (Centricity Radiology RA600, GE Healthcare) by 3 radiologists with more than 5 years of experience in the interpretation of head and neck images. All reviewers were blinded to the histopathologic results. Lesion sizes were measured as maximum diameter in axial planes. CT attenuation values of the lesions were measured in Hounsfield units by drawing 15 to 20 mm² circular regions of interest,^[8] taking care to exclude obvious hemorrhage, necrotic, or calcified areas, and avoid the most peripheral portions to exclude partial volume effects. Regions of interest were placed on the maximum axial slice of plain images and then propagated to the corresponding contrast enhanced images. CT characteristics of each lesion were evaluated, including the inner texture, margin, cortical involvement, and soft tissue extent. The internal texture character included homogeneous and heterogeneous. The margin of the lesion was considered as well defined if more than two-thirds of the margin was sharply demarcated from the surrounding tissue, and as ill-defined otherwise.^[9] The maxillary cortical involvement was evaluated both on the integrity and morphology. Cortical integrity was assessment of cortical continuation. Cortical morphology was classified as pressure remodeling/bowing or not. Soft tissue extent was an assessment of adjacent soft tissue infiltration including the muscle, fat, or neurovascular structures. The sizes of cervical lymph nodes were also measured. Lymphadenopathy was defined as a cervical lymph node with a minimal axial diameter larger than 10 mm or with visualized necrosis.^[10]

2.3. Statistical analysis

Statistical analysis was carried out using STATA version 10.0 (College Station, TX). $P < 0.05$ was considered as statistically significant. The clinical and imaging characteristics, including

sex, age, smoking status, alcohol use, tumor size, mean CT value, evaluation of inner texture, margin, cortical involvement, soft tissue extent, and cervical lymphadenopathy, were recorded. These characteristics were compared between METs and MNETs or between MOTs and MNOTs, using the χ^2 testing (the Fisher exact testing where appropriate) for categorical variables and unpaired t test for noncategorical data. Univariate and multivariable logistic regression analyses were performed to determine the association of these characteristics with tumor origin. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, with adjustment for possible confounding factors such as age, sex, smoking, alcohol use status, tumor size, and staging.

3. Results

3.1. Patients and clinical characteristics

We collected 164 patients (70 male, 94 female, age: 46.8 ± 18.3 years) with pathologically confirmed MC. Patients were divided into MET (n=88) and MNET (n=76), or MOT (n=15) and MNOT (n=149) groups. Their histologic classification was as follows: MET and MOT: ameloblastic carcinoma (AC, n=6), primary intraosseous squamous cell carcinoma (PIOSCC, n=5), and ghost cell odontogenic carcinoma (n=3); MNET and MOT: ameloblastic fibrosarcoma (n=1); MET and MNOT: squamous cell carcinoma (SCC, n=25), adenoid cystic carcinoma (ACC, n=25), mucoepidermoid carcinoma (MEC, n=10), myoepithelial carcinoma (n=4), malignant mixed tumor (n=3), spindle cell carcinoma (n=3), adenocarcinoma (n=2), giant cell carcinoma (n=1), and small cell carcinoma (n=1); MNET and MNOT: osteosarcomas (n=33), myofibroblastic sarcoma (n=11), synovial sarcoma (n=4), chondrosarcoma (n=3), undifferentiated high-grade pleomorphic sarcoma (n=3), spindle cell sarcoma (n=3), Ewing sarcoma (n=3), lymphoma (n=3), plasmacytoma (n=2), malignant peripheral nerve sheath tumor (n=2), malignant fibrous histiocytoma (n=2), malignant melanoma (n=2), malignant solitary fibrous tumors (n=1), chondromyxoid fibroma (n=1), and rhabdomyosarcoma (n=1). Patients with MET was significant older than those with MNET ($P < 0.001$). No statistical difference was found in sex, smoking, alcohol drinking, staging, and treatment between groups ($P > 0.05$). Clinical characteristics of patients are summarized in Table 1.

3.2. CT characteristics

The plain and contrast-enhanced CT images were available for 155 patients. All lesions showed enhancement after intravenous injection of contrast agent. All 15 cases of MOTs demonstrated heterogeneous enhancement, ill-defined margin, and impaired cortical integrity. CT characteristics of lesions with different tissue of origin are summarized in Table 2. No significant difference was found in mean of CT value as well as CT characteristics including inner texture, margin, cortical involvement, soft tissue extent, and cervical lymphadenopathy between MET and MNET, or between MOT and MNOT.

3.3. Association between CT characteristics and tumor origin

In univariate logistic regression analysis, no significant association was detected between tumor origin and CT characteristics. After adjusting for age, sex, smoking, alcohol use status, tumor size, and staging in the multivariable logistic regression model, we found the lesions with cortical bowing were approximately

Table 1
Clinical characteristics of patients with malignant maxillary neoplasm (n = 164).

Characteristics	Epithelial (88) n (%)	Nonepithelial (76) n (%)	P value*	Odontogenic (15) n (%)	Nonodontogenic (149) n (%)	P value*
Mean age ± SD, y	53.4 ± 16.8	39.1 ± 16.9	<0.001	51.9 ± 15.9	46.2 ± 18.4	0.258
Sex			0.433			0.586
Male	35 (39.8)	35 (46.1)		5 (33.3)	65 (43.6)	
Female	53 (60.2)	41 (53.9)		10 (66.7)	84 (56.4)	
Smoking			0.254			0.196
Ever	22 (25.0)	13 (17.1)		1 (6.7)	34 (22.8)	
Never	66 (75.0)	63 (82.9)		14 (93.3)	115 (77.2)	
Alcohol			0.416			1.000
Ever	10 (11.4)	5 (6.6)		1 (6.7)	14 (9.4)	
Never	78 (88.6)	71 (93.4)		14 (93.3)	135 (90.6)	
Staging			0.273			0.787
I-II	51 (58.0)	37 (48.7)		7 (46.7)	80 (50.3)	
III-IV	37 (42.0)	39 (51.3)		8 (53.3)	69 (49.7)	
Treatment						
S	22 (25.6)	27 (36.0)	0.172	6 (40.0)	43 (29.5)	0.392
C	1 (1.2)	0	—	0	1 (0.7)	—
X	1 (1.2)	1 (1.3)	1.000	0	2	—
Other†	62 (72.1)	47 (62.7)		9 (60.0)	100 (68.5)	

C=chemotherapy, CI=confidence interval, NA=not available, OR=odds ratio, S=surgery, SD=standard deviation, X=radiotherapy.

* P values of χ^2 testing (the Fisher exact testing where appropriate) for categorical variables and unpaired t test for noncategorical data.

† No treatment of surgery, chemotherapy, or radiotherapy was recorded in 2 epithelial and 1 nonepithelial tumors. No treatment of surgery, chemotherapy, or radiotherapy was recorded in 3 nonodontogenic tumors.

7 times more likely to be MET (OR=7.0, 95% CI, 1.4–36.1) rather than MNET. The lesions with cervical lymphadenopathy were approximately 13 times more likely to be MNET (OR=12.6, 95% CI, 1.1–140.0) rather than MOT. Results of multivariable logistic regression are listed in Table 3.

Nine of the 16 lesions demonstrating osseous expansion and cortical bowing were salivary gland-type carcinomas (Fig. 1).

Therefore, the logistic regression analysis was also performed to evaluate the association between cortical bowing and salivary gland-type origin. MCs with cortical bowing were 13 times more likely to be salivary gland type (OR=12.7, 95% CI, 2.8–57.8). When compared to the other epithelial cancers, tumors with cortical bowing were 14 times more likely to be salivary gland-type carcinomas (OR=13.8, 95% CI, 1.3–141.5).

Table 2
CT characteristics of patients with malignant maxillary neoplasms (n = 155).

Characteristic	Epithelial (86) n (%)	Nonepithelial (69) n (%)	P value*	Odontogenic (15) n (%)	Nonodontogenic (140) n (%)	P value*
CT value (mean ± SD) (HU)						
plain	40.6 ± 10.3	38.1 ± 11.1	0.223	38.8 ± 10.9	39.6 ± 10.7	0.587
CE	66.7 ± 15.2	67.0 ± 16.6	0.830	63.5 ± 8.9	67.1 ± 16.2	0.807
Increase†	26.7 ± 16.7	30.0 ± 18.6	0.325	25.4 ± 10.1	28.3 ± 18.1	0.959
Inner texture			1.000			1.000
Homogeneous	1 (1.2)	0 (0)		0 (0)	1 (0.7)	
Heterogeneous	85 (98.8)	69 (100)		15 (100)	139 (99.3)	
Margin			0.324			1.000
Well defined	1 (1.2)	3 (4.3)		0 (0)	4 (2.9)	
Ill defined	85 (98.8)	66 (95.7)		15 (100)	136 (97.1)	
Cortical integrity			0.324			1.000
Yes	1 (1.2)	3 (4.3)		0 (0)	4 (2.9)	
No	85 (98.8)	66 (95.7)		15 (100)	136 (97.1)	
Cortical bowing			0.183			1.000
No	75 (87.2)	64 (92.8)		14 (93.3)	125 (89.3)	
Yes	11 (12.8)	5 (7.2)		1 (6.7)	15 (10.7)	
Soft tissue extent			0.387			0.469
No	12 (16.3)	14 (20.3)		1 (6.7)	25 (17.9)	
Yes	74 (83.7)	55 (79.7)		14 (93.3)	115 (82.1)	
Lymphadenopathy			0.274			0.357
No	60 (69.8)	54 (78.3)		13 (86.7)	101 (72.1)	
Yes	26 (30.2)	15 (21.7)		2 (13.3)	39 (27.9)	

CE=contrast enhanced, CI=confidence interval, HU=Hounsfield units, NA=not available, OR=odds ratio, SD=standard deviation.

* P values of χ^2 testing (the Fisher exact testing where appropriate) for categorical variables and unpaired t test for noncategorical data.

† The value equals CT value in contrast enhanced image minus that in plain image.

Table 3**Multivariable analysis of CT characteristics in Malignant Maxillary tumors.**

Characteristic	Epithelial (86) n (%)	Non-epithelial (69) n (%)	Adjusted OR (95% CI)*	Odontogenic (15) n (%)	Non-odontogenic (140) n (%)	Adjusted OR (95% CI)*
Inner Texture						
Homogeneous	1 (1.2)	0 (0)		0 (0)	1 (0.7)	
Heterogeneous	85 (98.8)	69 (100)	NA	15 (100)	139 (99.3)	NA
Margin						
Well-defined	1 (1.2)	3 (4.3)	1.0	0 (0)	4 (2.9)	
Ill-defined	85 (98.8)	66 (95.7)	17.5 (0.6–551.2)	15 (100)	136 (97.1)	NA
Cortical integrity						
Yes	1 (1.2)	3 (4.3)	1.0	0 (0)	4 (2.9)	
No	85 (98.8)	66 (95.7)	0.7 (0.02–18.1)	15 (100)	136 (97.1)	NA
Cortical bowing						
No	75 (87.2)	64 (92.8)	1.0	14 (93.3)	125 (89.3)	1.0
Yes	11 (12.8)	5 (7.2)	7.0 (1.4–36.1)	1 (6.7)	15 (10.7)	1.1 (0.1–11.8)
Soft tissue extent						
No	12 (16.3)	14 (20.3)	1.0	1 (6.7)	25 (17.9)	1.0
Yes	74 (83.7)	55 (79.7)	0.8 (0.2–3.0)	14 (93.3)	115 (82.1)	8.9 (0.7–107.5)
Lymphadenopathy						
No	60 (69.8)	54 (78.3)	1.0	13 (86.7)	101 (72.1)	12.6 (1.1–140.1)
Yes	26 (30.2)	15 (21.7)	1.3 (0.5–3.5)	2 (13.3)	39 (27.9)	1.0

CI = confidence interval, NA = not available, OR = odds ratio.

* Adjusted for age, sex, smoking status, alcohol use, tumor size, and stage in a logistic regression model.

4. Discussion

Despite the broad spectrum of pathological processes that affect the maxilla, there could be considerable overlap in their imaging appearance. Radiologic findings might not allow a simple, precise diagnosis of a tumor. We expected them to narrow the differential diagnosis to a specific tissue of origin, which would benefit the treatment planning and prognostic prediction.

The CT characteristics of cortical bowing/remolding were found to be associated with tissue of origin in the present study. Bone changes could indicate the aggressive manner of lesion.^[11] In general, slowly growing lesions appear to push bone as they slowly remodel the osseous structure, while aggressive lesions tend to destroy bony walls and leave only remaining fragments.^[12] Occasionally, however, malignant lesions can cause bowing rather than directly infiltrate the bone.^[13] In the present

study, lesions with cortical bowing were approximately 7 times more likely to be epithelial rather than nonepithelial. Possible factors influencing tumor aggressiveness such as tumor size and grade have been adjusted in the multivariable model. Other contributors of the results might be histopathological constitution and patient distribution within groups. It is interesting to be noted that, 9 of the 44 salivary gland-type carcinoma cases under study (20.5%) demonstrated cortical bowing. Furthermore, within the epithelial group, cortical bowing were 14 times more likely to be salivary gland type. Salivary gland-type carcinomas typically arise in the salivary glands, oral mucosa, and sinonasal cavities, and secondarily invade the maxilla and the mandible, though scarcely they can also arise centrally within the maxilla itself.^[14,15] As previously reported, the lesion could be expansile or surrounded by sclerotic margins,^[16,17] which is consistent with the results of the present study.



Figure 1. A 32-year-old man with mucoepidermoid carcinoma in the right maxilla, which showed pressure remodeling and cortical bowing. (A) Plain CT (soft tissue window); (B) plain CT (bone window); and (C) enhanced CT (soft tissue window).

Odontogenic tumors (OTs) of the jawbones are reported to comprise only 0.74% to 9.6% of all oral tumors.^[18] OTs are relatively more prevalent in Africans and the highest reported frequency was 41%.^[19] MOTs represent only 0% to 6.1% of all OTs.^[18,20] The rarity of incidence, variations in pathogenesis, clinical-pathological features, and biological behavior all complicated the diagnosis.^[21,22] In the present study, all MOTs showed heterogeneous enhancement, ill-defined margin, and infiltration into cortical bone and adjacent soft tissue, suggestive of an aggressive nature. It is reported that involvement of local lymph nodes and distant metastases may occur early in MOTs.^[2] However, in the present study, only 2 patients of MOT showed cervical lymphadenopathy, and the cervical lymphadenopathy was more associated with MNOTs. Given the small sample size of MOT in the present study, due to the extremely low incidence, further study with larger population is warranted. We have also noticed that the mean tumor size of MOTs was smaller than that of MNOTs in the present study, which may result in a less possibility of nodal metastasis in MOTs; however, we have adjusted lesion size and also the tumor stage in logistic analyses to exclude the confounding effect. In fact, early infiltration of lymph nodes does not necessarily accompany lymph node enlargement or necrosis,^[23] which may induce false negative results on CT images. Due to the small sample size, which restricted further statistical analyses, and the lack of pathological diagnosis of each suspected lymph node, further studies are still worth to be conducted to verify the exact association between cervical lymphadenopathy and MOT.

Except for the small amount of MOT patients above-mentioned, the present study has several other limitations. First, we did not include all manifestation on CT images. We chose to evaluate CT characteristics more clinically applicable (measurable and reproducible) and not specific to a unique disease or location. Second, the patients' distribution in our study may not be the same as that in general population. We only included patients with histopathologically confirmed, previously untreated primary MC patients with preoperative CT scan. Patients with definite diagnosis after clinical and X-ray examination or without planning for surgical treatment might not undergo CT and biopsy. Therefore, we have not further discussed the epidemiological characteristics of patients. Third, the clinical and radiological data for the cohort were collected retrospectively and performed at 1 institution. Prospective and multicenter studies with large sample size are needed to validate our findings. Finally, magnetic resonance imaging (MRI) has been more and more used for detecting and assessing jaw lesions, which may better illustrate the inner texture and extent of soft tissue.^[24] Further studies could be performed to assess the association of MRI with tumor origin, and the correlation of MRI and CT characteristics, with special focus on the 2 CT characteristics we found with statistical significance.

5. Conclusion

Our findings indicate that CT characteristics of cortical remodeling and cervical lymphadenopathy could be suggestive of tissue origin in MCs. Lesions with cortical bowing were more likely to be epithelial rather than nonepithelial origin. Furthermore, within the epithelial cancers, the lesions with cortical bowing were more likely to be salivary gland type. Cervical lymphadenopathy was more associated with a

nonodontogenic origin rather than odontogenic. Due to the rarity of malignant OT and thus the small sample size restricting thorough statistical analyses, larger prospective studies are warranted.

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