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FULL PAPER

Palatal lesions: discriminative value of conventional MRI and diffusion weighted imaging

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Objective: To evaluate and compare the ability of conventional MRI, diffusion-weighted imaging (DWI) and a combination of both MRI techniques to differentiate malignant and benign palatal lesions.

Methods: A retrospective review of MRI findings was performed in patients with pathologically confirmed palatal lesions between January 2012 and December 2014. Each lesion was evaluated with conventional MRI characteristics, including enhancement, inner texture, margin, adjacent soft-tissue involvement and cervical lymph node, and/or apparent diffusion coefficient (ADC) value. Statistical analyses were performed to assess the differential performance of each parameter separately and together.

Results: A total of 42 patients (24 males, 18 females; age: 54.9 ± 16.4 years) were investigated. The optimal cut-off ADC value to distinguish malignant from benign lesions was $1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, with a sensitivity of 87.5% and

a specificity of 75.0%. Conventional MRI showed a sensitivity of 87.1% and a specificity of 63.6%. Combination of conventional MRI and ADC scores increased sensitivity to 100% and specificity to 75.0%. The AUCs did not differ significantly between conventional MRI alone, DWI alone and integration of both.

Conclusion: Additional DWI does not substantially improve differential ability of conventional MRI. However, combining ADC values with conventional MRI improves both sensitivity and specificity, which is of worth to be further validated in prospective studies with larger sample sizes.

Advances in knowledge: Combination of conventional MRI and ADC scores could increase the ability to differentiate malignant from benign palatal lesions, with a sensitivity of 100% and specificity of 75.0%, although without statistical significance.

INTRODUCTION

The palate separates the oral from the nasal cavity and is anatomically composed of soft and hard parts. The hard palate is composed of mucosal surface and minor salivary glands located between the mucosal surface and the underlying bone. The soft palate is formed by squamous mucosa and muscle fibers, and contains a smaller number of minor salivary glands compared with the hard part. Palatal lesions include a variety of pathological types,¹ and squamous cell carcinoma (SCC) is the most common malignancy. Tumours of the minor salivary glands are the most common type of submucosal masses, and malignant tumours account for approximately half of them.² Various types of mesenchymal tumours, such as fibromas, lipomas, schwannomas, neurofibromas, haemangiomas and lymphangiomas, also involve the palate.

Accurate differentiation between malignant and benign palatal lesions as well as assessment of the tumour extent on images are essential for directing further therapeutic approach and the extent of surgical intervention,³ especially for

submucosal masses which are relatively hard to identify by inspection and palpation. MRI is increasingly used because of its excellent soft-tissue contrast ability and milder distortions from dental metallic materials than CT. However, the information provided by conventional MRI may not be sufficient to accurately and consistently differentiate malignant from benign lesions.^{4,5} As a functional imaging method, diffusion-weighted imaging (DWI) quantifies the diffusional mobility of water protons in biological tissues with apparent diffusion coefficient (ADC),⁶ a quantitative index shown potential for correlating with histopathological characterization of lesions, differentiating benign from malignant tumours, assessing treatment response and detecting recurrence in head and neck tumours.⁷⁻¹⁰ Another advantage of DWI is that it does not require intravenous contrast media, thus enabling its use in patients with renal dysfunction. The purpose of this study was to evaluate and compare the morphological MRI characteristics and ADC values between malignant and benign palatal lesions and to assess the benefit of adding DWI to conventional MRI protocol for differential diagnosis of palatal lesions.

METHODS AND MATERIALS

Patient selection

A retrospective review of MRI findings was performed in patients with palatal lesions between 1 January 2012 and 31 December 2014. All lesions were confirmed by histopathological examination of specimens obtained at biopsy or surgery. Patients were excluded if any of the following conditions: (1) with artefacts interfering the diagnosis; (2) with a previously diagnosed head and neck cancer; or (3) with treatment of a head and neck lesion (surgical management or radiotherapy) before the MRI scan. Lesions < 10 mm were also excluded to reduce partial volume effects. The institutional review board of Shanghai Ninth People's Hospital approved this retrospective study.

MRI acquisition

All MRI examinations were performed using a 1.5-T imager (Signa Excite; GE Medical Systems, Milwaukee, WI) with a head and neck array coil. The conventional non-enhanced MRI protocol consisted of T_1 weighted (T1W) and T_2 weighted sequences (with fat suppression). DWI was performed using a single-shot spin-echo echoplanar imaging sequence with b -values of 0 and 800 s mm^{-2} . Gradients were applied in three orthogonal directions. Contrast-enhanced T1W images were obtained after intravenous injection of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) at a dosage of 0.1 mmol kg^{-1} of body weight. Details of the MRI protocol are provided in Table 1.

MRI interpretation

All MR images were interpreted by consensus by three radiologists with more than 8 years' of experience in the interpretation of head and neck MRI. All reviewers were blinded to the clinical, surgical and histopathological results. Tumour size was measured in maximal dimensions on the transverse plane. Each lesion was evaluated with regard to the enhancement, lesion texture, margin and adjacent structure involvement. The internal texture was classified as homogeneous or heterogeneous based on pre-contrast T1W imaging and T_2 weighted imaging, and post-contrast T1W imaging. The margin of the lesion was considered well defined if more than two-thirds of the margin

was sharply demarcated from the surrounding tissue and ill defined if less than one-third of the margin was sharply defined.¹¹ The size and signal intensity features of cervical lymphadenopathy were also evaluated. Lymphadenopathy was defined as a minimal axial diameter >10 mm or with visualized necrosis.¹² Using the post-processing software Functool from GE, ADC values were generated by drawing freehand regions of interest on images by consensus, taking care to exclude obvious haemorrhage, necrotic or other non-perfused areas by visual correlation with pre-contrast and post-contrast T1W images and avoiding the most peripheral portions to exclude partial volume effects of adjacent extraleisional tissue. ADC values were manually measured three times, and the average ADC was obtained as the representative value for each lesion.

Reading results of MRI characteristics were dichotomized into Score 1 (positive, suspicious of malignancy) or 0 (negative), including enhancement (with enhancement, 1; without, 0), inner texture (heterogeneous, 1; homogeneous, 0), margin (ill defined, 1; well defined, 0), adjacent structure invasion (with infiltration, 1; without, 0) and cervical lymph node (with cervical lymphadenopathy, 1; without, 0). The sum score was calculated for each lesion from the five variates of conventional MRI with or without ADC ($\leq$ cut-off value, 1; $>$ cut-off value, 0).

Statistical analyses

Statistical analyses were performed to determine the relationship between MRI results and malignancy. Demographic and imaging characteristics were compared between malignant and benign lesions using χ^2 testing or Fisher exact test for categorical variables and unpaired t test for non-categorical data. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression models to determine the association between malignancy and conventional MRI characteristics, as well as the ADC value. To find the optimal cut-off ADC value to distinguish malignant from benign masses, we conducted receiver operator characteristics (ROCs) analysis. We plotted the sensitivity vs 1-specificity for each cut-off value across the range of ADC value to generate the ROC curve, and the areas under

Table 1. Conventional MRI protocol

Sequences	T1WI	T2WI	T2WI	T2WI	DWI	T1WI ^a	T1WI ^a
Plane	Axial	Axial	Axial	Coronal	Axial	Axial	Coronal
TR (ms)	600	4200	4440	3700	2775	540	540
TE (ms)	9.9	94.6	94.6	81.4	70	8.8	9.4
NEX	2	2	2	3	8	2	2
Thickness/gap (mm)	5/1	5/1	5/1	5/1	5/0.5	5/1	5/1
Matrix (mm)	288 × 192	320 × 224	320 × 224	320 × 224	128 × 128	288 × 192	288 × 192
FOV (cm)	24 × 24	24 × 24	24 × 24	22 × 22	24 × 24	24 × 24	22 × 22
FS	No	No	Yes	Yes		No	Yes

DWI, diffusion-weighted imaging; FOV, field of view; FS, fat saturation; NEX, number of excitations; T1WI, T_1 weighted imaging; T2WI, T_2 weighted imaging; TE, echo time; TR, repetition time.

^aContrast-enhanced sequences.

the ROC curve (AUC) were assessed. The optimal cut-off value which maximized the sum of sensitivity and specificity was determined as the point in the upper left-hand corner. We then conducted and compared the ROCs of conventional MRI, DWI and combination of both techniques to evaluate the diagnostic ability. Statistical analysis was carried out using STATA® v. 10.0 (Stata Corp, College Station, TX). $p < 0.05$ was considered as statistically significant.

RESULTS

Patients and clinical characteristics

42 patients [24 males, 18 females; age: 54.9 ± 16.4 years (mean $\pm$ standard deviation)] with pathologically confirmed palatal lesions were enrolled. All included patients underwent conventional MRI, and DWI images were available for 32 patients. In 31 of the 42 patients, malignant palatal lesions were diagnosed as squamous cell carcinoma ($n = 14$), adenoid cystic carcinoma ($n = 6$), mucoepidermoid carcinoma ($n = 5$), mucosa-associated lymphoid tissue (MALT) lymphoma ($n = 3$), malignant pleomorphic adenoma ($n = 1$), malignant melanoma ($n = 1$) and lymphoepithelial carcinoma ($n = 1$). The remaining 11 patients with benign palatal lesions were diagnosed as pleomorphic adenoma ($n = 8$), benign lymphoepithelial lesion ($n = 2$) and inflammation ($n = 1$). The mean size of malignant tumours was significantly larger than that of benign lesions ($p = 0.031$). No statistical difference was found in sex and age of patients with benign vs malignant lesions ($p > 0.05$). Clinical characteristics of patients are summarized in Table 2.

Conventional MRI and diffusion-weighted imaging findings

All 42 lesions demonstrated enhancing after intravenous injection of gadopentetate dimeglumine. The conventional MRI manifestations of margin and adjacent structure invasion were significantly different between malignant and benign palatal lesions ($p = 0.019$ for margin, and $p = 0.004$ for adjacent structure invasion). Palatal lesions with ill-defined margins and invasion to adjacent structures were approximately 7 and 18 times more likely to be malignant than those with well-defined margins and without adjacent structure infiltration (OR = 7.3 and 95% CI, 1.6–33.3 for margin; OR = 18.2 and 95% CI, 2.0–161.3 for adjacent structure invasion). When adjusted for age, sex and tumour size, only lesions with adjacent structure infiltration showed association with malignancy (OR = 16.9, 95% CI, 1.2–230.4). MRI characteristics of patients are summarized in Table 2.

Malignant palatal lesions presented with significantly lower ADC values than benign palatal lesions ($p = 0.007$) (Figures 1 and 2). The ROC was generated for ADC in discriminating malignant palatal tumours, and the AUC was 0.797 ± 0.109 (mean $\pm$ standard error). The optimal differential performance was obtained using a cut-off ADC value of $1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, which suggested a malignant diagnosis with $\text{ADC} \leq 1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ and a benign diagnosis with $\text{ADC} > 1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, generating a sensitivity of 87.5% and a corresponding specificity of 75.0%. When adjusted for age, sex and tumour size in the logistic regression model, lesions with $\text{ADC} \leq 1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ were still about 43 times more likely to be a malignant tumour than

those with $\text{ADC} > 1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (OR = 42.9, 95% CI, 1.6–1155.2). ADC results and the association with malignancy are presented in Table 2.

Differential ability of conventional MRI and diffusion-weighted imaging

For the assessment of the combined influence of different MRI characteristics on the diagnosis, further analyses were performed. The cut-off ADC value $1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ was applied for assessment. For each lesion, the sum score was calculated from the five variates of conventional MRI with or without ADC. The ROC curves were generated respectively for conventional MRI, DWI and both of them, and the AUC of conventional MRI, DWI and both techniques for differentiating malignant palatal tumours was 0.812 ± 0.075 , 0.813 ± 0.089 and 0.888 ± 0.081 , respectively. The best differential performance for conventional MRI was obtained at a cut-off score of 3, which meant a malignant diagnosis with three or more positive results in the five conventional MRI variates, generating a sensitivity of 87.1% and a corresponding specificity of 63.6%. The best differential performance for combination of conventional and DWI was also obtained at a cut-off score of 3, which meant a malignant diagnosis with three or more positive results in the five conventional MRI variates and ADC value, generating a sensitivity of 100% and a specificity of 75.0%. No statistical difference was found between ROC of conventional MRI alone and DWI alone ($p > 0.05$). After combining the ADC results with conventional MRI, the diagnostic performance slightly improved from the AUC of 0.812–0.888, although still without statistical difference ($p > 0.05$).

DISCUSSION

For the diagnosis of palatal lesions, cross-sectional imaging studies such as conventional MRI cover both topography and fine structure of lesions and give information about tumour extension. DWI provides information related to cancer cellularity and the integrity of cell membranes and is clinically used for differentiating benign from malignant lesions, monitoring treatment response after chemotherapy or radiation, and detecting recurrent cancer. In this study, we evaluated and compared the performance of conventional MRI, DWI alone and a combination of both techniques in differentiating palatal lesions.

Invasion to adjacent structures and ADC value showed the best association with malignancy in the present study. The palatal lesions with MRI characteristics of invasion to adjacent structures and ADC value $\leq 1.02 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ were statistically 17 and 43 times more likely to be malignant, respectively. In general, infiltration of the adjacent structures may undeniably suggest malignancy. DWI has been showing promise in the diagnosis, staging and follow-up after treatment of head and neck tumours.⁸ Although exceptions and overlap in ADC results might exist due to the heterogeneous group of benign and malignant lesions, lower ADC values have been reported in the head and neck region for most malignant lesions.^{13,14} In the current study, the mean ADC value for malignant palatal lesions was significantly lower than that of benign palatal lesions. The reason why malignant tumours have lower ADC values are not

well understood but is probably related to a combination of higher cellularity, tissue disorganization and increased extracellular space tortuosity, all contributing to reduced motion of water.⁸

Although with different *b*-values and different optimal ADC thresholds, most previous studies inevitably proved the ability of DWI in differentiating malignant from benign head and neck tumours,^{15–24} except that diagnostic dilemma exists in cholesteatoma, salivary gland tumours and lymph nodes.^{8,25} However, the comparison of diagnostic ability between DWI and conventional MRI was less performed. In a comparison of conventional MRI and DWI in cervical lymph nodes,²⁶ the ADC value was proved as the strongest diagnostic method of

nodal metastases in head and neck squamous cell carcinoma, with 92.3% sensitivity and 83.9% specificity. A significant performance improvement was also found when the ADC value was added to conventional MRI criteria. In the present study, the AUC comparison revealed no significant difference between conventional MRI alone, DWI alone and combined conventional MRI and DWI. Although no superiority of DWI over conventional MRI could be shown, we still interpret the results as promising in that additional DWI has improved the differential ability of conventional MRI: AUC from 0.812 to 0.888; sensitivity from 87.1% to 100%; specificity from 63.6% to 75.0%. Some cases were detected solely by DWI but not by conventional MRI. Hence, in a single case, DWI could still provide additional information compared with conventional

Table 2. Clinical and MRI characteristics of patients

Characteristics	Malignant (31), <i>n</i> (%)	Benign (11), <i>n</i> (%)	<i>p</i> -value ^a	OR (95% CI)	Adjusted OR ^b (95% CI)
Clinical					
Age (years)	55.1 ± 13.4	54.2 ± 23.8	0.931		
Sex			0.159		
Male	20 (64.5)	4 (36.4)			
Female	11 (35.5)	7 (63.6)			
Size (cm)	3.1 ± 1.4	2.1 ± 0.8	0.031		
MRI					
Enhancement			–		
Yes	31 (100)	11 (100)			
No	0	0			
Inner texture			0.353		
Homogeneous	4 (12.9)	3 (27.3)		1.0	1.0
Heterogeneous	27 (87.1)	8 (72.7)		2.5 (0.5–13.7)	1.6 (0.3–9.9)
Margin			0.019		
Well defined	6 (19.4)	7 (63.6)		1.0	1.0
Ill defined	25 (80.6)	4 (36.4)		7.3 (1.6–33.3)	3.8 (0.6–22.8)
Adjacent structure invasion			0.004		
No	11 (35.5)	10 (90.9)		1.0	1.0
Yes	20 (64.5)	1 (9.1)		18.2 (2.0–161.3)	16.9 (1.2–230.4)
Lymphadenopathy			0.453		
No	20 (64.5)	9 (81.8)		1.0	1.0
Yes	11 (35.5)	2 (18.2)		2.5 (0.5–13.5)	2.1 (0.3–13.0)
ADC (× 10 ^{−3} mm ² s ^{−1}) ^c	0.89 ± 0.15	1.09 ± 0.20	0.007		
>1.02	3 (12.5)	6 (75.0)		1.0	1.0
≤1.02	21 (87.5)	2 (25.0)		21.0 (2.8–156.1)	42.9 (1.6–1155.2)

ADC, apparent diffusion coefficient; CI, confidence interval; NA, not available; OR, odds ratio.

^a*p*-values, the Fisher exact testing for categorical variables and unpaired *t*-test for non-categorical data.

^bAdjusted for age, sex and tumour size in a logistic regression model.

^cADC values were not available in 7 malignant and 3 benign lesions.

Figure 1. A 17-year-old female with a pathologically proven pleomorphic adenoma in the left palate. Axial T_1 weighted (T1W) imaging (a), T_2 weighted imaging without/with fat saturation (b, c), axial (d) and coronal (e) contrast-enhanced T1W imaging show a well-defined mass without infiltration into adjacent structure. The round cursors mark the regions of interest selected (f) for measurement of the apparent diffusion coefficient (ADC) value in the ADC map, and the ADC value is $1.28 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. Avg., average; Dev., deviation.

MRI and help in the detection of malignant lesions. Therefore, although AUC analysis did not reveal a superiority of DWI over conventional MRI, we recommend using DWI in differential diagnosis because it can be acquired fast, easily and without contrast agents, and it might help in individual cases. Additional integration of ADC scores to conventional MRI scores caused no false-negative results. Two false-positive findings included one pleomorphic adenoma, which demonstrated atypical hyperplasia in pathological evaluation making it different from other pleomorphic adenoma, and one benign lymphoepithelial lesion. Lesions of salivary glands with a prominent lymphoid component are a heterogeneous group of diseases that include benign reactive lesions and malignant neoplasms.¹⁶ Benign lymphoepithelial lesion, lymphoepithelial carcinoma and MALT lymphoma are examples of this pathology. DWI frequently shows restricted diffusion behaviour on lymphomas because of high cellular density.³ Although no previous articles have reported the diffusion characteristics of lymphoepithelial lesion in the palate, a restricted diffusion characteristic could be speculated, attributing to the general lymphoma feature. In the present study, the ADC values of one benign lymphoepithelial lesion, one lymphoepithelial carcinoma

and two MALT lymphomas were significantly lower than other lesions ($p = 0.009$).

Although the number of included patients was limited for further epidemiological analysis in our study, the demographic characteristics of patients was in consistence with previous reports.³ Palatal tumours commonly arise from the squamous mucosa and minor salivary glands. The majority of malignant tumours are squamous cell carcinomas (14/42). The majority of benign salivary gland tumours of the palate are pleomorphic adenomas, whereas the most common malignant salivary gland tumour is adenoid cystic carcinoma and mucoepidermoid carcinoma. In clinical characteristics, one noticed finding was from the sex distribution. Although no statistical difference was detected, patients with malignant lesions were mostly male (64.5%), whereas most patients with benign lesions were female (63.6%). The results are in consistence with previous study reporting 1.5 times more female patients having benign neoplasms in the hard palate.¹⁷ The predilection for sex in the present study might be attributed to disease composition. Both pleomorphic adenoma and benign lymphoepithelial lesion have relatively higher frequency in female patients.

Figure 2. A 54-year-old female with a pathologically proven squamous cell carcinoma in the right palate. Axial T_1 weighted imaging (a), T_2 weighted imaging without/with fat saturation (b, c), axial (d) and coronal (e) contrast-enhanced T_1 weighted imaging show a well-defined mass with infiltration into the right nasal cavity. The round cursors mark the regions of interest selected (f) for measurement of the apparent diffusion coefficient (ADC) value in the ADC map, and the ADC value is $0.81 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$.

Our study had some limitations. First and foremost, we included a small number of cases, mostly due to the low incidence rate of the disease and the inclusion criteria of the study. We only included the histopathologically proved palatal lesions with pre-operative conventional MRI, which dramatically reduced the number of eligible patients. A small number of patients in each disease group had inhibited some statistical analyses and reduced the convincingness of some results. Furthermore, the demographic, clinical and radiological data for the cohort were collected retrospectively, and the included patients were hospital based. Therefore, future prospective

and multicentre studies with large sample size are needed to validate our findings. Second, details on risk factors such as smoking, clinical staging and treatment are not presented and assessed in that the data were incomplete.

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