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두경부암 근치적 치료 후 추적 자기공명영상에서 국소 재발 진단에 확산강조영상의 추가적 진단능: 진단 정확도 및 관찰자간 일치도 향상

Adding DWI to surveillance MRI can improve inter-reader reliability as well as diagnostic accuracy to detect local tumor recurrence after definitive treatment for HNSCC

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이 논문을 의학석사학위 논문으로 제출함

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영문요약

Adding DWI to surveillance MRI can improve inter-reader reliability as well as diagnostic accuracy to detect local tumor recurrence after definitive treatment for HNSCC

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Background: To evaluate diagnostic performance and inter-reader reliability of additional ADC map for detecting tumor recurrence after definitive treatment for HNSCC, in readers with different experiences.

Methods: This retrospective study included consecutive patients with newly developed contrast-enhancing lesion at the primary cancer site on the surveillance MRI following definitive treatment of HNSCC from 2014 to 2018. Two radiologists with 2 and 18 years of experience evaluated MR images blinded to clinical information except the primary site using T2-, T1-, and contrast-enhanced T1-weighted imaging, and apparent diffusion coefficient (ADC) map. The radiologists performed sequential analysis and made diagnosis of the images as follows: 1) conventional images only, 2) conventional images and ADC map, 3) conventional images and ADC map assisted by circular ROI measurement of ADC values using cut-off value as 1.2×10^{-3} mm^2/sec. If there was discordance, findings of conventional image outweighed ADC map analysis unless the cases were inconclusive based only on morphologic criteria. Histopathologic results or follow-up imaging at least 6 months after regarded as a reference standard. The accuracy, sensitivity, and specificity of readers' classification were calculated for each analysis. Diagnostic accuracy and inter-reader agreement of each analysis by two radiologists were compared using generalized estimating equation (GEE) model and Cohen's Kappa coefficient, respectively.

Results: Total 177 patients (mean age, 62.17 years; range, 26-84 years) were included with 105 cases of local recurrence (59.3%) and 72 cases of posttreatment change (40.7%). Diagnostic accuracies for analysis of conventional MR imaging by two readers were significantly improved from 77% (72-81%) to 85% (80-89%) by adding visual analysis of ADC ($P = 0.002$). The specificities were also increased significantly from 73% (65-80%) to 90% (82-94%) by adding visual ADC analysis ($P < 0.001$) without compromising sensitivities (79% vs 82%; $P = 0.374$). Circular ROI measurement of ADC value showed no added value for diagnostic performance than visual analysis of ADC map**.** Inter-reader agreement became improved by adding ADC map regardless of circular ROI measurement: conventional image analysis, [$\kappa = 0.38$; 95% CI, 0.27-0.48); conventional image with visual analysis of ADC map, [$\kappa = 0.76$; 95% CI, 0.67-0.86]; conventional image analysis assisted with ADC value measurement using a circular ROI, [$\kappa = 0.81$; 95% CI, 0.72-0.89].

Conclusions: Adding qualitative/quantitative DWI to morphologic analysis can improve diagnostic performance including accuracy and specificity, and improve inter-observer reliability in differentiating tumor recurrence from treatment change, regardless of reader's experience in head and neck imaging.

목차

표 및 그림 차례

서론

Local recurrence after definitive treatment of HNSCC is main manifestation of disease relapse up to 40% in advanced cases and early detection of regional recurrence can enable salvage operation which improves overall survival [1, 2]. So timely detection of tumor recurrence with high accuracy at follow up imaging is critical in HNSCC patient while post-treatment surveillance.

Detection of local recurrence is more complicated than diagnosis of primary HNSCC because treatment including surgery and radiation therapy may distort the anatomy and induce inflammatory change such as edema, necrosis, granulation tissue, and progressed to fibrosis that can mimic or obscure recurred tumor [3, 4].

Combined DWI analysis with conventional MR imaging has been reported to improve diagnostic performance of differentiating tumor recurrence from post-treatment change showing lower ADC value of tumor than that of treatment-related change [3-11].

However, interpretation of head and neck imaging is difficult due to many interfaces between air, bone, and tissue, especially in DWI resulting in image distortion and quality degradation [12]. In this context radiologist may need learning period to make precise diagnosis with high agreement, so that imaging analysis were performed by experienced radiologists in most previous studies.

Although the inter-observer reliability in detecting tumor recurrence is critical factor in application of imaging in clinical practice, to our knowledge, there were limited studies for inter-reader agreement especially in inexperienced reader. Some previous study showed that radiologist's experience in head and neck imaging or DWI was not significantly related to diagnostic performance for recurred HNSCC, however the study population size was too small and imaging analysis was performed for DWI with conventional image together, not respectively [13]. Moreover in previous study about interpretation of prostate cancer using DWI, diagnostic performance and inter-observer agreement were significantly improved with reader's experience [14, 15]. Another study reported that adding DWI analysis to conventional liver MRI improved diagnostic performance of radiology residents for detecting liver metastasis while it showed no added value for board-certified radiologists [16].

So in this study, we aim to evaluate diagnostic performance and inter-observer reliability of the radiologists with different experience for differentiating tumor recurrence from post-treatment change in analysis of conventional image only and combined analysis with qualitative or quantitative DWI, respectively.

연구대상 및 연구방법

Study population

We reviewed electronic records of patients who underwent surveillance MRI after definitive treatment for HNSCC between January 2014 and June 2018. Among these follow up MRIs, we included consecutive patients which met the flowing criteria: 1) patients who had undergone definitive treatment for pathologically confirmed HNSCC according to the 8th edition of American Joint Committee on Cancer (AJCC) [17]; 2) new contrast-enhancing lesion was seen at the post-treated primary site. Exclusion criteria were as follows: 1) cases not confirmed whether recurred tumor or post-treatment change due to inadequate follow-up; 2) non-diagnostic DWI from poor quality.

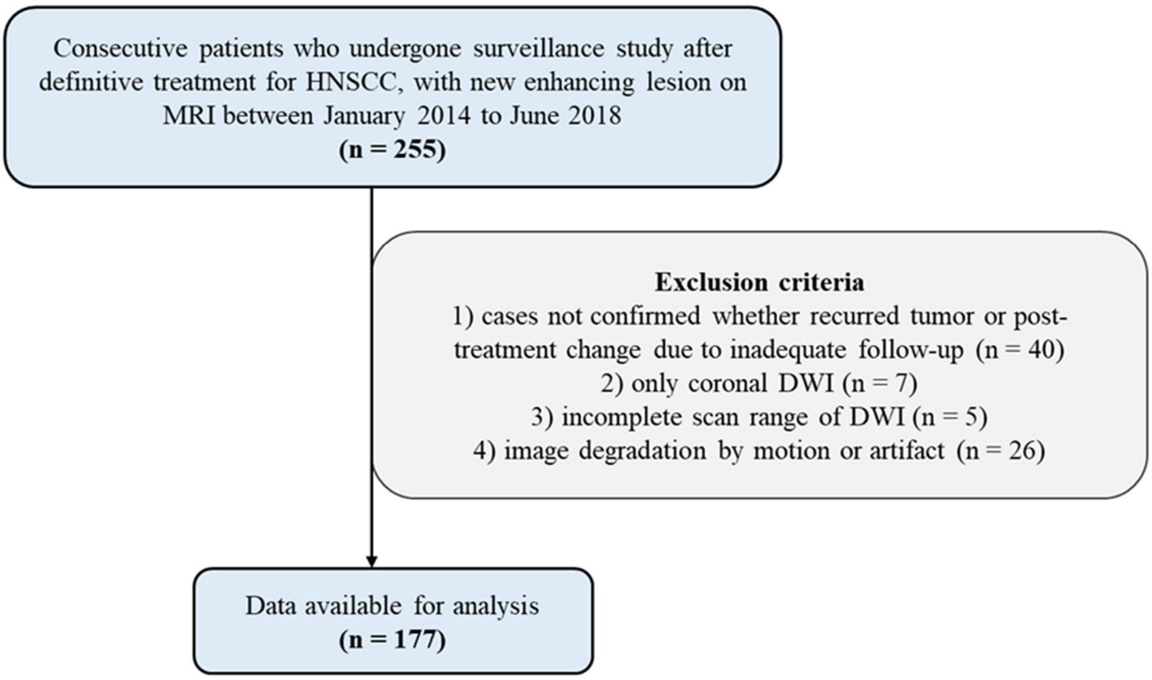

Figure 1. Flowchart of the patient inclusion process.

MR imaging protocol and image analysis

MRI was performed using a 3-T scanner with 64-channel head and neck coil (Skyra, Siemens Healthcare, Erlangen, Germany). MR imaging protocol for head and neck tumors included axial and coronal T1- and T2-weighted turbo spin-echo sequences with DWI. All of the axial T1- (repetition time (TR)/echo time (TE) = 790/11 ms) and T2-weighted images (T2WI) (TR/TE = 5470/85 ms) were acquired with field of view (FOV) = 190 × 190 mm^2, matrix size = 448 × 291, and slice thickness/gap, 3 mm/0 mm. DWI was obtained using the following parameters: TR/TE, 3000/56 ms; diffusion gradient encoding, b = 0, 1000 s/mm^2; FOV, 250 x 250 mm^2; matrix, 256 × 256; slice thickness/gap, 3 mm/0 mm; and acquisition time, 4 minutes and 12 seconds. The apparent diffusion coefficient maps were calculated using the b values of 0 and 1000 s/mm^2, using a two-point estimate of signal decay: $ADC = -\ln (S[b]/S[0])/b$, where b indicates the b value and S(0) and S(b) are the signal intensities of images with b values at 0 and 1000, respectively. Axial (TR/TE = 650/12 ms) and coronal (TR/TE = 540/11 ms) contrast-enhanced-T1 weighted images (CE-T1WI) with fat suppression were obtained after administration of gadolinium contrast agent.

MR images were reviewed by 2 neuroradiologists (with 2 and 18 years of experience in head and neck oncology, respectively) on a PACS monitor while blinded to all clinical information including histopathologic results, initial & follow-up imaging except the primary site of HNSCC.

Initial image interpretation was performed only with T1WIs, T2WIs, and contrast-enhanced axial T1WIs without DWI. We defined recurred tumor based on tumor site alterations such as moderately high signal intensity on T2WI, tissue volume increase, mass effect, and moderate contrast enhancement. If not, the cases were defined as post-treatment change [3, 4, 8, 11].

After the initial interpretation, radiologists reclassified the case into recurrence or treatment related changes using both conventional images and ADC map. ADC map of the index lesion was interpreted by visual analysis only, and then, assisted by an ADC value measured with a circular ROI. Visual analysis of DWI were made based on signal intensity on b=1000 image and value of the corresponding ADC map. The high signal intensity on b=1000 combined with low value on ADC map was interpreted as tumor recurrence.

Otherwise, the cases were considered as post-treatment change. In quantitative DWI analysis, measurement of ADC value was made using circular ROI placed on the most hypo-intensity area, avoiding necrotic/cystic portion. The cut-off value of ADC were set as 1.2 x 10^{-3} mm^2/sec referring to previous reports [4, 6, 8, 11].

If there was discordance between analysis of conventional image and ADC map, findings of conventional images outweighed ADC analysis unless the cases were inconclusive based on morphologic criteria only.

Final histopathologic results or clinico-radiologic consensus with follow up imaging at least 6 months after were considered as the standard of reference. In cases without pathologic confirmation, cases were classified as tumor recurrence when at least 20% or more growth of the enhancing lesion on follow up imaging or other evidence such as invasion or metastasis developed. When the enhancing lesion remains stable or regressed on follow up images at least 6 months after without any evidence of recurrence, the cases were classified as treatment change.

Statistical analysis

Statistical analyses were performed using SPSS statistical software (version 21.0, SPSS). A *p* value less than 0.05 was considered statistically significant. Patient demographics and clinical characteristics were compared between two subgroups using Chi-square test or Fisher's exact test for binary variables and Student's t test for continuous variables. Diagnostic performance was evaluated by calculating the accuracy, sensitivity, and specificity of each reader's classification for conventional image analysis, conventional image combined with visual ADC analysis or ADC value of circular ROI respectively. Percentage agreement and Cohen's k coefficient (k) was used to evaluate inter-observer reliability and κ coefficients were categorized as follows: poor ($0<\kappa w\leq 0\cdot 20$), fair ($0\cdot 20<\kappa w\leq 0\cdot 40$), moderate ($0\cdot 40<\kappa w\leq 0\cdot 60$), good ($0\cdot 60<\kappa w\leq 0\cdot 80$), and excellent ($0\cdot 80<\kappa w\leq 1\cdot 00$). Considering the correlation within the same patient, we used generalized estimating equation(GEE) model for comparing accuracy, sensitivity, and specificity of classified cases by conventional image analysis, conventional image with visual ADC analysis, and conventional image analysis with circular ROI ADC value.

연구결과

Patient characteristics

Two hundred and fifty-five patients were met to the inclusion criteria. Among them 78 patients were excluded due to inadequate follow-up (N=40), no available axial DWI (only coronal DWI, N=7), no available DWI slice corresponding to target lesion due to incomplete scan range (N=5), image degradation by motion or susceptibility artifact (N=26). Finally, total 177 MRIs of 177 patients were included in this study.

Of 177 patients, 72 cases (41 %) had post-treatment change and 105 cases (59 %) had tumor recurrence. Statistical analysis revealed no significant difference between recurrence and treatment change groups in demographic data including mean age or sex (62.8 $\pm$ 11.7 years vs 61.2 $\pm$ 11.3 years, P = .369; 79 men and 26 women vs 56 men and 16 women, P = .696).

The most frequent primary site of HNSCC was the oral cavity (44.1% [78/177]), followed by PNS (18.1% [32/177]), oropharynx (13.6% [24/177]), nasopharynx (12.4% [22/177]), larynx (6.8% [12/177]), and hypopharynx (5.1% [9/177]).

Most patients (63.3% [112/177]) underwent surgery as a standard treatment followed by adjuvant radiation therapy in 23.7% [42/177] and by concurrent chemoradiation therapy in 6.8% [12/177], and 28.2% [50/177] of patients underwent concurrent chemoradiation therapy only. The remaining 1.7% [3/177] of patients received only radiation therapy as definitive treatment for glottic cancer.

Initial clinical staging was classified according to the 8^{th} edition of AJCC for all patients and restaging was done for patients who diagnosed according to prior edition.

There was no significant difference in primary tumor location (P = .189), treatment modality (P = .612), and clinical staging (P = .48) between two subgroups.

In tumor recurrence group, the final diagnosis was confirmed by pathology in 87.6% [92/105] and by clinicoradiologic concordance in 12.4% [13/105], and in post-treatment group, by pathology in 22.2% [16/72] and by clinicoradiologic concordance in 77.8% [56/72].

Descriptive statistics including demographics and clinical characteristics for two groups were summarized in table 1.

Table 1. Demographics and clinical characteristics of the patients (n=177)

	Local tumor recurrence (n=105)	Post-treatment change (n=72)	*P*
Mean age (years)	62.8 ± 11.6	61.2 ± 11.3	0.369
No. of women	26 (24.7%)	16 (22.2%)	0.696
Primary site			0.189
Nasopharynx	16 (15.2%)	6 (8.3%)	
Oropharynx	10 (9.5%)	13 (18.1%)	
Hypopharynx	3 (2.9%)	6 (8.3%)	
Larynx	10 (9.5%)	2 (2.8%)	
Oral cavity	47 (44.8%)	31 (44.4%)	
PNS	18 (17.1%)	14 (19.4%)	
Final diagnosis			<0.001
Pathologic	92 (87.6%)	16 (22.2%)	
Clinico-radiologic	13 (12.4%)	56 (77.8%)	
Definite treatment			0.612
Surgery	38 (36.2%)	32 (44.4%)	
Surgery with RT	27 (25.7%)	15 (20.8%)	
CCRT	32 (30.5%)	18 (25%)	
RT only	2 (1.9%)	1 (1.4%)	
Surgery with CCRT	6 (5.7%)	6 (8.3%)	
TNM staging(clinical)			0.48
1	13 (12.4%)	15 (20.8%)	
2	15 (14.3%)	11 (15.2 %)	
3	36 (34.3%)	20 (27.8%)	
4A	27 (25.7%)	16 (22.2%)	
4B	6 (5.7 %)	7 (9.7%)	
N/A	8 (7.6 %)	3 (4.1%)	

Note: Data are expressed as the mean ± standard deviation. Numbers in parenthesis are percentage. N/A = not available

Comparison of imaging analysis

Table 2 shows the results of readers' classification for conventional image only, conventional image combined with visual analysis of ADC map, and conventional image with ADC value measured using a circular ROI, respectively.

Table 2. Results of conventional image analysis and combined interpretation of conventional image with visual analysis of ADC map or ADC value for differentiating tumor recurrence

	Local tumor recurrence (n = 105)			Post-treatment change (n = 72)		
	TP	FN	FNR (%)	TN	FP	FPR (%)
Reader 1						
Conventional image analysis	98	7	7	40	32	44
Conventional with visual analysis of ADC map	90	15	14	64	8	11
Conventional with ADC value using circular ROI	90	15	14	66	6	8
Reader 2						
Conventional image analysis	68	37	35	65	7	11
Conventional with visual analysis of ADC map	82	23	22	65	7	11
Conventional with ADC value using circular ROI	85	20	19	62	10	14

Note: FN indicates false negative; FNR, false-negative rate; FP, false-positive; FPR, false-positive rate; TN, true-negative; TP, true-positive

Inter-reader agreement for differentiating tumor recurrence was fair for conventional image analysis (κ = 0.38; 95% CI, 0.27-0.48; percentage agreement = 66.7%[118/170]), good for conventional image with visual analysis of ADC map (κ = 0.76; 95% CI, 0.67-0.86; percentage agreement = 88.1%[156/170]), and excellent for conventional image analysis combined with ADC value assisted by circular ROI measurement (κ = 0.81; 95% CI, 0.72-0.89; percentage agreement = 90.4%[160/170]).

For radiologist with 18 years of experience (reader 1), adding DWI analysis with ADC value measured using circular ROI decreased false positive rate from 44.4% to 8.3% preserving high sensitivity from 93.3% to 85.7% and decreased false negative rate from 35.2 % to 19.0 % preserving high specificity from 90.3% to 86.1% for radiologist with 2 years of experience (reader 2).

Diagnostic accuracies for analysis of conventional MR imaging by two readers were significantly improved from 77% (72-81%) to 85% (80-89%) by adding visual ADC analysis in all patients (P = 0.002). The specificities were also increased significantly from 73% (65-80%) to 90% (82-94%) by adding visual ADC analysis (P < 0.001) without compromising sensitivities (79% vs 82%; P = 0.374). There was no significant difference in accuracy and specificity between visual analysis of ADC map and quantitative analysis of ADC value with circular ROI. The results were summarized in table 3.

Table 3. Diagnostic accuracies of conventional image anlaysis and combined interpretation of conventional image with visual analysis of ADC map or ADC value for differentiating tumor recurrence

			Overall P value	Post-hoc P value	
Accuracy	Conventional image analysis	0.77(0.72-0.81)	0.004	Ref	
	Conventional with visual analysis of ADC map	0.85(0.80-0.89)		0.002	Ref
	Conventional with ADC value using circular ROI	0.86(0.80-0.90)		0.002	0.684
Sensitivity	Conventional image analysis	0.79(0.73-0.84)	0.374		
	Conventional with visual analysis of ADC map	0.82(0.75-0.88)			
	Conventional with ADC value using circular ROI	0.83(0.76-0.89)			
Specificity	Conventional image analysis	0.73(0.65-0.80)	0.001	Ref	
	Conventional with visual analysis of ADC map	0.90(0.82-0.94)		<0.001	Ref
	Conventional with ADC value using circular ROI	0.89(0.81-0.94)		0.002	0.763

See Figs 2,3 and 4 for examples of radiologist's case classification based on morphologic characteristics with analysis of ADC and final diagnosis.

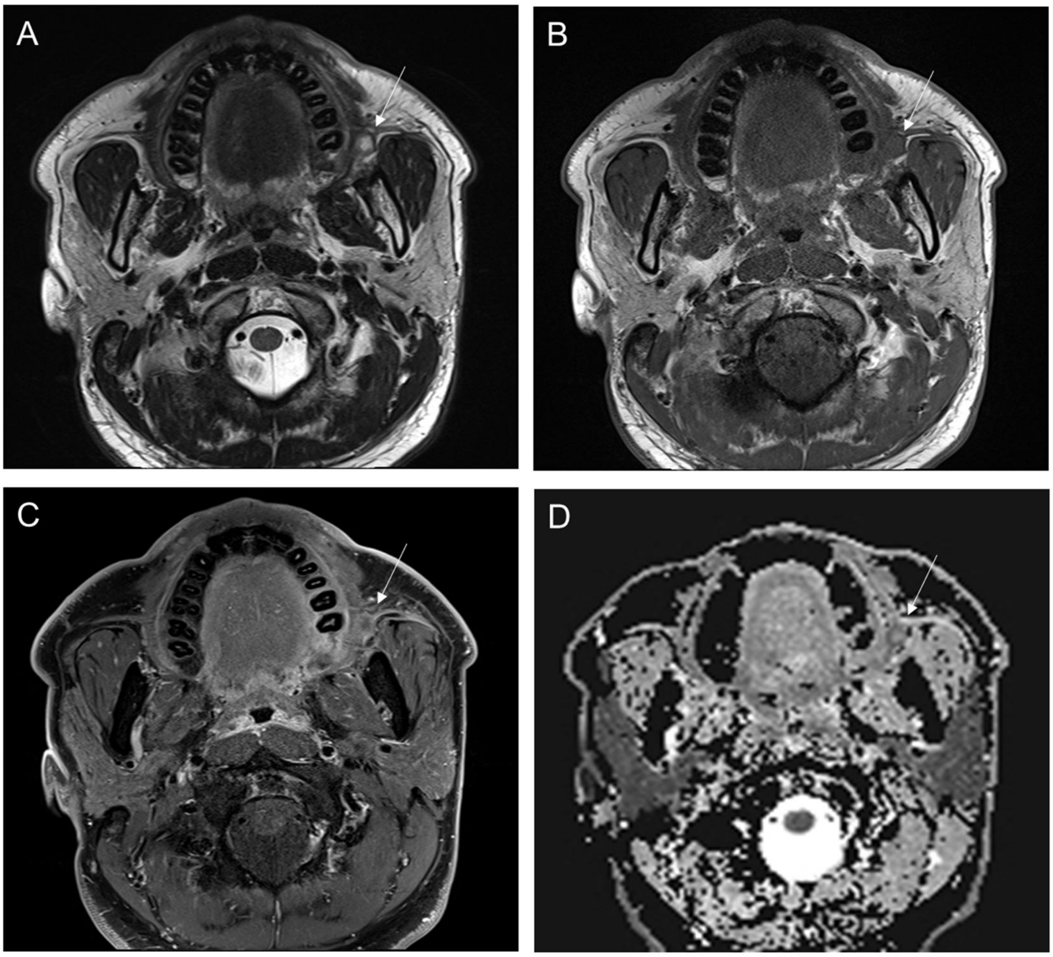

Figure 2. (A-D) Case of local recurrence. 53-year-old man with buccal cancer received marginal mandibulectomy and radical neck dissection. On surveillance MRI after 2 months, enhancing lesion was detected on operation site.

(A-B) T2WI & T1WI shows small ovoid shaped lesion with internal T2 hyper-intensity portion in left buccal mucosa, upper portion of the buccinator muscle. (C) CET1WI shows peripheral enhancement of lesion. (D) ADC map shows diffusion restriction of the lesion. Although two radiologists classified this case as post-treatment change on morphologic analysis, they revised the decision to tumor recurrence after analysis of ADC map. Histology confirmed recurrence of a squamous cell carcinoma.

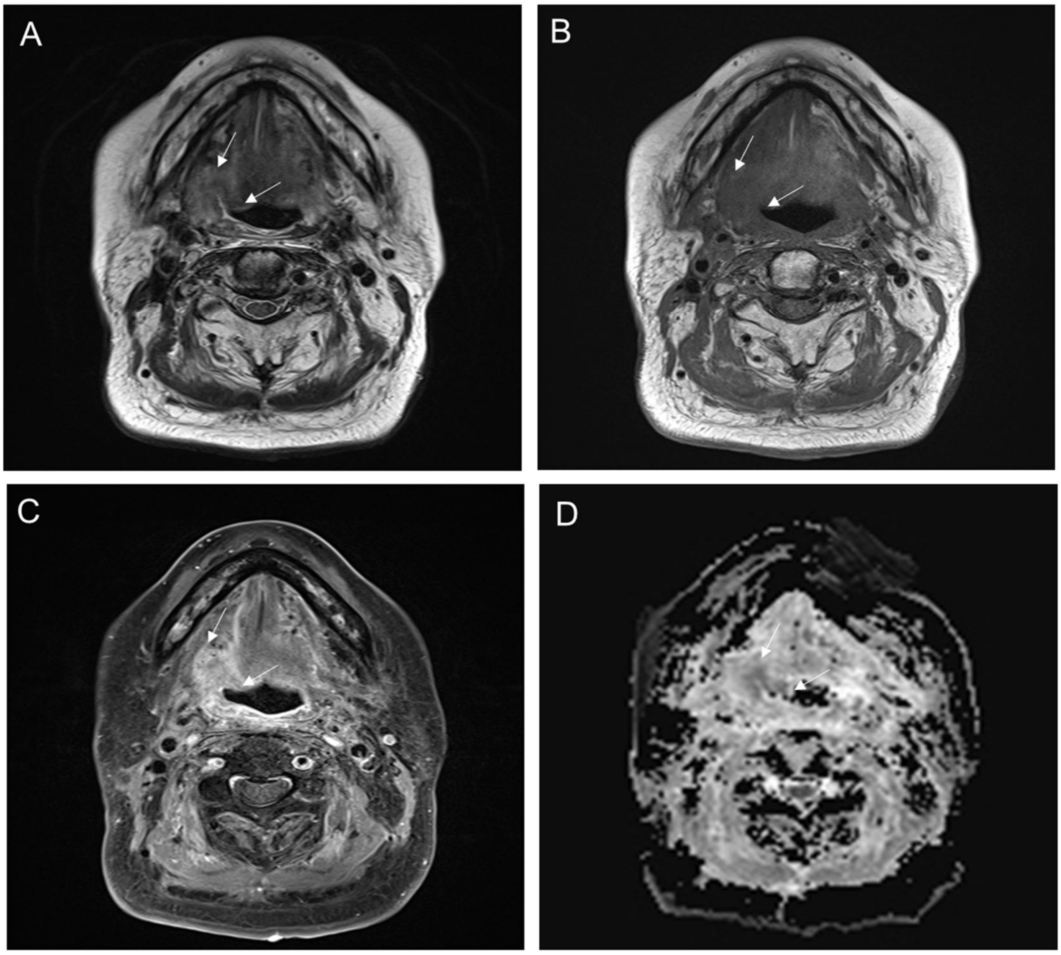

Figure 3. (A-D) Case of tumor recurrence. 85-year-old man with oral cavity (tongue) cancer received operation followed by chemo-radiation therapy. On MRI after 9 years, enhancing lesion was detected in the post-operation site. (A-B) T2WI & T1WI shows ill-defined superficial spreading mass involving right side of tongue base, right lateral oropharyngeal wall. (C) CET1WI shows moderate enhancement of lesion. (D) ADC map shows diffusion restriction of the lesion.

Although two radiologists made different diagnosis on morphologic analysis, they made consensus to tumor recurrence after analysis of ADC map. Histology confirmed recurrence of a squamous cell carcinoma.

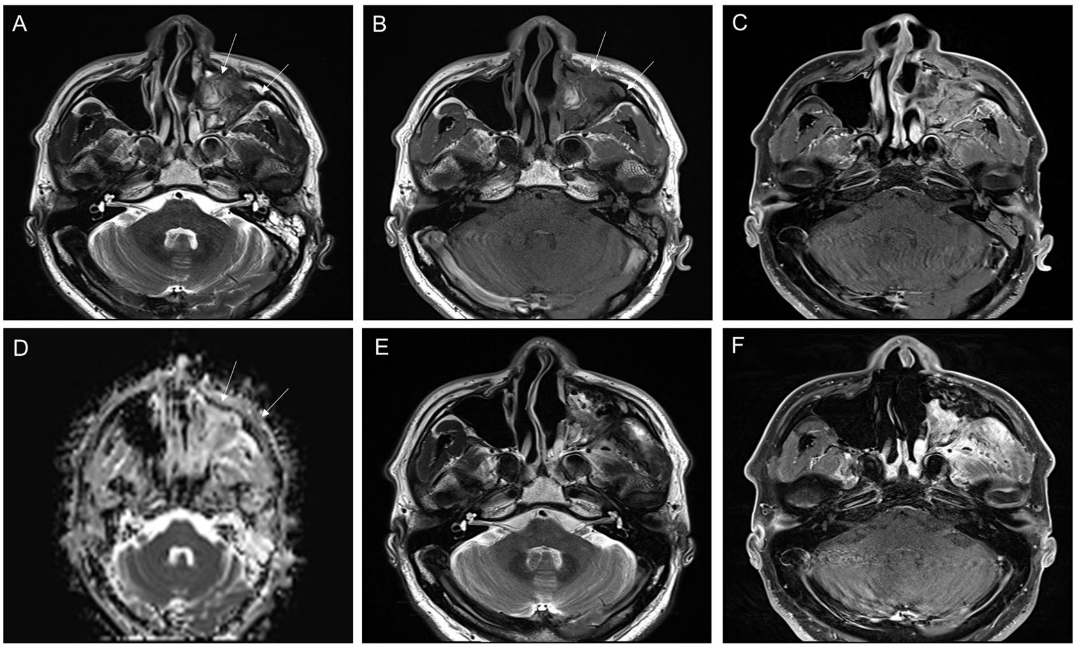

Figure 4. (A-D) Case of post-treatment change. 58-year-old man with left maxillary sinus cancer received operation. On surveillance MRI after 6 months, enhancing lesion was detected in the left maxillary sinus. (A-B) T2WI & T1WI shows heterogeneous signal intensity soft tissue in posterior portion of flap margin. (C) CET1WI shows mild enhancement of lesion. (D) ADC map shows no definite diffusion restriction of the lesion. Although two radiologists made different diagnosis on morphologic analysis, they made consensus to tumor recurrence after analysis of ADC map. The enhancing lesion remained stable on follow-up MRI after 3 years (E-F). So this case was regarded as post-treatment change.

고찰

Our study for detecting local recurrence after treatment showed that inter-observer agreement between readers with difference experiences improved from fair to good by adding visual analysis of ADC and improved from good to excellent by adding measured ADC value using a circular ROI. We confirmed added value of DWI to morphologic MRI by increasing accuracy and specificity, which was consistent with previous studies [6, 8]. Although ADC value measured using circular ROI (quantitative analysis) showed no added value for diagnostic performance than visual analysis of ADC map (qualitative analysis) in agreement with previous study of Minerva Becker et al [4] , it improved inter-reader reliability between different experiences.

The usefulness of DWI for differentiating tumor recurrence from post treatment change was proven in previous studies, showing significantly low value of ADC in recurred tumor group than that of post-treatment groups reflecting high cellularity of tumor. Also using quantitative analysis of ADC showed high diagnostic performance of sensitivity (78.9 – 100 %) and specificity (78 – 86.2 %) with optimal cutoff value of ACD_{mean} from 1.2 x 10^{-3} mm^2/sec to 1.53 x 10^{-3} mm^2/sec [4, 6, 8, 11]. Previous studies by Acampora et al [6] and Ailianou et al [8] reported DWI analysis combined with morphologic analysis of conventional image improved accuracy and specificity. Adding DWI also improved sensitivity in study of Ailianou et al [8], although our study showed no significant difference in sensitivity. This may be due to different study population that included only cases treated by radiation therapy with or without additional surgery, while our study also included cases treated only by operation without radiation therapy that accounts for 40%. Adding DWI analysis may enables detection of recurred tumor masked by radiation induced changes.

Contrary to our study, Ailianou et al [8] showed excellent interobserver-agreement for detecting tumor recurrence in both analysis, MRI (conventional MRI only) and qualitative DWIMRI (MRI combined with qualitative DWI). However in this case, the readers had more than 10 years of experience, different from our study with radiologist of 2 years of experience. Also Boris Peltenburg et al [13] reported that the reader’s experience had no significant influence in diagnostic accuracy for interpretation of MRI including DWI. This may be due to increased consent between readers by adding DWI analysis. So quantitative analysis of DWI using circular ROI may be useful especially for inexperienced readers, also supported by study of Fukumoto et al [16] showing additional value of DWI only for radiologic residents not for board certificated radiologists in detecting liver metastasis.

In clinical practice, false positive report for post-treatment change case is more endurable than missed recurrence case, so that experienced reader may prefer reporting inconclusive cases as local recurrence. That may explain our study result showing higher sensitivity of reader 1 (18 years of experience) for conventional image analysis than reader 2 (2 years of experience). However, high false positive rate may lead to invasive procedure for pathologic confirm with risk of complication. We validated usefulness of DWI for avoiding unnecessary invasive process by additional clarification for inconclusive cases, with improved specificity.

In addition to the retrospective nature of this study, there are several limitations. Although the number of cases are relatively big, the cases were from single tertiary hospital center and assessed only by two readers. The results of our study could be further validated with future multicenter study. Second, we did not subdivide posttreatment changes into late fibrosis and others. One report said the late fibrosis had significantly low ADC value similar to recurred tumor [8]. The potential to mis-diagnose late fibrosis as recurrent tumor by ADC value could be overcome by applying strict criteria of morphologic MRI. Third, there were relatively large proportion of oral cavity cancer patients in both tumor recurrence and treatment change groups accounting 44.8 and 44.4 % respectively. For consistence of staging, restaging according to the 8th edition of AJCC was done for previously diagnosed patients before 8th edition. So some patients received different treatment guided by previous edition of AJCC, especially in case of oropharyngeal cancer with HPV or p16 positivity.

결론

we proved adding DWI analysis to morphologic MRI can improve diagnostic performance including accuracy and specificity in differentiating tumor recurrence from treatment change and improve inter-observer reliability with measurement of ADC value using circular ROI, regardless of degree of experience in head and neck imaging.

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국문요약

연구제목: 두경부암 근치적 치료 후 추적 자기공명영상에서 국소 재발 진단에 확산강조영상의 추가적 진단능: 진단 정확도 및 관찰자간 일치도 향상

연구배경: 기존의 자기공명영상에 확산강조영상을 추가하는 것이 두경부암의 재발을 평가하는데 진단 정확도 및 관찰자간 일치도를 향상시킬 수 있는지 서로 다른 경력의 판독자에서 평가하고자 하였다.

연구방법: 두경부암에 대한 근치적 치료 후 2014년 1월부터 2018년 6월까지 시행한 추적관찰 자기공명영상에서 원발암 치료부위에 새로운 조영 증가 병변이 생긴 경우를 연구대상으로 포함하였다. 각각 2, 18년 경력의 영상의학과 의사 2명이 원발암부위를 제외한 다른 임상 정보는 제공받지 못한 상태로 먼저 T2, T1, 조영증강 T1 영상만을 이용하여 각 병변에 대해 재발 여부를 평가하였으며, 이후 확산강조영상에 대해 정성적 분석과 원형 관심영역을 (circular ROI) 이용한 정량적 분석을 추가하였을 때 각각에 경우에 대해 병변의 재발 여부를 재평가 하였다. 정략적 분석의 기준점은 이전 논문에 따라 1.2 x 10^{-3} mm^2/sec로 설정하였으며, 기존영상에서 병변에 대한 재발 여부 판단과 확산강조영상을 이용한 재발 여부 판단이 불일치하는 경우 형태학적 기준에 따른 판단이 불명확한 경우를 제외하고는 형태학적 기준에 의거 판단하였다. 표준진단방법은 병리결과에 따랐으며, 병리학적 진단이 시행되지 않은 경우에 최소 6개월 후의 영상 평가를 이용하여 진단하였다. 관찰자별로 각 분석에 대해 진단의 정확도, 민감도, 특이도를 구하였으며, 각 분석의 진단능을 비교하기 위해 일반화 추정방정식 (generalized estimating equation model) 을, 각 관찰자간 일치도를 평가하기 위해 코헨의 카파 (Cohen's Kappa coefficient) 를 이용하였다.

연구결과: 총 177명의 환자가 연구대상에 포함되었으며, 재발케이스가 105건, 치료관련변화의 경우가 72건이었다. 두 관찰자에서 확산강조영상의 정성적 분석을 추가하는 경우 진단의 정확도는 77% (신뢰구간, 72-81%) 에서 85% (신뢰구간, 80-89%) 로 향상되었으며 (P=0.002) , 민감도의 유의한 감소 없이 (79% vs 82%;

P = 0.374) 특이도를 73% (신뢰구간, 65-80%) 에서 90% (신뢰구간, 82-94%) 로 향상시켰다 (P<0.001). 확산강조영상의 정량적 분석은 정성적 분석과 비교해 유의한 진단능의 향상을 보이지 못했지만, 관찰자간 일치도 평가에서 일치도의 향상에 도움을 주었다.

연구결론: 두경부암 재발여부를 판단하는 데 있어 확산강조영상에 대한 정성적/정량적 분석을 추가하는 경우 정확도와 특이도를 포함한 진단능의 향상과 함께 서로 다른 경력의 관찰자간 일치도를 향상시키는 효과가 있었다.