ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Diffusion MR Imaging in Evaluation of Treatment Response in Patients with Lung Cancer

Akciğer Kanserli Hastalarda Tedavi Yanıtının Değerlendirilmesinde Difüzyon MR Görüntüleme

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ABSTRACT

Aim: *To observe the change in apparent diffusion coefficient (ADC) value after chemoradiotherapy in lung cancer and to investigate the ability of the change in ADC values to detect response to treatment earlier than computed tomography (CT).*

Material and Methods: *This prospective study was performed in patients with a confirmed diagnosis of stage III-IV lung cancer and included 25 patients who underwent T2-weighted MR, diffusion-weighted images (DWI), CT, and FDG PET/CT. Thoracic diffusion MRI and CT examinations were performed on patients who received chemoradiotherapy. Post-therapy; Thoracic diffusion MRI was repeated one week after the two cycles of chemotherapy and two weeks after the end of the radiotherapy, while post-therapy CT was performed four or five weeks after therapy. Before and after treatment, ADCmin, ADCmean, and SUVmax values were compared with each other.*

Results: *Data analysis revealed a statistically insignificant inverse correlation between the pre-therapy ADCmin and SUVmax (r=-0.36; p=0.077) with ADCmean and SUVmax (r=-0.283; p=0.170). Post-therapy repeated measures revealed that increased ADCmin values were significantly higher with the tumor size change (r=-0.872; p=0.000) and median size (r=-0.847; p=0.001) tumor on CT.*

Conclusion: *ADC measurements with DWI may be a new prognostic marker in lung cancers predicting early response to chemotherapy in lung cancer.*

Keywords: *diffusion; apparent diffusion coefficient; lung cancer; responce to treatment; magnetic resonance imaging*

ÖZET

Amaç: *Akciğer kanserinde kemoradyoterapi sonrası görünür difüzyon katsayısı (ADC) değerindeki değişimi gözlemlemek ve ADC değerlerindeki değişimin bilgisayarlı tomografi (BT)'den daha erken tedaviye yanıtı belirleme yeteneğini araştırmak.*

Materyal ve Metot: *Bu prospektif çalışma, evre III-IV akciğer kanseri tanısı doğrulanmış hastalarda yapıldı ve T2 ağırlıklı MR, difüzyon ağırlıklı görüntüler (DAG), BT ve FDG PET/BT yapılan 25 hastayı içeriyordu. Kemoradyoterapi alan hastalara torasik difüzyon MRG ve BT incelemeleri yapıldı. Tedavi sonrası; Torasik difüzyon MRG, iki kür kemoterapi bitiminden bir hafta sonra ve radyoterapi bitiminden iki hafta sonra tekrarlanırken, tedavi sonrası BT, tedaviden dört veya beş hafta sonra yapıldı. Tedavi öncesi ve sonrası ADCmin, ADCmean ve SUVmax değerleri birbirleri ile karşılaştırıldı.*

Bulgular: *Veri analizi, tedavi öncesi ADCmin ve SUVmax (r=-0,36; p=0,077) ile ADCmean ve SUVmax (r=-0,283; p=0,170) arasında istatistiksel olarak anlamsız bir ters korelasyon ortaya çıkardı. Tedavi sonrası tekrarlanan ölçümler, BT'de tümörün büyük boyutunun (r=-0,872; p=0,000) ve median boyutunun (r=-0,847; p=0,001) değişimiyle, artan ADCmin değerlerinin önemli ölçüde daha yüksek olduğunu ortaya koydu.*

Sonuç: *DAG ile ADC ölçümleri, akciğer kanserinde kemoterapiye erken yanıtı öngören yeni bir prognostik belirteç olabilir.*

Anahtar Kelimeler: *difüzyon; görünür difüzyon katsayısı; akciğer kanseri; tedaviye yanıt; manyetik rezonans görüntüleme*

Introduction

Lung cancer is the most common type of cancer in the world and in our country, as well as the most common cause of cancer-related deaths[1,2]. While it was a rare disease in the early 20th century, its frequency increased in parallel with the increase in smoking habits[3,4]. Lung cancer is responsible for 12.8% of cancer cases and 17.8% of cancer deaths worldwide[5].

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Determination of the individual response to treatment in lung cancer is extremely important in order to avoid unnecessary doses as well as to prevent unnecessary expenditure. The change in the size of the tumor may be behind the biological and molecular changes, therefore there may not be an early and sensitive indicator in the evaluation of response to treatment[6].

Due to the problems arising from the physics of the lungs, the use of MR in the evaluation of lung pathologies has lagged. However, with the new MR sequences and functional MRI applications, studies on the use of lung MRI in the early diagnosis, staging and follow-up of lung cancer have gained momentum. However, when applied after radiotherapy, MRI provides excellent soft tissue contrast and real-time adaptive therapy opportunity for tumor and normal tissue identification[7]. Computed tomography (CT) and Positron Emission Tomography / Computed Tomography (PET-CT), which are used routinely to evaluate tumor size and tumor metabolism after treatment, have some limitations in the differentiation of residual tumor tissue from necrotic tumor and fibrotic scar tissue. Diffusion-weighted imaging (DWI), which provides functional evaluation, provides additional important information in staging of lung cancer, calculating the true diameter of the tumor, separating tumor tissue from atelectasis, collapse, post-obstructive change, distinguishing high cell tumors from necrotic or normal tissue and evaluating early response to chemotherapy[8,9]. In lung cancer, DWI has been shown to more effectively delineate gross tumor volumes within the atelectatic lung than CT or PET/CT[7]. The ADC (Apparent Diffusion Coefficient), which shows the water mobility in the tumor and replaces the marker of tissue cellularity, can distinguish high cell tumor tissue from normal tissue or necrotic areas[8,9]. Therefore, changes in ADC values may be used in monitoring of response to treatment, which manifests itself as a change in the cellularity of the tumor[9,10].

Since diffusion MRI does not have a radiation risk, multiple examinations can be performed on the same patient and maybe an alternative to CT in follow-up[10,11]. Shorter examination time, noninvasive, relatively inexpensive examination and no need for contrast media are other advantages of the method. It has been shown in previous studies that the change of ADC values can be used as an indicator for the evaluation of response to treatment in many organ tumors.

The aim of our study was to investigate the ability of the change in ADC values after chemoradiotherapy in lung cancer in early detection of response to treatment.

Materials and Methods

Study Population

The study performed between February 2015 and December 2015. The patients were informed about the adverse effects of diffusion MRI and written informed consent was obtained from the patients who accepted the procedure. Computed tomography and PET-CT were performed according to the pre-treatment routine diagnosis and staging protocol. In addition, a thoracic MRI scan including axial T2-weighted MRI and Diffusion MR sequences was performed at 1.5 T MRI. Diffusion MRI was performed 1 week after two cycles of chemotherapy and 2 weeks after the radiotherapy. Post-control thorax CT imaging was performed 1 month after the treatment.

Inclusion Criteria

* Over 18 years old,
* Histopathologically diagnosed as primary lung cancer,
* Patients not previously treated for lung cancer
* Stage III and stage IV small cell and non-small cell lung cancers

The Criteria for Exclusion

* Contraindications to MRI
* Interruption of chemo-radiotherapy
* Tumor less than 1 cm in size
* DWI artifacts that prevent optimal evaluation
* Indeterminate tumor borders

In the axial plane, a single-shot inversion recovery echo-planar sequence (SSIR EPI) was administered without breath. SSEP-SE T2 was obtained by applying diffusion sensitive gradients at two different values in every 3 directions (x, y, z). 0 and 1000 s / mm^2 values were used for the b value. The mean duration of the test was about 5 minutes.

In addition to CT, PET-CT was performed for routine diagnosis and staging in the pre-treatment period, diffusion MRI and T2-weighted images were obtained in our study. In Fig. 1 and Fig. 2, there are pre-treatment images of the 84 years old male patient with SCC diagnosis.

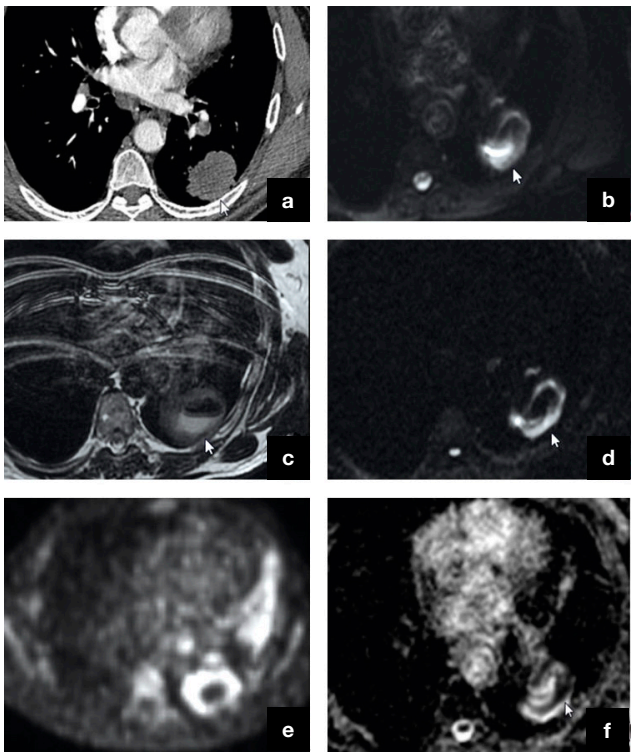

Figure 1. *Fifty-nine years old male patient with NSCLC. The central necrotic mass lesion is located in the left lung lower lobe superior segment, peripherally. Images are from the pre-treatment period.* ***a:*** *Enhanced CT;* ***b:*** *DWI 'b value 0 s/mm²';* ***c:*** *T2 weighted MRI;* ***d:*** *DWI 'b value 1000 s/mm²;* ***e:*** *PET* ***f:*** *ADC map.*

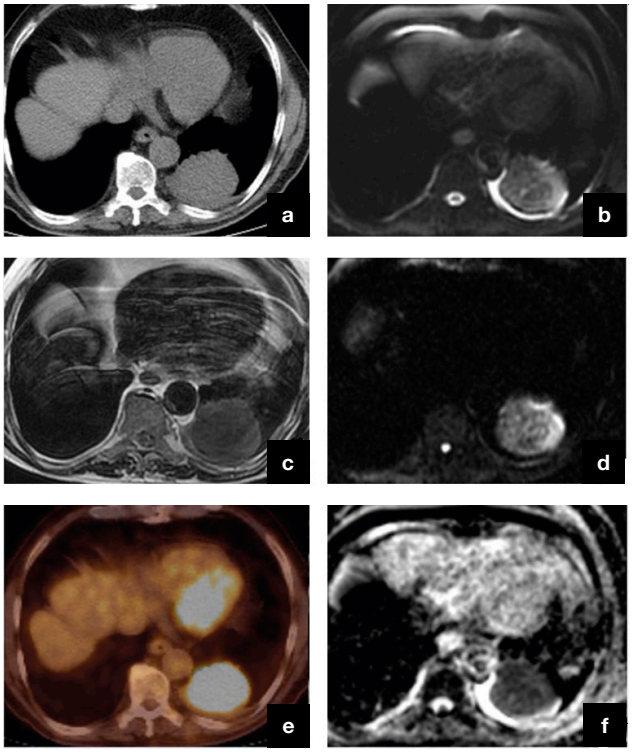

Figure 2. *Eighty-four years old male patient with SCC. A peripheral mass lesion is observed in the posterobasal segment of the lower lobe of the left lung. Images are from the pre-treatment period.* ***a:*** *Unenhanced CT;* ***b:*** *'b 0' value diffusion MR;* ***c:*** *T2 weighted MRI;* ***d:*** *'b 1000' weighted diffusion MR;* ***e:*** *PET-CT* ***f:*** *Apparent diffusion coefficient map. Minimal pleural effusion accompanying the mass lesion is observed in the images. The pleural fluid can be easily selected in b0 value diffusion MR images and on the ADC map, depending on the T2 shine effect.*

Table 1. *Recist guideline*[12]

Response assessment	RECIST guideline, version 1.1
Complete response (CR)	Disappearance of all target lesions and reduction in the short axis measurement of all pathologic lymph nodes to ≤10 mm.
Partial response (PR)	≥30% decrease in the sum of the longest diameter of the target lesions compared with baseline.
Progressive disease (PD)	≥20% increase of at least 5 mm in the sum of the longest diameter of the target lesions compared with the smallest sum of the longest diameter recorded. The appearance of new lesions, including those detected by FDG-PET.
Stable disease (SD)	Neither PR nor PD.

The images were evaluated by two radiologists and a nuclear medicine specialist. The anatomical information obtained from T2-weighted images was also used to evaluate the localization of the tumoral lesion while evaluating the diffusion-weighted images. Before ADC measurements were made, diffusion-weighted images obtained from b=0 sec / mm^2 and b=1000 sec / mm^2 were examined and localizations were determined. For each measurement, a circular shaped ROI (region of interest, interest) was placed on the ADC map of the hyperintense monitored view on b1000 images. The ADC measurements obtained from the imaging results were taken from the solid sections of the masses by considering the contour of the lesion on the ADC maps generated automatically by the device. When calculating ADCmean values, 2–5 times the mass lesion size and heterogeneity were taken into consideration, and these were averaged. Cystic and necrotic components were not included in ROI. The ROIs were circular and the surface area for each lesion was 0.3–0.7 cm^2.

In the pre-treatment period, the SUVmax value of each mass was calculated from the PET-CT images that were routinely performed for diagnosis and staging. The longest diameter of the tumor was determined from the axial sections according to RECIST 1.1 criteria[12] (Table 1) in CT examinations performed before and after treatment with or without contrast. Besides, mean diameters of short and long diameters were obtained. In addition, long dimensions of lesions were measured on axial T2-weighted images.

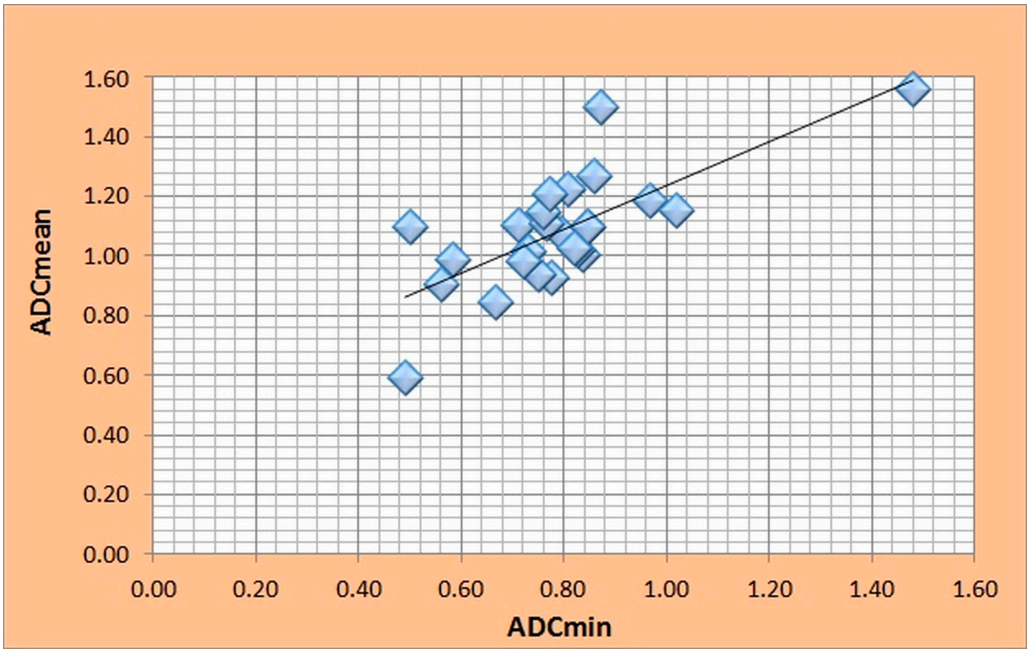

Figure 3. *The chart shows ADCmean and ADCmin values.*

Statistical Analysis

In cases without treatment, the correlation between SUVmax, ADCmin and ADCmean values obtained from the lesions before the treatment were investigated using Pearson's correlation coefficient (n=25). Figure 3 shows ADCmean and ADCmin values in this study.

In the cases treated; the percentage of ADC values and tumor diameters (long-short-mean dimensions in CT, long diameters in T2) were calculated. The rate of change between SUVmax, ADCmin, ADCmean values and the long, short and average diameters of the tumor before and after treatment was calculated as the percentage of four patients in whom the response to treatment with PET-CT in the post-treatment period was evaluated.

The correlation between tumor diameters, ADCmin and ADCmean values in the pre-treatment period, and the changes in the post-treatment period were investigated using the Wilcoxon signed ranks test (n=11). Spearman's statistical rho test was used to determine whether there was a statistically significant difference between ADCmin and ADCmean values and tumor diameters (n=11). $p<0.05$ was considered significant for statistical testing. Analyzes were done in the computer environment. IBM Statistical Package for Social Sciences program version 15.0 (USA) was used for statistical analysis.

Table 2. *Distribution of the data of the patient group according to histopathological typing (n=25)*

N=25	SCC	Adeno Ca	NSCLC	SCLC
Age range	44–86	65–69	58–80	56–70
Gender				
Male	16 –	2	4 –	2 –
Female		1		
Grade				
Stage 3	7	0	3	0
Stage 4	9	3	1	2
Placement				
Right lung	7	1	1	2 –
Left lung	9	2	3	
Intrapulmonary location				
Central	4	1	1	1
Peripheral	5	1	2	1 –
Central + peripheral	7	1	1	

SCC: Squamous Cell Cancer; NSCLC: Non-small cell cancer; SCLC: Small cell cancer.

Results

Twenty-five patients were included in the study. The mean age of the patients was 55.6 years (46–62) and 1 of the 25 patients (4%) was female and the others were male (96%). Pathological diagnosis of the patients was made by bronchoscopy in 17 (68%) and by transthoracic cutting needle biopsy in 8 (32%). Histopathological; 16 cases (64%) were diagnosed with squamous cell carcinoma, 3 (12%) adenocarcinoma, and 2 SCLC (8%). Subtyping was not performed in 4 cases (16%)

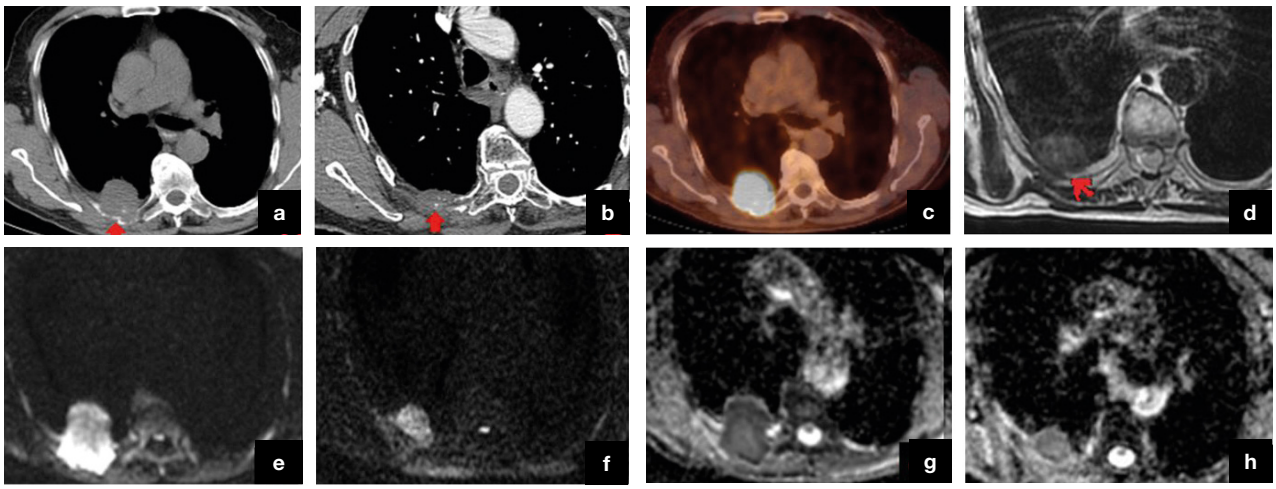

Figure 4. *Seventy-two years old male patient with SCC. The mass appears to have invaded the chest wall.* ***a:*** *Prettreatment non-enhanced CT imaging* ***b:*** *Posttreatment enhanced CT imaging* ***c:*** *pretreatment PET-CT* ***d:*** *Posttreatment T2 WI* ***e:*** *Pretreatment DWI* ***f:*** *Posttreatment DWI* ***g:*** *Pretreatment ADC* ***h:*** *Posttreatment ADC.*

diagnosed with NSCLC. There was no patient with a diagnosis of large cell lung cancer.

Tumoral lesions were located on the right lung in 11 patients (44%), and on the left in 14 patients (56%). Of these, 7 (28%) were central, 9 (36%) were peripheral, and 9 (36%) were both central and peripheral. In staging, 10 patients (40%) were classified as stage-III, and 15 patients (60%) as stage-IV. 9 patients (92%) were given cisplatin + gemcitabine, 1 patient (4%) gemcitabine + carboplatin treatment, and 1 patient (4%) radiotherapy (RT). In imaging modalities, the minimum and maximum diameters of the target lesions in the lungs were 94–16 mm according to RECIST 1.1 criteria. Table 2 shows the distribution of the data of the patient group participating in the study according to histopathological typing.

Thoracic CT, thorax diffusion MRI and PET-CT examinations of the patients were examined. ADC values were based on diffusion MR images obtained at our workstation before and 1 week after CRT; Mass sizes were also evaluated from thoracic CT images obtained before and 3–4 weeks after CRT. The correlation between SUVmax and ADCmin and ADCmean values in 25 cases in the pre-treatment period was evaluated using the Pearson correlation coefficient (r). The correlation coefficient is r=-0.36 between SUVmax-ADCmin values, and r=-0.283 between SUVmax-ADCmean values. According to these results, a negative but weak correlation was found between SUVmax and ADCmin-ADCmean. Table 3 shows the relationship between SUVmax and ADCmin and ADCmean values.

The correlation between ADCmin and ADCmean values is statistically significant (r=0.74, p=0.000).

Table 3. *Correlation of SUVmax with ADCmin and ADCmean values in the pre-treatment period*

Parameters	r	p
SUVmax-ADCmin	-0.360	0.077
SUVmax-ADCmean	-0.283	0.170

r: Pearson correlation coefficient.

Table 4. *Before and after treatment SUVmax, ADC values and tumor diameters change according to histopathological types*

Type	SUVmax (before)	ADCmin (before) (10^{-3} mm^2/s)	ADCmean (before) (10^{-3} mm^2/s)	Size (before) (mm)	SUVmax (after)	ADCmin (after) (10^{-3} mm^2/s)	ADCmean (after) (10^{-3} mm^2/s)	Size (after) (mm)
NSCLC	15.1	0.795	1.078	46	7.9	1.140	1.253	40
SCC	11.4	0.730	1.015	90	6	0.846	1.223	78
SCC	8.6	0.540	0.815	58	4.2	1.081	1.248	50
SCC	21.3	0.860	1.270	80	7.8	0.841	1.208	83

SCC: Squamous Cell Cancer; NSCLC: Non-small cell cancer.

Table 5. *Changes in ADC values and tumor diameters before and after treatment*

Parameters	Before treatment	After treatment	p	N
ADCmin (10^{-3} mm^2/s)	0.75±0.13	0.95±0.2	0.026	11
ADCmean (10^{-3} mm^2/s)	1.04±0.15	1.25±0.2	0.026	11
Longest diameter (cm)	6.7±2.2	6.3±2.8	0.248	11
Average diameter (cm)	5.5±2.2	4.8±2.3	0.130	11
Shortest diameter (cm)	4.7±1.8	3.8±2	0.083	11

Wilcoxon signed ranks test.

Table 6. *Correlation of the change in tumor size with ADCmin and ADCmean values in the post-treatment period (ρ=Spearman's rho coefficient)*

Parameters	r	p
ADCmin – long diameter	-0.870	0.000
ADCmin – average diameter	-0.774	0.005
ADCmin – short diameter	-0.450	0.165
ADCmin – T2 long diameter	-0.806	0.003
ADCmean – long diameter	-0.460	0.154
ADCmean – average diameter	-0.409	0.212
ADCmean – short diameter	-0.210	0.536
ADCmean – T2 long diameter	-0.473	0.142

PET-CT was performed on 4 patients for therapeutic evaluation after treatment. 3 of these were SCC and 1 of them was NSCLC with no subtype. In addition to ADC values and dimensions of the lesions in these patients, SUVmax values were noted, and percentage change values before and after treatment were calculated. Figure 4 shows the transformation of the tumoral lesion in the pre-treatment and post-treatment imaging. After therapy, a decrease in SUVmax values and in the longest diameter and an increase in ADC values were observed in tumoral lesions in all four patients. The change of tumor sizes in ADC, SUVmax and CT according to histopathological typing is shown in Table 4.

The change in ADC values and tumor diameters before and after the treatment is shown in Table 5. While the change of ADCmin and ADCmean values were found to be statistically significant (p <0.05), there was no statistically significant difference between the changes in lesion sizes (p >0.05).

In the post-treatment period, the relationship between ADCmin, ADCmean values and tumor size changes was evaluated with Spearman's rho test. (p=-0.870), long diameter of the tumor in ADCmin-T2AG (r=-0.806) and ADCmin-mean tumor diameter (p=– 0.774) after treatment (p <0.05). The correlation between ADCmean-tumor T2 long diameter (r=-0.473), ADCmean-tumor long diameter (p=– 0.460), ADCmin-short diameter (p=-0.450) and ADCmean-mean diameter (p=-0.409) and A statistically insignificant correlation was found (p >0.05). There was no correlation between ADCmean-tumor short diameter (Spearman's rho=-0.210, p=0.536) (Table 6).

Among the 11 patients who received treatment, post-treatment dimensional regression in 8 cases, whereas increase in ADCmin and ADCmean values; Dimensional progression and decrease in ADCmin and ADCmean values were observed in 3 cases. As a result, an inverse correlation was found between the post-treatment ADCmin and ADCmean values and the changes in lesion size.

When evaluated according to RECIST1.1; with a reduction of 47%, 32%, 33% and 30% in size, partial response was predicted in 4 patients, and progressive disease was predicted in 2 patients with a decrease of 10% and 13%.

Discussion

The most common histopathological type was squamous cell carcinoma with 16 cases (64%). Adenocarcinoma, the most common lung cancer besides SCC, was observed in only 3 of our cases. This may be because our working group is small-scale.

Approximately 30% of patients with NSCLC may have tumor progression after the onset of chemotherapy. It is important to recognize this situation as early as possible, to stop the treatment and apply an alternative treatment[13,14]. Thomas J. Vogl et al in their retrospective study, measured ADC values in 47 patients with 68 lung lesions, who underwent percutaneous microwave ablation with inoperable lung neoplasms. They found a statistically significant difference in ADC value measured 24 h after the ablation between the responding and non-responding groups[15]. In our study,

a decrease was observed in ADCmin and ADCmean values after treatment in 3 cases. Control CT examinations performed 1 month after the treatment showed an increase in tumor size. One of them was in the "stable disease" category according to RECIST 1.1, and the other two were in the "progressive disease" category. Changes in diameter and ADC values were found to be correlated with each other in all 11 cases.

Jagoda et al evaluated the tumor diameters and volumes in 20 patients with stage I-III NSCLC from CT i.v. contrast agent and non-enhanced MRI images before and 3, 6 and 12 months after radio-chemotherapy. They found no significant difference regarding longest longitudinal diameter and tumor volume between Diffusion MRI and CT in addition patients with a good tumor response have higher ADC values than non-responders[16]. In our study, we observed an inversely proportional change in the size of the tumor and ADCmin values after treatment, but we did not see a significant relationship between the categorization of treatment response according to the Recist's criteria and the percentages of changes in ADCmin values.

Apparent diffusion coefficient maps are generally not homogeneous on the normal and cancerous sides. Therefore, where the region of interest (ROI) is placed is very important. In our study, especially in ADC measurements performed several times from heterogeneous lesions, ADCmin values were obtained close to each other, while more variable values were obtained in repeated measurements in ADCmean values. For this reason, we think that ADCmin values give more stable and objective results than ADCmean. In our study, there was a significant correlation between ADCmin and the longest diameter and ADCmin and mean diameter changes in the post-treatment period, while there was no statistically significant correlation between ADCmean and tumor size changes (long-short-mean diameters). Significant values could not be obtained between ADCmin and the shortest diameter.

In one study, 45 FDG-PET / MRI scans were performed on 11 patients, and although the overall changes measured by ADC did not change significantly, a significant overall decrease in FDG uptake was found from pre-treatment scans to post-treatment scans[17]. In our study, the correlation between SUVmax-ADCmin and SUVmax-ADCmean values was investigated in 25 patients before treatment. Statistical significance was not detected between SUV and ADC values. Therefore, a negative correlation was found between SUVmax-ADCmin and SUVmax-ADCmean values. However, the correlation between SUVmax and ADCmin values was found to be more significant than the relationship between SUVmax and ADCmean values. In 4 of our patients who underwent PET after treatment, an inverse ratio was observed between the change in SUVmax values and the change in ADCmin values in all lesions. In three cases diagnosed with NSCLC, a strong relationship was observed in the change in ADCmin and SUVmax values compared to the case diagnosed with SCC. We have 3 cases with a dimensional progression and decrease in ADC values on CT and T2-weighted MR images. In these cases, pre-treatment SUVmax values were determined as 21.3, 15.5 and 10.5. SUVmax=21.3 also constitutes the highest SUV value in our patient group (n=25). In 2 of these 3 cases, SUVmax value was found to be above the average of 13.9 SUVmax values of 11 patients treated. ADCmin values are below the average value in all three cases and ADCmean values are above the average. Even though lesions showed an increase in size at CT, all 3 patients were stable according to the RECIST criteria. The change in SUVmax and ADCmin values were compatible and more pronounced than the change in tumor size.

In the case of SCC diagnosis, SUVmax value was 21.3 and ADCmin was 0.860×10^{-3} mm^2/s in central part of tumor. Posttreatment 1 week after chemotherapy ADCmin increased (51%) while 4 weeks after therapy SUVmax decreased (-63%). In the post-treatment period, SUVmax decreased by 178% and ADCmin value decreased by 53% in the peripheral part of the tumor. However long tumor diameter increased by 4 % were observed (Fig. 2). Brightening was detected in DWI compatible with PET-CT images. SUVmax and ADCmin values of the lesion, which was observed as a hilar localized mass in the post-treatment period it was interpreted as a significant regression. In the peripheral area, posttreatment SUVmax and ADCmin values were competent with progression. The increase in the size of the tumor also supported this. However, according to the RECIST criteria, it was categorized in the stable disease group.

In the study conducted by Komori et al on 16 patients with lung, colon, breast and parathyroid cancer, the examinations of the patients who underwent PET-CT and DWI were evaluated visually and more lesions were detected correctly in DWI than PET-CT[18]. As a result of the visual evaluations, we performed in our study, 2

tumoral lesions detected in PET-CT could not be observed in DWI, while all lesions detected in DAG were also observed in PET. These two lesions completely disappeared in post-treatment imaging. Considering the small number of patients, it is not possible to comment on the sensitivity of PET-CT and compare it with DWI for our study.

Thomas J. Vogl et al, performed ADC analysis on thirty-one patients with 13 primary and 29 secondary lung target lesions before and after the first session of trans arterial chemoperfusion or transpulmonary chemoembolization. They found that the ADC change showed a strong negative correlation with the change in diameter and volume in primary and secondary lung lesions, especially in primary lesions[19]. In our study, we obtained consistent directional changes in size measurements from ADC and post-treatment CT examinations in all patients who received treatment (n=11). However, in our study, there is a significant correlation between the changes in ADCmin values and the changes in the mean and long diameters of the tumor in the post-treatment period, and a negative correlation between the changes in the ADCmean and the tumor size (short-long-mean size). There was no correlation between the short dimension and ADCmin and ADCmean values.

There are some limitations of our study, the first of which is the small number of cases. Another limitation is the low histopathological diversity of our study group. Therefore, diffusion properties and ADC values of the lesions could not be compared according to histopathological types. Since PET-CT was performed on only 4 patients in the post-treatment period, the relationship between SUV and ADC values could not be investigated in the other 7 patients in the post-treatment period. Although there was a significant negative correlation between the post-treatment ADCmin values and the changes in the mean size and longest diameter of the tumor, statistically significant results could not be obtained due to the small number of patients who received treatment, and there is a need to study with larger patient groups.

In conclusion, Diffusion MR, which enables us to obtain information from tissues at a microscopic level; has very important advantages such as not using intravenous contrast material, no need for patient preparation, tolerable examination time (5 minutes), and obtaining PET-like images. In addition, the fact that it is relatively cheap and easily accessible, and most importantly, the absence of ionizing radiation exposure unlike CT, PET and PET-CT have accelerated the studies in this field.

Diffusion-weighted images can be used as an alternative method, especially in patients with a long life expectancy and PET-CT is contraindicated. Since it does not contain radiation, the radiation dose can be reduced with this method in patients who need to be followed up at short intervals.

The correlation of the change in ADC values after chemoradiotherapy (CRT) with the change in lesion sizes in patients with lung cancer can provide valuable information to the clinician in terms of evaluating the early response to CRT and establishing effective treatment protocols. In this way, patients can be protected from the toxicity of both ionizing radiation and contrast agents and chemo radiotherapeutics. We think that DWI and ADC measurements can be used as prognostic markers in evaluating the response to treatment in lung cancer.

Statement of Ethics

Our institutional human research ethics committee approved this prospective study (Approval no: 2015-20478486-66).

Conflict of Interest Statement

All the authors declare no conflict of interest.

References

1. Ferlay J, Shin HR, Bray F, et al. Estimates of worldwide burden of cancer in 2008: Int J Cancer. 2010;127:2893–2917.
2. Yilmaz HH, Yazihan N, Tunca D, et al. Cancer trends and incidence and mortality patterns in Turkey Jpn J Clin Oncol. 2011;41:10–16.
3. Loeb LA, Ernster VL, Warner KE, et al. Smoking and lung cancer: an overview. Cancer Res. 1984;44(12 Pt 1):5940-5958.
4. Spiro SG, Porter JC. Lung cancer--where are we today? Current advances in staging and nonsurgical treatment. Am J Respir Crit Care Med. 2002;166:1166–1196.
5. Cai Z, Liu Q. Understanding the Global Cancer Statistics 2018: implications for cancer control. Sci China Life Sci. 2021;64:1017–1020.
6. Desar IM, van Herpen CM, van Laarhoven HW, et al. Beyond RECIST. molecular and functional imaging techniques for evaluation of response to targeted therapy. Cancer Treat Rev. 2009;35:309–321.

7. Austin J. Sim, Evangelia Kaza, Lisa Singer, et al. A review of the role of MRI in diagnosis and treatment of early stage lung cancer. Clin Transl Radiat Oncol. 2020; 24:16–22.
8. Zhang Y, Chen J, Shen J, et al. Apparent diffusion coefficient values of necrotic and solid portion of lymph nodes: differential diagnostic value in cervical lymphadenopathy. Clin Radiol.2013;68:224-231.
9. Barnes A, Alonzi R, Blackledge M, et al. UK quantitative WB-DWI technical workgroup: consensus meeting recommendations on optimisation, quality control, processing and analysis of quantitative whole-body diffusion-weighted imaging for cancer. Br J Radiol.2018;91:20170577.
10. Cui Y, Zhang XP, Sun YS, et al. Apparent diffusion coefficient: potential imaging biomarker for prediction and early detection of response to chemotherapy in hepatic metastases. Radiology. 2008;248:894–900.
11. Chen L, Zhang J, Chen Y, et al. Relationship between apparent diffusion coefficient and tumour cellularity in lung cancer. PLoS One. 2014;9:e99865.
12. Eisenhauer E, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009; 45:228.
13. Lazzari C, Bulotta A, Ducceschi M, et al. Historical Evolution of Second-Line Therapy in Non-Small Cell Lung Cancer. Front Med (Lausanne). 2017;4:4.
14. Wei M, Ye Q, Wang X, et al. Early tumor shrinkage served as a prognostic factor for patients with stage III non-small cell lung cancer treated with concurrent chemoradiotherapy. Medicine (Baltimore)2018;97:e0632.
15. Vogl TJ, Emara EH, Elhawash E, et al. Feasibility of diffusion-weighted magnetic resonance imaging in evaluation of early therapeutic response after CT-guided microwave ablation of inoperable lung neoplasms. Eur Radiol. 2021;19.
16. Jagoda P, Fleckenstein J, Sonnhoff M, et al. Diffusion-weighted MRI improves response assessment after definitive radiotherapy in patients with NSCLC. Cancer Imaging. 2021;21:21.
17. Langer NH, Langer SW, Johannesen HH, et al. Very Early Response Evaluation by PET/MR in Patients with Lung Cancer-Timing and Feasibility. Diagnostics (Basel) 2019 26;9:35.
18. Komori T, Narabayashi I, Matsumura K, et al. 2-(Fluorine-18)-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography versus whole-body diffusion-weighted MRI for detection of malignant lesions: initial experience. Ann Nucl Med. 2007;21:209–215.
19. Vogl TJ, Hoppe AT, Gruber-Rouh T, et al. Diffusion-Weighted MR Imaging of Primary and Secondary Lung Cancer: Predictive Value for Response to Transpulmonary Chemoembolization and Transarterial Chemoperfusion. J Vasc Interv Radiol. 2020;31:301-310.