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Differences in Tumor Doubling Time Between Clinical and Pathological Parameters in The Treatment of Lung Cancer Chemotherapy

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ABSTRACT

Background: *Lung cancer is malignant disease with relatively high incidence in the setting of organ cancer, characterized by rapid tumor growth, low grade of differentiation and low 5-year survival. TDT has critical value in differentiating benign or active tumors with slow development. The shorter TDT means increase in rapid tumor development and thus decrease in survival. In the past, TDT has been used in many cases for both malignant screening and patient survival, but it is now attempt to evaluate the antitumor effect.* ***The Aim:*** *We aimed to investigate the differences in tumor doubling time between the clinical and pathological parameters of chemotherapy for lung cancer.* ***Patients and methods:*** *Ninety-seven patients with lung cancer who were received standard chemotherapy for indication. Patients with radiographic findings of lung tumors before and after treatment and who did not discontinue treatment were included. Treatment effect (CR; complete remission PR; partial remission PD; progression) after treatment was compared for several clinicopathological parameters such as lesion site, lesion size, histotype, and stage.* ***The results and conclusions:*** *The difference in tumor doubling time between treatment effects in the chemotherapy treatment of lung cancer is as follows. Tumor doubling time was significantly shorter in central and peripheral lung cancers in the affected site, in the lesion size ~5.0 cm, in the histological type squamous cell carcinoma, in the stage IA-B and IIIA-B compared with the partial remission in the complete remission. Tumor doubling time was -19.8±2.1days for complete remission, -52.9±2.1days for partial remission and 48.9±2.2days for progression.*

Keywords: Tumor doubling time, Lung cancer, Chemotherapy.

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INTRODUCTION

Lung cancer is malignant disease with a relatively high incidence in the setting of organ cancer, characterized by rapid tumor growth, low grade of differentiation and low 5-year survival[11,12]. If patients with lung cancer have natural course without surgical treatment soon after diagnosis, the tumor volume doubling time can be applied to estimate their prognosis and survival. Many researchers have advocated the introduction of Tumor Doubling Time (TDT) which is a notation for tumor volume doubling time (TVDT), emphasizing the accuracy of volume over tumor diameter. Some authors have also introduced the term Average Tumor Volume Doubling Time (midDT).

TDT is the rule of thumb for measuring and calculating the size of tumor on chest X-ray or CT, usually more than two measurements within period of no more than 25 days. TDT is calculated according to Collins Schwartz's formula (TDT = t × log 2/log (Vt/V0), t = time

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difference of imaging findings, Vt = volume at time difference, V0 = volume at first scan).

TDT has critical value in differentiating benign or active tumors with slow development[5,9].

Usually, TDT of less than 400 days is considered rapidly developing malignancy. The shorter TDT means increase in rapid tumor development and thus decrease in survival. TDT is highly reliable for solid tumors and non-small cell lung cancer (non-invasive lung cancer)[1,2,6]. We compared the 3D computed TDT estimates for solid, partial solid and non-solid tumors and found that the accuracy was high for solid tumors. Some data suggest that the TDT in non-small cell lung cancer in 70% of lung cancers is between 50 and 400 days on average with adenocarcinoma increasing more slowly than squamous cell carcinoma[3,4,7,8,10].

Some investigators have evaluated tumor doubling time with radiation therapy and have shown that patients receiving chemotherapy have a shorter tumor doubling time with radiation. In the past, TDT has been used in many cases for both malignant screening and patient survival but it is now attempt to evaluate the antitumor effect. Therefore, we aimed to investigate the differences in tumor doubling time between the clinical and pathological parameters of chemotherapy for lung cancer.

SUBJECTS AND METHODS

Patients and methods Ninety-seven patients with lung cancer who were admitted to the Oncology Institute and received standard chemotherapy for indication for chemotherapy. Patients with radiographic findings of lung tumors before and after treatment and who did not discontinue treatment were included. The following patients who did not have chemotherapy indications (cachexia with very poor systemic nutrition, very severe liver and kidney disease, severe anemia, severe anemia, poor seniority, poor cardiopulmonary function, severe infection, recurrent surgery, and discontinued chemotherapy) were excluded.

The sex and age group of the study population showed that both sexes had mean age of 55.5±0.8 years with significant 50-year age and male-to-female ratio of 15.2:1. Patients with stage I-IV lung cancer who were confirmed to have lung cancer and were treated with standard chemotherapy with chemicals such as CDDP, 5-Fu, CPA, and IL-2 in accordance with the indication for chemotherapy and patients with pre- and post-treatment chest radiographs were examined to determine the long-term and short-term tumor length and then tumor volume and length of treatment before and after treatment were calculated using the following formula :

$TDT=t\times\log 2/\ [\log(Vt)/(V0)]\quad V=\pi\ ab2/6$

Here, the difference in tumor doubling time according to the pretreatment tumor volume V0, bowel diameter a, and treatment effect (CR ; complete remission PR ; partial remission PD ; Progresive Desease) after treatment was compared for several clinicopathological parameters such as lesion site, lesion size, histotype and stage.

The TDT value was defined as tumor growth if positive, tumor shrinkage if negative, and rapid tumor shrinkage if TDT was positive and small, whereas the TDT was defined as rapid increase in tumor volume if it was negative and small and no response was observed.

The diagnosis and treatment effect of lung cancer were made according to clinicopathological diagnosis and treatment guidelines published by the Ministry of Public Health, DPRK.

RESULTS

Table 1. Differences in TDT between sites of lesions according to treatment effect ($\overline{X}$ ±SE, day)

Classification	Cases	Lesion site	
		central	peripheral
CR	55	-20.3±2.4* (44)	-16.5±3.6* (11)
PR	14	-50.8±7.3 (13)	-80.5 (1)
PD	13	45.3±8.1 (10)	61.0±16.0 (3)

():cases *; p<0.05 (compared with PR)

As shown in Table 1, tumor allocation time by site of focus according to treatment effect was significantly shorter in both central and peripheral lung cancers compared with partial remission in cases with complete remission.

Table 2. Differences in TDT by lesion size according to treatment effect($\overline{X}$ ±SE, day)

Classification	Cases	Lesion size			
		~3.0㎝	3.1~5.0㎝	5.1~7.0㎝	7.1㎝~
CR	55	-14.2±1.9* (5)	-15.8±2.7* (22)	-22.1±5.2 (17)	-26.9±3.5 (11)
PR	14	-98.2 (1)	-56.8±9.0 (6)	-40.4±10.9 (5)	-49.7±12.7 (2)
PD	13	-	34.9±9.0 (5)	43.4±9.9 (4)	71.9±10.6 (4)

():cases *; p<0.05 (compared with PR)

As shown in Table 2, tumor doubling time by lesion size according to treatment effect was significantly shorter for complete remission compared with partial remission for ~5.0 cm.

Table 3. Differences in TDT by histotype according to treatment effect($\overline{X}$ ±SE, day)

Classification	Cases	Histotype		
		Squamous carcinoma	Adenocarcinoma	Small cell carcinoma
CR	55	-20.7±2.3* (30)	-16.5±3.6 (11)	-20.6±4.8 (14)
PR	14	-66.2±7.4 (9)	-30.5±7.8 (4)	-22.7 (1)
PD	13	48.2±11.0 (5)	53.0±11.6 (6)	38.3±24.7 (2)

():cases *; p<0.05 (compared with PR)

As shown in Table 3, the tumor doubling time according to treatment effect was significantly shorter in squamous cell carcinoma compared with partial remission in cases with complete remission.

Table 4. Differences in TDT by stage according to treatment effect($\bar{X}$ ±SE, day)

Classification	Cases	Stage			
		Ⅰ A-B	Ⅱ A-B	Ⅲ A-B	Ⅳ
CR	55	-14.7±2.4* (4)	-11.4±4.7 (5)	-23.3±2.8* (37)	-12.6±3.2 (9)
PR	14	-60.8±37.4 (2)	-	-54.6±6.7 (11)	-17.9 (1)
PD	13	-	32.3 (1)	46.8±7.4 (11)	89.1 (1)

(): cases *; p<0.05 (compared with PR)

As shown in Table 4, the tumor time according to treatment effect was significantly shorter in both IA-B and IIIA-B compared with partial remission in the complete remission case.

Table 5. Differences in TDT with treatment effect

Classification	Cases	TDT ($\bar{X}$ ±SE, day)
CR	55	-19.8±2.1*
PR	14	-52.9±7.1
PD	13	48.9±7.2

*;p<0.05 (comparison with treatment effect)

As shown in Table 5, tumor doubling time following treatment effect was significantly shorter in the complete remission compared with the partial remission.

DISCUSSION

We observed differences in tumor doubling time between treatment effects in the chemotherapy treatment of lung cancer. Lung cancer is defined as multidisciplinary approach based on patient status, tumor pathology and clinical classification. The evaluation of treatment effects during chemotherapy is based on local and survival effects.

Complete remission (CR; Complete remission) with local effects is the case of no recurrence or new lesions over month after all of the original lesions have been removed, partial remission (PR; Partical remission) is the case of imaging tumour reduction rates greater than 50% and no new lesions more than one month and unchanged (NC; No Change) is the case of tumour reduction less than 50% or less than 25% or no change and no new lesions are present within one month, with no further improvement in the presence of new lesions (PD; Progresive Desease) or no change in the presence of new lesions or no change.

When we looked at tumor doubling times by site of focus according to treatment effect, complete remission was found to be -20.3±2.4 days for central lung cancer, -16.5±3.6 days for peripheral lung cancer, -50.8±7.3 days for central lung cancer, -80.5 days for peripheral lung cancer, 45.3±8.1 days for advanced central lung cancer, and 61.0±16.0 days for peripheral lung cancer, respectively with significant reduction in the case of peripheral lung cancer for complete remission in the peripheral lung cancer (Table 1). This suggests that chemotherapy for lung cancer may progress but that in remission, tumors shrink faster in complete remission compared to partial remission and peripheral lung cancer shrinks faster than central lung cancer. On the

other hand, we found that the difference in tumor doubling time by lesion size according to treatment effect was significantly shorter in complete remission at ~5.0 cm compared with partial remission and significantly shorter in advanced cases at 3.1-5.0 cm compared with 7.1 cm ($p < 0.05$ Table 2). This suggests that chemotherapy for lung cancer may progress but in remission, tumors shrink faster in complete remission compared with partial remission and tumors shrink faster with smaller size.

We found that tumor doubling times according to treatment effects were significantly shorter in patients with squamous cell carcinoma compared with those with partial remission in patients with complete remission ($p < 0.05$ Table 3). This suggests that chemotherapy for lung cancer may progress, but in remission, tumors shrink faster in complete remission compared with partial remission and more rapidly in adenocarcinoma. In our study, the tumor doubling time by stage according to treatment effect was significantly shorter in complete remission than in partial remission in both type IA-B and IIIA-B ($p < 0.05$ Table 4). This suggests that chemotherapy for lung cancer may progress but that in remission, tumors shrink faster in complete remission compared with partial remission and are more rapidly in stage IIA-B. We found that tumor doubling time according to treatment effect was significantly shorter in patients with complete remission compared with those with partial remission ($p<0.05$ Table 5), with complete remission of -19.8±2.1 days, partial remission of -52.9±7.1 days and progression of 48.9±7.2 days. This suggests that the tumor is reduced to two-times in complete remission with chemotherapy for lung cancer, which takes approximately 20 days to achieve 50 days in partial remission and that the tumor is doubled in progression and that 50 days.

CONCLUSION

The difference in tumor doubling time between treatment effects in the chemotherapy of lung cancer is as follows.

1) Tumor doubling time was significantly shorter in central and peripheral lung cancers in the affected site, in the lesion size ~5.0 cm, in the histological type squamous cell carcinoma, in the stage IA-B and IIIA-B compared with the partial remission in the complete remission.

2) Tumor doubling time was -19.8±2.1days for complete remission, -52.9±2.1days for partial remission and 48.9±2.2days for progression.

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