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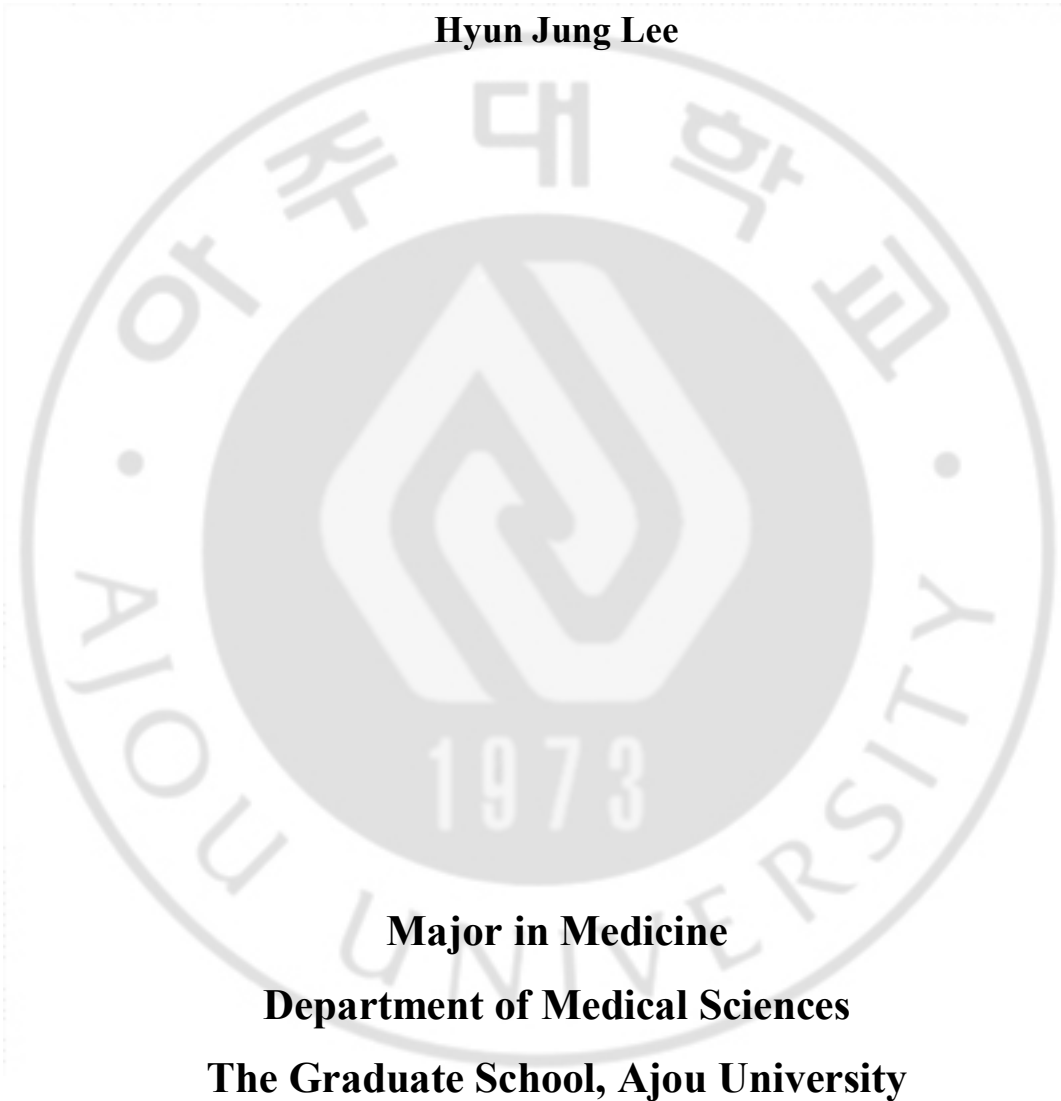
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**The threshold of clinical severity of cervical dystonia for  
positive  $^{18}\text{F}$ -FDG PET/CT study**

by

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**Major in Medicine**

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**A Dissertation Submitted to The Graduate School of  
Ajou University in Partial Fulfillment of the Requirements for the  
Degree of Master of Medicine**

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**July, 5th, 2013**

## **The threshold of clinical severity of cervical dystonia for positive <sup>18</sup>F-FDG PET/CT study**

**Background:** To examine whether there is a significant correlation between the clinical severity of cervical dystonia (CD) and <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography (<sup>18</sup>F-FDG PET/CT) findings and to determine the threshold of the clinical severity of CD for acquisition of positive <sup>18</sup>F-FDG PET/CT study findings.

**Methods:** Forty-seven subjects who showed torticollis as one of the symptoms of CD were included. The clinical severity of CD was evaluated with the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) at the time of the <sup>18</sup>F-FDG PET/CT study. The correlation between the clinical severity of CD and the highest SUVmax was examined. The threshold of the clinical severity of CD for obtaining positive <sup>18</sup>F-FDG PET/CT findings was determined using receiver operating characteristics curve analysis.

**Results:** Thirty-three subjects (70.21%) out of 47 showed positive <sup>18</sup>F-FDG PET/CT findings. The most frequently involved, top 3 rotators were ipsilateral splenius capitis/cervicis, oblique capitis inferior and longuscolli/capitis. The highest SUVmax of <sup>18</sup>F-FDG PET/CT showed a significant correlation with the TWSTRS. All subjects with a total TWSTRS of more than 39 showed positive <sup>18</sup>F-FDG PET/CT findings, and all subjects with a total TWSTRS of 22 or less showed negative <sup>18</sup>F-FDG PET/CT study results. The cutoff value of the total TWSTRS for positive <sup>18</sup>F-FDG PET/CT findings was set at 27.5, with 90.9% sensitivity and 64.3% specificity.

**Conclusions:** This study demonstrated a significant correlation between the clinical severity of CD and <sup>18</sup>F-FDG PET/CT findings, providing a threshold of the clinical severity of CD for acquisition of positive <sup>18</sup>F-FDG PET/CT findings. In conclusion, these findings are suggestive of the usefulness of <sup>18</sup>F-FDG PET/CT for identification of dystonic muscles of CD with moderate to severe severity and further studies are required to verify these findings.

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Keyword: Cervical dystonia, Fluorodeoxyglucose F18, Positron emission tomography

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## I.INTRODUCTION

Cervical dystonia is a chronic neurological disorder characterized by involuntary contractions of the cervical musculature that lead to abnormal movements and postures of the head and neck (Jankovic and Tolosa, 2007; Jankovic et al., 2007). Cervical dystonia is the most common form of focal dystonia with a prevalence of 0.006% in Europe (Epidemiological Study of Dystonia in Europe Collaborative, 2000) and 0.280% in the USA (Jankovic et al., 2007). While cervical dystonia causes variable postures of the head and neck, torticollis is the most common symptom of cervical dystonia (Camargo et al., 2008).

Botulinum neurotoxin (BoNT) injection, physical therapy, deep brain stimulation and oral medications such as anticholinergics and benzodiazepines have been used for the management of cervical dystonia. Among these treatments, BoNT injection has been known as the first-line therapy for cervical dystonia since 1989 (Albanese et al., 2006). Symptomatic relief has been reported with BoNT injection in more than 85% of those affected (Anderson et al., 1992; Comella et al., 1992; Brans et al., 1995; Jankovic, 2004; Truong et al., 2005). However, not all subjects show satisfactory improvement of abnormal posture of the head and neck after BoNT administration. The most important determinants in achieving a favorable response to BoNT treatment are proper identification of the involved muscles and appropriate dosage of BoNT (Jankovic, 2004).

Inspection and palpation of dystonic muscles, and electromyography have been used to identify the dystonic muscles in cervical dystonia (Brans et al., 1998). Sung et al. reported the usefulness of  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography ( $^{18}\text{F}$ -FDG PET/CT) for identification of dystonic muscles in subjects with cervical dystonia (Sung et al., 2007). Lee et al. compared the outcome of BoNT injection between a  $^{18}\text{F}$ -FDG PET/CT-assisted clinically targeting group and a clinically targeting group. The results showed that the  $^{18}\text{F}$ -FDG PET/CT-assisted clinically targeting group was superior to the clinically targeting group in terms of the reduction rate of the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and the BoNT-A reinjection-free living period (Lee et al., 2012). Therefore, the  $^{18}\text{F}$ -FDG PET/CT study is a useful tool in identification of dystonic muscles of

cervical dystonia, which ends up with better outcome with BoNT injection. However, not all subjects with cervical dystonia show positive  $^{18}\text{F}$ -FDG PET/CT study findings (Lee et al., 2012). According to our clinical experience with the  $^{18}\text{F}$ -FDG PET/CT study, it seems that the higher the clinical severity of cervical dystonia, the better the chance of positive findings of the  $^{18}\text{F}$ -FDG PET/CT study (Lee et al., 2012). However, it has not yet been established whether there is any correlation between the clinical severity of cervical dystonia and  $^{18}\text{F}$ -FDG PET/CT findings. If there is a significant correlation, the threshold of the clinical severity of cervical dystonia for acquisition of positive  $^{18}\text{F}$ -FDG PET/CT study findings would be able to be determined. This would help prevent clinicians from conducting negative  $^{18}\text{F}$ -FDG PET/CT studies.

The objectives of this study were 1) to examine whether there is a significant correlation between the clinical severity of cervical dystonia and  $^{18}\text{F}$ -FDG PET/CT findings; and 2) to determine the threshold of the clinical severity of cervical dystonia for acquisition of positive  $^{18}\text{F}$ -FDG PET/CT study findings.



## II. MATERIALS AND METHODS

This study was a retrospective study conducted at a clinic for torticollis in a tertiary medical center from November 2009 to May 2012. This research was approved by the Institutional Review Board of OO Medical Center.

### A. Subjects

Subjects with cervical dystonia who met the following two criteria were included: (1) subjects with torticollis as one of the symptoms of cervical dystonia; and (2) subjects who underwent a  $^{18}\text{F}$ -FDG PET/CT study. Cervical dystonia was diagnosed when subjects showed abnormal posture of the head and neck caused by involuntary contractions along with morning benefit, sensory trick or aggravation of physical/emotional stress (Lee et al., 2012). Torticollis was defined as a condition in which the head was turned toward the right or left side on the horizontal plane (Yim et al., 2009). Subjects who had one or more of the following criteria were excluded: 1) subjects who had surgery for cervical dystonia; 2) subjects who showed a limited range of motion of the head and neck; and 3) those who had generalized dystonia or other neurological symptoms; 4) those who had cervical dystonia caused by known gene mutations such as *TOR1* and *GCHI* or copper metabolism disorder such as Wilson disease. Clinical data were collected through a review of medical records for information on age, gender, duration of cervical dystonia, clinical severity of cervical dystonia and abnormal posture of the head and neck caused by cervical dystonia such as torticollis, laterocollis, retrocollis, anterocollis or combination of them. The clinical severity of cervical dystonia at the time of the  $^{18}\text{F}$ -FDG PET/CT study was measured using TWSTRS. The range of the total score of TWSTRS was 0 to 85 points on 3 subscales; severity (0-35 points), disability (0-30 points) and pain (0-20 points) (Consky and Lang, 1994; Salvia et al., 2006).

### B. Analysis of $^{18}\text{F}$ -FDG PET/CT findings

Subjects fasted for at least 4 hours before the  $^{18}\text{F}$ -FDG PET/CT study. The  $^{18}\text{F}$ -FDG PET/CT study was done as previously described (An et al., 2007; An et al., 2008). The  $^{18}\text{F}$ -FDG

PET/CT study was evaluated in two ways. First, by visual image interpretation of the second author (a nuclear medicine specialist), which was interpreted as either positive or negative according to the presence of increased uptake of  $^{18}\text{F}$ -FDG at any muscle among the rotators of the head and neck compared to the adjacent or contralateral muscles. The rotators of the head and neck with increased  $^{18}\text{F}$ -FDG uptake were listed for each subject with positive  $^{18}\text{F}$ -FDG PET/CT findings.

Secondly,  $^{18}\text{F}$ -FDG PET/CT findings were quantified using maximum standardized uptake value (SUVmax). SUV is defined as the amount of radioactivity released per 1 g of tissue divided by the amount of radioactivity administered per 1 kg of body weight (An et al., 2007; An et al., 2008). SUVmax was measured for 10 rotators of the head and neck for each subject by setting the globular-shaped volume of interest (VOI,  $0.96\text{ cm}^3$ ). Therefore, 10 SUVmax values were measured for each subject, after which the highest SUVmax among the SUVmax values of 10 rotators in each subject was determined. The rotators of the head and neck are the muscles causing torticollis of the head and neck. Based on functional anatomy of the head and neck, 10 rotators of the head and neck were identified as follows: the ipsilateral splenius capitis/cervicis, ipsilateral longus colli/capitis, ipsilateral oblique capitis inferior, ipsilateral oblique capitis superior, ipsilateral rectus capitis posterior major, contralateral semispinalis capitis, contralateral sternocleidomastoid, contralateral multifidus, contralateral trapezius and contralateral levator scapulae muscles.

### **C. The correlation between the clinical severity of cervical dystonia and the highest SUVmax of the $^{18}\text{F}$ -FDG PET/CT study**

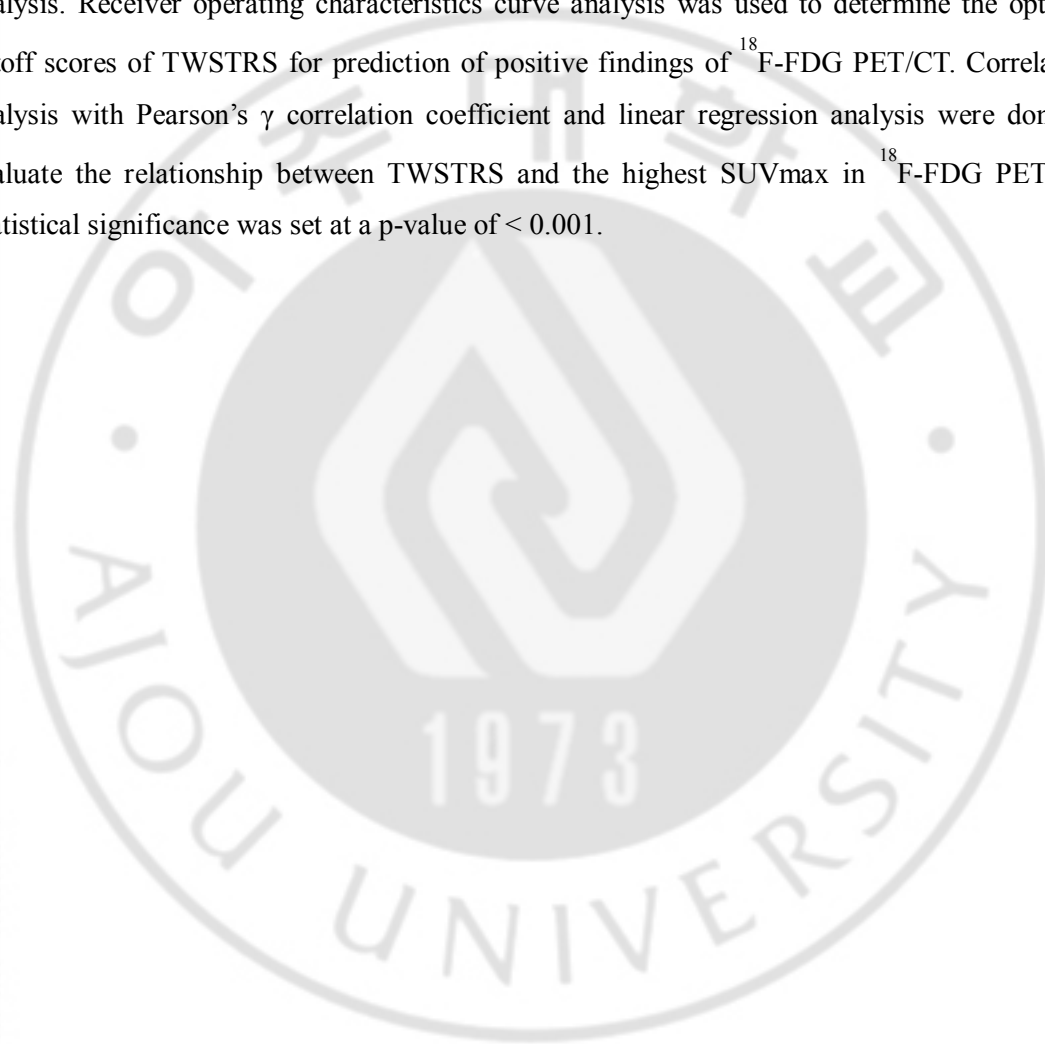
The correlation between the clinical severity of cervical dystonia and the highest SUVmax was examined through correlation analysis and linear regression analysis. The clinical severity of cervical dystonia and the extent of the related disability of activities of daily living were measured using TWSTRS. TWSTRS is composed of subscales on severity, disability and pain, and is used widely for assessment of clinical severity and treatment effect due to its outstanding inter-observer reliability (Consky and Lang, 1994; Salvia et al., 2006).

#### **D. The threshold of the clinical severity of cervical dystonia for positive <sup>18</sup>F-FDG PET/CT study findings**

The threshold of the clinical severity of cervical dystonia for obtaining positive <sup>18</sup>F-FDG PET/CT study findings was determined using the receiver operating characteristics curve analysis.

#### **E. Statistical analysis**

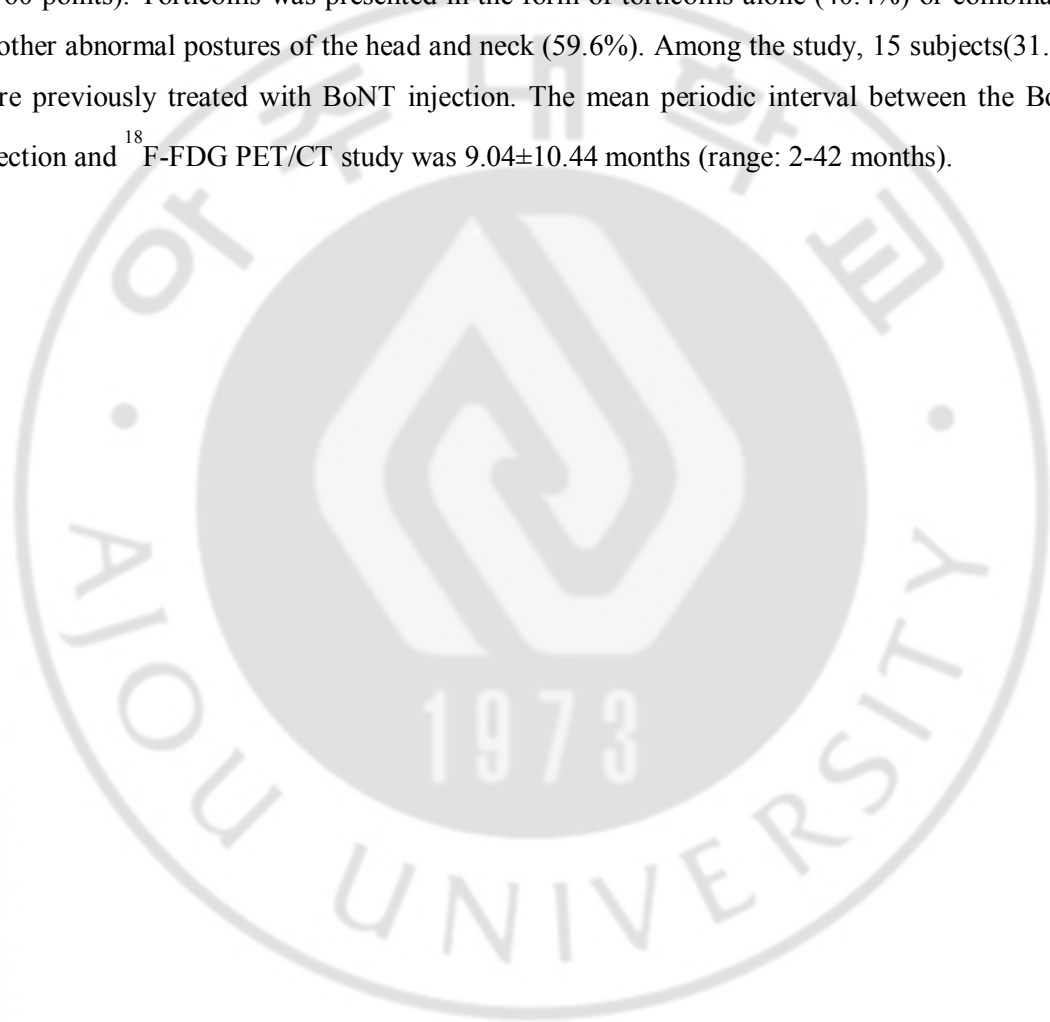
IBM SPSS Statistics version 20.0 (IBM, Co., Armonk, NY, USA) was used for statistical analysis. Receiver operating characteristics curve analysis was used to determine the optimal cutoff scores of TWSTRS for prediction of positive findings of <sup>18</sup>F-FDG PET/CT. Correlation analysis with Pearson's  $\gamma$  correlation coefficient and linear regression analysis were done to evaluate the relationship between TWSTRS and the highest SUVmax in <sup>18</sup>F-FDG PET/CT. Statistical significance was set at a p-value of  $< 0.001$ .



### III. RESULTS

#### A. The characteristics of the subjects

Forty-seven subjects were included in this study. The characteristics of the subjects are presented in Table 1. Among 47 subjects, 21 were men and 26 were women. The mean age was  $38.23 \pm 12.05$  years (range: 18-64 years). The mean duration of cervical dystonia was  $28.96 \pm 32.63$  months (range: 0.25-125 months). The total TWSTRS was  $34.26 \pm 10.08$  (range: 14-60 points). Torticollis was presented in the form of torticollis alone (40.4%) or combination of other abnormal postures of the head and neck (59.6%). Among the study, 15 subjects (31.9%) were previously treated with BoNT injection. The mean periodic interval between the BoNT injection and  $^{18}\text{F}$ -FDG PET/CT study was  $9.04 \pm 10.44$  months (range: 2-42 months).



**Table 1. Characteristics of the subjects**

|  | <b>Value</b> |
|--|--------------|
| <b>Characteristics</b>   |              |
| Age (year-old)   | 38.23±12.05  |
| Men:Women (n=47)   | 21:26        |
| Duration of cervical dystonia (months)   | 28.96±32.63  |
| <b>Toronto Western Spasmodic Torticollis Rating Scale</b>                        |              |
| Total Score  | 34.26±10.08  |
| Severity Score   | 14.21±4.28   |
| Disability Score   | 13.74±4.91   |
| Pain Score   | 6.15±5.21    |
| <b>Abnormal posture of the head and neck</b>                                     |              |
| Torticollis  | 19 (40.4%)   |
| Torticollis + Laterocollis   | 21 (44.7%)   |
| Torticollis + Retrocollis  | 2 (4.3%)     |
| Torticollis + Laterocollis + Anterocollis  | 3 (6.4%)     |
| Torticollis + Laterocollis + Retrocollis   | 2 (4.3%)     |
| <b>Number of the subjects previously treated with BoNT injection</b>             |              |
| Interval between the BoNT injection and <sup>18</sup> F-FDG PET/CT study(months) | 9.04±10.44   |

**B. The number of subjects showing increased <sup>18</sup>F-FDG uptake according to each of the 10 rotators of the head and neck in descending order**

Thirty-three subjects (90.9%) out of 47 showed positive <sup>18</sup>F-FDG PET/CT study findings. For 33 subjects, each of the 10 rotators of the head and neck was listed with the number of subjects who showed increased <sup>18</sup>F-FDG uptake in descending order (Table 2). The subjects showed increased <sup>18</sup>F-FDG uptake in 2.88 rotators on average. The most frequently involved, top 3 rotators were the ipsilateral splenius capitis/cervicis, oblique capitis inferior(OCI) and longuscolli/capitis, indicating frequent involvement of the deep-seated neck muscles in cervical dystonia.

**Table 2. The Number of subjects showing increased <sup>18</sup>F-FDG uptake according to each of 10 rotators of the Head and Neck**

| <b>Rotators of the head and neck</b>           | <b>Number of subjects (%)</b> |
|--|-------------------------------|
| Ipsilateral splenius capitis/splenius cervicis | 19 (40.4)                     |
| Ipsilateral oblique capitis inferior           | 18 (38.3)                     |
| Ipsilaterallonguscolli/longuscapitis           | 18 (38.3)                     |
| Contralateral sternocleidomastoid              | 15 (31.9)                     |
| Contralateral semispinaliscapitis/cervicis     | 7 (14.9)                      |
| Ipsilateral rectus capitis posterior major     | 6 (12.8)                      |
| Contralateral multifidus                       | 6 (12.8)                      |
| Contralateral trapezius                        | 5 (11.0)                      |
| Contralateral levator scapulae                 | 2 ( 4.2)                      |
| Ipsilateral oblique capitis superior           | 1 ( 2.1)                      |

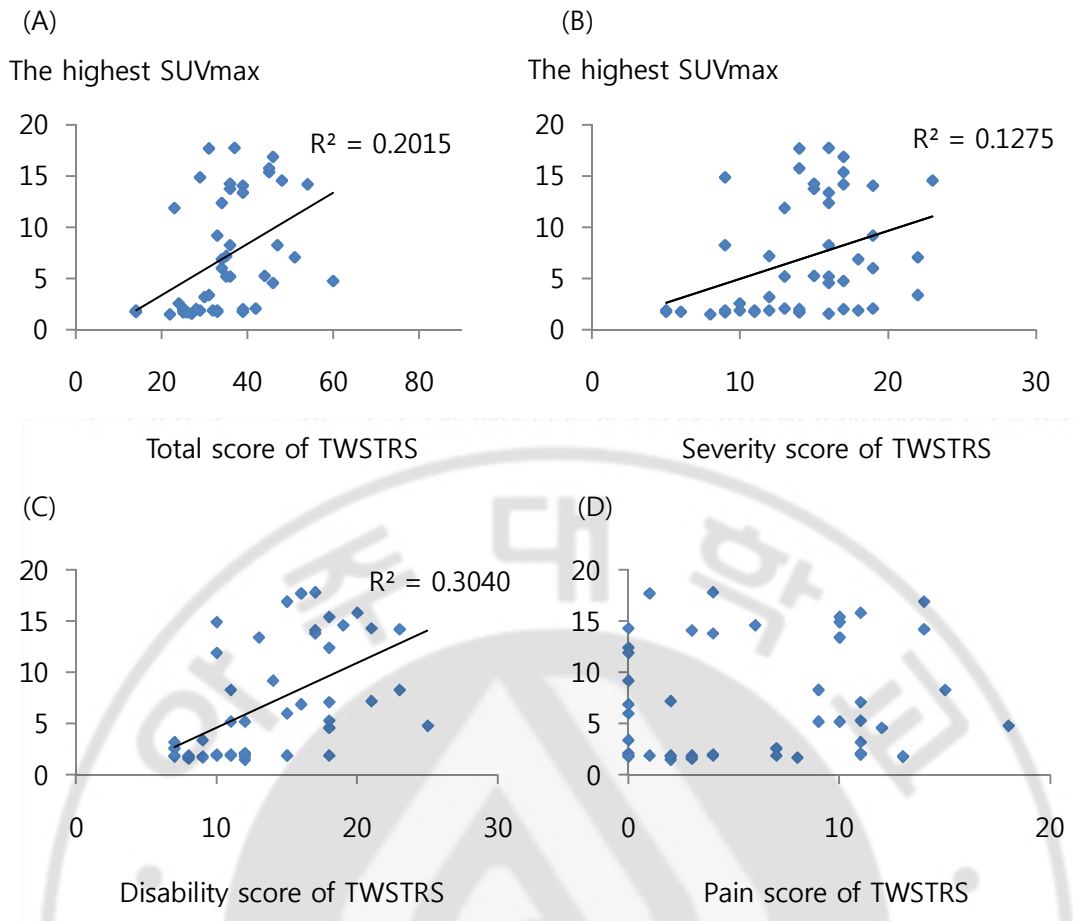
<sup>18</sup>F-FDG: <sup>18</sup>F-Fluorodeoxyglucose



**C.The correlation between the clinical severity of cervical dystonia and the highest SUVmax of the <sup>18</sup>F-FDG PET/CT study**

While the mean highest SUVmax of 14 negative <sup>18</sup>F-FDG PET/CT studies was  $1.79 \pm 0.13$  (range: 1.5~1.9), the mean highest SUVmax of 33 positive <sup>18</sup>F-FDG PET/CT studies was  $9.17 \pm 5.34$  (range: 2~17.8). The highest SUVmax of the <sup>18</sup>F-FDG PET/CT study showed a significant positive correlation with the total TWSTRS (Pearson  $\gamma$  correlation coefficient: 0.449,  $p=0.01$ ), the severity subscale score (Pearson  $\gamma$  correlation coefficient: 0.357,  $p=0.01$ ) and the disability subscale score (Pearson  $\gamma$  correlation coefficient: 0.551,  $p=0.01$ ). The linear regression analysis with  $R^2$  is shown in Figure 1. However, there was no significant correlation between the pain subscale score and the highest SUVmax ( $p=0.582$ ).



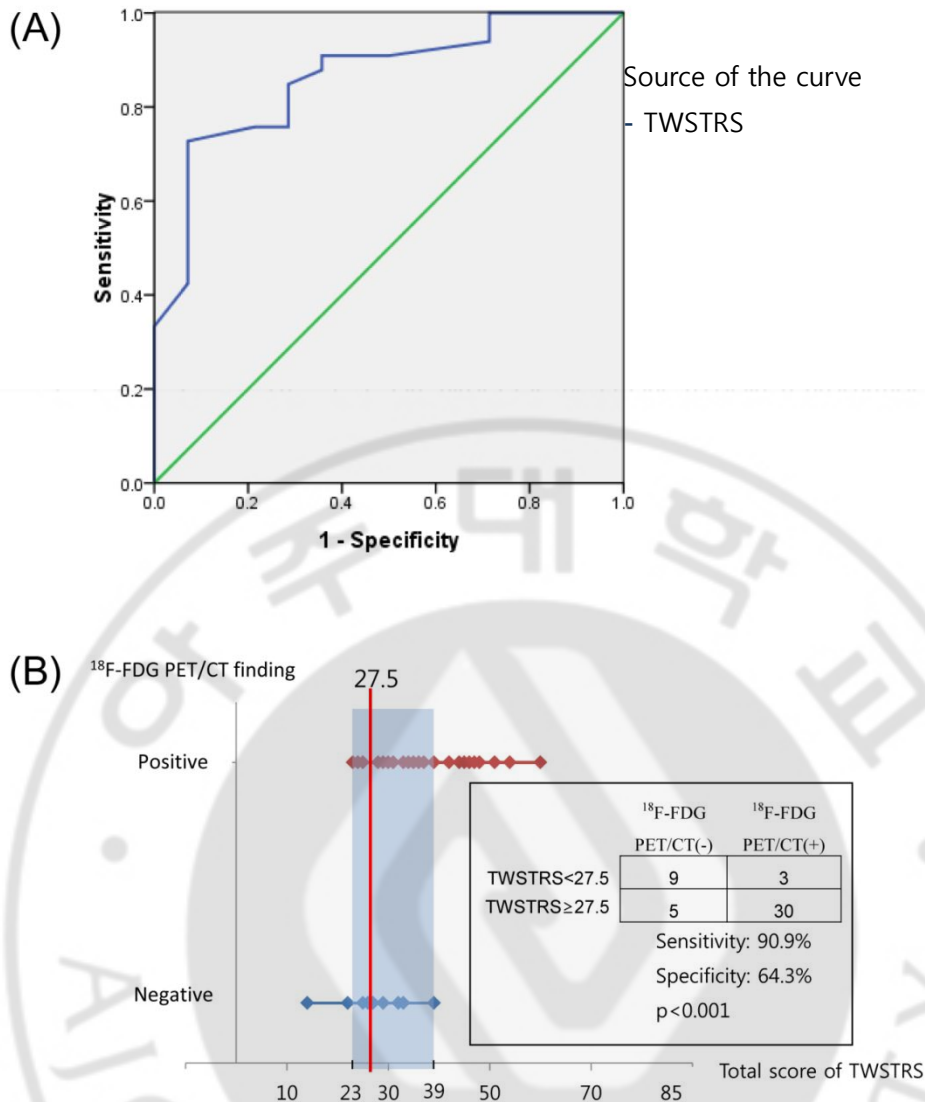


**Fig. 1. Correlation between TWSTRS and the highest SUVmax of  $^{18}\text{F}$ -FDG PET/CT study.** (A)(B)(C) The highest SUVmax showed significant correlation with the total TWSTRS, the scores of severity subscale, the scores of disability subscales of TWSTRS ( $p < 0.001$ ) (D) There was no correlation between the scores of pain subscale and the SUVmax ( $p = 0.582$ ). The highest SUVmax means the largest SUVmax among SUVmaxes of 10 rotators in each subject.  $^{18}\text{F}$ -FDG PET/CT:  $^{18}\text{F}$ -Fluorodeoxyglucose Positron emission tomography/computed tomography, SUVmax: Maximum standardized uptake value, TWSTRS: Toronto Western Spasmodic Torticollis Rating Scale.

#### **D. The threshold of the clinical severity of cervical dystonia for positive $^{18}\text{F}$ -FDG PET/CT study findings**

Among the 33 subjects with positive  $^{18}\text{F}$ -FDG PET/CT study findings, all subjects with a total TWSTRS of more than 39 showed positive  $^{18}\text{F}$ -FDG PET/CT study findings, and all subjects with a total TWSTRS of 22 or less showed negative  $^{18}\text{F}$ -FDG PET/CT study findings (Fig. 2). We performed receiver operating characteristics curve analysis in order to find the total TWSTRS score with reasonable sensitivity and specificity. This analysis set the cutoff value of the total TWSTRS for positive  $^{18}\text{F}$ -FDG PET/CT study findings at 27.5, with 90.9% sensitivity and 64.3% specificity (confidence interval[CI]=75.2%-97.3%) (Fig. 2).





**Fig. 2.** The ROC curve for predicting the positive <sup>18</sup>F-FDG PET/CT findings. (A) Area under the ROC curve is 0.836 corresponding to a sensitivity of 90.9% and specificity of 64.3%. (B) The optimal cutoff value of TWSTRS for <sup>18</sup>F-FDG PET/CT positive finding selected by ROC curve analysis: 27.5. The lowest total score of TWSTRS for the positive <sup>18</sup>F-FDG PET/CT findings was 23. All subjects with a total TWSTRS of more than 39 showed positive <sup>18</sup>F-FDG PET/CT findings.

TWSTRS: Toronto Western Spasmodic Torticollis Rating Scale, <sup>18</sup>F-FDG PET/CT: <sup>18</sup>F-Fluorodeoxyglucose Positron emission tomography/computed tomography.

## IV. DISCUSSION

To the best of our knowledge, this is the first report to demonstrate a significant correlation between the clinical severity of cervical dystonia and  $^{18}\text{F}$ -FDG PET/CT findings.

The present study aimed to examine the clinical usefulness of  $^{18}\text{F}$ -FDG PET/CT by assessing whether the degree of  $^{18}\text{F}$ -FDG uptake is related in accordance with the extent of clinical symptoms by examining the level of clinical severity that can result in positive findings under the  $^{18}\text{F}$ -FDG PET/CT test in cervical dystonia with torticollis symptoms. Until now, there have been studies reporting that  $^{18}\text{F}$ -FDG PET/CT is useful since it can determine the metabolism of the deep and superficial neck muscles simultaneously through a non-invasive method by overcoming the shortcomings of physical examination and electromyography mapping (Sung et al., 2007; Lee et al., 2009). In addition, the usefulness of  $^{18}\text{F}$ -FDG PET/CT in selection of muscles in cervical dystonia is already widely known as there are research results showing the influence of  $^{18}\text{F}$ -FDG PET/CT on the BoNT treatment effects (Lee et al., 2012). However, there has been no research on the correlation between the clinical severity expressed by means of TWSTRS score and SUVmax that illustrate the extent of increase in  $^{18}\text{F}$ -FDG uptake in  $^{18}\text{F}$ -FDG PET/CT. To study the relations between clinical severity and  $^{18}\text{F}$ -FDG PET/CT, we conducted a correlation analysis between the total TWSTRS score and the highest SUVmax. The highest SUVmax showed a significant correlation with TWSTRS, which is a new finding which has not been found in any previous research. Although there was a significant correlation in the total TWSTRS score, severity subscale score and disability subscale score, interestingly, there was no correlation with the pain subscale score. Pain is a relatively common symptom of cervical dystonia, with a reported rate of 68% (Jankovic et al., 1991). In the present study, 37 subjects (78.72%) had pain but 24 subjects (51.06%) including 10 patients without pain showed a low level of pain. This is deemed to be due to the fact that it is difficult to reflect the objective level of the severity of subjective symptoms only by means of pain since the pain subscale is the most subjective subscale of all the subscales of TWSTRS. Due to differences in pain perception and tolerance thresholds being associated with other factors such as ethnicity, genetics, and sex, pain is very subjective feeling.

Based on this correlation, we were able to provide the threshold of the clinical severity of

cervical dystonia for acquisition of positive  $^{18}\text{F}$ -FDG PET/CT study findings. The cutoff value of TWSTRS in order for  $^{18}\text{F}$ -FDG PET/CT to display positive findings was set at a score of 27.5 with 90.3% sensitivity and 64.3% specificity in this study. We set the sensitivity as the major value and, as such, we selected a point at which the specificity is at its peak when the sensitivity is high at 90.3%. It was possible to display the cutoff value of clinical symptoms on whether to perform the  $^{18}\text{F}$ -FDG PET/CT test, which is an expensive test, on patients with cervical dystonia with symptoms of torticollis in accordance with the results of the research. This makes it possible to determine whether  $^{18}\text{F}$ -FDG PET/CT will be useful in discriminating the dystonic muscles in patients with moderate severity. There has not been any research regarding guidelines on making decisions on whether to implement  $^{18}\text{F}$ -FDG PET/CT or not until now, and this study is the first thesis presenting the cutoff value for clinical severity that can be used in predicting the presence of  $^{18}\text{F}$ -FDG PET/CT positive findings.

Based on what has been disclosed by the majority of studies until now, the superficial neck muscle was the dystonic muscle in the majority of cervical dystonia patients and, there has been only few recent researches that used  $^{18}\text{F}$ -FDG PET/CT the reported deep neck muscles such as longuscolli/capitis, OCI and RCP major as the dystonic muscles (Sung et al., 2007; Lee et al., 2009; Lee et al., 2012). However, even these studies did not administer BoNT injections into these deep neck muscles. According to the results of the present study, the deep neck muscles such as longuscolli, OCI and RCP major in cervical dystonia with symptoms of torticollis displayed a high frequency of  $^{18}\text{F}$ -FDG uptake increase in  $^{18}\text{F}$ -FDG PET/CT, and therefore, illustrating that these should be considered as target muscles for BoNT injection.

The advantage of the present study is that we determined the cutoff value that can be used for deciding whether to implement  $^{18}\text{F}$ -FDG PET/CT in accordance with the severity of clinical symptoms, as the  $^{18}\text{F}$ -FDG PET/CT study with a high radiation dose, which is also an expensive test, should not be performed on all patients indiscriminately. Therefore, it was possible to confirm that  $^{18}\text{F}$ -FDG PET/CT is useful in determining dystonic muscles in cervical dystonia with higher than moderate severity. In addition, it was possible to present guidelines for prioritizing the muscles for BoNT injection in those who were not subjected to  $^{18}\text{F}$ -FDG PET/CT by computing the frequencies of the muscles for which the  $^{18}\text{F}$ -FDG uptake was increased under  $^{18}\text{F}$ -FDG PET/CT. This will provide assistance in selecting the appropriate muscle for BoNT injection by illustrating that not only the widely known superficial neck

muscles but also the deep neck muscles such as OCI, longuscollis and RCP major, etc are frequently involved in cervical dystonia. Lastly, the present study results would also be helpful in determining the dosage of BoNT injection in accordance with the extent of  $^{18}\text{F}$ -FDG uptake at the time of BoNT injection since the correlation between clinical severity and SUVmax was confirmed to be high.

However, this study also had several limitations. First, the results of this study cannot be applied if the symptoms of patients including laterocollis, anterocollis and retrocollis manifest singly or in combination since this study was subjected only to cervical dystonia with symptoms of torticollis. Second, the subjects of the research were not divided into a BoNT injection group and a non-BoNT injection group, and thus, the corresponding analysis was not performed. Therefore, it was not possible to determine the effect of previous BoNT injection on the results of  $^{18}\text{F}$ -FDG PET/CT. However, 8 subjects proceeded  $^{18}\text{F}$ -FDG PET/CT less than 6 months after BoNT injection and 2 subjects underwent  $^{18}\text{F}$ -FDG PET/CT less than 3 months. Thus, we presumed that the previous BoNT injection did not significantly effect on study results. Third, since we did not compare baseline TWSTRS with the TWSTRS score following BoNT injection treatment after  $^{18}\text{F}$ -FDG PET/CT, it was not possible to determine the resultant effect of  $^{18}\text{F}$ -FDG PET/CT on the treatment of cervical dystonia with BoNT. Therefore, the range of research subjects in future studies should be broadened to include patients with a diverse range of symptoms including laterocollis, retrocollis and anterocollis, and combinations thereof. Moreover, the scope of the analysis of the muscles should include not only the muscles that function as rotators but also those that cause a wide range of head and neck movements including flexion, lateral flexion and extension, etc. In addition, research on the extent of improvement of clinical symptoms prior to and following BoNT injection would enable us to determine the usefulness of  $^{18}\text{F}$ -FDG PET/CT not only in selection of muscles but also in the treatment effect.

## V. CONCLUSION

A significant correlation was identified between the clinical severity of cervical dystonia and  $^{18}\text{F}$ -FDG PET/CT findings. Based on this correlation, we were able to provide a threshold of the clinical severity of CD for acquisition of positive  $^{18}\text{F}$ -FDG PET/CT study findings. The  $^{18}\text{F}$ -FDG PET/CT study let us gain an in-depth understanding of frequent involvement of the deep-seated neck muscles in cervical dystonia. In conclusion, these findings are suggestive of the usefulness of  $^{18}\text{F}$ -FDG PET/CT for identification of dystonic muscles of cervical dystonia with higher than moderate severity. Further studies are required to verify these findings.





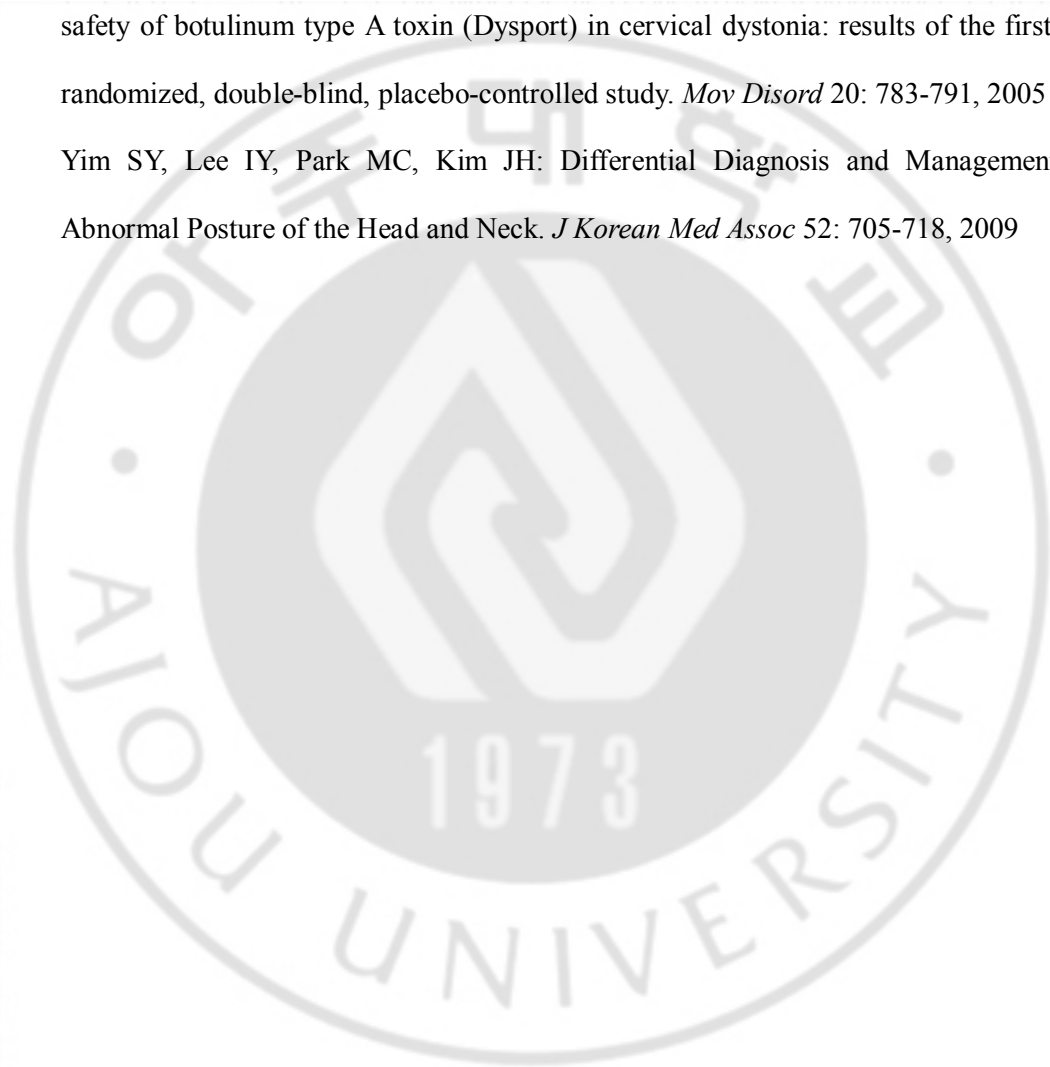
## REFERENCE

1. Albanese A, Barnes M, Bhatia K, Fernandez-Alvarez E, Filippini G, Gasser T, Krauss J, Newton A, Rektor I, Savoiaro M: A systematic review on the diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes: report of an EFNS/MDS-ES Task Force. *European journal of neurology* 13: 433-444, 2006
2. An YS, Sheen SS, Oh Y, Hwang SC, Yoon JK: Nonionic intravenous contrast agent does not cause clinically significant artifacts to 18 F-FDG PET/CT in patients with lung cancer. *Annals of nuclear medicine* 21: 585-592, 2007
3. An YS, Sun JS, Park KJ, Hwang SC, Park KJ, Sheen SS, Lee S, Lee KB, Yoon JK: Diagnostic performance of 18 F-FDG PET/CT for lymph node staging in patients with operable non-small-cell lung cancer and inflammatory lung disease. *Lung* 186: 327-336, 2008
4. Anderson TJ, Rivest J, Stell R, Steiger MJ, Cohen H, Thompson PD, Marsden CD: Botulinum toxin treatment of spasmodic torticollis. *J R Soc Med* 85: 524-529, 1992
5. Brans JW, Aramideh M, Koelman JH, Lindeboom R, Speelman JD, Ongerboer de Visser BW: Electromyography in cervical dystonia: changes after botulinum and trihexyphenidyl. *Neurology* 51: 815-819, 1998
6. Brans JW, de Boer IP, Aramideh M, Ongerboer de Visser BW, Speelman JD: Botulinum toxin in cervical dystonia: low dosage with electromyographic guidance. *J Neurol* 242: 529-534, 1995
7. Camargo CH, Teive HA, Becker N, Baran MH, Scola RH, Werneck LC: Cervical dystonia: clinical and therapeutic features in 85 patients. *Arq Neuropsiquiatr* 66: 15-21, 2008

8. Comella CL, Buchman AS, Tanner CM, Brown-Toms NC, Goetz CG: Botulinum toxin injection for spasmodic torticollis: increased magnitude of benefit with electromyographic assistance. *Neurology* 42: 878-882, 1992
9. Consky ES, Lang AE: Clinical assessments of patients with cervical dystonia. *Neurological Disease and Therapy* 25: 211, 1994
10. Epidemiological Study of Dystonia in Europe Collaborative G: A prevalence study of primary dystonia in eight European countries. *J Neurol* 247: 787-792, 2000
11. Jankovic J: Treatment of cervical dystonia with botulinum toxin. *Mov Disord* 19 Suppl 8: S109-115, 2004
12. Jankovic J, Leder S, Warner D, Schwartz K: Cervical dystonia Clinical findings and associated movement disorders. *Neurology* 41: 1088, 1991
13. Jankovic J, Tolosa E: Parkinson's disease and movement disorders. 5th ed. Philadelphia, Lippincott Williams & Wilkins, pp.330-334, 2007
14. Jankovic J, Tsui J, Bergeron C: Prevalence of cervical dystonia and spasmodic torticollis in the United States general population. *Parkinsonism Relat Disord* 13: 411-416, 2007
15. Lee HB, An Y-S, Lee HY, Hwang JH, Lee HJ, Jeong KY, Kim JW, Yim S-Y: Usefulness of 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Management of Cervical Dystonia. *Ann Rehabil Med* 36: 745-755, 2012
16. Lee IH, Yoon YC, Sung DH, Kwon JW, Jung JY: Initial experience with imaging-guided intramuscular botulinum toxin injection in patients with idiopathic cervical dystonia. *AJR Am J Roentgenol* 192: 996-1001, 2009
17. Salvia P, Champagne O, Feipel V, Rooze M, de Beyl DZ: Clinical and goniometric evaluation of patients with spasmodic torticollis. *Clin Biomech (Bristol, Avon)* 21: 323-

329, 2006

18. Sung DH, Choi JY, Kim DH, Kim ES, Son YI, Cho YS, Lee SJ, Lee KH, Kim BT: Localization of dystonic muscles with 18F-FDG PET/CT in idiopathic cervical dystonia. *J Nucl Med* 48: 1790-1795, 2007
19. Truong D, Duane DD, Jankovic J, Singer C, Seeberger LC, Comella CL, Lew MF, Rodnitzky RL, Danisi FO, Sutton JP, Charles PD, Hauser RA, Sheean GL: Efficacy and safety of botulinum type A toxin (Dysport) in cervical dystonia: results of the first US randomized, double-blind, placebo-controlled study. *Mov Disord* 20: 783-791, 2005
20. Yim SY, Lee IY, Park MC, Kim JH: Differential Diagnosis and Management of Abnormal Posture of the Head and Neck. *J Korean Med Assoc* 52: 705-718, 2009



## 경부근긴장이상증에서의 임상양상과 양전자 방출촬영의 결과

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**목적:** 본 연구는 경부근긴장이상증의 임상적 중증도와 양전자 방출 단층촬영 결과 간에 유의한 연관성이 있는지를 살펴보고 양전자 방출 단층촬영에서 양성 결과를 보이기 위한 경부근긴장이상증의 임상적 중증도의 역치 값을 알아보고자 하였다.

**방법:** 경부근긴장이상증 환자 중 사경의 증상을 보이는 47명의 환자가 연구에 참여하였으며 임상적 중증도는 Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)로 평가하였다. 경부근긴장이상증의 임상적 중증도와 양전자 방출 단층촬영에서 가장 높은 최대 표준화 섭취율 간의 상관성을 분석하였으며 수신자 판단 특성 곡선을 이용하여 양전자 방출 단층 촬영에서 양성 결과를 얻기위한 경부근긴장이상증의역치값을 결정하였다.

**결과:** 47명의 환자 중 33명의 환자에서 양전자 방출 단층 촬영에서 양성 결과를 보였다.가장 흔하게 침범한 근육으로는 동측두관상근/경관상근, 동측하두사근, 동측 경장근/머리긴근이었다. 가장 높은 최대 표준화 섭취율은 TWSTRS 값과 유의한 연관성을 보여주었으며 양전자 방출 단층촬영에서 양성 결과를 얻기위한 TWSTRS 점수의 역치는 27.5점으로 90.9%의 민감도와 64.3%의 특이도를 가질 때로 정하였다.

**결론:** 본 연구를 통해 경부근긴장이상증의 임상양상과 양전자 방출 단층 촬영결과 간에 유의한 연관성 및 양전자 방출 단층 촬영에서 양성 결과를 얻기위한 임상적

중증도의 역치 값을 알 수 있었다. 결론적으로, 본 연구 결과는 중증도 이상의 경부 근긴장이상증 환자에서 근긴장 유발 근육을 확인하는 데 양전자 방출 단층촬영이 유용함을 보여주었으며 추후 대규모 연구가 필요할 것으로 생각된다.

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핵심어: 경부근긴장이상증, Fluorodeoxyglucose F18, 양전자방출단층촬영

