INTRODUCTION:
We aimed to determine whether F-18 FDG PET/CT follow-up imaging after treatment in patients with spine infection (SI) could provide useful prognostic information and determine the residual SI.

METHODS:
Patients. This prospective study includes 30 patients (men; 11 patients, women; 19 patients, mean age; 55.5±18.4 years, range; 19–81 years old) with SI on the basis of clinical symptom and imaging procedure such as radiography and bone scan. All patients were operated and underwent histologic confirmation. Eleven patients had tuberculous spine infection (TSI) and 19 patients had pyogenic spine infection (PSI). In PSI, surgery was indicated when the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level did not become normal and the pain persisted even after administering antibiotics for more than 4 weeks or when neurological symptoms were expressed as a result of an abscess compressing the dura. Surgical indications for TSI was when severe back pain and/or radicular pain persisted even after conservative treatment, when neurological symptoms were expressed as a result of granulation tissue, abscess, sequestrated bone or disc fragment compressing the dura, or when instability or progressive deformity was expressed.

Operative technique. The infected end plate, disc and soft tissue were removed using anterior or posterior approach under general anesthesia. The disc material and infected end plate removed during surgery were sent for culture and histology. The space created after the meticulous debridement was filled with an autogenous iliac bone, and then posterior fusion with pedicle screw was performed. In fixing pedicle screw, the pedicle screw was not directly applied to the vertebral body causing the infection if possible. When the infection and destruction of the vertebral body was severe, we fixed one level above or below the segment.

Postoperative care. In PSI, the appropriate antibiotics were administered intravenously for mean 6.4 weeks (4 to 12) after surgery. After continuous intravenous antibiotic therapy, oral antibiotics were administered for mean 8.6 weeks (4 to 24). In addition to the antituberculous chemotherapy, intravenous antibiotic drug for 5 to 7 days was given to all the patients with TSI after surgery. Antituberculous chemotherapy was begun 1 week to 7 months before surgery for all the patients and was continued for 12 to 18 months. The standard four-drug therapy with isoniazid (5 mg/kg), rifampicin (10 mg/kg), ethambutol (15 mg/kg), and pyrazinamide (25 mg/kg) was administered as a first-line treatment for 4 months, and this was followed by isoniazid, rifampicin and ethambutol for 12 to 18 months. This treatment was regularly supervised by chest physicians. Ambulation was allowed 3 days after surgery and the patients wore a lumbar-sacral orthosis for 3 months.

Determination of residual spine infections. The residual SI was determined by presence of the preoperative symptoms including fever and back pain, hematological infection marker (ESR, CRP) and radiological findings during follow-up.

F-18 FDG PET/CT image analysis. F-18 FDG PET/CT image analyses were performed by two methods of lesion-based analysis and patient-based analysis. Image data sets of initial and follow-up scans were evaluated by two nuclear medicine physicians blinded to clinical and pathological results. Decisions concerning the analysis of F-18 FDG PET/CT data sets were reached by consensus. F-18 FDG PET/CT data sets of initial and follow-up images were analyzed quantitively by use of the SUV as index of F-18 FDG uptake. For quantitative analysis, all affected spine and soft tissue were evaluated by lesion-based analysis. Spherical regions of interest (ROIs) were placed over all affected spine lesions visible on PET images. The ROIs of lesions that were invisible on PET images were located by use of the corresponding CT images. ROIs were placed in the same area on the selected image for both of initial and follow-up. The maximal SUV of initial and follow-up images were calculated by manually drawing a region of interest (ROI) over the most intense slice of lesions visible on PET images. Also, with these ROIs, mean SUV of initial and follow-up calculated. From these quantitative indices, the % changes of SUVmax and SUVmean were calculated as following equations:

% change of SUVmean (%ΔSUVmean)= (SUVmean-initial−SUVmean-follow-up)/SUVmean initial X 100

After lesion-based analysis, we performed patient-based analysis. The patient-based analysis was conducted by using the mean values of SUVmax and SUVmean of all affected spines and adjacent soft tissues of individual patients.

RESULTS:
Patients Characteristics. Overall, 30 patients (11 men, 19 women with 89 lesions were assessed on F-18 FDG PET/CT. 31 lesions in 11 patients were TSI, and 58 lesions in 19 patients were PSI. Residual diseases were found in 17% of 4 patients. Among them, 4 lesions in 1 patient were TSI. The mean follow-up period was 423.8±258.8 days (range, 110–962 days; median, 370 days).

Comparison of quantitative indices of F-18 FDG PET/CT between residual and non-residual spine infection. The SUVmax were significantly declined after treatment in both of residual (2.35±1.7 to 2.06±1.03; p<0.0001) and non-residual SI (4.31±2.07 to 1.44±0.46; p=0.0001). The SUVmean were also decreased after treatment in both of residual (1.45±0.45 vs 1.04±0.29; p=0.0014) and non-residual SI (2.09±0.03 vs 0.81±0.25; p<0.0001).

The SUVmax were not significantly changed after treatment in residual SI (2.79±1.26 to 2.06±1.04; p=0.125). However, non-residual SI (4.24±1.9 to 1.53±0.47; p<0.0001) showed statistically significant decline in SUVmax after treatment. Also, the SUVmax were not significantly changed after treatment in residual SI (1.4±0.44 vs 1.02±0.32; p=0.125). However, non-residual SI (2.03±0.87 vs 0.83±0.19; p<0.0001) showed statistically significant decline in SUVmax after treatment.

The residual SI demonstrates significant lower values of %ΔSUVmax and %ΔSUVmean than those of non-residual SI by both of lesion-based analysis (%ΔSUVmax : 28.4±18 % vs 59.5±19.6 %, p<0.0001; %ΔSUVmean : 25.7±17.9 % vs 53.2±21.8 %, p=0.0001) and patient-based analysis (%ΔSUVmax : 25±19.2 % vs 57.8±18.4 %, p=0.0104; %ΔSUVmean : 24.7±15.8 % vs 53.4±15.8 %, p=0.0073).

Prediction of residual disease by lesion-based analysis. Receiver operating curve (ROC) analyses were performed to determine optimal cut-off values of %ΔSUVmax and %ΔSUVmean for the differentiation of residual and non-residual SI after treatment. When ±4.01 % of %ΔSUVmax was used as threshold value for differentiation of residual and non-residual disease, the area under curve (AUC) was 0.879 (standard error, 0.0391; 95% CI, 0.793-0.938; p=0.0001). The sensitivity and specificity were 85.7 %, 82.6 %, respectively. The positive and negative predictive values were 48 %, 96.9 %, respectively.

Prediction of residual disease by patient-based analysis. ROC analyses were also performed to determine optimal cut-off values of %ΔSUVmax and %ΔSUVmean for the differentiation of residual and non-residual SI after treatment by patient-based analysis. When ±46.14 % of %ΔSUVmax was used as threshold value for differentiation of residual and non-residual disease, AUC was 0.904 (standard error, 0.0621; 95% CI, 0.739-0.979, p=0.0001). The sensitivity and specificity were 100 %, 76.9 %, respectively. The positive and negative predictive values were 40 %, 100 %, respectively.

Residual disease free survival after treatment. Survival analysis was conducted by Kaplan-Meier and Cox proportional hazard model by patient-based analysis to define poternt preditors of residual disease after treatment of SI. The Kaplan-Meier survival curve illustrates the significant relationships between the %ΔSUVmax and %ΔSUVmean and residual disease free survival (%ΔSUVmax log rank statistic, 5.69; p=0.017: %ΔSUVmean log rank statistic, 11.24; p=0.0036). The Cox proportional hazard model using multivariate analysis for forward selection identified %ΔSUVmax as an independent prognostic factor for residual SI after treatment.

CONCLUSION:
F-18 FDG PET/CT is useful for discrimination of residual and non-residual SI after treatment. Among the various quantitative indices, %ΔSUVmax is a potent predictor of residual SI in the current study. However, these findings should be validated by large population based study.