Comparison of Disc Degeneration between Pyogenic Spondylitis and Noninfected Lumbar Spondylosis: A Multicenter Retrospective Study with Propensity Score Matching

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Abstract:

Introduction: Disc degeneration is a risk factor of pyogenic spondylitis. However, its degree in patients with pyogenic spondylitis is unknown. This study aimed to determine differences in disc degeneration between patients with pyogenic spondylitis and those with noninfectious lumbar spondylosis.

Methods: A total of 85 patients with lumbar pyogenic spondylitis (the infected group) and 156 with lumbar spondylosis who underwent posterior lumbar interbody fusion (the noninfected group) were retrospectively evaluated. Patients with a previous history of spinal fusion, tuberculous spondylitis, and multilevel infection and those receiving dialysis were excluded. Magnetic resonance imaging of the lumbar spine was conducted. Each disc at the L1/2-L5/S levels was graded. The total score of the four discs, excluding the affected disc, was used as the modified disc degenerative disease (DDD) score. Propensity score matching was performed using independent variables such as age, sex, diabetes mellitus, cancer, and steroid use. The modified DDD scores at all and each disc level were compared between the two matched groups.

Results: After matching, 48 patients in the infected group and 88 in the noninfected group were finally included in the study. The mean modified DDD scores of the infected and noninfected groups were 7.63 and 5.40, respectively. The modified DDD scores at all and each disc level were higher in the infected group than in the noninfected group.

Conclusions: The incidence of disc degeneration at all and each disc level was higher in patients with pyogenic spondylitis than in those with noninfectious lumbar spondylosis.

Keywords:

pyogenic spondylitis, disc degenerative, propensity score matching, multicenter study

Spine Surg Relat Res 2024; 8(6): 616-622
dx.doi.org/10.22603/ssrr.2024-0032

Introduction

Pyogenic spondylitis is a common disease among elderly individuals. The number of patients with this condition has been increasing in recent years due to the greater number of susceptible hosts caused by societal aging[1-3)]. This disease has different etiologies, such as bloodstream and abdominal-pelvic infections and other medical causes[1)]. It has been recently proposed that disc degeneration itself, as evidenced by Modic change, is a risk factor of pyogenic spondylitis[4,5)]. There have been various reports on disc degeneration and infection[6,7)]. However, the degree of disc degeneration in patients with pyogenic spondylitis is unknown. We hypothesized that lumbar disc degeneration can be more severe in patients with pyogenic spondylitis than in those with noninfected degenerative spinal diseases. This study aimed to determine differences in disc degeneration between patients with pyogenic spondylitis and those with noninfectious lumbar spondylosis using propensity score matching.

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Received: February 9, 2024, Accepted: March 15, 2024, Advance Publication: May 10, 2024

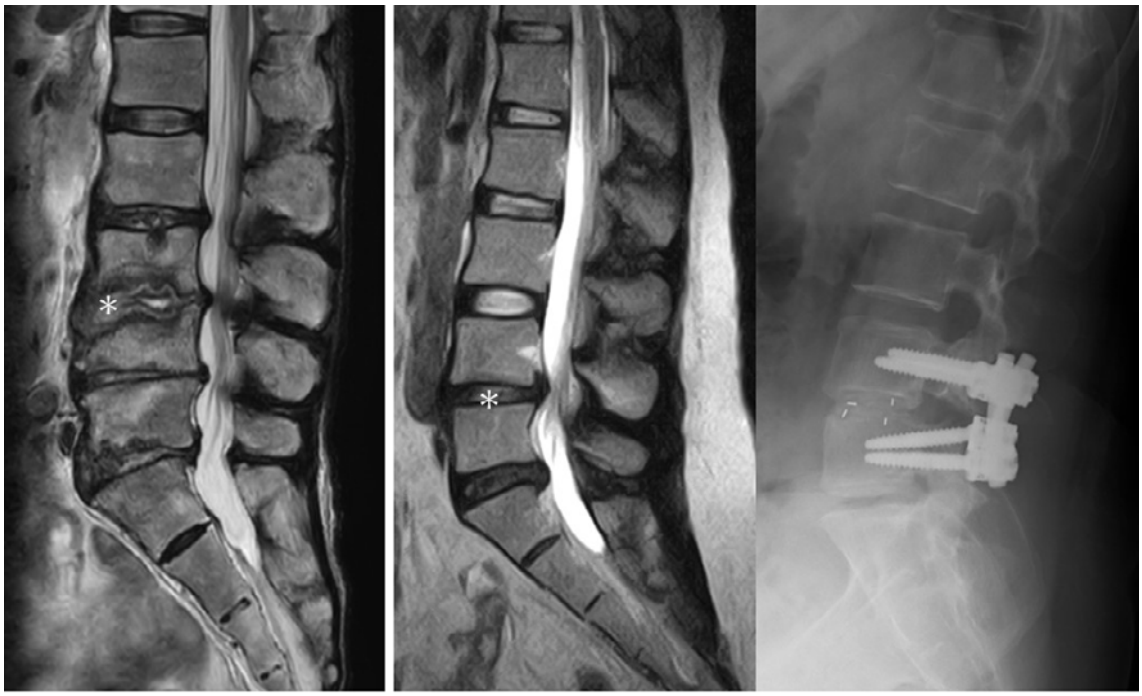

Figure 1. Illustrative examples of the infected and noninfected groups.
A: Infected group, pyogenic spondylitis at the L3/4 level (*). Degeneration of the whole lumbar spine.
B: Noninfected group, lumbar spondylosis at the L4/5 level (*) (B1). Posterior lumbar interbody fusion at the L4/5 level was performed (B2). There was disc degeneration at the L4/5 and L5/S levels.

Materials and Methods

This was a multicenter, retrospective cohort study, and the institutional review board approved the methodology of this study.

From 2012 to 2022, 85 patients with lumbar pyogenic spondylitis (the infected group) and 156 with lumbar spondylosis who underwent one-level posterior lumbar interbody fusion (the noninfected group), a common surgical procedure for lumbar degenerative disease, at four affiliated centers were evaluated (Fig. 1).

Patients with a single infected disc and lumbar spine (L1/2-L5/S level) in the infected group and those who underwent single-level lumbar surgery in the noninfected group were included in this study. The exclusion criteria were patients with a previous history of spinal fusion, tuberculous spondylitis, and multilevel infections and those receiving dialysis.

At the initial visit, data on age, sex, morbidity level, comorbidity (diabetes mellitus [DM] and cancer), and steroid use were assessed[2,3].

T2-weighted sagittal plane magnetic resonance imaging (MRI) of the lumbar spine was performed at the initial visit, and each disc at the L1/2-L5/S level was graded based on the study of Cheung[3,4,8]: 0, normal; 1, slight low signal in the disc; 2, low signal in the whole disc; and 3, low signal in the whole disc with intervertebral space narrowing. According to previous studies, the scores of the four discs, excluding the affected disc, were summed up to obtain a modified disc degenerative disease (DDD) score (0-12) (Fig. 2)[4,8]. The modified DDD score was independently assessed by two spine surgeons, each blinded to the other's evaluation, and a single assessment was conducted by each surgeon. In instances of divergent assessments, consensus discussions were held, resulting in a final decision.

Statistical analysis/propensity score matching

All statistical analyses used the JMP 10 (SAS Inc., Cary, NC, USA) and the Statistical Package for the Social Sciences software version 28.0.1.1 (IBM, New York, USA). Propensity score matching was performed on 61 and 146 patients in the infected and noninfected groups, respectively. The dependent variable was the presence or absence of infection, and the independent variables were age, sex, DM, cancer, and steroid use (prednisolone ≥1 mg per day), which are the risk factors of pyogenic spondylitis based on previous studies[2,3]. Propensity score was calculated with the logistic regression model, and the infected and noninfected groups were matched using propensity score matching with the nearest neighbor technique with a caliper of 0.2.

It has been reported that intraclass correlation coefficient (ICC) values, following Koo et al.'s classification, evaluate interobserver agreement in the modified DDD score. Classification categorizes values as follows: <0.50 for poor agreement, 0.50-0.75 for moderate agreement, 0.75-0.90 for good agreement, and >0.90 for excellent agreement[9]. Furthermore, modified DDD scores at all and each disc level were compared between the two matched groups according to previ-

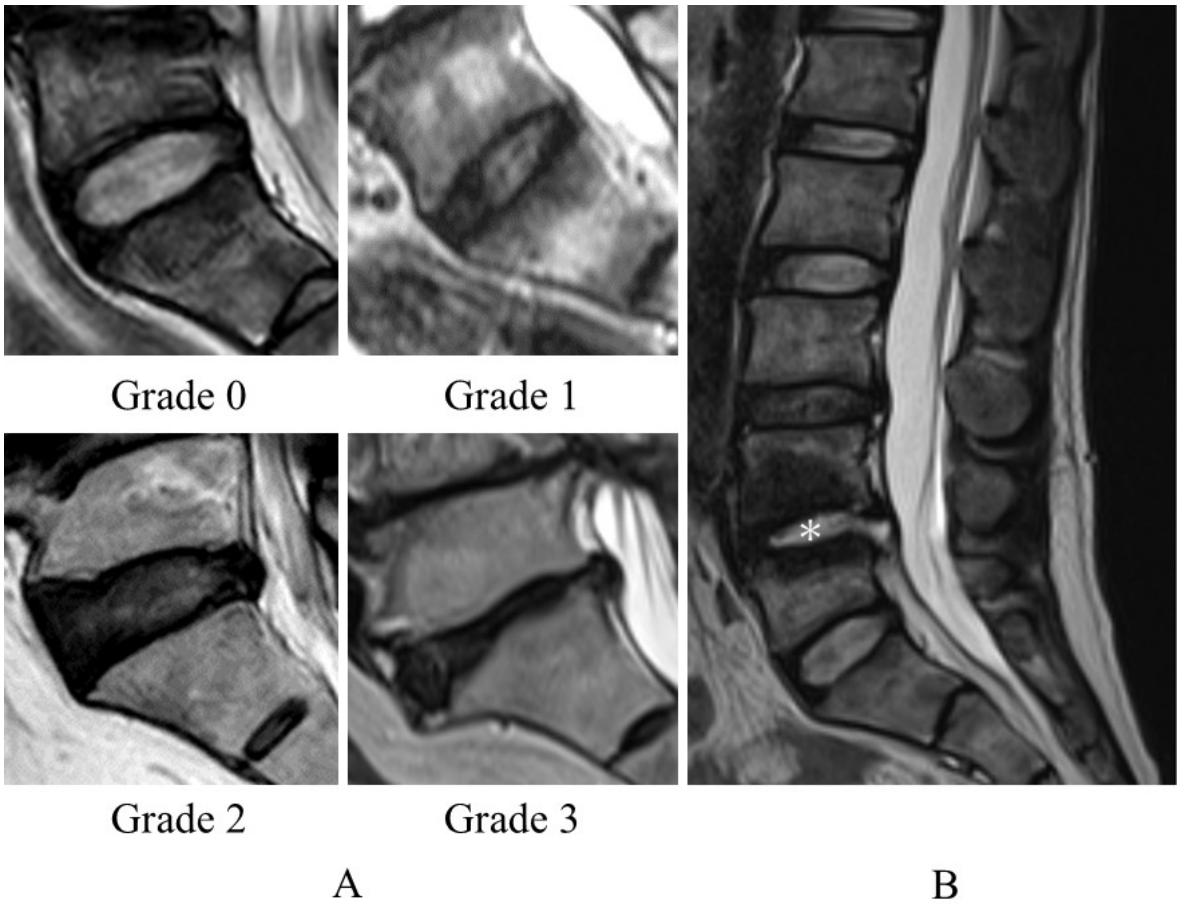

Figure 2. Evaluation of the modified DDD score.
Evaluation of the modified DDD score was performed via T2-weighted sagittal plane magnetic resonance imaging of the lumbar spine at the initial visit, and each disc at the L1/2–L5/S levels was graded as follows (A): 0, normal; 1, slightly low signal in the disc; 2, low signal in the whole disc; and 3, low signal in the whole disc with intervertebral space narrowing. The total score of the four discs, excluding the affected disc, was used as the modified DDD score (0–12).
Example (B): pyogenic spondylitis at the L4/5 level (*). Except for the affected disc, the L1/2 and L2/3 levels had 0 points, the L3/4 level had 2 points, and the L5/S level had 0 points. The total score was 2.
DDD, disc degenerative disease

ous studies[8]. Statistical analysis was performed to evaluate the association between variables using Fisher's exact test, Chi-square test, Mann-Whitney U test, and Kruskal-Wallis test. A p value of 0.05 was considered statistically significant.

Results

Demographic characteristics of the patients

A total of 61 patients in the infected group (mean age: 72.5 years) and 146 in the noninfected group (mean age: 68.7 years) were evaluated. After propensity score matching, 136 patients (48 in the infected group and 88 in the noninfected group) were finally included in the study (Fig. 3). Results showed that the patients were comparable in terms of age, sex, and comorbidity (Table 1).

ICC for interobserver agreement in modified DDD scores

The ICC for interobserver agreement regarding modified DDD scores was 0.92 (95% confidence interval 0.89-0.94), indicating excellent agreement.

Modified DDD scores according to disc level and demographic characteristics

The overall mean modified DDD score was 6.18 (standard deviation [SD]: 3.12, range: 0-12). The L4/5 level had the highest degenerative score at 1.89. There was a significant difference on the scores according to age groups (<60 years, 4.00; 60-79 years, 6.21; and >80 years, 7.69) (p=0.0005), but none according to sex and comorbidity (Table 2).

Comparison of the infected and noninfected groups

The mean modified DDD scores were significantly higher in the infected group than in the noninfected group (7.63 and 5.40, respectively; p<0.0001). The mean modified DDD

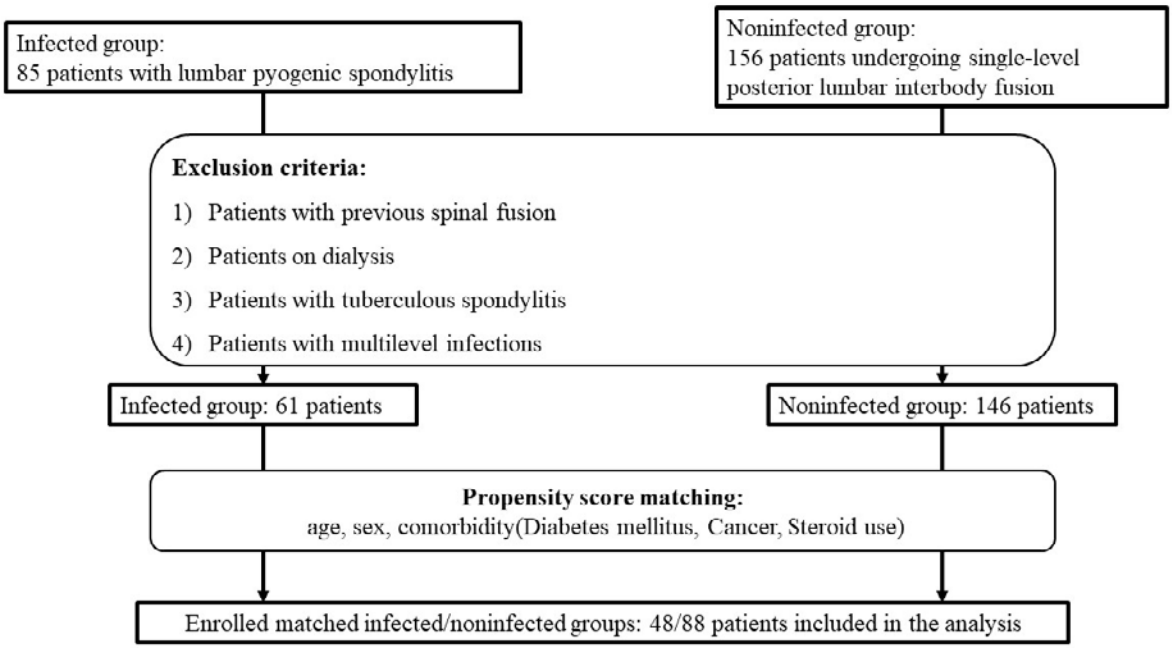

Figure 3. Inclusion and exclusion criteria.
A total of 85 patients were included in the infected group and 156 in the noninfected group. Furthermore, 61 patients in the infected group and 146 in the noninfected group were evaluated after applying the exclusion criteria (previous history of spinal fusion, tuberculous spondylitis, and multilevel infections and dialysis treatment). After propensity score matching using independent variables such as age, sex, comorbidity (diabetes mellitus and cancer), and steroid use, 48 patients in the infected group and 88 in the noninfected group were finally included in the study.

Table 1. Demographic Characteristics of Patients in the Infected and Noninfected Groups after Propensity Score Matching.

Variables	Infected group, n=48	Noninfected group, n=88	p value
Age			
Mean±SD	70.9±13.7	70.8±9.57	0.48[a]
Range	35–93	36–87	
Male/female	29/19	53/35	1.00[a]
Comorbidity			
DM	16 (33%)	27 (31%)	0.85[b]
Cancer	12 (25%)	15 (17%)	0.27[b]
Steroid use	7 (15%)	10 (11%)	0.60[b]

SD, standard deviation; DM, diabetes mellitus; [a], Mann-Whitney U test; b, Fisher's exact test.

score at each level was significantly higher than that at all levels in the noninfected group (p=0.009-0.014) (Fig. 4).

Discussion

The main findings of this study are as follows: First, older patients had a higher modified DDD score. Second, modified DDD scores at all and each disc level was higher in patients with pyogenic spondylitis than in those with noninfectious lumbar spondylosis.

It has been recently found that disc degeneration, as evidenced by Modic change, is associated with infection[4,5]. Furthermore, normal disc tissue is destroyed by disc degeneration, leading to hematogenous infection. Modic change and disc degeneration themselves are attributed to infection caused by bacteria such as *Propionibacterium acnes*[10-13]. There are cross-sectional and longitudinal reports using MRI, and disc degeneration progresses gradually beginning in the 20s[8]. Furthermore, older patients had a higher risk of severe disc degeneration[8,14,15].

Differentiating noninfected disc degeneration from infectious disc degeneration is a major clinical challenge. Previous studies have evaluated differences between the two conditions using artificial intelligence and other techniques[16].

Currently, the distinct characteristic between infected and noninfected discs is controversial, and it is difficult to differentiate the two conditions. Systematic reviews of disc degeneration often report an association between Modic change and infection[17,18].

Table 2. Modified DDD Scores according to Disc Level and Demographic Characteristics after Propensity Score Matching.

Variables	Mean	SD	p values
All levels	6.18	3.12	
L1/2	1.15	1.07	
L2/3	1.49	1.03	
L3/4	1.53	0.93	
L4/5	1.89	0.99	
L5/S	1.86	1.05	
Age (years)			
<60	4.00	3.46	0.0005[a]
60–79	6.21	3.04	
>80	7.69	2.26	
Male	5.93	3.03	0.25[b]
Female	6.57	3.19	
Comorbidity			
DM (+)	6.35	3.15	0.52[b]
DM (−)	6.11	3.14	
Cancer (+)	5.67	3.59	0.25[b]
Cancer (−)	6.31	3.01	
Steroid use (+)	5.65	3.66	0.40[b]
Steroid use (−)	6.26	3.06	

DDD, disc degenerative disease; SD, standard deviation; DM, diabetes mellitus; [a], Kruskal-Wallis test; b, Mann-Whitney U test.

With recent advancements in metagenomic techniques for bacterial analysis, the normal disc also contains good microflora, such as *Saccharopolyspora*, which does not cause infection[18-21]. With disc degeneration, the normal barrier function is disrupted, and neovascularization in the normal avascular disc increases[18]. Due to greater neovascularization, bad bacteria such as *Streptococcus* and *Staphylococcus*, which cause infection and degeneration, can reach the disc from the bloodstream and form bacterial flora leading to clinical pyogenic spondylitis[1,2,18].

One of the key findings of this study was that the risk of disc degeneration was higher in older patients. Moreover, previous reports have shown that disc degeneration progresses with age[14]. The average age of patients with pyogenic spondylitis is 59-69 years, and the incidence of pyogenic spondylitis increases with age[1,3]. This study may provide an explanation why pyogenic spondylitis is more common in elderly patients with advanced-stage disc degeneration.

The assessment of disc degeneration between patients with pyogenic spondylitis and those with noninfectious lumbar spondylosis using propensity score matching was the major novelty of this study.

In a recent systematic review of 34 articles on disc degeneration and infection, several reports have shown an association between Modic changes and infection, but none of them evaluated the degree of disc degeneration in patients with pyogenic spondylitis[17].

Disc degeneration leads to the formation of bad flora and the development of clinical pyogenic spondylitis. Hence, the high degree of disc degeneration in patients with pyogenic spondylitis, which was the main result of this study, may result in localized susceptibility to the infectious characteristics of pyogenic spondylitis, as opposed to systemic suscep-

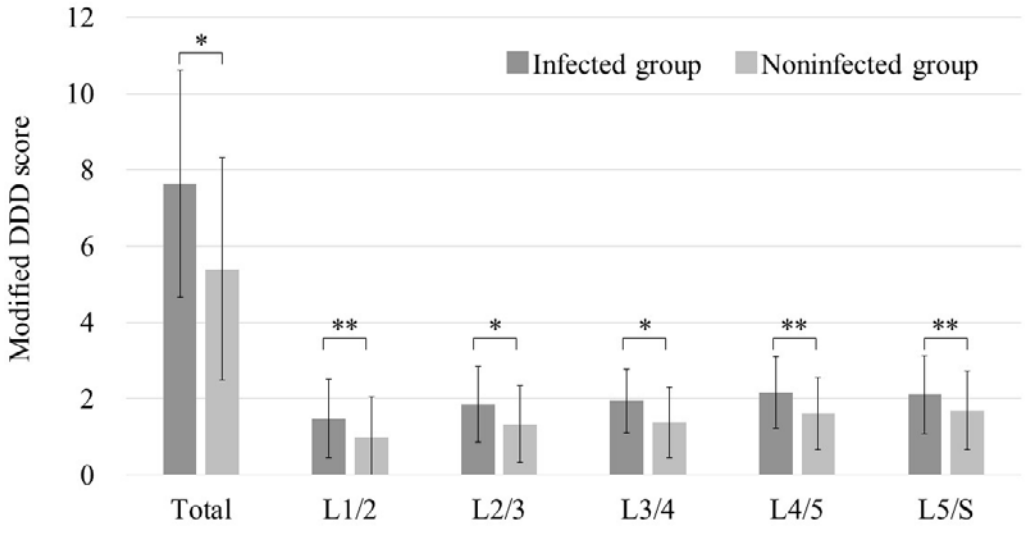

Figure 4. Modified DDD score in the infected or noninfected group after propensity score matching. The modified DDD scores at all and each disc level were higher in the infected group than in the noninfected group.
DDD, disc degenerative disease, * p<0.01, ** p<0.05.

tibility to DM or malignancy, which is the cause of systemic susceptibility to infection[1-3,18].

These results strongly support previous reports showing that disc degeneration, as evidenced by Modic change, is associated with pyogenic spondylitis.

This study had some limitations. First, although it was conducted at multiple centers, the patients were from the same race and an aging community (mean age, 71 years). Hence, the study results are not applicable to young patients with pyogenic spondylitis. Second, the condition of the disc before infection was not evaluated. Third, due to the retrospective nature of the study, it was impossible to conclude that disc degeneration is not a risk factor of infection. Fourth, the control group comprised patients who underwent posterior lumbar interbody fusion, a common surgery for lumbar degenerative disease. MRI was required for evaluating DDD scores and was appropriate for matching the characteristics of patients such as comorbidity and age. However, there might be a risk of selection bias because the patients were not volunteers of asymptomatic healthy patients. Fifth, our study design only has a small number of patients to perform statistical analysis for distinguishing infection and noninfection based on the modified DDD score. This challenge should be addressed in future investigations. Finally, the patient population in this study was predominantly elderly individuals, and disc degeneration might be a useful indicator of pyogenic spondylitis in elderly patients with degenerative disease.

Conclusion

Disc degeneration in pyogenic spondylitis and noninfectious lumbar spondylosis was compared using propensity score matching. The incidence of disc degeneration at all and each disc level was higher in patients with pyogenic spondylitis than in those with noninfected lumbar spondylosis.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

Sources of Funding: None.

Author Contributions: H.G., T.F., and M.K. conceived and designed the study. H.G., T.N., T.S., K.S., K.I., S.O., T.A., Y.S., K.M., H.N., H.T., I.S., and T.N. gathered and analyzed the data for the study. H.G., T.F., and M.K. drafted the paper. M.Y. and M.K. significantly revised the manuscript. All authors approved the version of the manuscript submitted for publication.

Ethical Approval: The institutional review board (IRB) of Ibaraki Western Medical Center approved all procedures including review of patient records used in this research (protocol code no. 21-07, approved on January 27, 2022). All procedures were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants of the study. The IRB also approved the procedures outlined for obtaining consent for this study.

Informed Consent: Informed consent was obtained from all patients to participate in this study and to publish this study.

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