Studies on the adjacent segment disease of the cervical spine in dogs

Summary of Doctoral Thesis

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Cervical intervertebral disc herniation (C-IVDH) and caudal cervical spondylotic myelopathy (CSM) are commonly diagnosed neurosurgical disorders in the cervical region of dogs. Clinically, as a treatment for C-IVDH and CSM, either ventral slot decompression (VS) or vertebral fixation (VF) is applied, based on the nature of the spinal cord compression (dynamic or static) of each individual case. Although postoperative instability and subluxation are serious complications with VS, these are considered preventable by combining VF. Typically, in caudal cervical lesions, when the slot width after VS is close to 50% of the vertebral body width, consideration of applying VF is necessary. However, after VF, the risk of similar lesions in the adjacent segment (domino lesions) has been reported. In domino lesions, abnormal mechanical environment occurs in the adjacent segment by vertebral fixation, promoting potential instability, and leading to extrusion of nucleus pulposus or hypertrophy of annulus fibrosus. Clinical symptoms secondary to domino lesions have been reported to occur in approximately 20 per cent of cases during the first 6 months to 4 years after surgery. In human medicine, similar lesions in adjacent intervertebral space after vertebral fixation of the cervical and lumbar spine has been reported (adjacent segment disease). In human cervical spines, it was demonstrated that the pressure or mobility of the adjacent segment increased after VF. Additionally, an increase in movement has also been observed at the upper and lower intervertebral spaces of the fixated segment in clinical studies using X-ray observations. However, there are only limited reports on the pathology of the adjacent segment disease and biomechanical and molecular mechanisms are still unknown in dogs. In order to clarify this pathology of the adjacent biomechanical disease, it is essential to study these mechanisms. Furthermore, it is necessary to consider the epidemiological features in order to make more detailed studies.

The purpose of this study is to clarify the pathology of the adjacent segment disease of the cervical spine in dogs. In chapter 2, in order to know the occurrence of adjacent segment disease

after surgical treatment with C-IVDH and CSM, we studied retrospectively with respect to various data that were collected from medical records of C-IVDH and CSM cases. In chapter 3, a cervical spine model was created using specimens obtained from healthy beagles, and the effect on the adjacent vertebral space after the vertebral fixation was examined using a 6-axis material tester for. In chapter 4, since the increase in range of motion (ROM) was observed in the adjacent segment in chapter 3, we reproduced the mechanical environment by creating an in vivo vertebral fixation model in dogs, and examined the effects of changes in the biomechanical environment in adjacent segment.

1. Occurrence of adjacent segment disease after surgical treatment of cervical spine in dogs.

In order to know the occurrence of adjacent segment disease after surgical treatment with cervical spinal disease in dogs, we studied retrospectively about C-IVDH and CSM cases. In this study, we difined the cases that recurrence of clinical symptoms such as neck pain or paresis and plegia of four limbs was observed as adjacent segment disease. As a result, the occurrence of adjacent segment disease was likely to occur after VF group (15.6%) compared to the after decompression group (5.2%), and significant association of adjacent segment disease was observed with respect to the combination of VF. Therefore, it was suggested that adjacent segment disease possibly associated with the stabilization surgery.

2. Changes in the biomechanical environment in the treated site and adjacent segment after the vertebral fixation.

A cervical spine model was created using specimens obtained from healthy beagles, and the effect on the adjacent vertebral space after VF was examined using a 6-axis material tester. As a result, the ROMs at the treated site (C5-6) was significantly decreased compared with the intact

model in both the PMMA and Plate models. Our results also showed that the ROM at the adjacent segment (C4-5) increased significantly in the PMMA and Plate models compared with the intact model. From these results, it was suggested that VF can change the mechanical environment at the adjacent segment and may cause adjacent segment disease. When ROM at C5-6 during the bending test in the PMMA and Plate models was compared, no significant difference was observed in flexion and extension movement. However, during lateral bending, ROM was significantly lower in the Plate model than in the PMMA model. In the rotational test, the ROM at C5-6 was significantly lower in the PMMA model than in the Plate Model. Since higher fixation strength was achieved in the Plate model in lateral bending and in the PMMA model in axial rotation, it was suggested that the effects on the adjacent segment differ according to the fixation method used.

3. Effect of changes in the biomechanical environment in adjacent segment after vertebral fixation.

Since the increase in range of motion was observed in adjacent segment after vertebral fixation in Chapter 3, we reproduced the mechanical environment of the adjacent segments by creating an in vivo vertebral fixation model in dogs, have examined the changes in the biomechanical environment of adjacent segments. As a result, in the adjacent segments of the vertebral fixation group, increase of chondrocyte-like cells and cell clusters were observed and histological scores increased in the nucleus pulposus. Also with respect to changes in the extracellular matrix of the nucleus pulposus, increase of Col1A1 and MMP13-positive cells and reduction of Col2A1-positive cells were observed in the vertebral fixed group. Therefore, it was suggested that degeneration progressed by the influence of the vertebral fixing. On the other hand, in the annulus fibrosus, a tendency for cell density to decrease and rounded cells to increase was

observed, in the vertebral fixation group. In addition, since some parts of the outer layer structure become unclear progressive degeneration due to vertebral fixation was suggested. With the examination of changes in the composition of the collagen fibers in the annulus fibrosus, reduction of Col1A1 positive region and regional replacement by cartilage matrix was also observed under the influence of the vertebral fixation. Therefore, the degradation of collagen fibers and the progress of cartilage metaplasia were suggested. Although there were no Col2A1 positive regions, positive cell rate was higher in the vertebral fixation group as compared to the control group. From these results, it suggested that due to vertebral fixation, degeneration of the intervertebral disc nucleus pulposus and annulus fibrosus progressed, leading to the adjacent segment disease to develop.

In summary, our findings suggested that the occurrence of adjacent segment disease possibly associated with the stabilization surgery. In addition, the range of motion at the adjacent segment increased, suggesting that VF can change the mechanical environment at the adjacent segment and may cause adjacent segment disease. Also, the results suggested that due to vertebral fixation, degeneration of not only the intervertebral disc nucleus pulposus but also the annulus fibrosus progressed, leading to the development of adjacent segment disease.