Title: Randomized Controlled Trial Comparing Clinical and Radiological Outcomes Between C3 Laminectomy with C4-C6 Laminoplasty and C3-C6 Laminoplasty

Study protocol (date: 2017-01-05)

Background

C3 laminectomy in cervical laminoplasty is a modified laminoplasty technique that can preserve semispinalis cervicis muscle attached to the C2 spinous process. Several previous studies have shown that this technique can lead to better outcomes of postoperative axial neck pain and C2-C3 range of motion (ROM) than conventional cervical laminoplasty. However, there is still a lack of understanding of total and proportional postoperative cervical sagittal alignment outcomes.

Study design

A randomized clinical trial will be conducted on patients with cervical laminoplasty for treating CSM or OPLL at a single tertiary referral university hospital. Patients will be randomly assigned to either the LN group (C4-6 laminoplasty with C3 laminectomy) or the LP group (C3-6 laminoplasty) at a 1:1 ratio. The sample size will be calculated to achieve a target of 80% power with a two-tailed significance level of 0.05, with a medium effect size (Cohen's d = 0.50), resulting in 63 patients per each group. The trial will enrolled consecutive patients who underwent cervical laminoplasty from March 2017. Participants' ages will ranged from 20 to 80 years. Patients with metastatic tumors, combined fractures, or previous posterior cervical surgeries will be excluded from this study. Patients with a diagnosis of CSM or OPLL will be assessed prior to randomization by a neurosurgical specialist through a combination of history-taking, clinical examination, and radiological workup, including dynamic radiographs and cervical spine computer tomography (CT) or magnetic resonance image (MRI) scans. Diagnosis of CSM will be based on symptoms of myelopathy and stenosis at two or more cervical levels on MRI. Diagnosis of OPLL will be made based on CT findings. The randomization process, surgical group options, and required follow-up evaluations and imaging will be fully explained to eligible patients by a neurosurgical

specialist. After obtaining informed consent, patients will be randomized using a computer-generated block design in 1:1 ratio with concealed assignment managed by an independent research nurse. The attending surgeons, patients, and staff members in the operating room will be blinded to the surgical method until the day of surgery. A concealed paper indicating the patient's assigned group will be provided in the operating room, and the surgeon will verify the patient's group just before commencing the surgery. This study was approved by the hospital's Institutional Review Board (IRB number: H-1610-136-804).

Data collection and outcomes

Data will be collected using patient-reported outcome questionnaires and plain x-rays taken at the outpatient clinic before surgery and at 1, 2, and 3 years postoperatively. Patients will record their outcomes directly without assistance of the surgeon or other study participants. Radiological parameters will be assessed using 150% magnified images by one of the authors (a fellow). Three measurements will be performed, and the median value will be selected as the final measurement. The measurements will be conducted utilizing the measuring tools within the institution's Picture Archiving and Communication System (M6, Infinitt Healthcare, Seoul, Korea) operating on a Microsoft Windows environment (Microsoft Corp., Redmond, WA, USA). We selected C2-C7 Cobb angle (C2-C7 CA) as the primary outcome measure, considering the importance of postoperative kyphotic changes in cervical laminoplasty, which have been associated with long-term recurrent myelopathy and chronic neck pain. Additionally, we chose the Neck Disability Index (NDI) as another primary outcome measure to evaluate axial neck pain, as it is commonly acknowledged as a potential advantage of C3 laminectomy. Secondary outcome measures included other radiologic parameters such as C2-C3 Cobb angle (C2-C3 CA), C4-C7 Cobb angle (C4-C7 CA), cervical sagittal vertical axis (cSVA), T1 slope (T1S) and T1 slope minus cervical lordosis (T1S-CL),

as well as presence of C2-C3 interlaminar fusion. Other clinical outcomes, such as numerical rating scores for neck (NRS-N) and limb (NRS-L) and the Euro-Quality of Life-5 Dimension (EQ-5D), will be also assessed. We will examine operation-related factors, including open side, presence of dome-like laminectomy at the C2 or C7 level, operative time, estimated blood loss, and complications such as hinge fracture, neural injury, dural injury, and wound infection.

Statistical analysis plan

Outcomes will be analyzed using the modified intention-to-treat (mITT) strategy. The mITT population will consist of all participants with randomly assigned surgery and have available at least a year of postoperative data from 1 to 3 years. Baseline and operation-related characteristics of the LN and LP groups will be compared using independent t-tests for continuous variables, and chi-square tests or Fisher's exact tests for categorical variables. Postoperative clinical outcomes and radiological parameters will be compared between groups and over time using linear mixed-effects models, with fixed effects including preoperative values of tested variables, group, time, interaction between group and time, other factors with possible relation with outcomes such as age, BMI and disease, and a random effect of subjects. Least squares mean for postoperative clinical outcomes and radiological parameters will be estimated. Comparisons will be made between the treatment groups. For variables with a significant difference in the interaction between time and group, post-hoc analysis will be performed for each time point and adjusted p-values will be evaluated using the Bonferroni method. All data will be analyzed using SPSS software version 27.0 (SPSS, Chicago, IL, USA), with statistical significance defined at $p < 0.05$ (two-sided).