國立臺灣大學醫學院物理治療學系暨研究所

碩士論文

School and Graduate Institute of Physical Therapy
College of Medicine
National Taiwan University

Master Thesis

頸椎脊髓神經病變患者之站立姿態控制研究

Study of the Upright Postural Control in Patients with Cervical Spondylotic Myelopathy

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中華民國 107 年 01 月

January, 2018

doi:10.6342/NTU201800337

國立臺灣大學（碩）博士學位論文
口試委員會審定書

頸椎脊髓神經病變患者之站立姿態控制研究
Study of the Upright Postural Control in Patients with Cervical Spondylotic Myelopathy

本論文係劉沛怡君（R04428004）在國立臺灣大學物理治療學系、所完成之碩（博）士學位論文，於民國 107 年 1 月 19 日承下列考試委員審查通過及口試及格，特此證明

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doi:10.6342/NTU201800337

誌謝

能完成這篇論文，我要特別感謝我的指導教授徐瑋勵老師,感謝她在實驗和寫論文的過程中，給予耐心和細心的指導。

我也要感謝實驗室的每一位成員對我的支持與鼓勵。感謝我的同學們－簡若恩、蘇姵宇、林昱瑄、莊貝愉、鄭亦珊和黃薇瑾，和研究助理魏玲芝，在研究的路上給予鼓勵及建議，也在每個重要時刻給予精神上的支持。

最後，感謝我的家人一直以來支持和鼓勵，讓我能在海外努力地完成我的學程。

再次誠心地感謝大家。

doi:10.6342/NTU201800337

中文摘要

背景：頸椎脊髓神經病變是近年來常見的退化性疾病，其會造成姿勢控制能力受損。而頸部減壓手術為針對頸椎脊髓神經病變的治療之一，其以侵入性方式直接去除造成脊髓壓迫的組織。然而，針對頸椎脊髓神經病變之功能性評估及站立時的姿勢控制之間的關係仍很少被探討，此外，過去也無研究探討頸椎脊髓神經病變患者在減壓手術前後之站立姿勢控制變化。

研究目的：（1）確立頸椎脊髓神經病變患者之功能性表現和站立姿勢控制能力的相關性，並比較不同程度之頸椎脊髓神經病變患者、頸椎神經根病變患者及健康對照者的平衡能力;（2）評估並追蹤頸椎脊髓神經病變患者接受減壓手術後之功能性表現及站立姿勢控制能力，並確立何種功能性評估最能反映出減壓手術後站立姿勢控制變化。

研究設計：觀察性研究

研究方法：在實驗一中，參與者會被分成為脊髓病變組（63名受試者），神經根病變組（24名受試者）和健康對照組（19名受試者）。脊髓神經病變組和神經根病變組會進行日常功能性評估，其包括功能性問卷（頸部失能量表（NDI）、日本骨科學會頸椎脊隨病變評估問卷（JOACMEQ）之下肢功能分數、Nurick量表以及改良式日本骨科學會（JOA）量表之下肢運動功能障礙分數）和功能表現（腳踏測試、五次坐到站測試和10秒原地踏步測試）。再者，三組的參與者皆會以自然站姿及雙腳併攏站姿站立於力板上，並分別在睜眼和閉眼情況下紀錄其壓力中心之前後側和左右側位移。在實驗二中，參與者被分成脊髓病變組（53名受試者）和健康對照組（22名受試者）。脊髓病變組會在術前與術後3個月、術後6個月和

doi:10.6342/NTU201800337

術後1年進行日常功能性表現評估（包括NDI，JOACMEQ下肢功能和10秒步進測試）以及在睜眼和閉眼下站立於力板上的姿勢控制評估。而對照組僅需參與站立姿勢控制評估。

結果：在實驗一中，日常功能性測試中的JOACMEQ下肢功能分數與站立時壓力中心參數(center of pressure variables)之間的有顯著的一般相關性（$r < 0.5$，$p < 0.05$）。以Nurick量表分數進行嚴重程度分組的兩組脊髓病變組之壓力中心參數在閉眼站立的情況下有顯著性差異（$p < 0.05$）。在Nurick量表分數為“2或3”的脊髓病變組之壓力中心參數明顯地比神經根病變組和健康對照組高（$p < 0.05$）。在實驗二中，脊髓病變組的NDI分數（$p = 0.036$）和JOACMEQ之下肢功能分數（$p = 0.036$）在減壓手術後均有顯著地改善，而在睜眼自然站立時，在壓力中心的95%置信橢圓面積（$p = 0.022$）、平均速度（$p = 0.019$）、前後向範圍（$p = 0.007$）、前後向均方根距離（$p = 0.023$）等壓力中心參數在術後有顯著地改善。然而，在所有的情況下，脊髓病變組之壓力中心參數在手術前後均顯著地高於健康對照組（$p < 0.05$）。若將術前之測量結果設置為基準，術後三個時間點的效應值和標準化反應平均值皆在-0.49至0.03的範圍內。以受試者工作特徵（Receiver operating characteristic，ROC）曲線方法分析並以JOACMEQ之下肢功能部分的第一題分數為依據，只有在術後3個月的壓力中心之95%置信區橢圓形區域、前後側範圍、左右側範圍和左右側均方根距離（面積> 0.70 ）的最小臨床重要差異能被計算出來。

結論：Nurick 量表適合被用於分類頸椎脊髓病變患者之姿勢不穩定的程度，Nurick 分數較高之頸椎脊髓神經病變患者相比於神經根病變患者或健康對照組，其姿勢控制有較明顯地受損。此外，在減壓手術後，主觀功能性評估問卷的分數

doi:10.6342/NTU201800337

和睜眼時前後方向相關的壓力中心參數皆有顯著地進步，然而站立壓力中心參數卻不適合作為評估減壓手術後短期變化的工具。

關鍵字：頸椎脊髓神經病變；減壓手術；功能性表現；站立姿勢控制；壓力中心

doi:10.6342/NTU201800337

ABSTRACT

Background: Cervical spondylotic myelopathy, which is a common degenerative disorder, may lead to impairment of upright postural control. The cervical decompression surgery is an invasive treatment for cervical myelopathy to remove the cord compression. However, there are few studies conducted on the relationship between functional outcomes and upright postural control, as well as effect of decompression surgery on upright postural control.

Purpose: (1) To determine the association between functional assessment with upright postural control of patients with myelopathy and to compare the upright postural control among patients with different severity of cervical myelopathy, patients with radiculopathy and healthy age-matched control; (2) To evaluate functional outcomes and upright postural control of patients with myelopathy after cervical decompression surgery and determine which statistical methods that reflect the clinically meaningful measure in upright postural control following cervical decompression surgery

Design: Observational study

Methods: In Experiment 1, participants were be recruited for myelopathy (63 subjects), radiculopathy (24 subjects) and age-matched control group (19 subjects). Only myelopathy and radiculopathy group were assessed by functional outcome measures, (i.e Neck Disability Index (NDI), Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire (JOACMEQ)-lower extremity function, Nurick scale, and

doi:10.6342/NTU201800337

modified Japanese Orthopaedic Association (JOA) scale-motor dysfunction of lower extremity (mJOA-MDLE)), and functional performances (i.e. foot taping test, five-times-sit-to-stand test and 10 second step test). Meanwhile, force platform was used to record the anteroposterior (AP) and mediolateral (ML) COP displacement of all participants in neutral and narrow stance with eyes-open and eyes-closed respectively. In Experiment 2, participants were recruited for myelopathy (53 subjects) and age-matched control group (22 subjects). The functional assessments, including NDI and JOACMEQ-lower extremity function and 10 second step test, were performed in myelopathy group at four phase: preoperative phase together with postoperative 3 months, 6 months and 1 year respectively. The standing balance assessment using force platform was performed in in myelopathy group at four phases and in age-matched control group only at recruitment day.

Results: In Experiment 1, the correlations between JOACMEQ-lower extremity function and COP variables were significantly fair ($r < 0.5$, $p < 0.05$). The COP variables of myelopathy group classify with Nurick score showed significant differences ($p < 0.05$) in all eyes-closed condition. The myelopathy group with Nurick score '2 or 3' demonstrated significantly increased COP variables than radiculopathy and age-matched control group ($p < 0.05$). In Experiment 2, the NDI score ($p = 0.036$) and JOACMEQ-lower extremity function score of myelopathy group ($p = 0.036$) improved after decompression surgery. Significant improvement was shown in 95% confidence ellipse area ($p = 0.022$), mean velocity ($p = 0.019$), range-AP ($p = 0.007$), and RMS distance-AP ($p = 0.023$) in neutral stance with eyes-opened. However, the COP variables was significantly instable than healthy age-matched control ($p < 0.05$) before and after surgery in all standing condition.

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The effect size and standard response mean of all three postoperative phases ranged from -0.49 to 0.03 if the preoperative phase was set as baseline. Only minimally clinically important difference (MCID) for 95% confidence ellipse area, range-AP, range-ML, root mean square (RMS) distance ML (area > 0.7) in eyes-closed condition at postoperative 3 months were determine with first question of JOACMEQ-lower extremity function as anchor by receiver operating characteristic (ROC) curve analysis.

Conclusion: The Nurick scale may reflect severity of postural instability in patients with myelopathy. The myelopathy patients with higher Nurick score had obviously impaired upright postural control compared to patients with radiculopathy or healthy age-matched control. Besides, the subjective functional outcomes and COP variables in eyes-open condition significantly improved after decompression surgery. The COP variables were more suitable to reflect long-term change after decompression surgery.

Keywords: Cervical myelopathy, decompression surgery, functional assessment, upright postural control, center of pressure (COP)

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Chapter 1 Introduction

Cervical myelopathy is one of the consequences of common degenerative change of cervical spine during aging.[1] Myelopathy is the clinical symptom caused by the compression of the spinal cord. The clinical manifestations of cervical myelopathy are determined by the severity or location of the spinal cord compression.[2] The signs and symptoms of cervical myelopathy, such as neck pain, upper and lower extremity paresthesia, muscle weakness, muscle spasticity and gait disturbance,[3] may deteriorate the functional activities and living quality.

The incidence of cervical myelopathy were estimated at a minimum of 41 and 605 per million in North America[1] and 349.5 per million person in Taiwan[4] annually. The conservative treatment for cervical myelopathy patients includes neck immobilization with cervical collar or head halter), bed rest, exercise and medication.[1] If the disorder becomes severe and progressive, the cervical decompression surgery may be suggested.[5]

The patients with myelopathy may have postural control impairment due lesion on spinal cord. The long-term outcome of surgical decompression was variable, and some patients may have late functional deterioration even after adequate decompression and initial improvement.[6] This purposes of this study were to investigate relationships between functional outcomes and postural control, as well as examine the progression of upright postural control after cervical decompression surgery.

doi:10.6342/NTU201800337

Chapter 2 Literature Review

2.1 Background and Epidemiology

Cervical spondylotic myelopathy is attributed to compression of the spinal cord secondary to degeneration change in cervical spine,[1] that can lead to direct injury to neurons and glia and may be followed by ischemia, excitotoxicity, and apoptosis[7] on nerve tissues. Symptoms of cervical myelopathy include gait imbalance, lower extremity stiffness and jerking, sensory loss, muscles weakness, loss of hand dexterity or bladder dysfunction, corresponding to the level of cervical spine.[8]

Cervical myelopathy may be caused by static or dynamic factor. Static factors of the cervical myelopathy include cervical spondylosis, disc degeneration and ossification of posterior longitudinal ligament/ ligamentum flavum,[7] hyperostosis (hypertrophy and osteophyte formation) of the vertebrae.[2] The dynamic factors of cervical myelopathy include increase spinal canal stenosis on flexion and extension of degenerative cervical spine,[2] which narrow the cervical spinal canal dynamically and place increased strain and shear forces on the spinal cord.[7]

Few researchers had depicted the epidemiology of cervical myelopathy. A study from the United Kingdom reported a total of 41 patients with averaged age of 68.7 years who presented with cervical myelopathy.[9] Cervical myelopathy was found to be more common in male patients to the ratio of approximately 2.7:1, whereas C5/6 being the most commonly affected level. This study also concluded that cervical myelopathy predominantly affects men after 70 years old.[9] A Japanese study indicated that the annual rate of operations per 100,000 residents in a north-eastern prefecture was 5.7% and that

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most of these patients were in their sixth or seventh decade of life.[10] In North America, the incidence and prevalence of cervical myelopathy were approximated at a minimum of 41 and 605 per million, respectively.[11] Incidence of myelopathy–related hospitalizations has been estimated at 4.04/100,000 person-years, and the surgical rates seem to be increasing.[11]

In Taiwan, from 1998 to 2009, National Health Insurance Research Database indicated that 349.5 million person-years was diagnosed with cervical myelopathy; 14,140 patients were admitted to hospital for cervical myelopathy.[4] The overall incidence of myelopathy-related hospitalization was 4.04 per 100,000 person-years with higher incidence in males and elderly.[12] During the follow-up of these patients for 13,461 person-years, a total of 166 patients were diagnosed with spinal cord injury.[4]

Apart from cervical myelopathy, cervical radiculopathy is another neurological disorder related to degenerative change of cervical spine, which is caused by dysfunction of nerve roots exiting cervical spinal cord.[13,14] The typical clinical presentations are arm pain, which can disrupt sensation, motor strength, and the reflex arc along the path of innervation of the affected root.[13,14] The etiology of cervical radiculopathy is commonly related to mechanical compression, neuropraxia, or chemical irritation of the nerve roots.[14] Degenerative change of joint and soft tissues in cervical spine can affect the neuroforamen from all directions, consequently limits nerve root excursion.[14] For instance, disk degeneration reduces foraminal height and alters the kinematics of the cervical spine, leading to osteophyte formation arising from the uncinate process and zygophophyseal joints.[14]

doi:10.6342/NTU201800337

The previous studies performed in Rochester Minnesota estimated the annual incidence of cervical radiculopathy to be 107.3 per 100,000 for men and 63.5 per 100,000 for women from 1976 to 1990.[15] The age-specific annual incidence rate per 100,000 population reached a peak of 202.9 for the age group 50 to 54 years within that 15 years.[15] Another more recent study in United States military indicated that 24,742 service members were diagnosed with cervical radiculopathy from 2000 to 2009 resulting in an incident rate of 1.79 per 1000 person-years.[16]

2.2 Postural Control System in Upright Position

Most of daily functional activities are performed in upright position, such as walking, jumping and squatting. In human upright standing position, approximately two-thirds of human body mass are insecurely balanced some distance from the ground (about two-thirds of human height) over two legs, which provide base of support.[17] The ability to stand upright on two feet is essential which work as a precursor to initiation of other daily living activities.[18] Previous study revealed that the poor functional outcome in modified Japanese Orthopaedic Association (JOA) scale for lower extremity function manifested worse postural stability in standing.[19] Hence, the postural control system is critical demand to execute movement in upright position.

The postural control system has two main functions.[20] The first function is mechanical antigravity function to build up posture against gravity and ensure that balance is maintained if center of gravity is under base of support under stance condition.[20] The second function is to serve as a reference frame to fix the orientation and position of the segments for perception and action as regards the external world.[20]

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Winter et al. (1990) suggested that the postural control system comprises three subsystem: the sensory system (consists of vestibular, visual and proprioception system), the central nervous system (CNS) and the musculoskeletal system.[17] The proprioception system which is made up by muscle, joint and cutaneous receptors provide two type of information: the information about the state if the effector system (such as muscle length, muscle force output and relative orientation of body segment) and the information about environment (such as temperature, contact surface condition, pressure distribution and presence of any noxious stimuli).[17] The vestibular system provides information about body orientation in the inertia frame of reference and acceleration of the body.[17] The visual system provides information about environment, body orientation and body movement.[17] The rich inputs from sensory system are evaluated and integrated by CNS to decide a suitable action plan.[17] The action plan is executed by the musculoskeletal system to regulate body posture and movement.[17]

Massion (1994) depicted that the central organization of posture involves interactions between external forces (such as gravity), the body mechanical properties and the neuromuscular forces. This postural control system involves the feedback and feedforward system. The human posture is the result of positioning and orientation of the body and limbs in equilibrium with motion and gravitation.[21] Postural adjustments are based on visual, vestibular and somatosensory input integrated into a complex feedback regulatory system.[20]

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2.3 Pathological Change in Spinal Cord of Patients with Cervical Myelopathy

Spinal cord plays important role for human movement. The cord compression may result in demyelination of spinal cord and apoptosis of spinal cord,[22] consequently lead to motor impairment if action potential conduction of muscle is affected. The space available for the cervical spinal cord decreases, thus, the compression on spinal cord increase.[23] The compression on white matter trigger long tract sign; the compression on grey matter trigger segmental sign.[24] Therefore, the spinal cord compression can lead to sensorimotor impairment which may affect functional activities.

The cervical myelopathy signs and symptoms are also based on the location of the associated cord compression, such as posterior, dorsolateral and ventrolateral columns, the ventral horns of the spinal cord.[7] For instance, the symptoms and signs in the trunk and lower limbs result from damaged white matter involvement of the long tracts at the cervical level.[19] The neural signals concerning proprioception ascend through the posterior columns of the spinal cord through the dorsal root ganglion on the same side of the peripheral nerve.[19]

Apart from location, the previous animal studies also indicated that severity[22] and duration[25] of compression on spinal cord also affect the clinical manifestation of cervical myelopathy. The greater compression on spinal cord may lead to more occurrence of microcirculation arrest, which is predominant in the watershed area of the cord and mostly affects the highly vulnerable anterior horn cells, give rises to neuronal death, necrosis, and eventual cavitation at the junction of the dorsal and anterior horns.[22] Longer period of compression on spinal cord also lead to complete ischemic blood flow in spinal cord

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and bring greater physiological damge.[25] Longer period of compression on spinal cord also lead to complete ischemic blood flow in spinal cord and bring greater physiological damge.[25]

The destruction of the axonal tissue and myelin sheath may lead to prolong conduction to peripheral muscle (such as leg muscles), eventually causing to conduction block. In normal human motor evoked potentials latency depends on the stimulus intensity and the state of the target muscles.[26] The stimulus intensity determines whether cortical motor neurons are activated directly or indirectly and also determines the site of activation.[26] Damage to spinal motor neurons could play an important role directly (loss of spinal motor neurons with faster conduction velocity) or indirectly (insufficiency of synapse from corticospinal tract to spinal motor neurons) in physiology of prolonged central motor conduction time.[26] Prolongation central motor conduction time in the patients with cervical myelopathy mainly manifested the severity of corticospinal conduction block, which may cause the loss of functional axons.[27]

The postural adjustment during standing and ambulation involved complex mechanism including polysynaptic spinal reflex mechanisms, depending on afferent sensory pathway, efferent motor pathway, and supraspinal influences.[3] The ascending tract (spinocerebellar tract) in the spinal cord mainly refers to the dorsal column, which conducts the deep joint sensation into cerebellum.[3] The long descending tracts, which consist of corticospinal tract (anterior and lateral), reticulospinal tract, tectospinal tract, vestibulospinal tract, raphespinal tract, function for motor control.[28]

The anterior corticospinal tract are with respect in paraspinal and axial muscle function.[28] The lateral corticospinal tract facilitates the performance of skilled movements,

doi:10.6342/NTU201800337

whereas the reticulospinal tracts act on motor neurons of axial and proximal limb muscles.[28] These tracts are considered part of the extra-pyramidal system of motor control (with the lateral vestibulospinal and tectospinal tracts), which are involved in locomotion as well as posture.[28] With damage to the corticospinal tract, which are related to motor system syndrome, the spasticity, or motor weakness of the lower extremities[19] may be manifested during maintenance of postural stability in upright standing.

2.4 Standing Balance in Patients with Cervical Myelopathy

Center of pressure (COP) is the location of the vertical reaction vector on the surface of a force platform on which the subject stands.[29] The COP indicates the orientations of the body segments (joint angles), and the movements of the body (joint angular velocities and accelerations) to hold the center of gravity over base of support.[30] Displacement of COP is measured by force platform in anteroposterior (AP) and mediolateral (ML) direction for evaluation of upright postural control.[30]

The deterioration of postural stability in quiet standing was identified in previous studies in patients with myelopathy. The patient with cervical myelopathy demonstrated broader sway area and longer locus length per environmental area comparing with age-matched control in eyes-closed stance.[19] The later study showed further support to instable standing balance in patient with cervical myelopathy based on body COP displacement in upright standing.[31] The body sway of patients with cervical myelopathy were larger comparing patients with cervical spondylosis and healthy normal in standing with and eyes-open and eyes-closed.[31] The tibialis anterior also delayed response to the perturbation during standing.[31]

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The sensorimotor dysfunction was suggested to be the primary cause of upright postural control impairment in patients with myelopathy.[31] The severe compression on spinal cord may damage the dorsal column and the ventral column, which neural signals referring to proprioception ascend through the dorsal columns of the spinal cord by way of the dorsal root ganglion on the same side of the peripheral nerve.[32] The delay of tibialis anterior antagonist reaction in patients with cervical myelopathy was consistent with an intensely abnormal transmission of the proprioceptive input to the suprasegmental centers during stance with perturbation.[31]

2.5 Functional Outcomes after Cervical Decompression Surgery

The conservative treatment is one of the selections for cervical myelopathy. The interventions of conservative management include cervical immobilization, head halter traction, plaster bed for head and trunk, exercises, bed rest and medication.[1] However, conservative methods were not always effective to reduce clinical presentations of cervical myelopathy and improve functional status.[33] Therefore, cervical decompression surgery is a common invasive intervention for cervical myelopathy. Two main approaches are usually used for cervical surgery: anterior and posterior approach. The anterior approaches of surgery include anterior decompression and fusion. Whereas, the posterior approaches of surgery include laminectomy and laminoplasty, which are usually indicated for multilevel myelopathy.[2]

After decompression surgery, recovery of daily functional activities is essential to determine whether surgery is beneficial to patients. The effectiveness of cervical

doi:10.6342/NTU201800337

decompression surgery was usually evaluated by the functional outcomes in research or clinical setting. The functional outcome measures for this cohort are related to the clinical manifestation such as neck pain, hand numbness and clumsiness, gait difficulties or sphincter dysfunction.[34] Several studies of functional outcomes in postoperative cervical myelopathy were published to determine effect of surgery.[35-37] Even though decompression surgery can stabilize or improve the sign or symptom of myelopathy, the surgical outcomes may be also affected by the age, preoperative severity and duration of symptoms.[38] Longer symptom duration was associated with worse outcomes measured with for leg assessment associated to functional activities requiring stability in upright position, such as standing and walking.[35]

One of the studies disclosed that pain were found improved but functional outcomes and quality of life were not improved after cervical decompression surgery.[35] However, some research results indicated different conclusion. A prospective study examined the potential effects of age, sex, duration of preoperative symptoms, and preexisting medical comorbidities on functional outcomes and postoperative complications in patients in cervical myelopathy underwent cervical decompression surgery.[36] The results showed that patients, who were significantly older and with more pre-existing medical comorbidities, had tendency to develop postoperative complications.[36] Overall, the mean Nurick grades, modified JOA score and Berg Balance Scale were significantly improved at 6 month and 1 year postoperatively,[36] whereas functional recovery reached a plateau at 6 months postoperatively.[36] The other studies also reported the remarkable improvement in JOA scale[37] (or modified JOA scale[39]), Neck Disability Index[37,39] and some component in SF-36 form[37,39] (physical functioning, physical role functioning, bodily pain, social role functioning and emotional role

doi:10.6342/NTU201800337

functioning), after 6 months,[37] 1 year[39] or 2 years[37] of surgery respectively.

Even though the balance performance had been evaluated at postoperative phase, no standing balance is assessed in biomechanical method yet after decompression surgery in patients with cervical myelopathy. However, several studies about gait analysis of patients with decompression surgery were published. Regarding to the biomechanical analysis on walking, some previous studies demonstrated the improvement of spatial-temporal gait parameter after decompression surgery, for instance, velocity,[40,41] step length,[40,41] cadence,[40] stance phase duration[41] and single-stance phase duration.[41] The vertical component of the ground reaction force, and maximal flexion angle of the hip joint, maximal flexion angle of the knee joint, extension angle of the knee joint (single-stance phase and swing phase) and dorsiflexion of the ankle joint[41] were also reported improving after decompression surgery.

A later study did not completely agree to previous postoperative gait analysis result of patients with cervical myelopathy.[42] None of the measured spatial-temporal parameters changed significantly. Gait speed slightly increased from a mean of 1.05 m/s preoperatively to 1.08 m/s at the 12-month postoperatively.[42] However, peak ankle plantarflexor moment and ankle power at pre-swing increased significantly.[42] Electromyography (EMG) analysis of the muscle activation timing demonstrated only significant increase in duration of activation of tibialis anterior from 37 % gait cycle duration preoperatively to 41.7 % postoperatively.[42] EMG change of tibialis anterior was suggested to be a compensatory strategy to improve control around the ankle during single limb support to create a more stable ankle joint.[42] This could then facilitate a higher plantarflexor moment and power burst at pre-swing to contribute greater power absorption by the knee during swing phase.[42]

doi:10.6342/NTU201800337

Generally, the patients with decompression surgery displayed improvement in functional outcomes and some of the gait parameters in the previous studies. However, the effect of surgery on postural control need to be investigated to identify the recovery sensorimotor dysfunction on upright standing. The COP also should be discussed whether applicable to reflect improvement after surgery.

2.6 Research Question

The association between functional assessment result and upright postural control in patients with myelopathy had not been discussed in previous studies. The upright postural control between patients with cervical myelopathy and radiculopathy also had not been distinguished in the previous studies. The research questions of experiment 1 in this study were:

1. Did the results of functional assessments associate with upright postural control in patients with myelopathy?
2. Was the upright postural control different between myelopathy group with radiculopathy group and age-matched control group?

Apart from investigation of upright postural control in patients without surgery, the change of upright postural control after cervical decompression surgery had not been determined in patients with myelopathy. The research questions of experiment 2 in this study were:

1. Did the functional outcomes and upright postural control change after cervical decompression surgery in patients with myelopathy?

doi:10.6342/NTU201800337

2. Can the upright postural control reflect the change after cervical decompression surgery in patients with myelopathy?

2.7 Study Objective

The purposes of experiment 1 in this study were:

1. To determine the association between functional assessments and upright postural control in patients with myelopathy

2. To compare upright postural control among patients with different severity of cervical myelopathy, patients with cervical radiculopathy, and healthy age-matched control

The purposes of experiment 2 in this study were:

1. To investigate change of functional outcomes and upright postural control in patients with myelopathy after cervical decompression surgery

2. To determine which statistical methods and minimally clinically importance difference thresholds representing the clinically meaningful measure in upright postural control following cervical decompression surgery

2.8 Hypotheses

The hypotheses of experiment 1 in this study were:

1. The results of functional assessments would associate with upright postural control in patients with myelopathy.

doi:10.6342/NTU201800337

2. The patients with myelopathy would show less stable upright postural control than patients with radiculopathy and healthy age-matched control group.

The hypotheses of experiment 2 in this study were:

1. The functional outcomes and upright postural control would be improved after cervical decompression surgery in patients with myelopathy.
2. The internal and external responsiveness characteristic would reflect the degree of change in upright postural control after cervical decompression surgery in patients with myelopathy.

doi:10.6342/NTU201800337

Chapter 3 Study Method

3.1 Experiment 1

3.1.1 Study Design

This study was cross-sectional observational study for determining the relationship between functional assessments and center of pressure (COP) in patients with cervical myelopathy. This study was approved by the National Taiwan University Hospital Research Ethics Committee (IRB reference number: 201505093RIN) and registered (ClinicalTrials.gov ID: NCT03396055).

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3.1.2 Study Procedure

This study flowchart is shown in Figure 2. The participants of myelopathy, radiculopathy and age-matched control group were assessed for eligibility. Before data collection, the recruited participants were provided the experimental explanation and written informed consent at Department of Surgery in National Taiwan University Hospital. For myelopathy and radiculopathy group, the data collection included demographic data, anthropometric data, functional assessments and standing balance assessment (Figure 2). For age-matched control group, the same data collection was applied, except functional assessments.

3.1.3 Participants

The participants of myelopathy and radiculopathy group were assessed by a same neurosurgeon for diagnosis.

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The inclusion criteria of the participants for myelopathy and radiculopathy group were:

1. Aged between 20 to 80 years old.
2. With diagnosis of cervical myelopathy or radiculopathy according to relevant imaging examination.

The exclusion criteria of the participants for myelopathy and radiculopathy group were:

1. Unable to stand upright for 1 minute without support.
2. With traumatic spinal injury.
3. With previous neurological dysfunction of central nervous system (CNS).
4. Unable to communicate or follow instruction.
5. With recent musculoskeletal injury on lower extremities.
6. With vestibular dysfunction.
7. With infection or metastasis on spine and lower extremities.

Besides, the inclusion criteria of the participants from age-matched healthy control group were:

1. Aged between 20 to 80 years old.
2. Without neck or back pain.
3. No history of severe musculoskeletal injury on lower extremities or spine, vestibular dysfunction and neurological dysfunction or neurosurgery.

doi:10.6342/NTU201800337

3.1.4 Data Collection

3.1.4.1 Functional Assessments

The functional assessments in this study included functional outcome measures and functional performances. The **functional outcome measures** were assessed in myelopathy and radiculopathy group using following assessments:

- ***Neck Disability Index (NDI)***

NDI is a questionnaire used to assess neck pain affecting functional activities, including pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreation. The total scores of this questionnaire is 50, which are converted to percentage to represent the level of severity.[43] The percentage of NDI correlates positively with the severity of neck functional loss. NDI is a valid and reliable clinical test.[43-49] The intraclass correlation coefficients (ICCs) range of NDI from 0.50 to 0.98.[46] The content validity as well as construct and convergent validity were proven in patient with neck disorder.[43-46,48]

- ***Japanese Orthopaedic Association Myelopathy Evaluation Questionnaire (JOACMEQ)***

Japanese Orthopaedic Association established JOACMEQ for self-administered assessment of patients with cervical myelopathy. The questionnaire is divided to 5 parts: cervical spine function, upper extremity function, lower extremity function, bladder function and quality of life.[50] The total mark of each division is higher since the patient condition of self-assessment is getting better.

doi:10.6342/NTU201800337

In this study, the lower extremity function (JOACMEQ-lower extremity function) was prioritized. This section includes 5 questions corresponding to ability of walking on flat surface, single leg stand, going up stairs, bending forward, kneeling or stooping and walking more than 15 minutes.[12,50] JOACMEQ is the highly valid clinical assessment tools.[12,34] The test-retest reliability of JOACMEQ is 0.79-0.00 and the correlation coefficient between JOACMEQ-quality in life and NDI is -0.76.[12]

- ***Modified Japanese Orthopaedic Association Scale (Modified JOA scale)***

Modified JOA scale is common multidirectional assessment tool for cervical myelopathy. This scale is an investigator-administered scale separately assessing motor dysfunction of the upper extremity, motor dysfunction of the lower extremity, sensory loss of the upper extremity, and sphincter dysfunction.[50] The motor dysfunction of the upper extremity component was modified from the original Japanese Orthopaedic Association (JOA) scale to adapt for non-Japanese culture.[51]

In this study, the motor dysfunction of lower extremity (mJOA-MDLE) was prioritized. The score was determining in regards to the ability of ambulation as well as sensory and motor function of lower extremities,[51] which could be classified into 0 grades from 7. The participant with complete loss of sensory and motor function was scored with 0. Conversely, the participant without dysfunction was scored with 7.[51]

The inter- and intra-observer reliabilities of the JOA scoring system for cervical myelopathy were high.[52] For modified JOA scale motor dysfunction of the lower extremity, the internal consistency was moderate with a Cronbach α of 0.63.[53] Regarding to the convergent and divergent validity, modified JOA scale correlated with the Nurick score ($r = -0.625$) but was not associated with subscales of the Short-Form 36 that

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measure different constructs.[53] The modified JOA scale was responsive to change as reflected by a Cohen effect size of 1 after 12 months of decompression surgery.[53]

- ***Nurick Scale***

The Nurick scale is an investigator-administered scale to assess walking ability of patients regarding to severity of gait impairment.[54] The higher score reflects more unstable gait. Nurick scale was reported as an appropriate outcome measure in prior studies focused on its reliability and construct validity in the patients with cervical myelopathy.[55] Nurick grade also well correlated with motor dysfunction of lower extremity in modified JOA scale (Spearman's ρ 0.901 and 0.886).[56] Cervical cord compression and intrinsic magnetic resonance imaging (MRI) signal change was also correlated with Nurick grading.[57]

The **functional performances** were assessed in myelopathy and radiculopathy group using following assessments:

- ***Foot Taping Test***

Foot tapping test is a quantitative analysis of lower limb motor dysfunction that was widely used for other neurological disorder.[58] The participant was seated on a chair with hips and knees at approximate 90º flexion.[58] The sole of the foot tap as many times as possible for 10 seconds while keeping the heel in contact with the floor.[58] The number of foot taping within the 10 seconds was recorded. This test was repeated on the other side. This whole process was repeated once. The mean of the results was adopted for data analysis.

doi:10.6342/NTU201800337

The mean of foot tapping test was 23.8±7.2 in patients with myelopathy, which was significantly lower than 31.7±6.4 in healthy age-matched controls and reduced with age.[58] The number of foot tap in 10 seconds significantly correlated with the lower extremity motor function of modified JOA score and results of grip and release test.[58] This test can detect the effect of decompression surgery on patients with myelopathy. This test showed postoperative improvement among myelopathy patient with decompression surgery after 12 months of surgery.[58] Postoperative gain of foot taping test significantly correlated with the gain of JOA score.[58]

- ***Five-times-sit-to-stand Test***

Five-times-sit-to-stand test is a test used to assess the muscle strength of the lower extremity. The participant sat on chair with back support for the preparation position, which was standing upright with the arm crossed front of the chest. When the timer started, the participant was instructed to sit to stand five times at the fastest speed. The timer was stopped as the patient sat on the chair after the last count of standing up.

If the patient completed the test for more than 15 seconds, he/she was at high risk of falling.[59] The sensitivity of this test is 55% and specificity is 65%.[59] Discriminant analysis demonstrated that the test correctly identified 65% of subjects with balance dysfunction.[60] Previous study demonstrated that individuals with times for 5 repetitions sit-to-stand exceeding the following can be considered to have worse than average performance: 11.4 seconds for 60 to 69 years, 12.6 seconds to 70 to 79 years and 14.8 seconds 80 to 89 years.[61]

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- ***10 Second Step Test***

10 second step test was recognized as a quantifiable measure of severity in cervical myelopathy.[62] The participants were instructed to take a step by lifting their thighs parallel to the floor (hip and knee joints in 90° flexion) in the same place without support to maintain balance.[62] The number of steps in 10 seconds was counted. Each participant was requested to perform the test at maximum speed.[62] For purpose of safety, the examiner stood at side of participant for close supervision to prevent fall incident.

Previous study indicated that average number of steps in myelopathy patients was 10.7±5.5 before surgery whereas the average number of steps in the control was 19.6±5.5.[62] Number of steps significantly correlated with the number of grip and release, walking grade of JOA scores, and total JOA score.[62] This test was responsive to reflect effect of decompression surgery on patients with myelopathy.[62] This test showed significant postoperative improvement ($p < 0.01$) among myelopathy patient with decompression surgery after 12 months of surgery.[62]

3.1.4.2 Standing Balance Assessment

- ***Procedure of Standing Trial***

The standing balance assessment was conducted on all participant to determine the static balance performance in upright standing. The participants were asked to stand on a force platform (Kistler, Switzerland) for 30 seconds with sampling rate of 1000Hz in each standing trial. The participants performed the standing task with eyes-open and eyes-closed in two different foot positions (Figure 3). Overall, four trials were performed for each participant: neutral stance with eyes-open (OE) and eyes-closed (CE) as well as

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narrow stance with eyes-open (RSOE) and eyes-closed (RSCE). Participants were allowed to rest if they felt tired or leg soreness.

- ***Data Processing of Center of Pressure (COP)***

Force platform signals were analogue-to-digital converted at a sampling rate of 1000 Hz. LabVIEW (National Instruments Corp., Austin, TX) software was used to compute the COP regarding ground reaction force and moment in anteroposterior (AP) and mediolateral (ML) direction. Then the data was processed and filtered with second order of Butterworth low-pass filter at 5 Hz by Matlab R2010a software.

COP were further analyzed for time domain measures.[30] First, 95% confidence ellipse area was defined as area enclosed approximately 95% of the points on the COP path. Next, mean velocity was defined as length of the COP path per second. Third, range was defined as maximum distance between any two points on the COP path, which was calculated in AP and ML direction respectively. Lastly, root mean square (RMS) distance was defined as RMS distance from the mean COP, which was calculated in AP and ML direction respectively.

3.1.5 Statistical Analysis

Descriptive data of participants from three groups (myelopathy group, radiculopathy group and age-matched group) were presented as means with standard deviation. Statistical analysis was performed using PASW Statistics 18 for Macintosh (SPSS, Chicago, IL). The normality of the functional assessments and COP variables were determined by Shapiro–Wilk test. The nonparametric tests were used for all data

doi:10.6342/NTU201800337

analysis as the variables were not normally distributed. P value of less than 0.05 (alpha, α) was considered statistically significant.

The data of NDI, JOACMEQ-lower extremity function, foot taping test, 5-times sit-to-stand test, and 10 second step test were continuous variables. Within myelopathy group, the correlations between COP variables and results of NDI, JOACMEQ-lower extremity function, foot taping test, 5-times-sit-to-stand test, and 10 second step test were determined by non-parametric Spearman test. The correlation coefficient within 0.00 to 0.25 represents little or no relationship between two variables.[63] The correlation coefficient within 0.25 to 0.50 represents fair relationship between two variables.[63] The correlation coefficient within 0.50 to 0.75 represents moderate to good relationship between two variables.[63] The correlation coefficient above 0.75 represents good to excellent relationship between two variables.[63]

The Nurick scale and modified JOA scale-motor dysfunction of lower extremity (mJOA-MDLE) were ordinal variables. The COP variables (95% confidence ellipse area, mean velocity, range-AP, range-ML, RMS distance-AP, and RMS distance-ML) were categorized based on the score of Nurick scale and mJOA-MDLE. Kruskal-Wallis test was used to test the differences among groups in COP variables with different scores of Nurick scale and mJOA-MDLE respectively.

The functional variables with most considerable association with COP variables would be selected for subgrouping participants in myelopathy group to compare COP variables among myelopathy, radiculopathy and age-matched control groups. The myelopathy group was classified into two subgroups: group with Nurick score ‘0 or 1’ and group with Nurick score ‘2 or 3’. Main effect of group difference among myelopathy

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group with Nurick score '0 or 1', radiculopathy, and age-matched control group was examined by Kruskal-Wallis test. The same test was repeated among myelopathy group with Nurick score '2 or 3', radiculopathy, and age-matched control group. If the main effect of group difference was significant, each pairwise comparisons between two groups were performed by Mann-Whitney U test. The level of significance was adjusted by Bonferroni correction ($\alpha/3$) to avoid Type I error. The effect size of each pairwise comparison was calculated by the below equation[63]:

$$Effect\ size = \frac{mean\ of\ group\ A - mean\ of group\ B}{pooled\ standard\ deviation} \qquad \text{(Equation 1)}$$

where $mean\ from\ group\ A$ and $mean\ of group\ B$ is the mean of myelopathy group or radiculopathy group or age-matched control group in pairwise comparison between two different groups.

3.2 Experiment 2

3.2.1 Study Design

This study was longitudinal observational study for determining the progression of functional outcomes and COP variables during postoperative 3 months, 6 months and 1 year. This study was approved by the National Taiwan University Hospital Research Ethics Committee (IRB reference number: 201505093RIN) and registered (ClinicalTrials.gov ID: NCT03396055).

doi:10.6342/NTU201800337

3.2.2 Study Procedure

This study flowchart is shown in Figure 5. The participants of myelopathy, and age-matched control group were assessed for eligibility. Before data collection, the recruited participants were provided the experimental explanation and written informed consent at Department of Surgery in National Taiwan University Hospital. For myelopathy group, the data collection included demographic data, anthropometric data, functional assessments (NDI, JOACMEQ-lower extremity function and 10 second step test) and standing balance assessment. The data collections of myelopathy group were initiated before decompression surgery and repeated at postoperative 3 months, 6 months and I year as follow-up (Figure 5 and 6). For age-matched control group, the same data collection was applied, except functional assessments.

3.2.3 Participants

The participants of myelopathy group were assessed by a same neurosurgeon to determine the requirement of the decompression surgery.

The inclusion criteria of the participants were:

1. Aged between 20 to 80 years old
2. With diagnosis of cervical myelopathy according to MRI imaging

The exclusion criteria of the participants were:

1. Unable to stand upright for 1 minutes
2. With traumatic spinal injury
3. Unable to communicate or follow instruction

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4. Not suit to cervical decompression surgery due to other medical conditions
5. With previous neurological dysfunction of CNS
6. With recent musculoskeletal injury on lower extremities
7. With vestibular dysfunction
8. With infection or metastasis on spine and lower extremities

Besides, the inclusion criteria of the participants from healthy age-matched control group were:

1. Aged between 20 to 80 years old
2. Without neck or back pain
3. No history of severe musculoskeletal injury on lower extremities or spine, vestibular dysfunction and neurological dysfunction or neurosurgery

3.2.4 Data Collection and Data Analysis

3.2.4.1 Functional Assessments

The following functional assessments were conducted in myelopathy group:

- ***Neck Disability Index (NDI)***

NDI is a self-administered assessment for level of neck pain effect on functional activities, including different level of the patient on pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreation.[43] Higher NDI score reflects higher severity of pain on functional activities.[43,46]

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- ***Japanese Orthopaedic Association Myelopathy Evaluation Questionnaire (JOACMEQ)***

JOACMEQ is a self-administered assessment of patients with cervical myelopathy for function loss, health condition and satisfaction. The questionnaire assessed cervical spine function, upper extremity function, lower extremity function, bladder function and quality of life.[50] The total mark of each division is higher since the patient condition of self-assessment is getting better. In this study, the lower extremity function (JOACMEQ-lower extremity function) was prioritized. The evaluated lower extremity function includes 5 questions corresponding to ability of walking on flat surface, single leg stand, going up stairs, bending forward, kneeling or stooping and walking more than 15 minutes.[12,50]

The 5 questions of lower extremity function in JOACMEQ were listed as below:[50]

1. "Can you walk on a flat surface?"
2. "Can you stand on either leg without the support of your hand? (the need to support yourself)?"
3. "Do you have difficulty in going up the stairs?"
4. "Do you have difficulty in one of the following motions; bending forward, kneeling or stooping?"
5. "Do you have difficulty in walking more than 15 minutes?"

doi:10.6342/NTU201800337

- ***10 Second Step Test***

10 second step test is recognized as a quantifiable measure of severity in cervical myelopathy.[62] The participants were instructed to take a step by lifting their thighs parallel to the floor (hip and knee joints in 90° flexion) in the same place without support at maximum speed.[62] The number of steps in 10 seconds was counted. Each participant was requested to perform the test at maximum speed.[62] For purpose of safety, the examiner supervised at side of participant to prevent fall incident.

3.2.4.2 Standing Balance Assessment

- ***Procedure of Standing Trial***

The standing balance assessment was conducted on myelopathy group at four phase of surgery and age-matched control group on the recruitment day. 16 participants were asked to stand on a force platform (Kistler, Switzerland) for 30 seconds with sampling rate of 1000Hz in each standing trial. All participants stood in neutral stance (feet shoulder-width apart) with eyes-open (OE) and eyes-closed (CE) respectively (Figure 7). The other 37 participants were conducted the same standing balance assessment on different force platform (AMTI Newton, MA) with sampling rate of 1000Hz. Participants were allowed to rest if they felt tired or soreness on legs.

- ***Data Processing of Center of Pressure (COP)***

Force platform signals were analogue-to-digital converted at a sampling rate of 1000 Hz. LabVIEW (National Instruments Corp., Austin, TX) software was used to compute the COP based on ground reaction force and moment in AP and ML direction.

doi:10.6342/NTU201800337

Then the data was processed and filtered with second order at Butterworth low-pass filter of 5 Hz by Matlab R2010a software.

COP were further analyzed for time domain measures.[30] First, 95% confidence ellipse area was defined as area enclosed approximately 95% of the points on the COP path. Second, mean velocity was defined as length of the COP path per second. Third, range was defined as maximum distance between any two points on the COP path, which was calculated in AP and ML direction respectively. Lastly, RMS distance was defined as RMS distance from the mean COP, which was calculated in AP and ML direction respectively.

3.2.5 Statistical Analysis

Descriptive data of participants from myelopathy group and age-matched control group were presented as means with standard deviation. Statistical analysis was performed using PASW Statistics 18 for Macintosh (SPSS, Chicago, IL). The normality of the functional outcomes and COP variables were determined by Shapiro-Wilk test. The nonparametric tests were used for data analysis as the results of functional assessments and COP variables were not normally distributed. *P* value of less than 0.05 (alpha, α) was considered statistically significant.

Myelopathy group was assessed at the preoperative phase, as well as postoperative 3 months, 6 months and 1 year. The main effect of differences on four phases in functional outcomes (NDI, JOACMEQ-lower extremity function, and 10 second step test) and in COP variables were tested by Friedman test. If the main effect of phase difference was significant, the pairwise comparisons of the variables between two

doi:10.6342/NTU201800337

phases were examined by Wilcoxon signed-rank test with Bonferroni adjustment ($\alpha/6$). The difference in COP variables between the myelopathy group and age-matched control group was determined by Mann-Whitney U test at four phases, respectively.

To assess degree of change in the myelopathy group after surgery, the effect size (ES), standardized response mean (SRM), standard error of measurement (SEM), and minimal detectable difference on 95% confidence interval (MDD_{95}) were calculated for all COP variables. The following equations were used for calculation:[63]

a) $ES = \frac{\overline{X}_{post} - \overline{X}_{pre}}{\sigma_{pre}}$

(Equation 2)

where $\overline{X}_{post}$ is the mean of COP variables at postoperative 3 months, 6 months and 1 year respectively; $\overline{X}_{pre}$ is the mean of COP variables at preoperative phase; σ_{pre} is the standard deviation of COP variables data at preoperative phase.

b) $SRM = \frac{\overline{X}_{post} - \overline{X}_{pre}}{\sigma_d}$; $d = x_{post} - x_{pre}$ (Equation 3)

where $\overline{X}_{post}$ is the mean of COP variables at postoperative 3 months, 6 months and 1 year respectively; $\overline{X}_{pre}$ is the mean of COP variables at preoperative period; σ_d is the standard deviation of COP variables data change between postoperative period and preoperative phase; d is the change between preoperative period and postoperative 3 months, 6 months and 1 year respectively; x_{post} is COP variables at postoperative 3 months, 6 months and 1 year respectively; x_{pre} is COP variables at preoperative period.

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c) $SEM = \sigma_X \sqrt{1 - r_{xx}}$ (Equation 4)

where σ_X is the standard deviation of COP variables at postoperative 3 months, 6 months and 1 year respectively, r_{xx} is test-retest reliability coefficient form previous studies[64,65]

d) $MDD_{95} = 1.96 * SEM * \sqrt{2}$ (Equation 5)

To determine the cutoff score for minimally clinically importance difference (MCID), the receiver operating characteristic (ROC) curve analysis was used to analyze the change of COP variables between preoperative phase vs. postoperative 3 months, preoperative phase vs. 6 months, and preoperative phase vs. 1 year. External responsiveness reflected that the relationship between the change of COP variables against the change in a reference measurement, that is, JOACMEQ-lower extremity function, was determined by calculating the area under the ROC curve and its 95% confidence interval (CI).[12] The change of each question of JOACMEQ-lower extremity function scoring was set as anchor, as the question reflected the lower extremity function in upright position.

The data in each COP variables was dichotomized in "improved" group and "non-improved" group regarding to change of score occurring on five questions of JOACMEQ-lower extremity function between preoperative phase vs. postoperative 3 months, preoperative phase vs. postoperative 6 months, and preoperative phase vs. postoperative 1 year. If the score was improved at postoperative phase, the data would be classified as "improved" group. The other participants without change or with worsening score would

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be classified as “non-improved” group. The point on the ROC curve closest to the upper left corner representing the optimal trade-off between sensitivity and specificity for detecting clinical improvement was used to determined MCID.[66] (Figure 8)

The ROC analysis was repeated with dichotomization COP variables to “worsen” group and “non-worsen” group. If the score was worsened at postoperative phase, the data would be classified as “worsen” group. The other participants without change or with improving score would be classified as “non-worsen” group.

doi:10.6342/NTU201800337

Chapter 4 Study Results

4.1 Experiment 1

4.1.1 Demographic Data

Descriptive characteristics of the participants in myelopathy group, radiculopathy group and healthy age-matched control are summarized in Table 1. The results of functional assessments in myelopathy and radiculopathy group are listed in Table 1.

4.1.2 Association between Center of Pressure Variables and Results of Functional Assessment in Myelopathy Group

Table 2 shows the Spearman correlation between center of pressure (COP) variables and results of Neck Disability Index (NDI), Japanese Orthopaedic Association Myelopathy Evaluation Questionnaire (JOACMEQ)-lower extremity function (JOACMEQ-lower extremity function), foot taping test, 5-times-sit-to-stand test and 10 second step test for 63 participants in myelopathy group. The JOACMEQ-lower extremity function score displayed significant fair correlation with COP variables. The number of foot taping test displayed significant fair correlation with mean velocity and root mean square (RMS) distance-mediolateral (ML) in neutral stance with eyes-open (OE) and all COP variables in neutral stance with eyes-closed (CE).

The length of time for 5 times sit-to-stand displayed significant fair correlations with 95% confidence ellipse area, range-ML, and RMS distance-ML in OE condition. The length of time for 5 times sit-to-stand also displayed significant fair correlations with

doi:10.6342/NTU201800337

95% confidence ellipse area, range, and root mean square (RMS) distance of both anteroposterior (AP) and ML direction in CE condition. The number of steps in 10 second step test displayed significant fair correlations with 95% confidence ellipse area and mean velocity in OE condition. The number of steps in 10 second step test also displayed significant fair correlations with 95% confidence ellipse area, range-AP, and RMS distance-AP in CE condition.

Figure 9 shows the results of Kruskal-Wallis test for relationship between modified Japanese Orthopaedic Association scale- motor dysfunction of lower extremity (mJOA-MDLE) score and COP variables. The results of Kruskal-Wallis test for relationship between mJOA-MDLE and COP variables show less remarkable significant differences. In OE condition, significant differences were found between score of the mJOA-MDLE and all COP variables (95% confidence ellipse area: $p = 0.002$; mean velocity: $p = 0.025$; range-AP: $p = 0.022$; range in mediolateral (ML) direction: $p = 0.003$; RMS distance-AP: $p = 0.025$; RMS distance-ML: $p = 0.003$). In CE condition, significant differences were also found between score of mJOA-MDLE and most of COP variables expect RMS distance-AP (95% confidence ellipse area: $p = 0.001$; mean velocity: $p = 0.012$; range-AP: $p = 0.031$; range-ML: $p < 0.001$; RMS distance-ML: $p < 0.001$). In narrow stance with eyes-open (RSOE) condition, significant differences were found in range-AP ($p = 0.049$) and RMS distance-AP ($p = 0.024$). In narrow stance with eyes-closed (RSCE) condition significant difference was found in RMS distance-AP ($p = 0.046$).

Figure 10 shows the results of Kruskal-Wallis test for relationship between Nurick score and COP variables. The significant differences between COP variables with Nurick score 0 and 3 was most remarkable ($p < 0.05/6$). Higher Nurick score demonstrated

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increased upright postural instability in participants with myelopathy. Therefore, Nurick scale was selected to be reference for subgrouping the participants in myelopathy group. The two myelopathy subgroups were then used to compare the upright postural stability with radiculopathy group and age-matched control group.

4.1.3 Comparison COP Variables among Myelopathy Subgroup, Radiculopathy Group and Age-matched Control Group

The myelopathy group was classified to two subgroups: first subgroup with Nurick score ‘0 or 1’ (n = 33) and second subgroup with Nurick score ‘2 or 3’ (n = 30). Table 3 summarizes the results of Kruskal-Wallis test for COP variables among group with Nurick score ‘0 or 1’, radiculopathy group, and age-matched control group. Significant differences were found in 95% confidence ellipse area in RSCE condition, range-AP in RSCE condition as well as RMS distance-AP in OE condition, in RSOE condition and in RSCE condition. Table 4 shows the pairwise comparisons of COP variables between myelopathy group with Nurick score ‘0 or 1’ vs. radiculopathy group, myelopathy group with Nurick score ‘0 or 1’ vs. age-matched control group, and radiculopathy vs. age-matched control group. Significant difference was found in pairwise comparison between myelopathy group with Nurick score ‘0 or 1’ vs. age-matched control group in 95% confidence ellipse area, range-AP and, RMS distance-AP in RSCE condition.

Table 5 shows the results of Kruskal-Wallis test for COP variables among group with Nurick score ‘2 or 3’, radiculopathy group and age-matched control. Significant differences were identified in most COP variables among three groups of participants,

doi:10.6342/NTU201800337

except range-ML in OE condition. Table 6 shows the pairwise comparisons of COP variables between myelopathy group with Nurick score ‘2 or 3’ vs. radiculopathy group, myelopathy group with Nurick score ‘2 or 3’ vs. age-matched control group, and radiculopathy vs. age-matched control group. No significant difference was found in pairwise comparison between myelopathy group with Nurick score ‘2 or 3’ vs. radiculopathy group in all COP variables in OE condition, and in all pairwise comparison between radiculopathy vs. age-matched control group.

4.2 Experiment 2

4.2.1 Demographic Data

Descriptive characteristics and surgical information of the patients are summarized in Table 7. The most common surgical method for patients with myelopathy was anterior cervical discectomy and fusion (ACDF).

4.2.2 Functional Outcomes after Decompression Surgery

Figure 11 shows the Friedman test results for phase factor in functional outcomes (i.e., NDI, JOACMEQ-lower extremity function and 10 second step test). Significant difference was found between phases in NDI ($p = 0.036$) and JOACMEQ-lower extremity function ($p = 0.036$). The pairwise comparison between preoperative phase vs. postoperative 1 year displayed significant difference in NDI ($p = 0.007$). The pairwise comparison between postoperative 3 months vs. 1 year displayed significant difference in JOACMEQ-lower extremity function ($p = 0.002$).

doi:10.6342/NTU201800337

4.2.3 COP Variables after Decompression Surgery

Figure 12 shows the results of Friedman test results for phase factor in COP variables in OE condition. Significant differences were found between phases of decompression surgery in all COP variables (95% confidence ellipse area: $p = 0.022$; mean velocity: $p = 0.019$; range-AP: $p = 0.007$; range-ML: $p = 0.017$; RMS distance-AP: $p = 0.023$; RMS distance-ML: $p = 0.028$) in OE condition. The pairwise comparison identified significant differences between preoperative phase vs. postoperative 6 months in 95% confidence ellipse area ($p = 0.006$), mean velocity ($p = 0.008$) and RMS distance-AP ($p = 0.004$; Figure 12). The pairwise comparison identified significant differences between preoperative phase vs. postoperative 1 year in mean velocity ($p = 0.004$), range-AP ($p = 0.001$) and RMS distance-AP ($p = 0.004$; Figure 12). Figure 13 shows no significant was found between phases of decompression surgery in all COP variables in CE condition.

Figure 12 and Figure 13 shows the results of Mann-Whitney U test between age-matched control and myelopathy group from four phases of surgery in OE and CE conditions respectively. The 95% confidence ellipse area showed significant differences between age-matched control and myelopathy group during preoperative phase, postoperative 3 months and 1 year respectively ($p < 0.05$) in both OE and CE conditions (Figure 12 and 13). The mean velocity, range-AP and RMS distance-AP displayed significant differences between age-matched control and myelopathy group from four phases of surgery ($p < 0.05$) in in both OE and CE conditions (Figure 11 and 12).

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4.2.4 Responsiveness of COP variables

Internal responsiveness results of the all participants in myelopathy group (n =53) are summarized in Table 8. Generally, from postoperative 3 months to 1 year, the effect size (ES) and standardized response mean (SRM) showed an increasing trend. However, the standard error of measurement (SEM) and minimal detectable difference on 95% confidence interval (MDD_{95}) showed decreasing trend.

Receiver operating characteristic (ROC) curve analysis was used to determine the minimally clinically importance difference (MCID) for the COP variables. The MCID was not be determined when the area under the ROC curve of a given COP variable was below the threshold of considerable acceptance (i.e., 0.7).[67] With dichotomization to "improved" group vs. "non-improved" group, MCID for all COP variables was not able to be determined in both OE and CE conditions at all phases.

With dichotomization to "worsen" group vs. "non-worsen" group, MCID for all COP variables was also not able to be determined in OE condition at all phases. However, in CE condition, when the first question of JOACMEQ-lower extremity function was used as the anchor, MCID for 95% confidence ellipse area, range-AP, range-ML and RMS distance-ML were able to be determined in postoperative 3 months (Table 9). When the second to fifth questions of JOACMEQ-lower extremity function were used as the anchor, MCID was not able to be determined for COP variables in both OE and CE conditions at all phases. Therefore, Table 9 summarizes the result of ROC analysis of COP variables at postoperative 3 months under dichotomization to "worsen" group vs. "non-worsen" group when the first question of JOACMEQ-lower extremity function was used as the anchor. Since no other MCID of COP variables are significant to be displayed, only the ROC analysis shown in Table 9 is reported.

doi:10.6342/NTU201800337

Chapter 5 Discussion

5.1 Experiment 1

This study is proposed to investigate the association between the functional assessments result and upright postural control to determine the most applicable assessment tool for reflecting postural stability in clinical setting. The findings of the study indicate that Nurick scale is the most remarkable assessment tool to reflect upright postural control, as myelopathy patients with instable upright postural control demonstrated a high Nurick score. Meanwhile, the upright postural control of myelopathy patients with a high Nurick score was less stable than patients with radiculopathy or age-matched control.

Relationship between Functional Outcomes and Upright Postural Control

Continuous variables

This study demonstrates the significant fair correlation between functional assessment results (i.e. JOACMEQ-lower extremity function, foot taping test, five-times-sit-to-stand test and 10 second step test) and upright postural control, which are consistent with some previous studies.[68-72] For example, the Dizziness Handicap Inventory[71] scores showed significant association with results of posturography in patients with traumatic brain injuy.[71] In another study, both timed-up-and-go scores and Dizziness Handicap Inventory scores showed significant correlation with results of posturography in patients with peripheral vestibular hypofunction.[72] All participants of these studies demonstrated

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somatosensory impairment which can affect the regulation of postural stability. However, some other studies did not show correlation between functional outcomes and upright postural control. For example, the functional performances (i.e. functional reach,[68,73] timed 10-meter walk,[68] chair rise,[68] chair stand,[73] Duke Functional Mobility Skills[68] and six-minute walk[68]) did not exhibit association with postural sway area in community-dwelling elderly. The patients with myelopathy demonstrated impaired proprioception in distal lower extremities.[3,74] Thus, the association between functional assessment result and postural stability may appear in patients with neurological involvement.

In this study, NDI did not exhibit significant association to upright postural control. NDI contents are related to neck pain and also neck movement in various functional activities. The previous study revealed that only concentration score of NDI was related to postural sway in patients with chronic neck pain.[75] The NDI is more suitable to assess the level of neck pain severity affecting general daily living activities, such as self-care, reading, driving, work and recreation activities. Hence, NDI is not applicable to assess the postural stability or specific lower extremities function.

The JOACMEQ-lower extremity function displayed fair association with COP variables in this study. The functional activities evaluated in JOACMEQ-lower extremity function, including walking, standing with one foot and going up stairs.[50] The ability to stand upright is essential to perform functional activities.[18] The gait performance of patients with peripheral neuropathy in lower extremities also correlated with standing balance control like the present study.[76] However, functional activities in standing position also can be affected by other factor, such as leg strength.[77] Hence, the JOACMEQ-lower extremity function score did not display strong association with upright postural control.

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The number of foot taping and stepping within 10 seconds showed fair association with the upright postural control of patients with myelopathy in neutral stance. The ankle dorsiflexion and plantarflexion control is essential to maintain anteroposterior (AP) balance during normal standing[78] and also to perform fast repetitive foot taping movement.[58] The ankle joint was also suggested to provide the correcting action during single leg stance on ground.[79] The patients with spinal cord compression on corticospinal tract may have sensorimotor impairment in the lower extremities, which could affect foot motor control. Besides, the number of foot taping and stepping within 10 seconds was more related to postural stability with eyes-closed rather than eyes-open. Therefore, the upright standing with eyes-closed required more efficient somatosensory and motor control in the lower extremities,[80] which are reflected in foot tapping test and 10 second step test.

The five-times-sit-to-stand test displayed fair association with upright postural control of patients with myelopathy in neutral stance. The sit-to-stand movement is a particular transfer skill, which requires efficient muscle control of the lower extremities,[81] to shift the center of mass forward and upward to rise the body from sitting to upright position.[82,83] The compensation strategy adapt to musculoskeletal disorder may change the joint coordination of lower extremities during sit-to-stand. The previous study has reported that the range and velocity of the hip movement during sit-to-stand reduced in patients with low back pain because of compensatory responses to pain.[84] Patients with myelopathy may have impaired motor control and proprioception in the lower extremities. They may need greater contribution from the hip joint (more related in ML stability) to maintain postural steadiness. In addition, the sit-to-stand performance may also be

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affected by other factors, such as sensorimotor function, balance control, and psychological status[85], which may cause fair correlation with upright postural control.

Ordinal variables

The upright postural stability decreased when score of mJOA-MDLE increased. In this evaluation, the participants were scored regarding to their ability of walking without aids, walking up/down stairs or walking pattern based on their walking performance. The ability of upright postural control is critical for successful performance of daily activities, including ambulation and transferring activities.[86]

The upright postural stability decreased when Nurick score decreased. The participants were scored regarding to the sign of spinal cord dysfunction, walking ability during working, ability to walk without aids and ability to stand upright. Nurick scale is used to assess the ability of ambulation, full-time employment and doing housework. Previous studies demonstrated that the instable postural control was related to poor socioeconomic conditions.[87] Therefore, our findings showed the Nurick score is postulated to be related to upright postural control in all standing position.

The mJOA-MDLE and Nurick scale are considered to be used to classify the severity of patients in myelopathy. Using Nurick scale to classify postural stability of patients with myelopathy showed more distinguishable results when compared to using mJOA-MDLE, especially in eyes-closed condition. The patients with myelopathy may tend to have instable postural control without vision input due to sensorimotor impairment in lower extremities. Hence, Nurick scale was more appropriate to be used in classification in postural stability for patients with myelopathy.

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Group Comparisons in Upright Postural Control

The myelopathy group with Nurick score ‘0 or 1’ showed significant increased 95% confidence ellipse area, range-AP and, RMS distance-AP in narrow stance with eyes-closed compared to radiculopathy and age-matched control groups. The ML postural stability, which is related to hip control,[18] did not significantly deteriorate in the myelopathy group with Nurick score ‘0 or 1’ (mild myelopathy). The spinal cord compression might have cause more impairment to the muscle control of ankle dorsiflexor/plantarflexor than hip abductor/adductor.

The study finding implied that the mild myelopathy group may appear postural instability in narrow stance, but not in natural stance. During neutral stance, the postural control mostly relied on passive stiffness of the legs-pelvis complex with less active neural control,[18,88] i.e., lower extremity muscles were activated in larger magnitude during narrow stance compared with neutral stance.[88] The patients with myelopathy may have delayed muscle activation in tibialis anterior if the lateral corticospinal tract was compressed.[31] Hence, the postural control of patients with myelopathy become instable in AP direction due to inefficient motor control on the distal end of lower limbs during narrow stance.

The study results also indicated that patients in myelopathy group with Nurick score ‘2 or 3’ (severe myelopathy) showed instable upright postural control compared to radiculopathy and age-matched control group in both AP and ML direction. This finding may suggest that the compression on spinal cord of myelopathy group with Nurick score ‘2 or 3’ were more severe than with Nurick score ‘0 or 1’. Therefore, the muscle control

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of both ankle dorsiflexor/plantarflexor and hip abductor/adductor may be impaired in severe myelopathy group.

Besides, the postural instability of severe myelopathy group also decreased in the most of conditions except in neutral stance with eyes-open compared to other participants. This study finding may suggest that the proprioception of the severe myelopathy group may be impaired, as the postural stability decreased with diminished visual input and reduced base of support. The sensorimotor impairment secondary to cord compression, which included impaired proprioception in lower extremities, may weaken the passive stiffness of legs-pelvis complex[3,31] in standing. The transmission of nerve impulse in the corticospinal tract may be impaired or delayed, consequently affect the active ankle control.[89] The previous study reported that increased sway was correlated with delayed latency of 'antagonist reaction' between tibialis anterior and soleus.[31] Thus, the severe myelopathy group may have inefficient upright postural control.

Overall, the RMS distance-AP in narrow stance during eyes-closed (RSCE) was the best COP variables to identify the myelopathy patients. All the patients with myelopathy of this study had notably less stable postural control compared to other participants corresponding to 95% confidence ellipse area, range-AP and RMS distance-AP in RSCE condition. However, 95% confidence ellipse area can be affected by COP displacement to ML direction; RMS distance-AP may give misleading information if participants swayed forward-backward abruptly during standing. Besides, the RMS distance of COP is related to the effectiveness of, or the stability achieved by the postural control system.[30] The RMS distance-AP provide more holistic results with quadratic mean of COP displacement in AP direction for standing trial. Lastly, postural stability was not distinguishable statistically between radiculopathy group and age-matched

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control group. The cervical radiculopathy is associated to nerve root compression, which is more relevant to the signs and symptoms of the upper limb function.[90]

Clinical Relevance

This study denoted that the upright postural control may partially reflect clinical functional outcomes, or vice versa. The Nurick scale can be used as a screening tool for the assessment of postural stability and for the evaluation of the intervention effect in patients with myelopathy. The patients with high Nurick score are recommended to have standing balance assessment on force platform for further understanding of sensorimotor deficit. Besides, using force platform to evaluate postural stability may be an easy way in a clinical and rehabilitation setting[31] to distinguish severity of myelopathy. The RMS distance-AP was suggested to be the most representative COP variable for identifying patients with myelopathy.

Limitation and Future Studies

Our study has several limitations. First, the participants may have minor psychosocial problems which may not be detected in the short-time assessment periods. The participants might not honestly enlighten their real condition. This might affect the credibility of subjective assessment results. Second, this study was only limited to the participants whom were able to stand without support. The patients with walking aids who could not stand for one minute were excluded in this study. Therefore, the results

doi:10.6342/NTU201800337

were not generalized to all patients with myelopathy because more severe patients, such as patients with wheelchair, were not included.

This study illustrated the static balance of patients with myelopathy. Thus, the future studies should incorporate dynamic balance of patients with myelopathy, such as walking and postural perturbation. Besides, the advanced biomechanical studies for the static and dynamic balance should be conducted to identify the postural control mechanism for patients with myelopathy. For example, the change of angles between COP and center of mass, and comprehensive electromyography in lower extremity muscles should be further investigated.

5.2 Experiment 2

The first aim of this study was to investigate the changes of functional activities and upright postural control of patients with myelopathy after cervical decompression surgery. The finding suggested the improvement appeared in functional outcomes (NDI and JOACMEQ-lower extremity function) and in upright postural control with visual input. However, compared to healthy age-matched control, the upright postural control of myelopathy group was less stable both before and after surgery.

The second aim of this study was to determine the internal and external responsiveness characteristic of COP variables to decompression surgery. The postural control variables in AP direction were more responsive to reflect the important change after 1 year of surgery compared to ML direction. However, the minimally clinically importance difference (MCID) could not be determined for COP variables as the change of score in each question in JOACMEQ-lower extremity function as anchor by receiver

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operating characteristic (ROC) curve analysis. The exception was the 95% confidence ellipse area, range-AP, range-ML and RMS distance-ML in eyes-closed stance at postoperative 3 months with first question of JOACMEQ-lower extremity function as anchor when COP variables were dichotomized to "worsen" group and "non-worsen" group.

Functional Outcomes after Surgery

The subjective functional assessments for this study were NDI and JOACMEQ-lower extremity function. The NDI score, which is related to neck pain, improved at 1 year postoperatively and showed consistency with previous studies using numerical rating scale[33] and NDI.[39] The JOACMEQ-lower extremity function score did not improve immediately after surgery but demonstrated the improvement at 1 year postoperatively as previous studies using Nurick score.[36,39] However, the objective functional assessment, i.e. 10 second step test, did not show significant improvement after surgery. The movement in 10 second step test may relied on the loading and unloading of lower extremities in the ML plane by hip abductor/adductor.[91] In our study, the patients with myelopathy showed AP postural control impairment. Thus, the 10 second step test may not reflect the recovery in these patients.

Upright Postural Control Before and After Surgery

The upright postural control gradually improved in patients with myelopathy at 6 months and 1 year postoperatively. The slow healing of the injured neural tissues in spinal

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cord may cause the delayed improvement of upright postural control at the early stage of postoperative phase. Previous animal study about spinal cord injury reported that sprouting of corticospinal tract fibers occurred between 3 weeks and 3 months after injury, with penetration of the axons of this tract into the lesion matrix occurring over a long period of time.[92] Besides, patients were usually asked to wear neck collar, which limited the neck movement for the first three months after surgery. The patients may also become inactive postoperatively due to postoperative fear of movement at early 3 months.[93] Thus, the improvement of postural steadiness started after termination of the immobilization phase. Postoperative motor re-learning and balance training should be initiated before 6 months to accelerate the recovery in postural control. Patients with shorter time between symptom onset and rehabilitation are expected to achieve better improvement in functional outcomes.[94]

The upright postural control gradually was improved in patients with myelopathy in eyes-open condition but not in eyes-closed condition. The sensorimotor impairment should be considered, as the ascending (sensory) and descending (motor) fibers in spinal cord may be injured or damaged after chronic compression.[31] Patients with myelopathy may be more mobile and active in daily functional with upright position in eyes-open condition. To maintain postural stability, various sensory input may be reweighted by the CNS.[95,96] In this study, the visual input may outweigh the proprioceptive input of lower extremities to regulate postural control in patients with myelopathy during eyes-open stance.[3,74] The delayed recovery of proprioception may increase postural sway of patients with myelopathy during eyes-closed stance.[68] Impaired proprioception could trigger inefficient sensory integration for upright postural control. Proprioception impairment may decrease sensory information about external environment and internal state of the

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muscle of lower limbs.[17] Therefore, the recovery of eyes-closed postural stability of the patients were delayed postoperatively.

Either before or after decompression surgery, the postural steadiness of patients with myelopathy (particularly in AP direction) were less stable than healthy age-matched control in both eyes-open and eyes-closed stance. Several assumptions were suggested to explain the poor upright postural control in patient in myelopathy:

1. Incomplete recovery of sensorimotor deficit

Firstly, the sensorimotor deficit may not fully recover after 1 year of surgery. Patients with chronic compressive spinal cord which could trigger pathological change in spinal cord, particularly in gray matter of corticospinal tract.[22] The tissue displacement secondary to compression on spinal cord may cause changes of viscoelastic properties[25] and internal stress.[97] A long period of spinal cord compression may further induce delayed nerve conduction and more extensive tissue damage, then would impair functional recovery.[25]

Decompression surgery was indicated to expanse the transverse area of the cervical canal for reversible cord injury. The expansion in the spinal canal may facilitate morphological plasticity of the injured nerve tissues.[97] However, various pathological processes may eventually reduce the viscoelasticity of the cervical spinal cord, thus reflecting the delay and small degree of gradual expansion of spinal cord.[97] The remodeling duration for spinal cord injury could last for months to years and become difficult to be predicted.[98] The delayed recovery of injured cord tissues may impair ankle dorsiflexor and plantarflexor control in upright standing, which are responsible to AP balance control.[78,99]

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2. Irreversible damage of the spinal cord

Secondly, some patients with myelopathy may sustained irreversible damage on part of spinal cord,[100] particularly on corticospinal tract. The severe compression on spinal cord may lead to permanent destruction on cord nerve tissues. The decompression surgical outcomes was indicated to be affected by the severity of histological change secondary to spinal cord compression.[100,101] The histological changes, such as gliosis,[100] demyelination,[100] or microcavities,[100] necrosis,[101,102] myelomalacia[101,102] or spongiform change[101,102] of neuronal cells may be caused by severe spinal compression or repetitive microtrauma in spinal cord.[103]

The irreversible pathological change in spinal cord would lead to permanent impairment in proprioception of lower limbs and in control of distal muscles (such as tibialis anterior). Thus, the patients' recovery may not in further progress at 1 year postoperatively. The sensory integration may be improved after decompression surgery but later the recovery was halted by the permanent damage on some of neuronal cells.

3. Cortical reorganization and sensorimotor network plasticity

Thirdly, the cortical reorganization and sensorimotor network plasticity before and after surgery may retard the recovery of upright postural control to level of healthy age-matched control, particularly in eyes-closed condition. Previous study of brain functional MRI suggested that the intrinsic functional plasticity in the sensorimotor network of patients with myelopathy become responsive to the insufficient sensory and motor experience[104] due to prolong motor conduction impairment. This phenomenon may be adaptive mechanism followed by the loss of afferent sensory conditions, which attributed to the inefficient funneling of neural processing under decreased sensory

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impulse conduction.[104]

The improvement of postural control may denote that the cortical reorganization was triggered[105,106] since the decompression surgery terminate the chronic or repetitive injury mechanism in corticospinal tract on spinal cord. Surgical decompression may induce cortical reorganization by allowing recovery of conduction in injured and reversible damaged axons.[105] This may result in growing cortical activation (recruitment) or reduced extent of cortical activation (focusing), depending on the availability of cortical neuron pools and the ability of existing corticospinal projections to activate spinal motor pools.[105] The plasticity of sensorimotor network in brain may facilitate postoperative recovery of postural control in participants with myelopathy.

However, the patients with decompression surgery may have fear of falling or perceived lack of stability as they were adapted to previous compensatory strategy as 'safer way' to move.[42] The patients with lumbar spinal fusion in previous studies may reduce distance to reach forward due to fear avoidance.[107,108] This may cause them stand in a compensatory pattern, even when sensorimotor spinal pathway was recovering. Previous studies implied that recovery of ankle dorsiflexion[105] were associated with change toward normal control in cerebral activation pattern. Consequently, the cortical reorganization of the patients toward normal may be delayed due to lack of task-specific practice.[105,109]

4. Adaptive or compensatory mechanism in motor function

Lastly, the adaptive or compensatory mechanism are not only occurring in brain, but also in musculoskeletal system. In patients with cervical myelopathy, the sensorimotor dysfunction is predominantly related to the local injury of the ascending or

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descending tract fiber[104,110] in spinal cord. The pathological change in spinal tract may trigger altered movement strategy in lower extremities to compensate the sensorimotor dysfunction.[111] For instance, to maintain postural stability, the delayed antagonist reaction of tibialis anterior[31] may trigger correcting responses of trunk and proximal joint.[112] The habitual compensatory pattern may persist after surgery if the patients have not learned the correct movement pattern.

Besides, the impairment on ascending and descending pathway in CNS may induce compensation or adaptation secondary to fatigability after repetitive functional actitivities.[113] The fatigability with incomplete spinal cord lesion may associated with muscle properties alteration and poor control, such as-muscle weakness, muscle atrophy and delayed activation[113] in distal end of lower extremities. The patients with myelopathy may have abnormal muscle co-activation and torque coupling[113,114] of ankle dorsiflexior and plantarflexor under compensated central and peripheral pathways of motor control during task in upright posture, such as walking.[113] The compensatory pattern may need time and practice to reverse back to normal pattern although the injured cord tissue recovered.

Responsiveness of COP variables

In this study, the internal and external responsiveness of COP variables were attempted to be determined. No previous study had been done to reveal the responsiveness COP variables in patients with cervical myelopathy to detect the effect of cervical decompression surgery. The COP variables of this group of patients did not reflect obvious change corresponding to the meaningful change determined by distribution

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method. The effect size (ES) and standardized response mean (SRM) of COP variables ranged from -0.49 to 0.09 for all postoperative phases with preoperative as baseline.

The ES and SRM of the COP variables overall displayed increasing trend from 3 months to 1 year postoperatively. COP is one of the neural controlled variable,[78] which may suitable to evaluate participants with myelopathy in sensorimotor impairment. The remodeling of injured nerve tissues may need longer time compared to other soft tissue injury.[98] This may suggest that COP variables would be more responsive in long-term evaluation for surgical effect on the neurological impaired patients.

The range and RMS distance in AP direction demonstrated the highest ES and SRM at 1 year postoperatively. These results also could be caused by the pathophysiology of cervical myelopathy. The patients with myelopathy commonly sustained the compression injury on corticospinal tract.[115] The corticospinal tract is motor pathway for movement of the distal end of lower extremities, which is associated to ankle control for postural stability in AP direction.[78] Therefore, the postural sway of AP direction would be more obviously change also compared to ML direction.

We had attempted to determine minimally clinically importance difference (MCID) of COP variables by ROC curve as the change of JAOCMEQ-lower extremities function was set as anchor. MCID of 95% confidence ellipse area, range-AP, range-ML and RMS distance in ML direction during eyes-closed stance were able to be determined as change of first question of the JOACMEQ-lower extremity function as anchor,[50] which was associated to ambulation on flat surface at only 3 month postoperatively. However, most of MCID for COP variables could not be determined at 3 month, 6 month and 1 year postoperatively if other questions were set as anchor. The results reflected that the

doi:10.6342/NTU201800337

question of JOACMEQ-lower extremity function may not suitable as anchors for determining MCID of COP variables. The multiple selection for answer in the questions of JOACMEQ may display high variability to reflect improvement or worsening in upright postural control.

Although human walking is essential to move body forward, but patients' perception only allows MCIDs related to side-by-side trunk control to be determined. ROC analysis need external outcome criterion,[116] which is based on what the patients figure out. Regarding to Figure 12, the participants with myelopathy have less stable postural control in AP direction than in ML direction, either preoperatively or after postoperatively. The patients may more depend on postural control in ML, which was controlled by more proximal segment[112] from ankle to compensate the AP control dysfunction. They may be more sensitive to the change of ML postural control as this can affect their postural stability.

Clinical Relevance

This study revealed the progression of functional outcomes and upright postural control until postoperative 1 year. The finding of this study provides biomechanical evidence of postural control after decompression surgery. Besides, the incomplete recovery of upright postural control indicates a theoretical evidence that postoperative rehabilitation should be launched at 3 months. The motor re-learning program and customized balance training should be introduced in the postoperative rehabilitation as soon as possible. The standing balance assessment should be conducted for long-term follow-up, as the postural control would indicate recovery of sensorimotor function.

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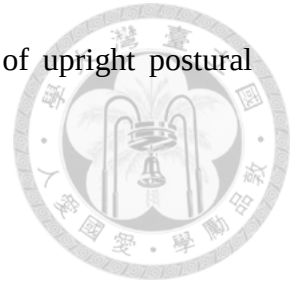
Therefore, COP variables can be used for objective examination of upright postural control for patients with myelopathy in clinical setting.



Limitation and Future Studies

Our study has several limitations. First, the lifestyles and the exercise habits of our participants were not fully under control after decompression surgery. The participants may live in remote area from our hospital and only seek for consultation and attend to our follow-up assessment regarding given appointment time. This may cause high variability of patients in postoperative recovery. Second, the participants with minor psychosocial problems may not provide real information during assessments with questionnaires. Third, our control group was not followed-up till 1 year. Thus, the aging effect of control group within one year could not excluded in this study.

The current study only investigated the static balance in neutral stance. The future study should include challenging balance position, such as narrow stance and tandem stance, to obviously reveal the proprioception recovery. Besides, the future studies should incorporate dynamic balance of patients with myelopathy, such as walking and postural perturbation. Furthermore, the advanced biomechanical studies for the static and dynamic balance should be conducted to identify the postural control mechanism for patients with myelopathy postoperatively. For instance, the angle between COP and center of mass, kinetic and kinematic analysis, as well as comprehensive electromyography on head, trunk and lower extremities, may provide further information about change of mechanism of postural control after surgery.

doi:10.6342/NTU201800337

Chapter 6 Conclusion

In conclusion, the functional assessments, including JOACMEQ-lower extremity function, foot taping test, 5-times-sit-to-stand test and 10 second step test, were fairly correlated with upright postural control, typically in AP direction. This may be results from the corticospinal tract dysfunction, which may impair ankle control in upright postural stability. Compared to modified Japanese Orthopaedic Association (JOA) scale-motor dysfunction of lower extremities, the Nurick scale was suggested to be more suitable to classify the severity of postural instability in patients with myelopathy. The upright postural control of myelopathy group with higher Nurick score was less stable than non-myelopathy group. In general, the COP variables can differentiate between the patients with myelopathy and age-matched control in eyes-closed narrow stance. The RMS distance-AP was suggested to be most representative COP variable for identifying patients with myelopathy.

In addition, the functional outcomes overall were improved after the cervical decompression surgery. The postoperative improvement of upright postural control was only during eyes-open stance. The upright postural control in patients with myelopathy were less stable than healthy age-matched control. These results may be caused by incomplete recovery of cervical spinal cord injury, permanent damage on spinal cord cell, on-going cortical reorganization and musculoskeletal adaptation change of patients with decompression surgery. The biomechanical parameter such as COP can reflect the long-term change of upright balance control after decompression surgery. The distribution-based responsiveness characteristic demonstrated highest responsiveness at 1 year postoperatively. At the same time, the external responsiveness of COP variables was

doi:10.6342/NTU201800337

difficult to be determined with either improved or worsen JOACMEQ-lower extremity function as anchor.

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Table 1 Descriptive characteristic and functional outcomes of the participants.

	Myelopathy Group	Radiculopathy Group	Age-matched Control Group	*p* value
Subject Number (male: female)	63 (45:18)	24 (12:12)	19 (4:19)	-
Age (years)	58.34 ± 9.16	59.08 ± 7.62	58.16 ± 8.06	0.924
Height (m)	1.64 ± 0.08	1.62 ± 0.07	1.61 ± 0.07	0.170
Weight (kg)	68.89 ± 11.42	63.97 ± 8.99	63.05 ± 10.66	0.064
BMI (kg/m^2)	25.49 ± 3.31	24.26 ± 2.76	24.34 ± 3.71	0.234
Functional Outcomes				
NDI (%)	19.92 ± 19.27	25.68 ± 19.88	NA	0.210
JOACMEQ-lower extremity function	83.40 ± 21.44	90.91 ± 13.67	NA	0.247
mJOA-MDLE	5.87 ± 1.11	6.83 ± 0.48	NA	<0.001*
Nurick Scale	1.44 ± 0.86	0.17 ± 0.48	NA	<0.001*
Foot Taping (repetition/10 secs)	24.59 ± 6.14	25.36 ± 5.28	NA	0.890
5-times-sit-to-stand Test (secs)	9.85 ± 3.37	8.91 ± 1.48	NA	0.144
10 Seconds Step Test (steps/10 secs)	6.16 ± 1.70	6.80 ± 0.99	NA	0.115

***Statistical significance between groups ($p < 0.05$).**
BMI: body mass index; NDI: Neck Disability Index; JOACMEQ: Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire; mJOA-MDLE: modified Japanese Orthopaedic Association scale-motor dysfunction of lower extremity; NA: not available

doi:10.6342/NTU201800337

Table 2 Correlation between COP variables and functional assessments in myelopathy group (n = 63).

Variables	Standing Condition	NDI		JOACMEQ-Lower extremity function		Foot Taping Test		5-times-sit-to-stand Test		10 Second Step Test	
		r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
95% Confidence Ellipse Area ($mm^{2)}$	OE	0.188	0.140	**-0.344**†	0.006	-0.218	0.086	**0.310***	0.013	**-0.248***	0.050
	CE	0.147	0.251	**-0.496**†	<0.001	**-0.287***	0.023	**0.307***	0.014	**-0.267***	0.034
	RSOE	0.144	0.260	**-0.385**†	0.002	-0.111	0.386	0.169	0.187	-0.239	0.059
	RSCE	0.188	0.140	**-0.421**†	0.001	-0.167	0.190	**0.265***	0.036	-0.145	0.256
Mean Velocity (mm/s)	OE	0.001	0.992	**-0.275***	0.029	**-0.255***	0.044	0.181	0.155	**-0.271***	0.031
	CE	0.071	0.578	**-0.409**†	0.001	**-0.264***	0.037	0.233	0.066	-0.227	0.073
	RSOE	-0.032	0.801	**-0.300***	0.017	-0.170	0.183	0.025	0.847	-0.177	0.165
	RSCE	0.031	0.811	**-0.385**†	0.002	-0.172	0.178	0.163	0.202	-0.167	0.192
Range-AP (mm)	OE	0.237	0.062	**-0.392**†	0.002	-0.096	0.455	0.195	0.126	-0.219	0.085
	CE	0.137	0.283	**-0.517**†	<0.001	**-0.271***	0.032	**0.308***	0.014	**-0.338**†	0.007
	RSOE	0.104	0.419	**-0.252***	0.046	-0.013	0.918	0.148	0.248	-0.193	0.129
	RSCE	0.158	0.215	**-0.442**†	0.000	-0.175	0.170	0.242	0.056	-0.177	0.166
Range-ML (mm)	OE	0.121	0.344	**-0.305***	0.015	-0.240	0.058	**0.298***	0.018	-0.245	0.053
	CE	0.089	0.489	**-0.477**†	<0.001	**-0.276***	0.029	**0.255***	0.044	-0.229	0.072
	RSOE	0.112	0.384	**-0.376**†	0.002	-0.159	0.215	0.142	0.266	-0.242	0.056
	RSCE	0.115	0.371	**-0.364**†	0.003	-0.117	0.360	0.156	0.223	-0.055	0.669
RMS distance-AP (mm)	OE	0.245	0.053	**-0.292***	0.020	-0.121	0.346	0.206	0.106	-0.204	0.110
	CE	0.208	0.102	**-0.487**†	<0.001	**-0.276***	0.029	**0.301***	0.017	**-0.292***	0.020
	RSOE	0.157	0.219	**-0.282***	0.025	0.033	0.799	0.099	0.438	-0.160	0.210
	RSCE	0.188	0.141	**-0.427**†	0.000	-0.163	0.202	0.247	0.051	-0.155	0.226
RMS distance-ML (mm)	OE	0.088	0.492	**-0.296***	0.018	**-0.251***	0.048	**0.304***	0.016	-0.223	0.079
	CE	0.105	0.412	**-0.465**†	<0.001	**-0.263***	0.038	**0.290***	0.021	-0.228	0.073
	RSOE	0.096	0.454	**-0.399**†	0.001	-0.206	0.105	0.211	0.097	**-0.288***	0.022
	RSCE	0.128	0.317	**-0.373**†	0.003	-0.132	0.304	0.213	0.093	-0.124	0.335

*** Statistical significance for 2-tailed correlation ($p < 0.05$).**

† Statistical significance for 2-tailed correlation ($p < 0.01$).

NDI: Neck Disability Index; JOACMEQ: Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire; OE: eyes-open in neutral stance; CE: eyes-closed in neutral stance; RSOE: eyes-open in narrow stance; RSCE: eyes-closed in narrow stance; AP: anteroposterior; ML: mediolateral; RMS: root mean square

doi:10.6342/NTU201800337

Table 3 Comparison COP variables among myelopathy with Nurick score '0 or 1', radiculopathy group and age-matched control group.

Variable	Standing Condition	Myelopathy (n = 33) Mean	(SD)	Radiculopathy (n = 24) Mean	(SD)	Age-matched Control (n = 19) Mean	(SD)	χ^2 value	*p* value
95% Confidence Ellipse Area (mm^2)	OE	108.16	(106.45)	147.66	(116.64)	88.42	(83.41)	3.633	0.163
	CE	157.24	(160.62)	144.97	(155.41)	119.35	(108.43)	1.009	0.604
	RSOE	332.66	(196.11)	287.09	(196.74)	239.47	(143.38)	4.202	0.122
	RSCE	963.19	(599.24)	660.46	(393.70)	551.10	(248.57)	6.603	**0.037***
Mean Velocity (mm/s)	OE	6.40	(2.29)	6.51	(1.80)	6.12	(1.66)	0.760	0.684
	CE	11.79	(6.31)	9.45	(3.18)	8.61	(2.49)	2.046	0.360
	RSOE	13.01	(4.18)	10.63	(3.02)	10.89	(2.93)	5.454	0.065
	RSCE	25.47	(10.43)	21.21	(6.79)	19.11	(4.70)	4.548	0.103
Range-AP (mm)	OE	17.41	(4.90)	18.39	(6.08)	15.24	(4.97)	3.158	0.206
	CE	26.22	(12.51)	20.99	(6.77)	19.81	(6.89)	3.568	0.168
	RSOE	20.42	(7.82)	19.79	(9.20)	15.85	(4.60)	5.364	0.068
	RSCE	34.73	(13.24)	28.67	(10.46)	25.82	(6.97)	7.996	**0.018***
Range-ML (mm)	OE	8.32	(7.64)	10.57	(7.36)	8.46	(4.62)	1.477	0.478
	CE	7.99	(4.08)	8.79	(5.49)	8.06	(4.34)	0.215	0.898
	RSOE	22.38	(7.33)	19.75	(6.29)	20.64	(7.48)	2.571	0.276
	RSCE	36.67	(11.57)	33.42	(12.08)	31.02	(10.49)	2.827	0.243
RMS distance-AP (mm)	OE	3.56	(0.93)	3.76	(1.12)	2.96	(1.10)	6.146	**0.046***
	CE	5.15	(2.54)	4.08	(1.28)	3.86	(1.25)	3.879	0.144
	RSOE	4.06	(1.77)	3.65	(1.35)	3.15	(1.09)	6.246	**0.044***
	RSCE	6.76	(2.60)	5.26	(1.63)	5.08	(1.54)	8.233	**0.016***
RMS distance-ML (mm)	OE	1.74	(1.69)	2.04	(1.31)	1.59	(0.91)	1.255	0.534
	CE	1.50	(0.76)	1.72	(1.14)	1.57	(1.07)	0.484	0.785
	RSOE	4.30	(1.52)	3.99	(1.24)	1.50	(1.50)	0.914	0.633
	RSCE	7.07	(2.42)	6.28	(2.04)	5.79	(1.76)	3.641	0.162

***Statistical significance ($p < 0.05$) between groups.**
†Statistical significance ($p < 0.01$) between groups.
SD: standard deviation; OE: eyes-open in neutral stance; CE: eyes-closed in neutral stance; RSOE: eyes-open in narrow stance; RSCE: eyes-closed in narrow stance; AP: anteroposterior; ML: mediolateral; RMS: root mean square

doi:10.6342/NTU201800337

Table 4 The pairwise comparisons of COP variables between two groups among myelopathy group with Nurick score '0 or 1', radiculopathy group and age-matched control.

		Myelopathy vs. Radiculopathy			Myelopathy vs. Control			Radiculopathy vs. Control		
Variable	Standing Condition	Effect size	U value	*p* value	Effect size	U value	*p* value	Effect size	U value	*p* value
95% Confidence Ellipse Area (mm^2)	OE	-3.75	315.00	0.190	2.00	265.00	0.357	5.86	156.00	0.078
	CE	0.98	369.00	0.663	3.20	261.00	0.318	2.21	205.00	0.574
	RSOE	3.25	312.00	0.175	7.03	213.00	0.056	3.62	198.00	0.463
	RSCE	13.43	289.00	0.084	19.11	185.00	**0.015***	6.02	201.00	0.509
Mean Velocity (mm/s)	OE	-0.08	356.00	0.518	0.19	305.00	0.872	0.29	190.00	0.353
	CE	1.05	353.00	0.487	1.44	237.00	0.146	0.49	202.00	0.525
	RSOE	1.24	271.00	0.043	1.10	217.00	0.067	-0.15	211.00	0.678
	RSCE	1.44	323.00	0.238	2.22	208.00	0.045	0.87	181.00	0.250
Range-AP (mm)	OE	-0.42	366.00	0.628	0.98	241.00	0.168	1.33	158.00	0.087
	CE	1.66	309.00	0.160	1.99	224.00	0.089	0.45	212.00	0.696
	RSOE	0.22	333.00	0.309	1.78	191.00	0.020	1.47	178.00	0.221
	RSCE	1.75	279.00	0.059	2.70	172.00	**0.007***	0.95	197.00	0.448
Range-ML (mm)	OE	-0.82	327.00	0.265	-0.05	270.00	0.408	0.85	213.00	0.714
	CE	-0.37	372.00	0.698	-0.04	310.00	0.947	0.33	211.00	0.678
	RSOE	1.00	306.00	0.146	0.64	254.00	0.258	-0.34	210.00	0.660
	RSCE	0.95	343.00	0.392	1.69	225.00	0.093	0.71	197.00	0.448
RMS distance-AP (mm)	OE	-0.20	365.00	0.616	0.60	206.00	0.041	0.76	133.00	0.020
	CE	0.76	302.00	0.129	0.90	223.00	0.085	0.20	210.00	0.660
	RSOE	0.33	309.00	0.160	0.75	189.00	0.018	0.45	176.00	0.203
	RSCE	1.02	255.00	0.023	1.13	182.00	**0.012***	0.14	219.00	0.826
RMS distance-ML (mm)	OE	-0.25	328.00	0.272	0.13	303.00	0.842	0.43	196.00	0.434
	CE	-0.22	367.00	0.639	-0.08	305.00	0.872	0.13	198.00	0.463
	RSOE	0.26	350.00	0.457	0.29	269.00	0.398	0.03	224.00	0.922
	RSCE	0.53	320.00	0.219	0.87	219.00	0.073	0.36	199.00	0.478

***Statistical significance ($p < 0.05/3$ after Bonferroni's adjustment)**
SD: standard deviation; OE: eyes-open in neutral stance; CE: eyes-closed in neutral stance; RSOE: eyes-open in narrow stance; RSCE: eyes-closed in narrow stance; AP: anteroposterior; ML: mediolateral; RMS: root mean square

doi:10.6342/NTU201800337

Table 5 Comparison COP variables among myelopathy group with Nurick score '2 or 3', radiculopathy group and age-matched control group.

Variable	Standing Condition	Myelopathy (n = 30) Mean	(SD)	Radiculopathy (n = 24) Mean	(SD)	Age-matched Control (n = 19) Mean	(SD)	χ^2 value	*p* value
95% Confidence Ellipse Area (mm^2)	OE	294.92	(326.73)	147.66	(116.64)	88.42	(83.41)	8.349	**0.015***
	CE	466.87	(369.99)	144.97	(155.41)	119.35	(108.43)	20.917	**<0.001†**
	RSOE	510.19	(330.45)	287.09	(196.74)	239.47	(143.38)	16.288	**<0.001†**
	RSCE	1578.54	(1220.06)	660.46	(393.70)	551.10	(248.57)	18.764	**<0.001†**
Mean Velocity (mm/s)	OE	9.28	(5.04)	6.51	(1.80)	6.12	(1.66)	6.720	**0.035***
	CE	18.22	(10.70)	9.45	(3.18)	8.61	(2.49)	27.686	**<0.001†**
	RSOE	14.89	(5.29)	10.63	(3.02)	10.89	(2.93)	13.173	**0.001***
	RSCE	31.60	(12.480	21.21	(6.79)	19.11	(4.70)	20.311	**<0.001†**
Range-AP (mm)	OE	24.89	(15.00)	18.39	(6.08)	15.24	(4.97)	6.327	**0.042***
	CE	39.35	(17.87)	20.99	(6.77)	19.81	(6.89)	26.255	**<0.001†**
	RSOE	25.35	(9.76)	19.79	(9.20)	15.85	(4.60)	16.072	**<0.001†**
	RSCE	45.05	(19.20)	28.67	(10.46)	25.82	(6.97)	18.187	**<0.001†**
Range-ML (mm)	OE	15.59	(11.99)	10.57	(7.36)	8.46	(4.62)	4.835	0.089
	CE	17.65	(9.53)	8.79	(5.49)	8.06	(4.34)	19.116	**<0.001†**
	RSOE	28.18	(7.87)	19.75	(6.29)	20.64	(7.48)	17.183	**<0.001†**
	RSCE	49.66	(21.17)	33.42	(12.08)	31.02	(10.49)	12.683	**0.002†**
RMS distance-AP (mm)	OE	4.78	(2.34)	3.76	(1.12)	2.96	(1.10)	9.677	**0.008†**
	CE	7.41	(3.30)	4.08	(1.28)	3.86	(1.25)	24.169	**<0.001†**
	RSOE	4.95	(1.96)	3.65	(1.35)	3.15	(1.09)	15.122	**0.001†**
	RSCE	8.50	(3.41)	5.26	(1.63)	5.08	(1.54)	21.065	**<0.001†**
RMS distance-ML (mm)	OE	3.05	(2.28)	2.04	(1.31)	1.59	(0.91)	6.333	**0.042***
	CE	3.15	(1.60)	1.72	(1.14)	1.57	(1.07)	17.998	**<0.001†**
	RSOE	5.29	(1.67)	3.99	(1.24)	3.96	(1.21)	12.555	**0.002†**
	RSCE	9.03	(3.98)	6.28	(2.04)	5.79	(1.76)	11.979	**0.003†**

***Statistical significance ($p < 0.05$) between groups.**
†Statistical significance ($p < 0.01$) between groups.
SD: standard deviation; OE: eyes-open in neutral stance; CE: eyes-closed in neutral stance; RSOE: eyes-open in narrow stance; RSCE: eyes-closed in narrow stance; AP: anteroposterior; ML: mediolateral; RMS: root mean square

doi:10.6342/NTU201800337

Table 6 The pairwise comparisons of COP variables between two groups among myelopathy group with Nurick score '2 or 3', radiculopathy group and age-matched control.

		Myelopathy vs. Radiculopathy			Myelopathy vs. Control			Radiculopathy vs. Control		
Variable	Standing Condition	Effect size	U value	*p* value	Effect size	U value	*p* value	Effect size	U value	*p* value
95% Confidence Ellipse Area (mm^2)	OE	9.63	271.00	0.121	13.51	155.00	**0.008***	5.86	156.00	0.078
	CE	19.41	141.00	**<0.001***	21.16	98.00	**<0.001***	2.21	205.00	0.574
	RSOE	13.54	178.00	**0.002***	16.83	112.00	**<0.001***	3.62	198.00	0.463
	RSCE	31.41	170.00	**0.001***	35.28	94.00	**<0.001***	6.02	201.00	0.509
Mean Velocity (mm/s)	OE	1.46	260.00	0.082	1.63	167.00	**0.015***	0.29	190.00	0.353
	CE	3.23	111.00	**<0.001***	3.50	68.00	**<0.001***	0.49	202.00	0.525
	RSOE	2.06	180.00	**0.002***	1.91	142.00	**0.003***	-0.15	211.00	0.678
	RSCE	3.29	167.00	**0.001***	4.05	87.00	**<0.001***	0.87	181.00	0.250
Range-AP (mm)	OE	1.95	298.00	0.280	2.89	170.00	0.018	1.33	158.00	0.087
	CE	5.10	113.00	**<0.001***	5.29	76.00	**<0.001***	0.45	212.00	0.696
	RSOE	1.80	203.00	**0.006***	3.40	101.00	**<0.001***	1.47	178.00	0.221
	RSCE	4.18	169.00	**0.001***	5.05	101.00	**<0.001***	0.95	197.00	0.448
Range-ML (mm)	OE	1.59	259.00	0.079	2.35	192.00	0.056	0.85	213.00	0.714
	CE	3.18	147.00	**<0.001***	3.49	109.00	**<0.001***	0.33	211.00	0.678
	RSOE	3.14	145.00	**<0.001***	2.71	132.00	**0.002***	-0.34	210.00	0.660
	RSCE	3.92	201.00	**0.006***	4.51	132.00	**0.002***	0.71	197.00	0.448
RMS distance-AP (mm)	OE	0.76	294.00	0.251	1.33	145.00	**0.004***	0.76	133.00	0.020
	CE	2.15	126.00	**<0.001***	2.24	82.00	**<0.001***	0.20	210.00	0.660
	RSOE	1.00	194.00	**0.004***	1.42	117.00	**0.001***	0.45	176.00	0.203
	RSCE	2.00	136.00	**<0.001***	2.08	100.00	**<0.001***	0.14	219.00	0.826
RMS distance-ML (mm)	OE	0.74	261.00	0.085	1.11	170.00	0.018	0.43	196.00	0.434
	CE	1.21	153.00	**<0.001***	1.33	116.00	**0.001***	0.13	198.00	0.463
	RSOE	1.07	183.00	**0.002***	1.09	146.00	**0.004***	0.03	224.00	0.922
	RSCE	1.55	212.00	**0.010***	1.83	131.00	**0.002***	0.36	199.00	0.478

***Statistical significance ($\alpha < 0.05/3$ after Bonferroni's adjustment)**
SD: standard deviation; OE: eyes-open in neutral stance; CE: eyes-closed in neutral stance; RSOE: eyes-open in narrow stance; RSCE: eyes-closed in narrow stance; AP: anteroposterior; ML: mediolateral; RMS: root mean square

doi:10.6342/NTU201800337

Table 7 Descriptive characteristic of myelopathy group with surgery and healthy age-matched control group.

	Myelopathy Group	Age-matched Control Group	*p* value
Subject Number (Male: Female)	53 (40:13)	22 (6:16)	-
Age (years)	55.50 ± 9.63	56.41 ± 9.66	0.861
Height (m)	1.65 ± 0.08	1.62 ± 0.07	0.087
Weight (kg)	68.73 ± 11.28	63.32 ± 9.90	0.054
BMI (kg/m^2)	25.19 ± 3.33	24.24 ± 3.32	0.268
Surgical Method			
ACDF	24	NA	
Laminoplasty	15	NA	
Arthroplasty	1	NA	
ACDF + Arthroplasty	12	NA	
Other	1	NA	

BMI: body mass index; ACDF: anterior cervical discectomy and fusion; NA: not available

doi:10.6342/NTU201800337

Table 8 Responsiveness of COP variables determined by distribution method.

Variables	Standing Condition	Post-op 3 months				Post-op 6 months				Post-op 1 year			
		ES	SRM	SEM	MDD_{95}	ES	SRM	SEM	MDD_{95}	ES	SRM	SEM	MDD_{95}
95% Confidence Ellipse Area (mm^2)	OE	-0.10	-0.09	96.92	268.64	-0.30	-0.34	53.32	147.79	-0.29	-0.33	47.31	131.12
	CE	-0.19	-0.32	118.98	329.78	-0.12	-0.10	195.29	541.31	-0.27	-0.35	88.54	245.41
Mean Velocity (mm/s)	OE	-0.21	-0.22	1.28	3.55	-0.30	-0.39	0.86	2.38	-0.31	-0.44	0.90	2.49
	CE	-0.15	-0.33	2.88	7.98	-0.19	-0.38	2.37	6.56	-0.17	-0.26	2.27	6.28
Range-AP (mm)	OE	-0.17	-0.16	7.92	21.94	-0.29	-0.30	5.76	15.95	-0.40	-0.49	4.96	13.76
	CE	-0.20	-0.29	11.14	30.89	-0.22	-0.26	10.12	28.06	-0.27	-0.35	7.22	20.02
Range-ML (mm)	OE	-0.02	-0.02	4.25	11.79	-0.23	-0.26	2.62	7.26	-0.20	-0.23	2.05	5.69
	CE	-0.20	-0.24	2.67	7.40	-0.25	-0.29	2.75	7.61	-0.26	-0.29	2.61	7.24
RMS distance-AP (mm)	OE	-0.19	-0.18	1.54	4.26	-0.36	-0.38	1.21	3.36	-0.40	-0.47	1.16	3.23
	CE	-0.24	-0.34	1.67	4.64	-0.16	-0.16	1.97	5.46	-0.26	-0.34	1.26	3.49
RMS distance-ML (mm)	OE	0.03	0.03	0.65	1.81	-0.25	-0.31	0.39	1.09	-0.12	-0.13	0.47	1.31
	CE	-0.12	-0.14	0.50	1.38	-0.16	-0.17	0.56	1.56	-0.20	-0.22	0.49	1.37

ES: effect size; SRM: standardized response mean; SEM: standard error of measurement; MDD_{95}: minimal detectable difference on 95% confidence interval; OE: eyes-open on neutral stance; CE: eyes-closed on neutral stance; AP: anteroposterior; ML: mediolateral; RMS: root mean square

doi:10.6342/NTU201800337

Table 9 ROC analysis of COP variables for postoperative 3 months with dichotomization to "worsen" group vs. "non-worsen" group when the first question of JOACMEQ-lower extremity function was used as the anchor (total n = 31).

Variables	Standing condition	Area under ROC curve	95% Confidence interval	*p* value	Cutoff point (Sensitivity, Specificity)
95% confidence ellipse area (mm^2)	OE	0.712	0.468-0.965	0.078	-
	CE	**0.832**	0.000-1.000	**0.006***	**24.671 (0.750,0.870)**
Mean Velocity (mm/s)	OE	0.565	0.312-0.818	0.588	-
	CE	0.690	0.459-0.921	0.114	-
Range-AP (mm)	OE	0.587	0.345-0.829	0.470	-
	CE	**0.745**	0.525-0.954	**0.042***	**5.615 (0.500,0.957)**
Range-ML (mm)	OE	0.620	0.375-0.865	0.321	-
	CE	**0.826**	0.000-1.000	**0.007***	**3.156 (0.750,0.913)**
RMS distance-AP (mm)	OE	0.565	0.338-0.793	0.588	-
	CE	0.723	0.519-0.927	0.064	-
RMS distance-ML (mm)	OE	0.652	0.413-0.891	0.206	-
	CE	**0.799**	0.380-1.000	**0.013***	**0.592 (0.750,0.913)**

***Statistical significance ($p < 0.05$)**

OE: eyes-open on neutral stance; CE: eyes-closed on neutral stance; AP: anteroposterior; ML: mediolateral; RMS: root mean square

doi:10.6342/NTU201800337

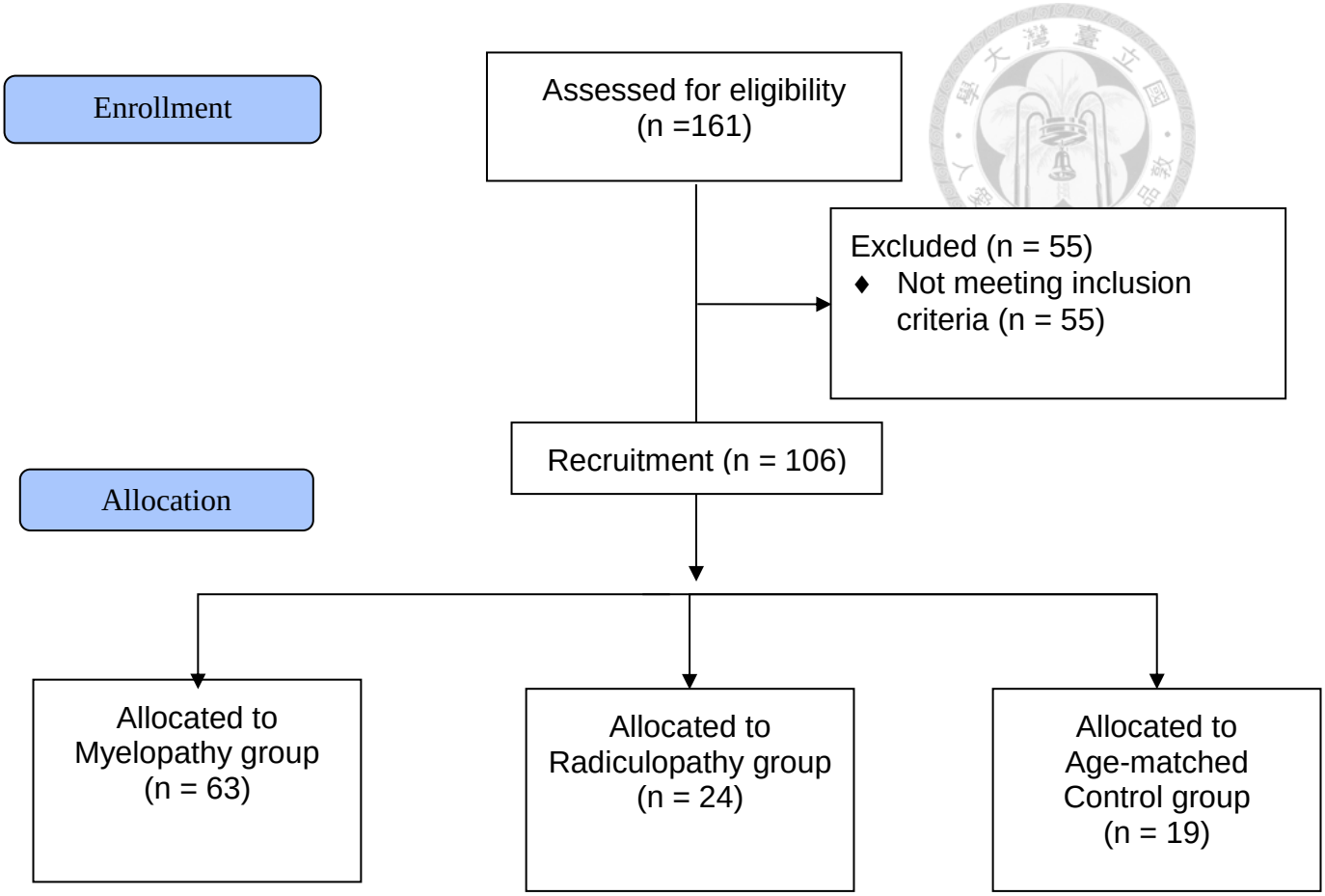

Figure 1 Allocation participants to myelopathy, radiculopathy and age-matched control group.

doi:10.6342/NTU201800337

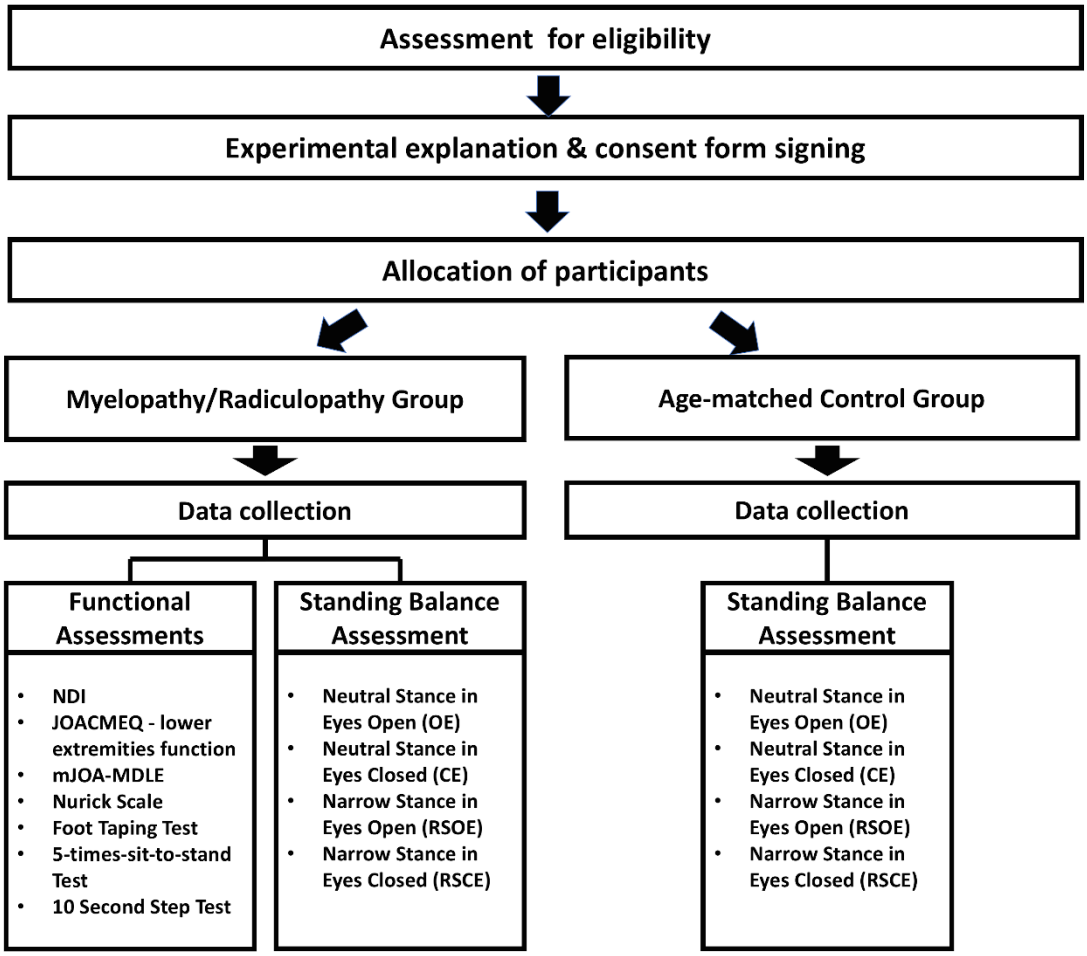

Figure 2 Flowchart of the assessment in Experiment 1.
NDI: Neck Disability Index; JOACMEQ: Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire; mJOA-MDLE: modified Japanese Orthopaedic Association scale-motor dysfunction of lower extremity

doi:10.6342/NTU201800337

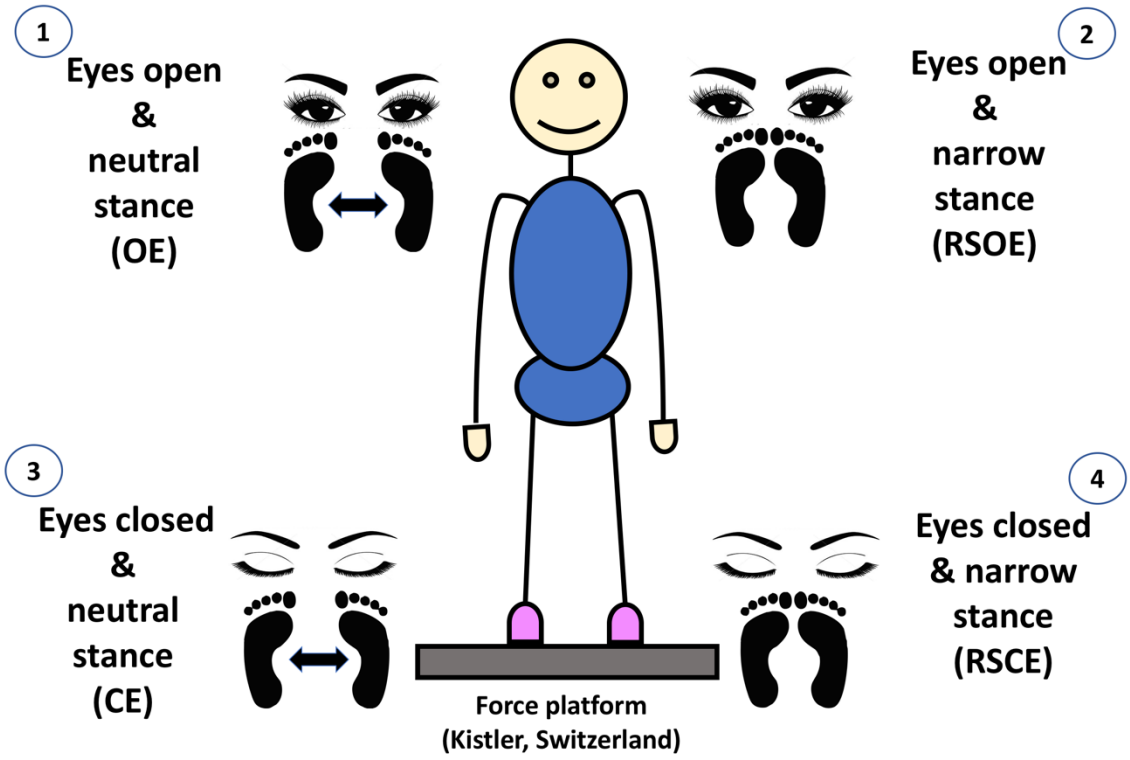

Figure 3 Standing trials in Experiment 1.

doi:10.6342/NTU201800337

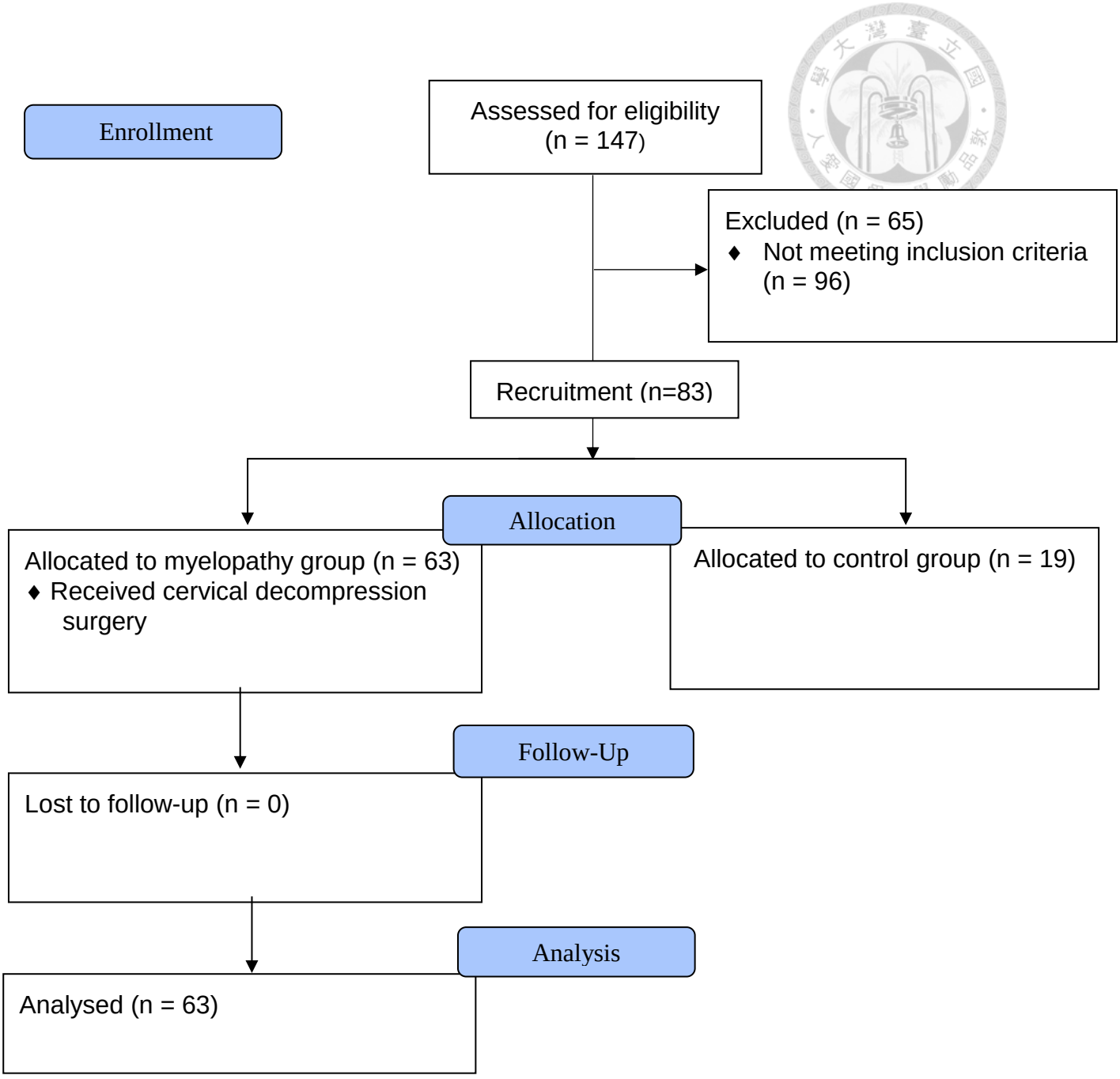

Figure 4 Flowchart of participant recruitment in Experiment 2.

doi:10.6342/NTU201800337

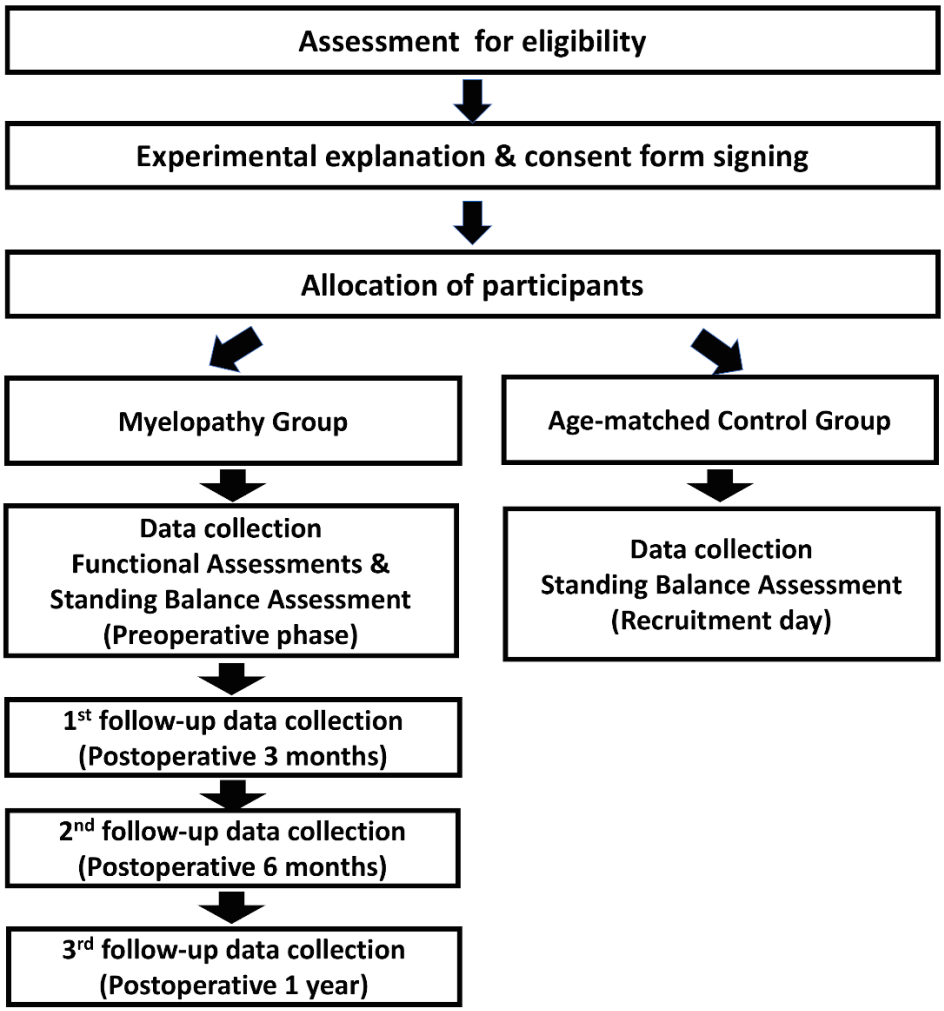

Figure 5 Flowchart of the assessment in Experiment 2.

doi:10.6342/NTU201800337

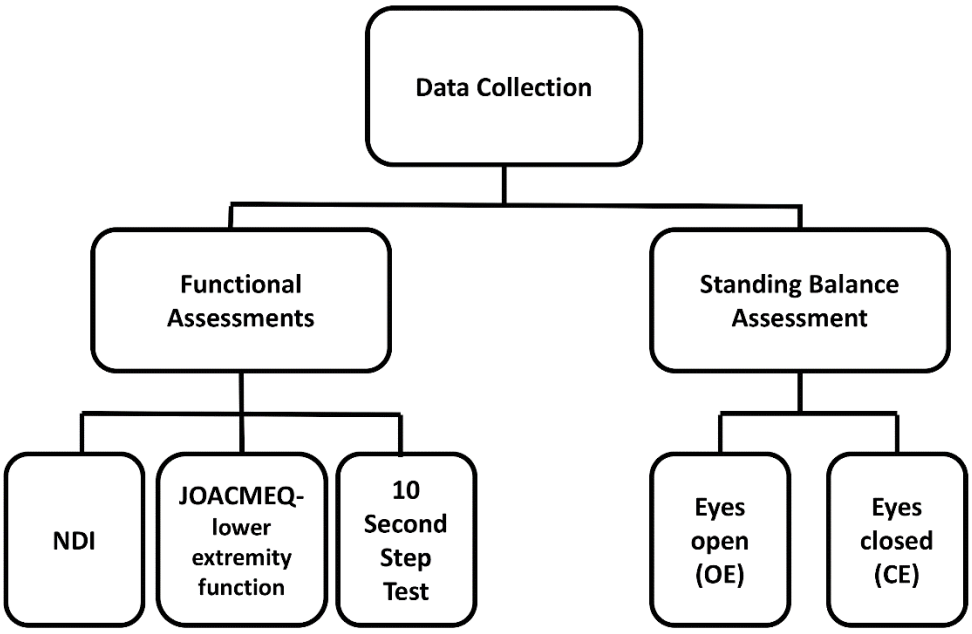

Figure 6 Experimental setup for single session of assessment for myelopathy group.

doi:10.6342/NTU201800337

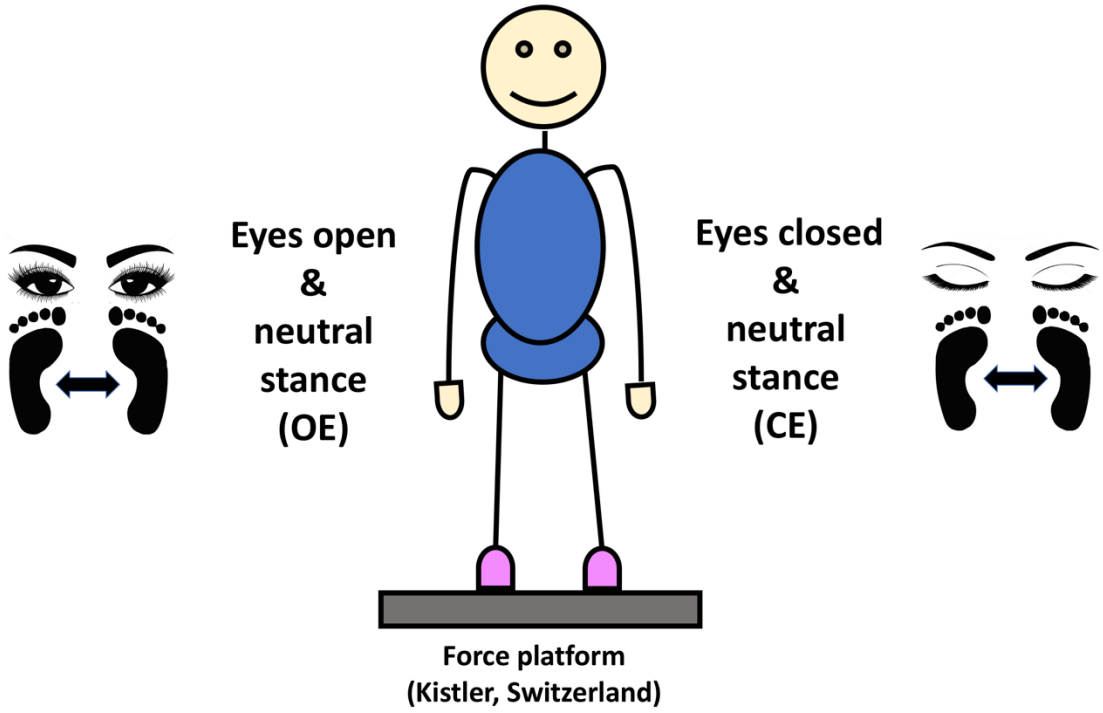

Figure 7 Standing trials in Experiment 2.

doi:10.6342/NTU201800337

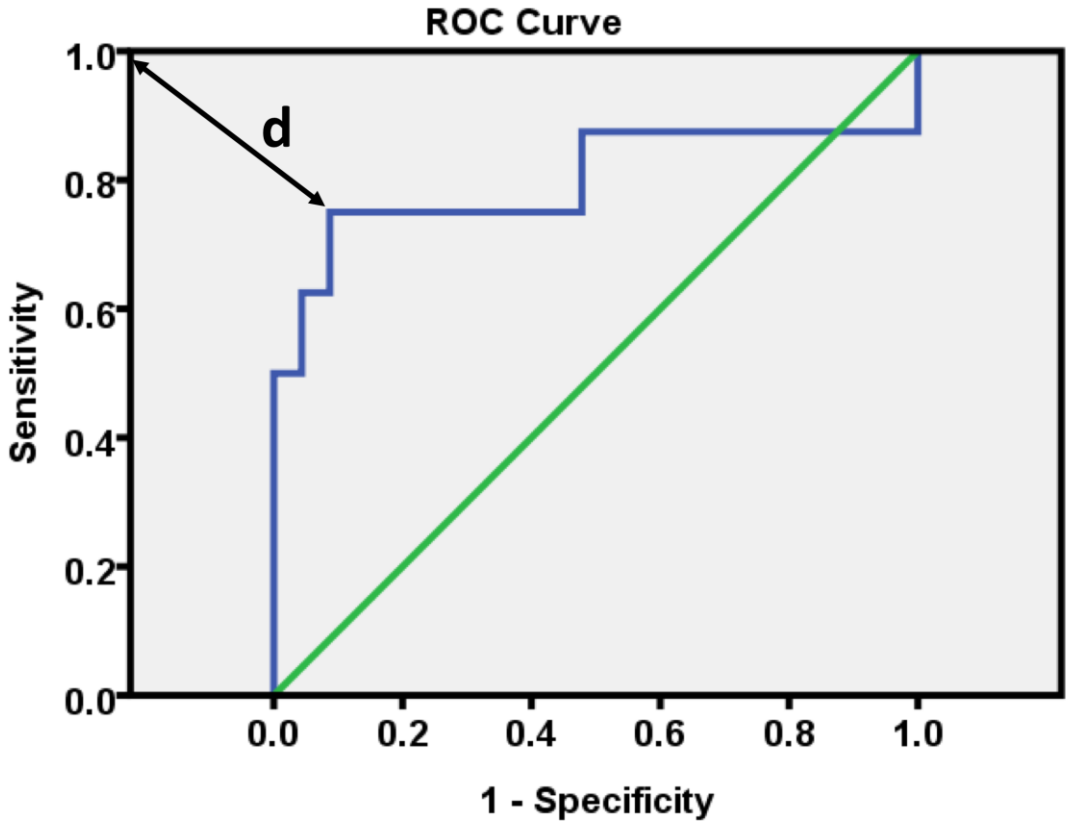

Figure 8 The example of ROC curve of RMS distance-ML for determining the MCID at postoperative 3 months. The cutoff point for MCID was determined based on the point on the ROC curve closest to the upper left corner (d is the shortest distance between ROC curve and upper left corner of y-axis).

doi:10.6342/NTU201800337

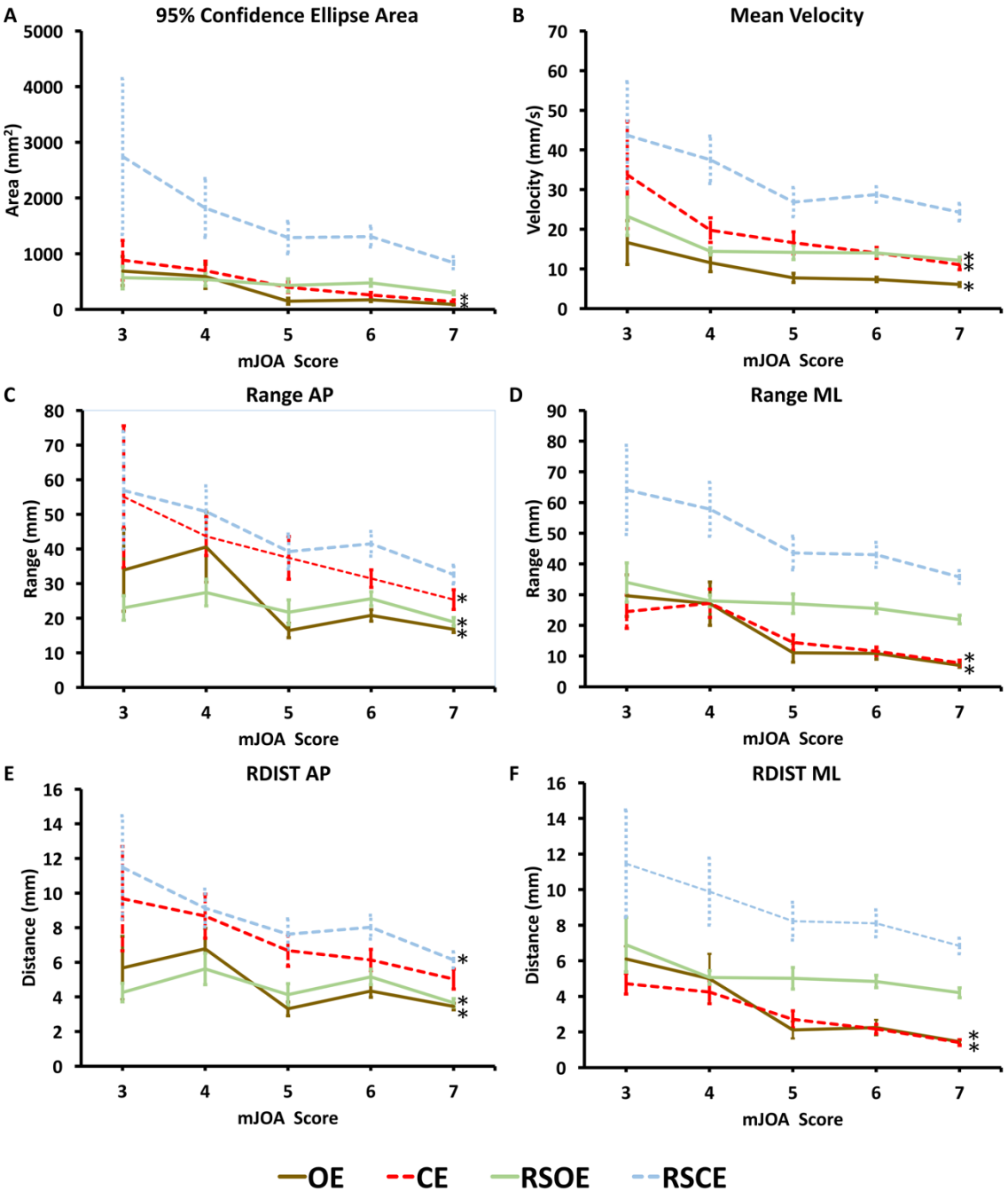

Figure 9 COP variables of myelopathy group in different mJOA-MDLE score: (A) 95% confidence ellipse area, (B) mean velocity, (C) range-AP, (D) range-ML, (E) RMS distance-AP and (F) RMS distance-ML.

mJOA-MDLE: modified Japanese Orthopaedic Association scale-motor dysfunction of lower extremity; OE: Eyes-open in neutral stance; CE: Eyes-closed in neutral stance; RSOE: Eyes-open in narrow stance; RSCE: Eyes-closed in narrow stance

***Statistical significance ($p < 0.05$) among different scores**

doi:10.6342/NTU201800337

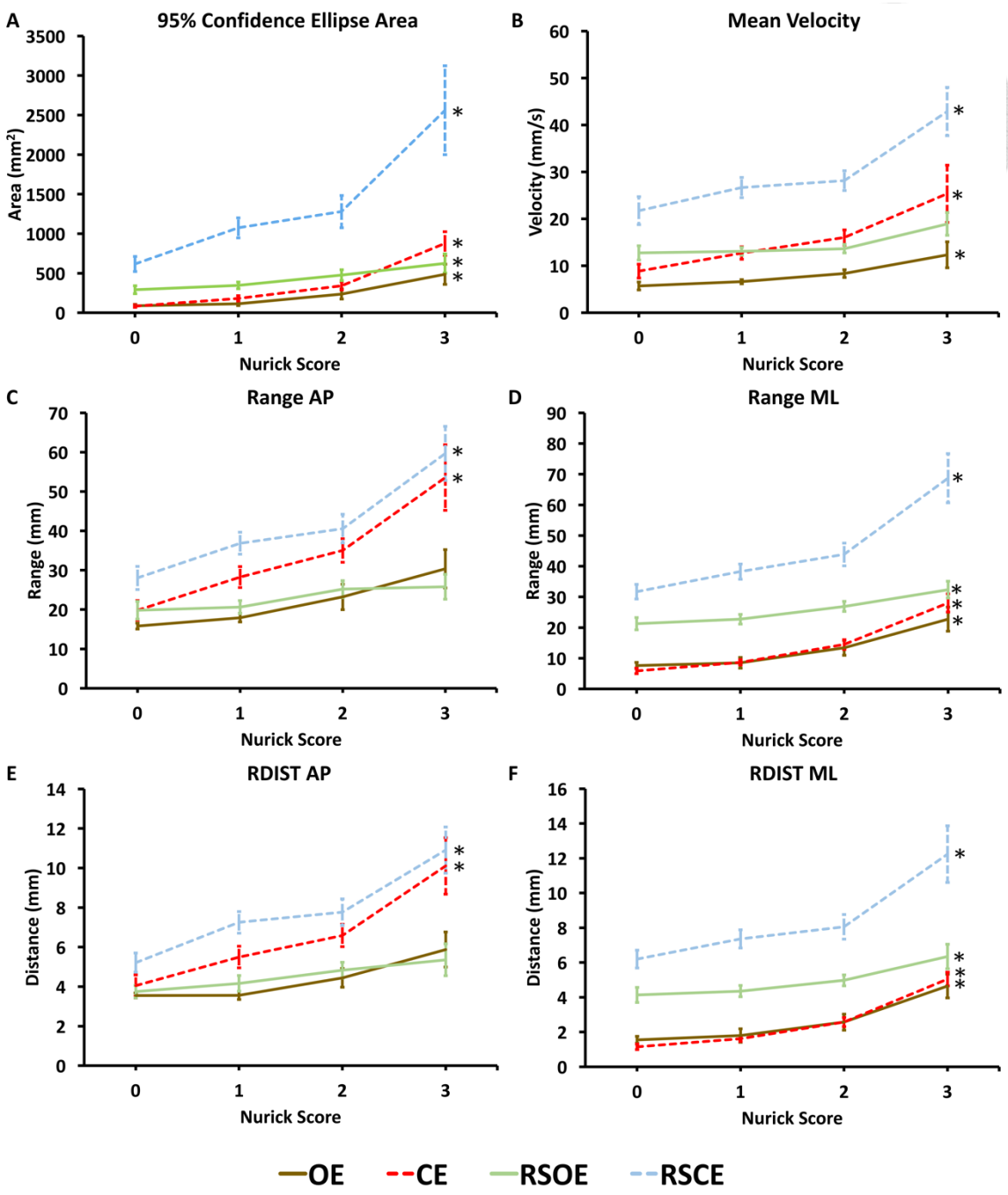

Figure 10 COP variables of myelopathy group in different Nurick score: (A) 95% confidence ellipse area, (B) mean velocity, (C) range-AP, (D) range-ML, (E) RMS distance-AP and (F) RMS distance-ML.
OE: Eyes-open in neutral stance; CE: Eyes-closed in neutral stance; RSOE: Eyes-open in narrow stance; RSCE: Eyes-closed in narrow stance
***Statistical significance ($p < 0.05$) among different scores**

doi:10.6342/NTU201800337

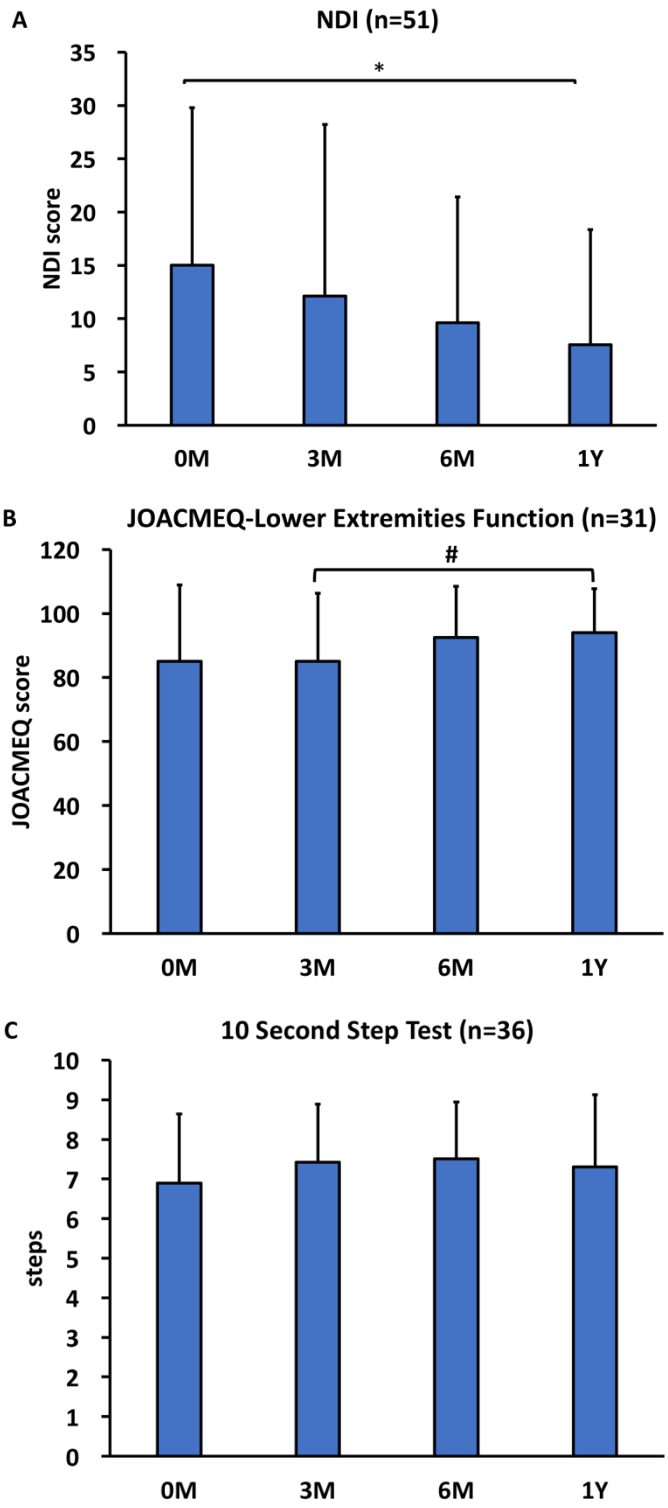

Figure 11 Comparison of Neck Disability Index (NDI), Japanese Orthopaedic Association Myelopathy Evaluation Questionnaire(JOACMEQ)-lower extremities function and 10 second step test after 3 months, 6 months and 1 year of surgery (preoperative phase as baseline).

0M: preoperative phase; 3M: postoperative 3 months; 6M: postoperative 6 months; 1Y: postoperative 1 year

*** Significant difference between 0M and 1Y ($p < 0.05/6$ after Bonferroni's adjustment)**

 # Significant difference between 3M and 1Y ($p < 0.05/6$ after Bonferroni's adjustment)

doi:10.6342/NTU201800337

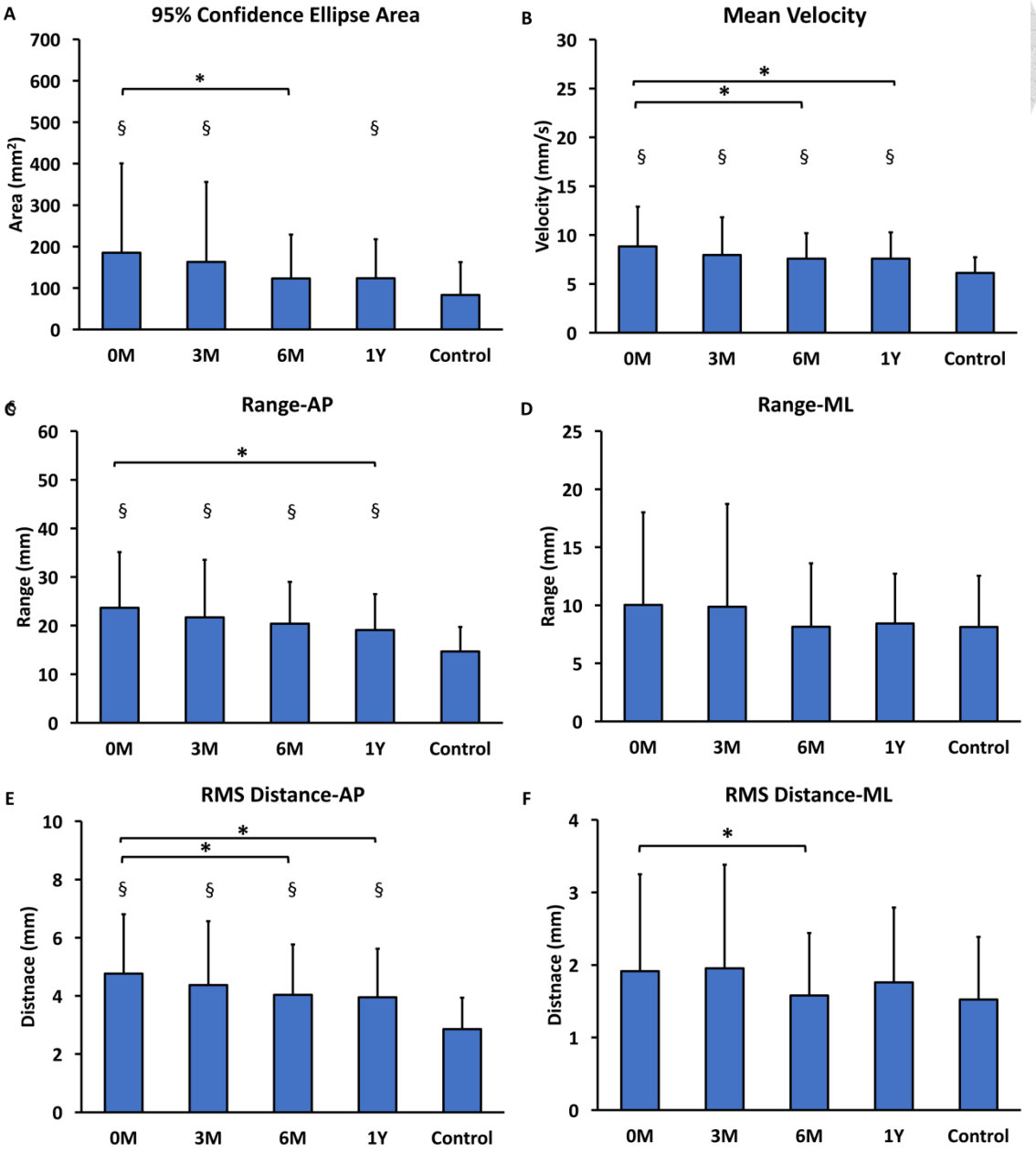

Figure 12 Comparison between phases and groups in COP variables during eyes-open condition (OE) in (A) 95% confidence ellipse area, (B) mean velocity, (C) range-AP, (D) range-ML, (E) RMS distance-AP and (F) RMS distance-ML.
0M: myelopathy group at preoperative phase; 3M: myelopathy group at postoperative 3 months; 6M: myelopathy group at postoperative 6 months; 1Y: myelopathy group at postoperative 1 year; Control: age-matched control group
*** Significant difference between phases of surgery (p <0.05)**
§ Significant difference between myelopathy group and age-matched control group (p<0.05)

doi:10.6342/NTU201800337

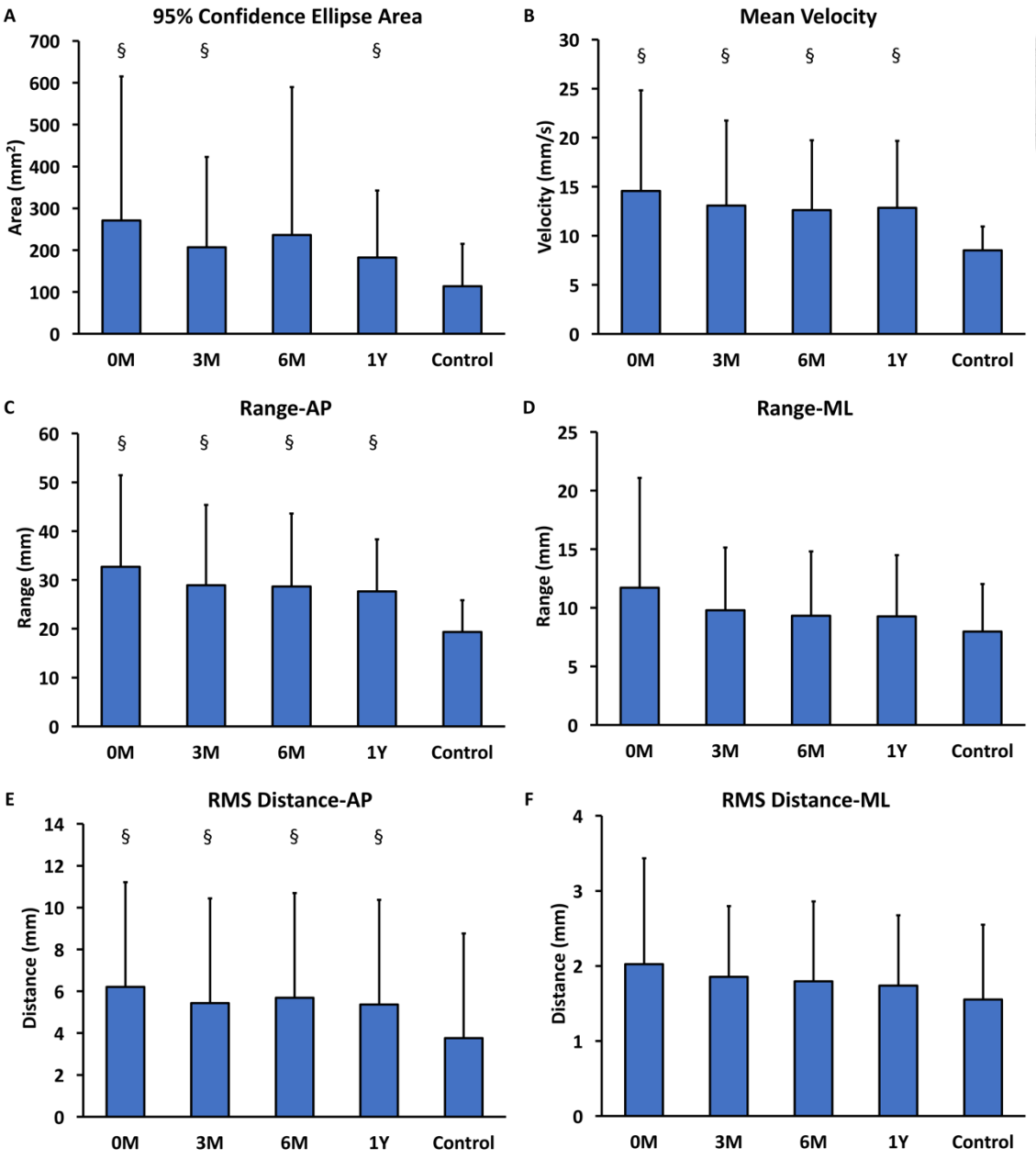

Figure 13 Comparison between phases and groups in COP variables during eyes-closed condition (CE) in (A) 95% confidence ellipse area, (B) mean velocity, (C) range-AP, (D) range-ML, (E) RMS distance-AP and (F) RMS distance-ML.
0M: myelopathy group at preoperative phase; 3M: myelopathy group at postoperative 3 months; 6M: myelopathy group at postoperative 6 months; 1Y: myelopathy group at postoperative 1 year; Control: age-matched control group
*** Significant difference between phases of surgery (p<0.05)**
§ Significant difference between myelopathy group and age-matched control group (p<0.05)

doi:10.6342/NTU201800337

APPENDICES

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Appendix 1:臨床實驗/研究許可書

國立臺灣大學醫學院附設醫院A研究倫理委員會

Research Ethics Committee A
National Taiwan University Hospital
7, Chung-Shan South Road, Taipei, Taiwan 100, R.O.C
Phone: 2312-3456 Fax: 23951950

臨床試驗/研究許可書

許可日期：2017 年 6 月 30 日

倫委會案號：201505093RINA
計畫名稱：頸椎脊髓神經病變之手術選擇、心理諮詢介入、神經肌肉代償、復健運動療效與生物力學之研究。。
試驗機構：國立臺灣大學醫學院附設醫院
部門/計畫主持人： 外科部 賴達明醫師
上述計畫持續審查申請業經 2017 年 6 月 30 日本院 A 研究倫理委員會第 93 次會議審查同意，符合研究倫理規範。本委員會的運作符合優良臨床試驗準則及政府相關法律規章。
本臨床試驗許可書之有效期限自 2017 年 7 月 2 日起至 2018 年 7 月 1 日止，計畫主持人須依國內相關法令及本院規定通報嚴重不良反應事件及非預期問題，並應於到期日至少 6 週前提出持續審查申請表，本案需經持續審查，方可繼續執行。

主任委員 蔡甫昌

Clinical Trial /Research Approval

Date of approval: June 30, 2017

NTUH-REC No.：201505093RINA
Title of protocol：Investigation of the relationship between surgical approaches, psychological intervention, neuromuscular control, rehabilitation exercise and biomechanical characteristics in radiculomyelopathy patients.
Trial/Research Institution：National Taiwan University Hospital
Department/ Principal Investigator：Department of Surgery / Dr. Dar-Ming Lai

The continuing review of the protocol has been approved by the 93rd meeting of Research Ethics Committee A of the National Taiwan University Hospital on June 30 2017. The committee is organized under, and operates in accordance with, the Good Clinical Practice guidelines and governmental laws and regulations.

The duration of this approval is from Jul 2, 2017 to Jul 1, 2018. The investigator is required to report serious adverse events and unanticipated problems in accordance with the governmental laws and regulations and NTUH requirements and apply for a continuing review not less than six weeks prior to the approval expiration date.

Daniel Fu-Chang Tsai, M.D.
Chairman
Research Ethics Committee A Daniel Fu-Chang Tsai

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Appendix 2: 臨床試驗/研究受試者說明暨同意書

病歷號：
姓　名：
生　日：西元　　年　月　日

國立臺灣大學醫學院附設醫院
National Taiwan University Hospital

臨床試驗/研究受試者說明暨同意書

研究倫理委員會案號：**201505093RIN**　　Ver3.20151028

臨床試驗/研究受試者說明書

您被邀請參與此臨床試驗/研究，這份表格提供您本試驗/研究之相關資訊，本試驗/研究已取得研究倫理委員會審查通過，研究主持人或其授權人員將會為您說明試驗/研究內容並回答您的任何疑問，您不須立即決定是否參加本試驗，請您經過慎重考慮後方予簽名。您須簽署同意書後才能參與本試驗/研究。

中文計畫名稱：頸椎脊髓神經病變之手術選擇、心理諮詢介入、神經肌肉代償、復健運動療效與生物力學之研究。

英文計畫名稱：Investigation of the relationship between surgical approaches, psychological intervention, neuromuscular control, rehabilitation exercise and biomechanical characteristics in radiculomyelopathy patients

執行單位：台大醫院外科部/物理治療系　　委託單位/藥廠：無

經費來源：科技部

主要主持人：賴達明　　職稱：主治醫師　電話：0972-651428

協同主持人：王淑芬　　職稱：教授　　電話：02-33668139

協同主持人：徐瑋勵　　職稱：助理教授　電話：02-33668149

協同主持人：鄭智修　　職稱：助理教授　電話：03-2118800#3714

協同主持人：王兆麟　　職稱：教授　　電話：02-33665269

※二十四小時緊急聯絡人：賴達明　　電話：0972-651428

受試者姓名：

性別：　　出生日期：

病歷號碼：

通訊地址：

聯絡電話：

法定代理人、輔助人或有同意權人之姓名：

與受試者關係：

性別：　　出生日期：

身分證字號：

通訊地址：

聯絡電話：

一、藥品、醫療技術、醫療器材全球上市現況簡介：

嚴重的頸椎脊髓病變患者手術，主要在解除被擠壓的脊椎神經以及脊柱不穩定的問題，視患者情況，來選擇前路減壓融合術以及後路椎板成形術的手術方式，而此二種手術方式皆為目

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前世界上用來治療頸椎脊髓病變的治療方法。

二、試驗/研究目的：

在本研究中，將分析您的頭部動作和身體平衡控制能力，並深入探討這些能力與臨床評估量表的相關性。本研究結果將有助於，針對個別動作控制能力的問題、提供最佳的復健運動訓練計劃。

三、試驗/研究之主要納入與排除條件：

負責本研究的人員會幫您做評估，並與您討論參加本研究所必需的條件。您必須在進入研究前簽屬本受試者說明及同意書。

納入條件：

您必須符合以下所有條件方能參加本研究：

脊髓神經病變病人

1. 年齡介於 20-80 歲之間
2. 依據核磁共振影像診斷有脊髓病變者
3. 後縱韌帶鈣化肥厚

神經根病變病人（醫生診斷結果）

1. 符合 Dermatone 分部
2. 理學檢查(Spuring test)

排除條件：

若有下列任何情況者，不能參加本研究：

1. 在參與本次研究前一年內未曾頸痛超過一個禮拜的時間或曾痛到無法繼續工作
2. 僵直性脊椎炎、類風溼性關節炎、多發性硬化症等內科性關節病變
3. 腫瘤
4. 患有精神或神經疾病（如憂鬱症、膽妄症、斜頸、舞蹈症、唐氏症等）
5. 因嚴重內科疾病而不適合接受正規手術或物理治療處方者

四、試驗/研究方法及相關檢驗：

本研究之脊髓神經病變病患，將分為不須手術組以及手術組。分別進行以下治療。

1. 手術診斷：手術治療前，將為您進行術前診斷，包含 X 光攝影、核磁共振影像，如必要在進行電腦斷層掃瞄。X 光攝影用於檢驗頸椎活動能力與僵硬程度，並可量得相關參數以利醫師診斷。核磁共振影像可檢查軟組織病變，有利於判斷病症嚴重程度。依據診斷結果，將手術方式將分為前開以及後開兩種。

A. 若您為前開手術，手術將遵行以下步驟進行:

I. 手術於全身麻醉下進行，採正躺的姿勢。

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II. 切開前頸皮膚，分開肌肉，以牽引器將氣管、食道及頸動脈隔開，露出頸椎間盤及椎體。
III. 於手術顯微鏡下，將椎間盤／錐體切除，並將壓迫脊髓或神經根之骨刺，韌帶，或腫瘤等移除減壓。
IV. 從腸骨切取適當大小之自體移植骨塊，或使用人工植入物，遷入上下椎體之間，此為骨融合。
V. 視需要於上下錐體分別打入骨釘，嵌上骨板，此為內固定。
VI. 檢查有無出血點並給予止血，視情況需要放置引流管，縫合肌肉及皮膚傷口。
VII. 病患於手術後拔管轉至恢復室觀察。

B. 若您為後開手術，則手術將遵守以下步驟:
I. 手術於全身麻醉下進行。
II. 切開後頸部（或背部）皮膚，玻璃肌模肌肉，直到露出脊椎棘突及兩側椎弓。
III. 切除脊椎棘突及椎弓，或視情況予以椎弓整型術（多為頸椎）。
IV. 如需骨融合，視情況施予後側／後外側骨融合，或經椎孔／後方椎體間骨融合。可選擇使用自體移植骨、人工骨或人工植入物做為融合材料。
V. 如需內固定，則施予骨釘固定術。
VI. 檢查有無出血點並予以止血，縫合肌膜，置放引流管，縫合皮膚傷口。
VII. 變換於手術後拔管轉至恢復室觀察。

C. 術後追蹤：術後持續為您追蹤病情改善程度。
D. 術後物理治療介入：包含被動性的熱敷和牽引治療，以及居家運動訓練。

2. 不須開刀者將納入物理治療，並隨機分配為被動治療組與主動治療組，至台大物理治療中心進行每周一次，為期六週之物理治療。

臨床檢測流程:

1. 超音波影像：檢測前將塗抹超音波膠以利檢測。接著利用常規物理治療檢測，測量您關節活動度、肌力、神經症狀以及疼痛指數。
2. 肌電圖：以肌電圖量測肌群，包括頸部左右兩側共計三對六條肌肉，此肌群負責頸部動態平衡，測驗前將進行皮膚酒精消毒及清除受測部位體毛。
3. 運動學量測：將請您戴上一付具有三個定位點的頭套，並穿上同樣具有三個定位點的背架，另外分別於頸椎第二節、第三節、第五節、及第七節貼上單顆定位點。可以描述各節與頭部的相對運動。測試時要請您採取坐姿，頭擺在正中位置做為起始位置。執行下列三個階段的指令。
I. 在第一階段時，您需頭頂住垂直於牆面的測力儀器，執行頸部前、後兩個方向上的最大自主等長收縮各五秒鐘。每個動作間會讓您休息兩分鐘以避免肌肉疲乏而影響出力。
II. 第二階段根據測力儀器的量值，您必需在頭部維持正中姿勢下，執行不出力、維持向前/向後 33%最大出力、及維持向前/向後 67%最大出力等五種出力條件。出力程度超過±5%則視為失敗試驗。每個條件記錄五秒鐘。
III. 第三階段您則需以慢速動作執行頸屈曲及頸伸展兩個方向上的頸部自主活動。過程中必須以等速和固定時間內完成所有動作。

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IV. 您將可在正式量測之前練習幾次上述動作。每一個動作都會記錄三次。為確保實驗的可重複性，全部的實驗流程和資料收集分析，都將由同一位物理治療師來執行。

4. 問卷資料評估：研究人員將問您一些問卷以及做一些功能性動作，以評估您的心智與功能性動作表現。
5. 脊椎的曲度：脊椎的曲度將使用非侵入性之測量器，儀器類似滑鼠，沿著您的背部脊椎表面皮膚滑過，可測得脊椎曲度。
6. 肌肉力量測試：我們將使用酒精清潔皮膚，若有過多毛髮將使用拋棄式剃刀為您剃除，之後將黏上一非侵入性的反光球及表面肌電感測貼片在您的皮膚，這些儀器不會產生任何電流及不適，實驗進行將請您用最大力氣收縮肌肉約 5 秒，共測試 3 次。
7. 步態分析測試：您將被要求使用自選速度在裝有力板的地面和跑步機上行走。
8. 上述所有檢測約需時 2~2.5 小時。

檢測時間點:

上述所有的臨床檢測將於術前、術後一個月、術後三個月、六個月與十二個月等五個時間點進行評估。

五、剩餘檢體處理情形：

此研究未使用病人檢體

六、可能產生之副作用、發生率及處理方法：

1. 目前脊椎手術的成功率極高，依個別患者的情形，可能產生下列副作用，國內外的統計報告發生率約 1-2%:

i. 神經根或脊髓傷害，導致癱瘓、麻痺、括約肌排泄功能障礙、呼吸衰竭
ii. 傷口血腫、上呼吸道阻塞
iii. 聲音沙啞、吞嚥困難
iv. 氣胸
v. 食道傷害
vi. 血管（頸動脈或脊椎動脈）傷害
vii. 傷口感染：<1%
viii. 骨融合不良
ix. 椎關節不穩定
x. 高位頸椎手術可能有植物人與死亡風險
xi. 脊柱變形
xii. 內固定失效
xiii. 假性脊膜膨出
xiv. 假性骨融合

doi:10.6342/NTU201800337

xv. 其他：如心肌梗塞、深部靜脈栓塞、肺炎等，視病患身體健康狀況而有所不同關於手術的副作用若有任何疑慮，建議於手術前與本研究之總主持人(神經外科醫師)討論。手術後若有副作用，將針對您的情況給予適當的醫療處置。

2. X 光攝影: 本研究中的 X 光攝影檢查的劑量相當低，造成的致命癌症機率風險是在萬分之一至百萬分之一之間。
3. 核磁共振: 核磁共振會釋放磁波，對於裝有心律調整器、接受腦血管動脈瘤結紮、腦部留有血管夾、及體內裝置各類電擊傳導器的患者，會干擾體內的醫療器械的運作。本研究人員會在病患受檢時再次確認，以免發生有任何意外。
4. 超音波影像: 超音波檢查的能量密度低，目前尚未知有長期副作用，一般不會造成患者不適。
5. 肌電圖、運動學量測: 此類量測屬於非侵入式分析，不會對於人體造成不良反應。

七、其他替代療法及說明：

1. 藥物：非類固醇類止痛劑
2. 復健物理治療
3. 使用各式輔具（如背架、頸部支撐輔具）
4. 不實施醫療處置可能的後果：症狀持續惡化、癱瘓、麻痺、括約肌功能障礙等。

八、試驗/研究預期效益：

1. 可改善因椎間盤突出、脊椎退化、腫瘤或後縱韌帶鈣化導致頸部脊髓或神經根壓迫所造成的神經病變
2. 可改善因外傷性骨折、退化、腫瘤病變等原因導致頸椎不穩定的情況
3. 椎骨整型手術、骨融合或內固定可增加脊椎穩定度
4. 手術／醫療處置的成功率：60-90%（依您的病情而定）

九、試驗/研究進行中受試者之禁忌、限制與應配合之事項：

受試者於試驗中無任何禁忌、部分量測可能會到台灣大學物理治療系系館、台大醫院影像醫學部及台大身體、心靈與文化整合影像研究中心進行

十、機密性：

臺大醫院將依法把任何可辨識您的身分之記錄與您的個人隱私資料視為機密來處理，不會公開。如果發表試驗/研究結果，您的身分仍將保密。您亦瞭解若簽署同意書即同意您的原始醫療紀錄可直接受監測者、稽核者、研究倫理委員會及主管機關(若試驗受美國食品藥物管理局管轄，則主管機關包含美國食品藥物管理局)檢閱，以確保臨床試驗/研究過程與數據符合相關法律及法規要求；若試驗受美國食品藥物管理局管轄，美國食品藥物管理局亦可能會檢視提供給您的文件，試驗結果將公佈於一個公開的臨床試驗資訊網站：Clinicaltrials.gov.，但您的個人資料仍將保密，該網站只會有試驗之結果摘要，您可以在任何時候搜尋該網站。上述人員並承諾絕不違反您的身分之機密性。

doi:10.6342/NTU201800337

十一、損害補償與保險：

(一) 如依本研究所訂臨床試驗/研究計畫，因而發生不良反應造成損害，本醫院願意提供專業醫療照顧及醫療諮詢。您不必負擔治療不良反應或傷害之必要醫療費用。

(二) 本研究不提供其他形式之補償。若您不願意接受這樣的風險，請勿參加試驗。

(三) 您不會因為簽署本同意書，而喪失在法律上的任何權利。

十二、受試者權利：

(一) 試驗/研究過程中，與您的健康或是疾病有關，可能影響您繼續接受臨床試驗/研究意願的任何重大發現，都將即時提供給您。

(二) 本試驗/研究已經過本院研究倫理委員會審查，並已獲得核准。本院研究倫理委員會委員由醫事專業人員、法律專家、社會工作人員及其他社會公正人士所組成，每月開會一次，審查內容包含試驗/研究之利益及風險評估、受試者照護及隱私保護等。如果您在試驗/研究過程中對試驗/研究工作性質產生疑問，對身為患者之權利有意見或懷疑因參與研究而受害時，可與本院之研究倫理委員會聯絡請求諮詢，其電話號碼為： **(02)2312-3456** 轉 **63155**。

(三) 為進行試驗/研究工作，在試驗事項上您必須接受計畫主持人或協同主持人：賴達明的照顧。如果您現在或於試驗/研究期間有任何問題或狀況，請不必客氣，可與在外科部的黃千聯絡(24 小時聯繫電話：0916643292　)。

本同意書一式 2 份，醫師已將同意書副本交給您，並已完整說明本研究之性質與目的。計畫主持人或協同主持人：賴達明已回答您有關試驗/研究的問題。

(四)本研究預期不會衍生專利權或其他商業利益。

十三、試驗/研究之退出與中止：

您可自由決定是否參加本試驗/研究；試驗/研究過程中也可隨時撤銷同意，退出試驗/研究，不需任何理由，且不會引起任何不愉快或影響日後醫師對您的醫療照顧。計畫主持人或贊助廠商亦可能於必要時中止該試驗/研究之進行。受試者若於中途退出，其先前資料將保留以利分析，但不再進行資料收集。

主要主持人、協同主持人已詳細解釋有關本研究計畫中上述研究方法的性質與目的，及可能產生的危險與利益。

主要主持人/協同主持人簽名：_____

日期：西元_____年_____月_____日

臨床試驗/研究受試者同意書

受試者：_____，已詳細瞭解上述研究方法及其所可能產生的危險與利益，有關本試驗/研究計畫的疑問，業經計畫主持人詳細予以解釋。本人經充分的時間考慮及閱讀同意書後，同意接受為臨床試驗/研究計畫的自願受試者。

doi:10.6342/NTU201800337

受試者簽名：_____

日期：西元_____年_____月_____日

法定代理人或輔助人或有同意權人簽名：_____

身分為（請圈選）：法定代理人、輔助人、有同意權人

與受試者之關係（請圈選）：本人、配偶、父、母、兒、女、其他：_____

日期：西元_____年_____月_____日

* 受試者為無行為能力(未滿七歲之未成年人者或受監護宣告之人)，由法定代理人簽名；受監護宣告之人，由監護人擔任其法定代理人。

* 受試者為限制行為能力者(滿七歲以上之未成年人或因精神障礙、其他心智缺陷，致其為意思表示、受意思表示、辨識其意思表示效果之能力，顯有不足，而受法院之輔助宣告者)，應得其本人及法定代理人或輔助人之同意。

* 受試者雖非無行為能力或限制行為能力者，但因意識混亂或有精神與智能障礙，而無法進行有效溝通和判斷時，由有同意權之人簽名。有同意權人順序如下：
(1)配偶。(2)成年子女。(3)父母。(4)兄弟姊妹。(5)祖父母。
依前項關係人所為之書面同意，其書面同意，得以一人行之；關係人意思表示不一致時，依前項各款先後定其順序。前項同一順序之人，以親等近者為先，親等同者，以同居親屬為先，無同居親屬者，以年長者為先。(人體研究法第 12 條)

見證人 **1**：　　（簽名）　見證人 **2**：　　（簽名）

見證人 **1** 身分證字號：　　見證人 **2** 身分證字號：

聯絡電話：　　聯絡電話：

通訊地址：　　通訊地址：

日期：西元　　年　月　日　　日期：西元　　年　月　日

*受試者、法定代理人、輔助人或有同意權之人皆無法閱讀時，應由見證人在場參與所有有關受試者同意之討論。並確定受試者、法定代理人、輔助人或有同意權之人之同意完全出於其自由意願後，應於受試者同意書簽名並載明日期。試驗/研究相關人員不得為見證人。

*若意識清楚，但無法親自簽具者且無親屬或關係人在場，得以按指印代替簽名，惟應有二名見證人。

doi:10.6342/NTU201800337

Appendix 3: 頸部失能量表 (Neck Disability Index, NDI)

Ver.1, 2011/12/30

頸部失能量表

填寫這份問卷能幫助治療師了解因為頸部造成的頭、頸、與上肢的不適症狀，影響妳日常生活活動的情況。在每一題請選擇一個最能形容妳今天狀況的答案回答：

問題 **1**—疼痛程度

- ☐ 我現在並不覺得疼痛。
- ☐ 我現在有很輕微的頸部疼痛。
- ☐ 我現在有中等程度的頸部疼痛。
- ☐ 我現在有相當嚴重的頸部疼痛。
- ☐ 我現在有非常嚴重的頸部疼痛。
- ☐ 我現在有就自己認知中最嚴重的頸部疼痛。

問題二—自我照顧能力 **(**例如：洗澡，穿衣服**)**

- ☐ 我能完成一般自我照顧的日常活動，且不會有任何疼痛。
- ☐ 我能完成一般自我照顧的日常活動，但會產生疼痛。
- ☐ 我在一般自我照顧的日常活動時會產生疼痛，所以我必須小心且緩慢。
- ☐ 我可以完成大部分自我照顧的活動，但需要一些協助。
- ☐ 我大部分的日常活動都需要別人協助才能完成。
- ☐ 我無法自己穿衣、洗澡，且總是必須待在床上。

問題三—抬起或提起重物

- ☐ 我可以提起重物且不產生疼痛。
- ☐ 我可以提起重物但會產生疼痛。
- ☐ 因為頸部疼痛，我無法自地面提起重物，但如果這個重物放置在桌面上我能使用它。
- ☐ 因為頸部疼痛，我無法自地面提起重物，但如果這個中等重量物體放置在桌面上我能使用它。
- ☐ 我只能提起很輕的物體。
- ☐ 我無法提起或提起任何物體。

問題四—閱讀 **(**例如：報紙、雜誌、書籍…**)**

- ☐ 我可以如我所願的閱讀，且不會產生頸部的疼痛。
- ☐ 我可以如我所願的閱讀，但會產生輕微的頸部疼痛。
- ☐ 我可以如我所願的閱讀，但會產生中等程度的頸部疼痛。
- ☐ 因為頸部中等程度的疼痛，使我不能如我所願的閱讀。
- ☐ 因為頸部嚴重的疼痛，我幾乎不能閱讀。
- ☐ 我完全無法閱讀。

問題五—頭部疼痛

- ☐ 我不覺得頭痛。
- ☐ 我偶爾會有輕微頭痛。
- ☐ 我偶爾會有中等程度的頭痛。
- ☐ 我常常會有中等程度的頭痛。
- ☐ 我常常會有嚴重的頭痛。
- ☐ 我幾乎一直感覺到頭痛。

doi:10.6342/NTU201800337

問題六—注意力

- ☐ 我能毫無困難的完全集中注意力。
- ☐ 我能完全集中注意力但覺得有一點點困難。
- ☐ 我有一點困難去完全的集中注意力。
- ☐ 我很難完全的集中注意力。
- ☐ 我非常困難完全的集中注意力。
- ☐ 我完全無法集中注意力。

問題七—工作

- ☐ 我能完成所有我想要做的工作。
- ☐ 我僅能完成一般日常工作。
- ☐ 我僅能完成大部分一般日常工作。
- ☐ 我無法完成一般日常工作。
- ☐ 我幾乎無法做任何的工作。
- ☐ 我完全無法做任何的工作。

問題八—開車

- ☐ 我開車時，不會產生疼痛。
- ☐ 我開車一段時間，就會產生輕微的頸部疼痛。
- ☐ 我開車一段時間，就會產生中等程度的頸部疼痛。
- ☐ 因為頸部中等程度的疼痛，所以我不能開太久的車。
- ☐ 因為頸部嚴重的疼痛，所以我不太能開車。
- ☐ 我無法開車。

問題九—睡眠

- ☐ 我沒有睡眠的問題。
- ☐ 頸部的疼痛很輕微的干擾了我的睡眠 (影響睡眠時間小於 1 小時) 。
- ☐ 頸部的疼痛輕微的干擾了我的睡眠 (影響睡眠時間約 1-2 小時) 。
- ☐ 頸部的疼痛中等程度的干擾了我的睡眠 (影響睡眠時間約 2-3 小時) 。
- ☐ 頸部的疼痛嚴重的干擾了我的睡眠 (影響睡眠時間約 3-5 小時) 。
- ☐ 頸部的疼痛非常嚴重的干擾了我的睡眠 (影響睡眠時間約 5-7 小時) 。

問題十 —休閒娛樂活動

- ☐ 我能參與各種休閒娛樂活動。
- ☐ 我能參與各種休閒娛樂活動但會感覺頸部有些疼痛。
- ☐ 因為頸部的疼痛，我僅能參與大部分的休閒娛樂活動。
- ☐ 因為頸部的疼痛，我僅能參與少部分的休閒娛樂活動。
- ☐ 因為頸部的疼痛，我難以參與休閒娛樂活動。
- ☐ 我無法參與任何的休閒娛樂活動。

doi:10.6342/NTU201800337

Appendix 4: 日本骨科學會脊髓型頸椎病評估問卷 (Japanese Orthopaedic Association Myelopathy Evaluation Questionnaire, JOACMEQ)

版本日期 ：2013/5/15 ver. 1

日本骨科學會脊髓型頸椎病評估問卷

關於您上個禮拜的健康狀況，請圈選最適當的項目號碼。如果您的狀況隨時或每天在變化，請就最嚴重的狀況圈選適當號碼。

問題 1-1 當您坐著時，您是否能抬頭仰看天花板？

1）不可能　2）可以到某個程度（需要用點力氣）　3）可以，沒有困難

問題 1-2 即使頸椎有症狀，您是否能不間斷喝完一杯水？

1）不可能　2）可以到某個程度　3）可以，沒有困難

問題 1-3 當您坐著時，您是否能將頭轉向坐在您側後方的人，並看著他 / 她的臉說話？

1）不可能　2）可以到某個程度　3）可以，沒有困難

問題 1-4 您是否能在下樓梯時看著您的腳？

1）不可能　2）可以到某個程度　3）可以，沒有困難

問題 2-1 您是否能用雙手扣上您上衣或襯衫的釦子？

1）不可能　2）可以，要花點時間　3）可以，沒有困難

問題 2-2 您是否能用慣用手持湯匙或筷子吃完一餐？

1）不可能　2）可以，要花點時間

3）可以，沒有困難

問題 2-3 您是否能抬起雙臂？（以無力的那側為主）

1）不可能　2）可以舉到肩膀高度

3）可以，雖然手肘以及 / 或是手腕需要微彎

4）我可以將整隻手直直舉高

doi:10.6342/NTU201800337

問題 3-1 您是否能在平地行走？

1）不可能　　2）可以，但是緩慢且需要支持

3）可以，只需欄杆、枴杖或助行器的支持

4）可以，雖然緩慢但是不需任何支持

5）可以，沒有困難

問題 3-2 您是否能用任一隻腳單腳站立而不需手扶？（來支撐你自己）

1）任一隻腳皆不可能

2）兩腳中有一隻腳可以獨自站立超過 10 秒

3）兩腳皆可以個別獨自站立超過 10 秒

問題 3-3 您上樓梯是否有困難？

1）我有很大的困難　2）我有一些困難　3）我沒有困難

問題 3-4 您是否有困難做下列其中一種動作；往前彎腰，跪下，或蹲著？

1）我有很大的困難　2）我有一些困難　3）我沒有困難

問題 3-5 您是否有困難走路超過 15 分鐘？

1）我有很大的困難　2）我有一些困難　3）我沒有困難

問題 4-1 您是否有尿失禁？

1）總是　　2）很頻繁　　3）憋尿超過兩小時

4）打噴嚏或用力　　5）沒有

問題 4-2 您夜裡上廁所的頻率為何？

1）三次或以上　2）一次或兩次　3）極少

問題 4-3 您是否在小便完仍覺得膀胱有殘餘尿液？

1）多數時候 2）有時候　3）極少

問題 4-4 當您有尿意時是否能立即（開始）排尿？

1）通常不行 2）有時候　3）多數時候

doi:10.6342/NTU201800337

問題 5-1 您現在的健康狀況如何？

1）差　2）尚可 3）好　4）非常好　5）好極了

問題 5-2 對於您想做的工作或日常活動，您是否無法完成過？

1）我從來無法做這些事　2）多數時候我無法做這些事

3）有時候我無法做這些事　4）多數時候我可以做這些事

5）我總是可以做這些事

問題 5-3 您曾因為疼痛而使工作習慣受阻嗎？

1）很大程度　2）中等程度

3）輕微程度（稍微）　4）少數程度（極少）

5）完全沒有

問題 5-4 您曾經覺得沮喪或憂鬱嗎？

1）總是 2）很頻繁　3）有時候　4）極少 5）從不

問題 5-5 您是否覺得精疲力盡？

1）總是 2）很頻繁　3）有時候　4）極少 5）從不

問題 5-6 您曾經覺得開心？

1）從不　2）極少　3）有時候

4）幾乎總是　5）總是

問題 5-7 您是否認為您的健康狀況還不錯？

1）一點也不（我的健康狀況非常差）　2）幾乎不（我的健康狀況差）

3）不太常（我的健康狀況一般）　4）尚可（我的健康狀況比一般狀況好些）

5）是（我很健康）

問題 5-8 您是否覺得您的健康會變差？

1）極有可能　2）隨著時間逐漸變差

3）有時候是有時候不是　4）不太可能

5）絕不可能

doi:10.6342/NTU201800337

0 分是“完全不痛（麻）”，10 分是“可以想像得到最強烈的痛（麻）”，在下列 0 到 10 分的直線上標示上星期中，您的疼（麻）痛症狀最嚴重時的程度。

如果您覺得脖子或肩膀有疼痛或僵硬，請標示程度

0 _____ 10

如果您覺得胸部緊繃，請標示程度

0 _____ 10

如果您覺得手臂或手掌有疼痛或僵硬，請標示程度

（如果雙臂都有疼痛，請標示嚴重側的疼痛程度）

0 _____ 10

如果您覺得從胸部到腳趾有疼痛或痠麻，請標示程度

0 _____ 10

0：完全不痛（麻）

10：可以想像得到最嚴重的程度

姓名：_____ 病歷號碼：_____ 性別：M / F 出生日期：_____

填寫日期：_____

請將填妥的問卷寄回，賴醫師的團隊謝謝您的配合。

doi:10.6342/NTU201800337

Appendix 5: The Modified Japanese Orthopaedic Association Scale and Grading of Nurick Scale

TABLE 1. The Modified Japanese Orthopaedic Association Scale
Motor Dysfunction score of the upper extremity
0 – Inability to move hands
1 – Inability to eat with a spoon, but able to move hands
2 – Inability to button shirt, but able to eat with a spoon
3 – Able to button shirt with great difficulty
4 – Able to button shirt with slight difficulty
5 – No dysfunction
Motor dysfunction score of the lower extremity
0 – Complete loss of motor and sensory function
1 – Sensory preservation without ability to move legs
2 – Able to move legs, but unable to walk
3 – Able to walk on flat floor with a walking aid
4 – Able to walk up and/or down stairs with hand rail
5 – Moderate-to-significant lack of stability, but able to walk up and/or down stairs without hand rail
6 – Mild lack of stability but walks with smooth reciprocation unaided
7 – No dysfunction
Sensory dysfunction score of the upper extremities
0 – Complete loss of hand sensation
1 – Severe sensory loss or pain
2 – Mild sensory loss
3 – No sensory loss
Sphincter dysfunction score
0 – Inability to micturate voluntarily
1 – Marked difficulty with micturation
2 – Mild-to-moderate difficulty with micturation
3 – Normal micturation

Table 1 Nurick grades(7)

0 Signs or symptoms of root involvement but without evidence of spinal cord disease

1 Signs of spinal cord disease but no difficulty in walking

2 Slight difficulty in walking which did not prevent full-time employment

3 Difficulty in walking which prevented full-time employment or the ability to do all housework, but which was not so severe as to require someone else's help to walk

4 Able to walk only with someone else's help or with the aid of a frame

5 Chair bound or bedridden

doi:10.6342/NTU201800337