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Clinical Study

# Geographic variations in clinical presentation and outcomes of decompressive surgery in patients with symptomatic degenerative cervical myelopathy: analysis of a prospective, international multicenter cohort study of 757 patients

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**Abstract**

**BACKGROUND CONTEXT:** Degenerative cervical myelopathy (DCM) is a progressive degenerative spine disease and the most common cause of spinal cord impairment in adults worldwide. Few studies have reported on regional variations in demographics, clinical presentation, disease causation, and surgical effectiveness.

**PURPOSE:** The objective of this study was to evaluate differences in demographics, causative pathology, management strategies, surgical outcomes, length of hospital stay, and complications across four geographic regions.

**STUDY DESIGN/SETTING:** This is a multicenter international prospective cohort study.

**PATIENT SAMPLE:** This study includes a total of 757 symptomatic patients with DCM undergoing surgical decompression of the cervical spine.

**OUTCOME MEASURES:** The outcome measures are the Neck Disability Index (NDI), the Short Form 36 version 2 (SF-36v2), the modified Japanese Orthopaedic Association (mJOA) scale, and the Nurick grade.

**MATERIALS AND METHODS:** The baseline characteristics, disease causation, surgical approaches, and outcomes at 12 and 24 months were compared among four regions: Europe, Asia Pacific, Latin America, and North America.

**RESULTS:** Patients from Europe and North America were, on average, older than those from Latin America and Asia Pacific (p=.0055). Patients from Latin America had a significantly longer duration of symptoms than those from the other three regions (p<.0001). The most frequent causes of myelopathy were spondylosis and disc herniation. Ossification of the posterior longitudinal ligament was most prevalent in Asia Pacific (35.33%) and in Europe (31.75%), and hypertrophy of the ligamentum flavum was most prevalent in Latin America (61.25%). Surgical approaches varied by region; the majority of cases in Europe (71.43%), Asia Pacific (60.67%), and North America (59.10%) were managed anteriorly, whereas the posterior approach was more common in Latin America (66.25%). At the 24-month follow-up, patients from North America and Asia Pacific exhibited greater improvements in mJOA and Nurick scores than those from Europe and Latin America. Patients from Asia Pacific and Latin America demonstrated the most improvement on the NDI and SF-36v2 PCS. The longest duration of hospital stay was in Asia Pacific (14.16 days), and the highest rate of complications (34.9%) was reported in Europe.

**CONCLUSIONS:** Regional differences in demographics, causation, and surgical approaches are significant for patients with DCM. Despite these variations, surgical decompression for DCM appears effective in all regions. Observed differences in the extent of postoperative improvements among the regions should encourage the standardization of care across centers and the development of international guidelines for the management of DCM. 

*Keywords:* Decompression; Geographic variation; Myelopathy; Surgical; Treatment efficacy; Treatment outcome

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## Introduction

Degenerative cervical myelopathy (DCM) is a progressive spine disease and is the most common cause of spinal cord impairment in adults worldwide [1]. The degenerative process is initiated by desiccation and fibrillation of the intervertebral disc, which disrupts the biomechanical homeostasis of the spinal column and leads to disc herniation, osteophyte formation, hypertrophy of the ligamentum flavum (HLF), and facet subluxation. These changes may narrow the

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spinal canal and result in compression of the spinal cord [1–3].Myelopathy may also develop from ossification of the posterior longitudinal ligament (OPLL) [4].

Compression of the spinal cord initiates a cascade of pathobiological events, including ischemia, endothelial cell impairment, disruption of the blood spinal cord barrier, neuroinflammation, and apoptosis of the neurons and oligodendrocytes [5]. Disruption of the neuronal circuitry manifests clinically as an array of signs and symptoms ranging from fingertip numbness to spasticity, ataxia, and incontinence [6]. Although non-surgical management strategies may initially optimize the musculoskeletal function and control symptoms, the physical compression of the cord can only be addressed effectively surgically [7–10].

Degenerative cervical myelopathy is present in patients from around the world. There are regional differences in opinions on the optimal management strategy for patients with DCM, as well as cultural variations in the perception of illness. The present study evaluates differences in disease causation, demographics, surgical techniques, treatment outcomes, length of hospital stay, and treatment complications across four geographic regions. This observational prospective international study was intended to identify regional variations in management strategies, which could serve as a baseline to establish global standards of management. As such, this information could be an important step in developing international guidelines for the treatment of DCM.

## Materials and methods

Data were obtained after a preplanned merger of two prospective observational studies conducted under the same investigational protocol, the CSM-North America (CSM-NA) study (clinicaltrial.gov NCT00285337) and the CSM-International (CSM-I) study (clinicaltrial.gov NCT00565734). The primary objective of the CSM-I study was to investigate if there are global differences in neurologic presentation, treatment approaches, and surgical outcomes. Between December 2005 and January 2011, 757 patients (278 in the CSM-NA study and 479 in the CSM-I study) were enrolled at 26 sites in Asia Pacific (n=150), Europe (n=126), Latin America (n=80), and North America (CSM-I: n=123, CSM-NA: n=278) (Table 1).

Participating centers in the CSM-NA study were members of the AOSpine North America Clinical Research Network consortium, whereas participating centers in the CSM-I study were recruited through an open call via AOSpine International. Interested sites were selected if they had adequate patient availability and experience in conducting prospective clinical research. Principal investigators were spinal neurosurgeons or orthopedic surgeons.

Table 1
Distribution of patients by region, country, and study center

| Region | Country | City or town | Study center | Principal investigator | Enrolled |
|---|---|---|---|---|---|
| Latin America | Venezuela | Caracas | Blinded | Blinded | 4 |
| | Brazil | São Paulo | Blinded | Blinded | 17 |
| | Brazil | São Paulo | Blinded | Blinded | 59 |
| Europe | Ireland | Dublin | Blinded | Blinded | 4 |
| | The Netherlands | Nijmegen | Blinded | Blinded | 42 |
| | Turkey | Izmir | Blinded | Blinded | 29 |
| | Italy | Ancona | Blinded | Blinded | 9 |
| | Italy | Catania | Blinded | Blinded | 42 |
| Asia Pacific | India | New Delhi | Blinded | Blinded | 57 |
| | Japan | Nagoya | Blinded | Blinded | 19 |
| | Japan | Okayama | Blinded | Blinded | 7 |
| | P.R. China | Chongqing | Blinded | Blinded | 41 |
| | R. Singapore | Singapore | Blinded | Blinded | 19 |
| | Japan | Chiba | Blinded | Blinded | 7 |
| North America | United States | Boston, MA | Blinded | Blinded | 2 |
| | United States | Atlanta, GA | Blinded | Blinded | 50 |
| | United States | Carmel, IN | Blinded | Blinded | 6 |
| | United States | Baltimore, MD | Blinded | Blinded | 4 |
| | United States* | Kansas City, KS | Blinded | Blinded | 79 |
| | United States | Sun City West, AZ | Blinded | Blinded | 1 |
| | United States | Boston, MA | Blinded | Blinded | 13 |
| | United States | Denver, CO | Blinded | Blinded | 6 |
| | United States | Philadelphia, PA | Blinded | Blinded | 30 |
| | Canada* | Toronto, Ontario | Blinded | Blinded | 175 |
| | United States | Salt Lake City, UT | Blinded | Blinded | 18 |
| | United States | Charlottesville, VA | Blinded | Blinded | 17 |

* These centers participated in both the CSM-North America and CSM-International studies.

The patient population consisted of those referred for surgical consultation by clinicians from multidisciplinary backgrounds. Patients were eligible for entry into the present study if they met the following key inclusion criteria: (1) age 18 years or older; (2) symptomatic with at least one clinical sign of myelopathy (corticospinal motor deficits, atrophy of intrinsic hand muscles, hyperreflexia, a positive Hoffman sign, upgoing plantar responses, lower limb spasticity, and broad-based unstable gait); (3) imaging evidence of cervical cord compression; and (4) no previous surgery for DCM. Patients were excluded if they had asymptomatic cervical spondylosis, active infection, neoplasia, rheumatoid arthritis, ankylosing spondylitis, or concomitant lumbar stenosis. Ethical approval was obtained from each site. All participating patients provided verbal and written informed consent.

### *Surgical techniques*

All participants underwent anterior and/or posterior surgical decompression of the cervical spine. The choice of surgical approach, the number of levels decompressed, and the option for instrumentation were left at the discretion of the attending surgeon. Anterior procedures included cervical discectomy and/or corpectomy with or without fusion. Posterior procedures included laminectomy with or without fusion and laminoplasty. Circumferential surgery consisted of a combination of both anterior and posterior approaches.

### *Data collection and quality assurance*

For each participant, extensive data were collected on personal characteristics; neurologic presentation; medical, social, and drug histories; causative pathology; surgical summary; functional status; disability; and health-related quality of life. Data were obtained preoperatively and at 6, 12, and 24 months postoperatively using electronic case report forms. Adverse events and complications were documented using standardized forms with a predetermined list of anticipated complications as well as an "other" option. Adverse events were adjudicated by a panel of investigators and classified as either related to DCM, related to surgery, or unrelated to either. External investigators performed both on- and off-site monitoring to confirm compliance with the study protocol and to ensure the data were authentic, accurate, and complete.

### *Outcome measures*

Validated functional assessment tools and quality of life questionnaires were used to evaluate preoperative and postoperative status. These included the modified Japanese Orthopaedic Association (mJOA) scale [11], the Nurick scale [12], the Neck Disability Index (NDI) [13,14], and the Short Form 36 version 2 (SF-36v2) [15]. The mJOA and Nurick scales are clinician-administered DCM-specific measures of impairment and disease severity, whereas the NDI and SF-36v2 are patient-reported questionnaires that evaluate disability and overall health status, respectively. The mJOA scale allocates scores between 0 (worst) and 18 (best) based on motor dysfunction of the upper and lower extremities, sensory impairment of the upper extremity, and sphincter dysfunction. The Nurick scale is a six-grade ordinal scale primarily based on gait dysfunction and ranges from 0 (best) to 5 (worst). The NDI, a modification of the Oswestry Disability Index, is a self-reported, disease-specific, and reliable measure of disability that evaluates performance in 10 different categories, including personal care, sleep, and driving; this score ranges from 0% (best) to 100% (worst). The NDI was unavailable in Chinese; thus, NDI data from 41 Chinese patients were not collected. The SF-36v2 is a widely used health status survey that combines physical component summary (PCS), a mental component summary (MCS), and pain levels; these scores were calculated using the 1998 US norms and the orthogonal approach to transformation. The minimum clinically important differences have been established for the mJOA (1.1), SF-36v2 PCS (4.1), SF-36v2 MCS (5.7), and NDI (7.5) scores in a degenerative spine population but not for the Nurick scores [13,16–19]. An improvement by one grade on the Nurick, however, likely reflects a clinically significant change.

## Analysis

For this analysis, outcomes at 12 and 24 months' follow-up were selected. Differences in baseline characteristics and surgical details were compared between the four regions using analysis of variance and the Pearson chi-square test for quantitative and qualitative variables, respectively. Nine patients died of unrelated causes and 25 patients withdrew from the study by 24 months postoperatively. Of the 735 subjects eligible for the 12-month follow-up, 628 (85.44%) attended. Of the 723 who were eligible for the 24-month follow-up, 566 (74.77%) attended the visit. Missing follow-up outcome scores were assumed to be missing at random, except for the patients who expired, and were accounted for using a multiple imputation procedure that created 10 multiply imputed samples. Such imputation is recommended as being less susceptible to bias and more efficient than performing a completed case analysis and dropping cases with incomplete data [20,21]. Using the imputed sets, patient outcomes at 12- and 24-month follow-ups were compared between the four regions (North America, Latin America, Europe, and Asia Pacific) using the mixed models analytic approach available in SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA). The dependent variable was the change between the preoperative and the 12- or 24-month scores (mJOA, Nurick, NDI, SF-36v2 PCS, and SF-36v2 MCS). A two-way repeated measurement of covariance was conducted that included a visit factor (12 and 24 months), a region factor, and an interaction term between the visit and the region factors. A p-value of $<.05$ for region indicates a significant difference in outcomes across the four geographic regions. A p-value of $<.05$ for visit indicates a significant difference in outcomes between the 12- and 24-month postoperative visits. Finally, a p-value for the

interaction term "region×visit" indicates that different regions exhibit different patterns of improvements in outcomes between the 12- and 24-month follow-ups.

Unadjusted and adjusted models were created. In the adjusted model, patient, disease severity, and surgical characteristics were controlled for, including gender, age, duration of symptoms, smoking status, years of education, sources of stenosis (spondylosis, intervertebral disc, OPLL, HLF, congenital stenosis, and subluxation), affected cervical levels, comorbidities by body system (cardiovascular, respiratory, gastrointestinal, renal, endocrine, psychiatric, rheumatologic, and neurologic), duration of operation, surgical approach, and surgical technique (anterior discectomy, anterior corpectomy, anterior fusion, anterior fixation, laminectomy without fusion, laminectomy and instrumented fusion, and laminoplasty). Further, the model included the preoperative value of the analyzed outcome (eg, preoperative NDI for the change in NDI model). The adjusted model controlled for known patient, disease, and surgical covariates to reduce selection bias caused by the non-randomized nature of the comparisons. The study had 90% power to detect a difference of 0.7 in the mJOA scores between the regions based on an observed standard deviation of 2.8. An unadjusted sensitivity analysis was performed using non-imputed data.

All statistical analyses were performed using SAS/STAT version 9.4 (SAS Institute Inc.).

## Results

### *Patient demographics*

Of the 757 patients, 80 (10.57%) were from Latin America, 126 (16.64%) were from Europe, 150 (19.82%) were from Asia Pacific, and 401 (52.97%) were from North America. The overall mean age was 56.4±11.83 years (range 21–87 years), and the majority were men (62.75%). The patients' demographics differed among the regions (Table 2). Patients from Europe (57.44±11.85 years) and North America (57.33±11.77 years) were, on average, older than those from Latin America (54.23±10.65 years) and from Asia Pacific (53.95±12.20 years) (p=.0055). The region with the highest proportion of men was Asia Pacific (74.00%), followed by Latin America (67.50%), Europe (59.52%), and North America (58.60%) (p=.0061). Race was different across regions (p<.0001). Patients from Latin America (37.96±30.92 months) had a longer duration of symptoms than those from Asia Pacific (22.04±35.68 months), Europe (24.89±32.48 months), and North America (26.55±42.92 months) (p<.0001).

### *Variations in the etiology of cervical myelopathy*

Sources of stenosis differed across regions (Table 2). Patients were often diagnosed with multiple degenerative changes and causes of myelopathy. The three most common etiologies in North America were spondylosis (75.31%), disc herniation (68.08%), and HLF (18.45%). In Europe, the most common pathologies were spondylosis (92.06%), disc herniation (73.02%), and OPLL (31.75%). In Asia Pacific, the most common causes of myelopathy were disc herniation (84.67%) followed by spondylosis (66.67%) and OPLL (35.33%). Finally, in Latin America, spondylosis was the most common etiology (80.00%), followed by disc herniation (63.75%) and HLF (61.25%).

In terms of regional differences in causative pathology, spondylosis was most common in Europe (92.06%) and least common in Asia Pacific (66.67%) (p<.0001). Disc herniation was most common in Asia Pacific (84.67%) and least common in Latin America (63.75%) (p=.0005). Hypertrophy of the ligamentum flavum was most common in Latin America (61.25%) and least common in North America (18.45%) (p<.0001). Finally, OPLL was most common in Asia Pacific (35.33%) and least common in North America (11.72%) (p<.0001). Except for one case in Asia Pacific, congenital stenosis was reported only in North American patients (16.46%) (p<.0001). There were no differences in the rates of subluxation among the regions (p=.2307).

### *Preoperative functional status*

There were no regional differences in mean preoperative mJOA and NDI scores (p=.2729 and p=.3364, respectively). There were, however, baseline differences in SF-36v2 PCS and MCS (p<.0001 and p=.0012, respectively) and Nurick grades (p<.0001). Patients from Asia Pacific had the highest preoperative SF-36v2 PCS (36.63±8.33) and the lowest SF-36v2 MCS (37.46±12.57). In contrast, patients from Latin America scored the lowest on the SF-36v2 PCS (30.30±8.60) but the highest on the SF-36v2 MCS (43.52±15.01).

About half (51.25%) of Latin American patients had a Nurick grade of IV (gait abnormality prevents employment) or worse. Only 43.33% of Asia Pacific, 34.13% of European, and 32.92% of North American patients exhibited a similar level of disability.

### *Variations in surgical approaches*

Surgical approaches also varied by region (p<.0001) (Table 3). Surgery was performed anteriorly most commonly in Europe (71.43%) and least commonly in Latin America (32.50%). The majority of patients from Asia Pacific (60.67%) and North America (59.10%) also underwent anterior-only surgery.

Circumferential surgery was rarely performed; only 5.24% of North American patients, 3.17% of European patients, and one patient from Latin America underwent a two-stage surgery. The length of surgery (skin-to-skin time) was the longest in Latin America (230.39±66.62 minutes), and the shortest in Europe (129.67±53.67 minutes). Mean surgical time in North American patients was 194.06±81.82 minutes and was significantly longer than that in Asia Pacific patients (159.96±72.57 minutes) (p<.0001). After adjusting for surgical characteristics, surgical time was still the longest in Latin

Table 2
Demographics, disease characteristics, and preoperative status by region

| Category | Values | Statistics | Latin America (N=80) | Europe (N=126) | Asia (N=150) | North America (N=401) | p-Value |
|---|---|---|---|---|---|---|---|
| Gender | Female | n (%) | 26 (32.50) | 51 (40.48) | 39 (26.00) | 166 (41.40) | .0061 |
| Race | Black or African-American | n (%) | 13 (16.25) | 0 (.00) | 0 (.00) | 34 (8.48) | <.0001 |
| | East Asian (Japanese, Chinese, Malay, Polynesian, Micronesian, etc.) | | 0 (.00) | 1 (0.79) | 92 (61.33) | 22 (5.49) | |
| | Native American (Latin American, Alaskan, Indian, Eskimo, etc.) | | 2 (2.50) | 0 (.00) | 0 (.00) | 2 (0.50) | |
| | Native Hawaiian or other Pacific Islander | | 0 (.00) | 0 (.00) | 0 (.00) | 1 (0.25) | |
| | Oceanian (New Guinean, Australian, Aborigine, etc.) | | 0 (.00) | 0 (.00) | 0 (.00) | 1 (0.25) | |
| | Other | | 20 (25.00) | 0 (.00) | 6 (4.00) | 10 (2.49) | |
| | White or Caucasian (Italian, English, Indian, Iranian, Lapps, etc.) | | 45 (56.25) | 125 (99.21) | 52 (34.67)* | 331 (82.54) | |
| Age (y) | | Mean | 54.23 | 57.44 | 53.95 | 57.33 | .0055 |
| | | SD | 10.65 | 11.85 | 12.2 | 11.77 | |
| Duration of symptoms (mo) | | Mean | 37.96 | 24.89 | 22.04 | 26.55 | <.0001 |
| | | SD | 30.92 | 32.48 | 35.68 | 42.92 | |
| | | Median | 36 | 16.5 | 8 | 12 | |
| Source of stenosis | Spondylosis | n (%) | 64 (80.00) | 116 (92.06) | 100 (66.67) | 302 (75.31) | <.0001 |
| | Disc | n (%) | 51 (63.75) | 92 (73.02) | 127 (84.67) | 273 (68.08) | .0005 |
| | Ossified posterior longitudinal ligament | n (%) | 19 (23.75) | 40 (31.75) | 53 (35.33) | 47 (11.72) | <.0001 |
| | Hypertrophic ligamentum flavum | n (%) | 49 (61.25) | 34 (26.98) | 28 (18.67) | 74 (18.45) | <.0001 |
| | Subluxation | n (%) | 2 (2.50) | 6 (4.76) | 6 (4.00) | 29 (7.23) | .2307 |
| | Congenital stenosis | n (%) | 0 (.00) | 0 (.00) | 1 (0.67) | 66 (16.46) | <.0001 |
| | Other | n (%) | 2 (2.50) | 1 (0.79) | 0 (.00) | 10 (2.49) | .1732 |
| mJOA score | | Mean | 12.59 | 12.93 | 12.29 | 12.65 | .2729 |
| | | SD | 3.15 | 2.94 | 2.96 | 2.63 | |
| Nurick classification | Grade 0 (no root or cord symptoms) | n (%) | 0 (.00) | 0 (.00) | 2 (1.33) | 1 (0.25) | <.0001 |
| | Grade I (root signs or symptoms, no evidence of cord involvement) | n (%) | 9 (11.25) | 6 (4.76) | 5 (3.33) | 15 (3.74) | |
| | Grade II (signs of cord involvement, normal gait) | n (%) | 14 (17.50) | 33 (26.19) | 25 (16.67) | 75 (18.70) | |
| | Grade III (mild gait abnormality, able to be employed) | n (%) | 16 (20.00) | 44 (34.92) | 53 (35.33) | 178 (44.39) | |
| | Grade IV (gait abnormality prevents employment) | n (%) | 27 (33.75) | 29 (23.02) | 35 (23.33) | 95 (23.69) | |
| | Grade V (able to ambulate only with assistance) | n (%) | 8 (10.00) | 5 (3.97) | 16 (10.67) | 32 (7.98) | |
| | Grade VI (chair bound or bedridden) | n (%) | 6 (7.50) | 9 (7.14) | 14 (9.33) | 5 (1.25) | |
| NDI | | n | 76 | 124 | 82 | 378 | .3364 |
| | | Mean | 38.36 | 36.85 | 40.1 | 40.4 | |
| | | SD | 19.52 | 20.53 | 19.23 | 21.06 | |
| SF-36v2 PCS | | n | 80 | 124 | 150 | 380 | <.0001 |
| | | Mean | 30.30 | 33.92 | 36.63 | 34.46 | |
| | | SD | 8.60 | 8.27 | 8.33 | 9.86 | |
| SF-36v2 MCS | | n | 80 | 124 | 150 | 380 | .0012 |
| | | Mean | 43.52 | 38.67 | 37.46 | 41.16 | |
| | | SD | 15.01 | 11.5 | 12.57 | 13.99 | |

mJOA, modified Japanese Orthopedic; NDI, Neck Disability Index; SF-36v2 PCS, Short Form 36 Physical Component Score; SD, standard deviation; SF-36v2 MCS, Short Form 36 Mental Component Score.

* Caucasians in Asia were from sites in India and Turkey.

Table 3
Characteristics of decompressive surgery by region

| Category | Values | Statistics | Latin America (N=80) | Europe (N=126) | Asia Pacific (N=150) | North America (N=401) | p-Value |
|---|---|---|---|---|---|---|---|
| Type of surgery | Anterior only | n (%) | 26 (32.50) | 90 (71.43) | 91 (60.67) | 237 (59.10) | <.0001 |
| | Posterior only | n (%) | 53 (66.25) | 32 (25.40) | 59 (39.33) | 143 (35.66) | |
| | Circumferential (both posterior and anterior) | n (%) | 1 (1.25) | 4 (3.17) | 0 (.00) | 21 (5.24) | |
| Number of levels decompressed | | Mean | 3.41 | 3.19 | 3.99 | 3.96 | <.0001 |
| | | SD | 1.24 | 0.99 | 1.16 | 1.31 | |
| Length of surgery (skin-to-skin time) | | Mean | 230.39 | 129.67 | 159.96 | 194.06 | <.0001 |
| | | SD | 66.62 | 53.67 | 72.57 | 81.82 | |
| Duration of hospital stay | | Mean | 9.96 | 11.25 | 14.16 | 5.70 | <.0001 |
| | | SD | 9.11 | 11.17 | 8.52 | 9.45 | |
| | | Median | 7 | 6 | 14 | 3 | |
| Surgical level | C1–C2 | n (%) | 0 (.00) | 1 (0.79) | 1 (0.67) | 9 (2.24) | .2654 |
| | C2–C3 | n (%) | 9 (11.25) | 4 (3.17) | 8 (5.33) | 59 (14.71) | .0003 |
| | C3–C4 | n (%) | 52 (65.00) | 57 (45.24) | 73 (48.67) | 205 (51.12) | .0407 |
| | C4–C5 | n (%) | 69 (86.25) | 86 (68.25) | 103 (68.67) | 293 (73.07) | .0192 |
| | C5–C6 | n (%) | 74 (92.50) | 113 (89.68) | 139 (92.67) | 381 (95.01) | .1912 |
| | C6–C7 | n (%) | 73 (91.25) | 95 (75.40) | 132 (88.00) | 367 (91.52) | <.0001 |
| | C7–T1 | n (%) | 42 (52.50) | 46 (36.51) | 56 (37.33) | 274 (68.33) | <.0001 |

SD, standard deviation.

America and the shortest in Europe; no surgical time differences were observed between cases from North America and Asia Pacific. The duration of hospital stay also differed across the regions. The median hospital stay was the longest in Asia Pacific (14 days) and the shortest in North America (3 days) (p<.0001).

The mean number of levels decompressed was 3.73±1.27 (range 1–7). The mean number of levels decompressed was lower in anterior surgeries (2.97±0.88) than in posterior surgeries (4.87±0.88) (p<.0001). The mean number of decompressed segments was the highest in Asia Pacific (3.99±1.16) and in North America (3.96±1.31), and the lowest in Europe (3.19±0.99) (p<.0001). Overall, C5–C6 (93.39%), C6–C7 (88.11%), and C4–C5 (72.79%) were the most commonly treated levels across all regions. There were no significant differences in the frequency of C5–C6 decompression among the regions. Surgery for C6–C7 was performed most frequently in North America (91.52%) and in Latin America (91.25%), and least commonly in Europe (75.40%) (p<.0001). C4–C5 decompression was performed in 86.25% of cases in Latin America and in approximately 70% of cases in the other three regions (p=.0192). The least frequently decompressed level was C1–C2 (0%–2.24% of cases), with no significant regional differences (p=.2654). C2–C3 decompression was performed in 14.71% of cases in North America but in only 3.17% of cases in Europe and in Asia Pacific (p=.0003).

### *Postoperative outcome measures*

The differences in outcomes at 12 and 24 months among patients from Latin America, Europe, Asia Pacific, and North America are summarized in Table 4A and B.

#### *mJOA*

Patients from all regions showed significant improvements in mJOA scores at 12 and 24 months after surgery (Table 4A). At 24 months, patients from North America (3.15, 95% confidence interval [CI]: 2.88–3.42) and Asia Pacific (2.95, 95% CI: 2.56–3.35) exhibited the greatest improvements on the mJOA scale. In contrast, patients from Europe (1.50, 95% CI: 1.07–1.93) and Latin America (1.88, 95% CI: 1.36–2.40) improved the least. After adjusting for relevant patient factors and surgical factors, differences in mJOA outcomes across regions remained significant (p=.0002) (Table 4B).

#### *Nurick grade*

At 24 months, patients from North America achieved the greatest improvements in the Nurick grade (1.66, 95% CI: 1.51–1.81), followed by those from Asia Pacific (1.57, 95% CI: 1.31–1.83), Europe (1.09, 95% CI: 0.83–1.35), and Latin America (0.87, 95% CI: 0.53–1.21) (p<.0001); (Table 4A) After adjustment for patient factors and surgical characteristics, these differences remained significant (p=.0037) (Table 4B).

#### *NDI*

At 24 months, patients from Asia Pacific (19.62, 95% CI: 15.53–23.72) and Latin America (15.05, 95% CI: 11.11–19.00) exhibited greater improvements on the NDI than those from North America (10.76, 95% CI: 8.69–12.83) and Europe (9.96, 95% CI: 6.67–13.24) (p=.0003) (Table 4A). These differences remained significant following adjustment for relevant patient and surgical characteristics (p=.0035) (Table 4B).

Table 4
Changes in outcome parameters at 12 and 24 months compared with baseline by region: (A) unadjusted analysis and (B) adjusted analysis

| | Visit | Latin America | Europe | Asia Pacific | North America | Region | Region ×visit | Visit |
|---|---|---|---|---|---|---|---|---|
| A | | | | | | | | |
| mJOA | 12M follow up | 1.96 (1.43–2.48) | 1.46 (1.02–1.91) | 2.83 (2.40–3.26) | 2.88 (2.63–3.12) | <.0001 | 0.3547 | 0.3045 |
| | 24M follow up | 1.88 (1.36–2.40) | 1.50 (1.07–1.93) | 2.95 (2.56–3.35) | 3.15 (2.88–3.42) | | | |
| Nurick | 12M follow up | 0.79 (0.47–1.11) | 1.11 (0.85–1.38) | 1.45 (1.20–1.69) | 1.59 (1.44–1.73) | <.0001 | 0.7060 | 0.2890 |
| | 24M follow up | 0.87 (0.53–1.21) | 1.09 (0.83–1.35) | 1.57 (1.31–1.83) | 1.66 (1.51–1.81) | | | |
| NDI | 12M follow up | 11.55 (7.52–15.59) | 11.52 (8.20–14.83) | 19.35 (15.19–23.52) | 10.43 (8.54–12.31) | .0003 | .0734 | 0.3814 |
| | 24M follow up | 15.05 (11.11–19.00) | 9.96 (6.67–13.24) | 19.62 (15.53–23.72) | 10.76 (8.69–12.83) | | | |
| SF-36 | 12M follow up | 6.70 (4.57–8.83) | 4.71 (2.92–6.51) | 9.71 (8.08–11.34) | 5.42 (4.37–6.47) | <.0001 | 0.2751 | .0482 |
| PCS | 24M follow up | 5.29 (3.14–7.43) | 3.26 (1.55–4.96) | 9.89 (8.18–11.60) | 5.14 (4.15–6.13) | | | |
| SF-36 | 12M follow up | 10.05 (7.45–12.65) | 3.71 (1.41–6.01) | 7.07 (4.97–9.16) | 5.78 (4.51–7.05) | <.0001 | 0.1309 | 0.6936 |
| MCS | 24M follow up | 11.56 (8.88–14.25) | 3.17 (0.97–5.37) | 7.09 (4.99–9.19) | 4.39 (3.07–5.71) | | | |
| B | | | | | | | | |
| mJOA | 12M follow up | 2.33 (0.63–4.04) | 2.02 (0.44–3.61) | 2.94 (1.26–4.62) | 3.11 (1.53–4.69) | .0002 | 0.3605 | 0.3261 |
| | 24M follow up | 2.26 (0.55–3.96) | 2.05 (0.45–3.65) | 3.06 (1.40–4.72) | 3.37 (1.77–4.98) | | | |
| Nurick | 12M follow up | 0.90 (−.08 to 1.88) | 1.25 (0.31–2.19) | 1.30 (0.35–2.26) | 1.60 (0.72–2.47) | .0037 | 0.6884 | 0.2283 |
| | 24M follow up | 1.02 (.01–2.03) | 1.23 (0.29–2.17) | 1.43 (0.48–2.38) | 1.67 (0.78–2.55) | | | |
| NDI | 12M follow up | 7.31 (−6.32 to 20.93) | 3.91 (−8.88 to 16.70) | 11.05 (−2.36 to 24.47) | 3.22 (−9.08 to 15.52) | .0035 | .0946 | 0.3836 |
| | 24M follow up | 10.66 (−2.98 to 24.31) | 2.41 (−10.51 to 15.32) | 11.44 (−199 to 24.87) | 3.53 (−8.79 to 15.84) | | | |
| SF-36 | 12M follow up | 4.09 (−3.03 to 11.21) | 1.78 (−4.70 to 8.26) | 5.13 (−1.62 to 11.88) | 2.49 (−3.77 to 8.76) | .0109 | 0.2330 | .0423 |
| PCS | 24M follow up | 2.60 (−4.58 to 9.79) | 0.27 (−6.24 to 6.78) | 5.33 (−1.49 to 12.16) | 2.22 (−4.08 to 8.51) | | | |
| SF-36 | 12M follow up | 3.44 (−6.07 to 12.94) | −4.13 (−12.74 to 4.48) | −2.34 (−11.23 to 6.56) | −1.63 (−10.11 to 6.85) | <.0001 | 0.1059 | 0.7314 |
| MCS | 24M follow up | 5.12 (−4.10 to 14.34) | −4.62 (−13.31 to 4.07) | −2.28 (−11.10 to 6.55) | −3.04 (−11.47 to 5.38) | | | |

mJOA, modified Japanese Orthopedic; NDI, Neck Disability Index; SF-36 PCS, Short Form 36 Physical Component Score; SF-36 MCS, Short Form 36 Mental Component Score.

Values are given as mean changes scores with 95% confidence intervals.

A p-value of <.05 for "region" indicates a significant difference in outcomes across the four geographic regions. A p-value of <.05 for "Visit" indicates a significant difference in outcomes between 12- and 24-month postoperative visits. Finally, a p-value for the interaction term "region×visit" indicates that different regions exhibit different patterns of improvements in outcomes between 12 and 24-month follow-ups.

Adjusted for gender, age, log of duration of disease, smoking status, years of education, sources of stenosis (spondylosis, intervertebral disc, ossified posterior longitudinal ligament, hypertrophic ligamentum flavum, congenital stenosis, and subluxation), affected cervical levels, comorbidities by body system cardiological, respiratory, gastrointestinal, renal, endocrinological, psychiatric, rheumatologic, and neurologic), plus duration of surgery, anterior approach, posterior approach, anterior discectomy, anterior corpectomy, anterior fusion, anterior fixation, laminectomy without fusion, laminectomy and instrumented fusion, and laminoplasty.

### *SF-36v2 PCS and MCS*

At 24 months, improvements in the SF-36v2 PCS were higher in patients from Asia Pacific (9.89, 95% CI: 8.18–11.60) than those from Latin America (5.29, 95% CI: 3.14–7.43), North America (5.14, 95% CI: 4.15–6.13), and Europe (3.26, 95%: 1.55–4.96) (p<.0001) (Table 4A). The differences among the regions remained significant after adjusting for patient and disease covariates (p=.0109) (Table 4B).

With respect to the SF-36v2 MCS, improvements at 24 months were the highest in Latin America (11.56, 95% CI: 8.88–14.25) and in Asia Pacific (7.09, 95% CI: 4.99–9.19) and lowest in North America (4.39, 95% CI: 3.07–5.71) and in Europe (3.17, 95% CI: 0.97–5.37) (p<.0001). These differences among the regions remained statistically significant following adjustment for confounders (p<.0001).

### *Sensitivity analysis*

Results from a sensitivity analysis using non-imputed data did not differ from those of the imputed analysis.

### *Complications*

Overall, 24.8% of patients experienced one or more treatment complications in the first year after surgery (Table 5). The three most common complications were dysphagia (4.6%), neck or arm pain (4.9%), and progression of myelopathy (3.0%). The complication rate was highest in Europe (34.9%), followed by Latin America (33.8%), North America (22.2%), and Asia Pacific (18.7%) (p<.0001). The highest reported rate of dysphagia was in Europe (10.3%) as was the highest rate of myelopathy progression (7.1%). The rate of neck or arm pain was highest in Latin America (17.5%).

## Discussion

The present study represents the first prospective evaluation of geographic variations in the presentation and management of DCM. We identified regional differences in demographics, myelopathy severity, causative pathology, surgical approach, and extent of postoperative improvements. This evidence is an important step in optimizing treatment strategies, standardizing care across regions,

Table 5
Complications in the first year after decompressive surgery by region and category

| | Latin America | | | | Europe | | | | Asia Pacific | | | | North America | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0–30 d | 31–365 d | All | | 0–30 d | 31–365 d | All | | 0–30 d | 31–365 d | All | | 0–30 d | 31–365 d | All | | 0–30 d | 31–365 d | All | |
| Pseudarthrosis | 0 | 0 | 0 | .0% | 2 | 1 | 3 | 2.4% | 0 | 0 | 0 | .0% | 0 | 3 | 3 | 0.7% | 2 | 4 | 6 | 0.8% |
| Hardware failure | 0 | 0 | 0 | .0% | 0 | 1 | 1 | 0.8% | 1 | 1 | 2 | 1.3% | 0 | 1 | 1 | 0.2% | 1 | 3 | 4 | 0.5% |
| C5 radiculopathy | 2 | 0 | 2 | 2.5% | 1 | 0 | 1 | 0.8% | 1 | 2 | 3 | 2.0% | 5 | 0 | 5 | 1.2% | 9 | 2 | 11 | 1.5% |
| Dural tear | 1 | 0 | 1 | 1.3% | 0 | 0 | 0 | .0% | 6 | 0 | 6 | 4.0% | 8 | 0 | 8 | 2.0% | 15 | 0 | 15 | 2.0% |
| Deep infection | 1 | 0 | 1 | 1.3% | 1 | 0 | 1 | 0.8% | 0 | 0 | 0 | .0% | 2 | 0 | 2 | 0.5% | 4 | 0 | 4 | 0.5% |
| Iatrogenic fracture | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 0 | 1 | 0.2% | 1 | 0 | 1 | 0.1% |
| DVT | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 0 | 1 | 0.2% | 1 | 0 | 1 | 0.1% |
| Adjacent segment degeneration | 0 | 2 | 2 | 2.5% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 0 | 4 | 4 | 1.0% | 0 | 6 | 6 | 0.8% |
| Superficial infection | 1 | 1 | 2 | 2.5% | 4 | 2 | 6 | 4.8% | 1 | 1 | 2 | 1.3% | 7 | 2 | 9 | 2.2% | 13 | 6 | 19 | 2.5% |
| Dysphagia | 0 | 1 | 1 | 1.3% | 12 | 1 | 13 | 10.3% | 0 | 2 | 2 | 1.3% | 16 | 3 | 19 | 4.7% | 28 | 7 | 35 | 4.6% |
| Dysphonia | 0 | 0 | 0 | .0% | 2 | 0 | 2 | 1.6% | 0 | 0 | 0 | .0% | 1 | 1 | 2 | 0.5% | 3 | 1 | 4 | 0.5% |
| Residual or progressing symptoms of myelopathy | 0 | 3 | 3 | 3.8% | 3 | 6 | 9 | 7.1% | 1 | 2 | 3 | 2.0% | 4 | 4 | 8 | 2.0% | 8 | 15 | 23 | 3.0% |
| New radiculopathy (not C5) | 1 | 0 | 1 | 1.3% | 1 | 0 | 1 | 0.8% | 0 | 1 | 1 | 0.7% | 3 | 1 | 4 | 1.0% | 5 | 2 | 7 | 0.9% |
| Perioperative worsening of myelopathy | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 0 | 1 | 0.7% | 1 | 0 | 1 | 0.2% | 2 | 0 | 2 | 0.3% |
| Graft site pain | 0 | 0 | 0 | .0% | 1 | 1 | 2 | 1.6% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 1 | 2 | 0.3% |
| Postoperative kyphosis | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 1 | 2 | 1.3% | 6 | 2 | 8 | 2.0% | 7 | 3 | 10 | 1.3% |
| Cardiopulmonary event | 1 | 0 | 1 | 1.3% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 0 | 1 | 0.2% | 2 | 0 | 2 | 0.3% |
| Relevant bleeding | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 4 | 0 | 4 | 1.0% | 4 | 0 | 4 | 0.5% |
| Thromboembolism | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 0 | 1 | 0.2% | 1 | 0 | 1 | 0.1% |
| Stroke | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 0 | 0 | 0 | .0% | 1 | 0 | 1 | 0.2% | 1 | 0 | 1 | 0.1% |
| Instrumentation malposition or migration | 1 | 1 | 2 | 2.5% | 3 | 1 | 4 | 3.2% | 0 | 1 | 1 | 0.7% | 2 | 2 | 4 | 1.0% | 6 | 5 | 11 | 1.5% |
| Neck or arm pain | 4 | 10 | 14 | 17.5% | 5 | 6 | 11 | 8.7% | 3 | 3 | 6 | 4.0% | 3 | 3 | 6 | 1.5% | 15 | 22 | 37 | 4.9% |
| Surgical wound problems (eg, hematoma and dehiscence) | 0 | 0 | 0 | .0% | 2 | 0 | 2 | 1.6% | 0 | 0 | 0 | .0% | 4 | 0 | 4 | 1.0% | 6 | 0 | 6 | 0.8% |
| **deep vein thrombosis** Other | 3 | 0 | 3 | 3.8% | 1 | 1 | 2 | 1.6% | 2 | 2 | 4 | 2.7% | 14 | 5 | 19 | 4.7% | 20 | 8 | 28 | 3.7% |
| Any complication | 13 | 15 | 27 | 33.8% | 29 | 17 | 44 | 34.9% | 17 | 13 | 28 | 18.7% | 66 | 27 | 89 | 22.2% | 125 | 72 | 188 | 24.8% |

DVT, deep vein thrombosis.

and developing international guidelines for the management of DCM.

Patients from Asia Pacific were, on average, younger than those from North America and Europe. This finding is likely a consequence of the fact that patients from Asia Pacific have congenitally narrower spinal canals and a higher rate of OPLL. In a recent subanalysis of the AOSpine dataset, patients diagnosed with congenital spinal stenosis (spinal canal occupying ratio ≥70%) were, on average, 5.5 years younger than those with an occupying ratio <70%; this result is expected as patients with a decreased space available for the spinal cord require less substantial degenerative changes to cause compression. Patients from Latin America had a significantly longer duration of symptoms than those from the other three regions; this difference may reflect a more conservative approach to the treatment of DCM in Latin America or a delayed recognition and diagnosis of myelopathy. Despite these demographic differences, preoperative mJOA and NDI scores were similar across regions. In contrast, there were significant geographic differences in the SF-36v2 PCS and MCS, which likely reflect sociocultural differences in the perception of illness.

Among regions, the most common causes of spinal stenosis and myelopathy were spondylosis and disc herniation. This finding is to be expected as the degenerative process is typically initiated at the level of the intervertebral discs [6]. Changes to the disc include dehydration, loss of height, and an increase in proteases responsible for the enzymatic degradation process [22]. These changes ultimately result in disc degeneration, alterations in the weight-bearing function of the intervertebral joint, and increased stress on the end plates [6]. Consequences of disc desiccation include facet hypertrophy, subluxation, osteophyte formation, and buckling and stiffening of the supporting ligament [23]. Myelopathy secondary to OPLL was the most common in Asia Pacific and accounted for over one-third of the cases in this region. Individuals from these regions may have a certain genetic predisposition that, when combined with specific environmental and occupational factors, may increase the risk of OPLL development. Surprisingly, OPLL was almost equally common in Europe, although this finding was mostly due to a high prevalence in patients from Turkey. Potential explanations for an increased rate of OPLL in Turkey include the following: (1) inter-racial marriages are common in these areas and result in greater genetic diversity, and (2) historically, individuals migrated from Central Asia to Turkey [24]. Furthermore, regional differences may exist in the methods of diagnosis and classification of OPLL; there is a pressing need to standardize diagnostic criteria for this disease and to further consider factors such as type, extent, and occupying ratio of ossification. The rate of degenerative HLF was surprisingly high in Latin America compared with the other regions, which is likely attributed to both genetic and environmental factors.

Surgical decision making is often influenced by sagittal alignment, extent of pathology, location of compression, the presence of radiculopathy or axial pain, age, comorbidities, and the surgeon's familiarity with the procedure [25]. The majority of cases in North America and in Europe were performed anteriorly. Interestingly, 60.67% of patients were also treated anteriorly in Asia Pacific, despite the popularity of the laminoplasty procedure. Contributing factors to this preference include younger age, high frequency of disc herniation, and low frequency of HLF. Furthermore, in several studies, anterior surgery results in superior surgical outcomes in patients with a high occupying ratio of OPLL as this approach facilitates direct removal of the source of compression [26–28]. In contrast, most patients from Latin America were treated posteriorly; this surgical decision may have been influenced by the high rate of HLF in this region. The number of decompressed levels and operative duration also varied across regions; these differences likely reflect differences in the surgical technique and the extent of compressive pathology.

Although patients across centers exhibited gains in function, disability, and quality of life following surgery, there were significant regional differences in the extent of improvement. Specifically, patients from North America and Asia Pacific achieved greater improvements in functional impairment, as evaluated by change in mJOA scores and Nurick grades, than those from Europe and Latin America. These differences in functional outcomes were statistically significant even after adjusting for patient, disease, and surgical confounders such as age, gender, number of decompressed levels, and surgical techniques. In contrast, patients from Asia Pacific and Latin America exhibited greater improvements in disability and quality of life than those from the other two regions. This finding likely reflects differences in sociocultural perceptions of illness and indicates that similar improvements in function (ie, between North America and Asia Pacific) do not necessarily translate to similar gains in disability and quality of life. Unfortunately, we were unable to control for socioeconomic and cultural influences as well as other possibly relevant factors.

The duration of hospital stay varied significantly across regions and was the longest in Asia Pacific. These variations likely reflect local hospital discharge policies and cultural practices rather than patient needs or outcomes. The overall rate of complications in our study was 24.8%, which is within the range of reported rates in the literature. Common complications were dysphagia, superficial infection, dural tear, and C5 radiculopathy. There were significant variations in complication rates among the regions, which may be partly explained by variations in surgical approaches. Specifically, patients from Europe had the highest rate of anterior surgery as well as the highest rate of dysphagia. Furthermore, neck pain was a particularly common complication in Latin America, where most patients underwent posterior surgery.

### *Limitations*

There are important limitations to the present study. First, this evaluation was based on a non-randomized comparison study. Although extensive statistical adjustments were performed, there may have been confounding covariates

unaccounted for in our statistical models. Second, not all countries were represented in the study, and any generalization of results to different regions should be done with caution. Third, although the follow-up rate was high, outcome data from some patients were missing and accounted for using a multiple imputation procedure. The robustness of our conclusions from the imputed data was validated through a sensitivity analysis using non-imputed data. Fourth, preoperative NDI data were unavailable for 68 patients (45.33%) from Asia Pacific. The majority, however, were from centers in China where a translated version of the NDI had not been validated at the time of the study. Fifth, we were unable to evaluate regional differences with respect to the selection of conservative versus surgical intervention for patients with varying severities of myelopathy; future studies are required to investigate these types of preferences in management strategies. Finally, the causative pathology was determined by the attending surgeon without the use of standardized imaging criteria. As a result, variations in diagnosis may be due to differences in definitions of degenerative changes.

## Conclusion

Surgical decompression for DCM results in improvements in function, disability, and the quality of life of patients from around the world and should be recommended as a treatment option for symptomatic myelopathy. This observational study, however, revealed significant differences in outcomes among regions and summarized expected results following surgical treatment in different centers. Standardization of management strategies and development of evidence-based clinical guidelines are necessary because of regional differences in patient outcomes, significant variations in surgical practices, and discrepancies in rates of complications and the length of hospital stay.

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