■ SPINE

Defining multilevel developmental cervical spinal stenosis using MRI

A POPULATION-LEVEL STUDY

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Aims

Developmental cervical spinal stenosis (DcSS) is a well-known predisposing factor for degenerative cervical myelopathy (DCM) but there is a lack of consensus on its definition. This study aims to define DcSS based on MRI, and its multilevel characteristics, to assess the prevalence of DcSS in the general population, and to evaluate the presence of DcSS in the prediction of developing DCM.

Methods

This cross-sectional study analyzed MRI spine morphological parameters at C3 to C7 (including anteroposterior (AP) diameter of spinal canal, spinal cord, and vertebral body) from DCM patients (n = 95) and individuals recruited from the general population (n = 2,019). Level-specific median AP spinal canal diameter from DCM patients was used to screen for stenotic levels in the population-based cohort. An individual with multilevel (≥ 3 vertebral levels) AP canal diameter smaller than the DCM median values was considered as having DcSS. The most optimal cut-off canal diameter per level for DcSS was determined by receiver operating characteristic analyses, and multivariable logistic regression was performed for the prediction of developing DCM that required surgery.

Results

A total of 2,114 individuals aged 64.6 years (SD 11.9) who underwent surgery from March 2009 to December 2016 were studied. The most optimal cut-off canal diameters for DcSS are: C3 < 12.9 mm, C4 < 11.8 mm, C5 < 11.9 mm, C6 < 12.3 mm, and C7 < 13.3 mm. Overall, 13.0% (262 of 2,019) of the population-based cohort had multilevel DcSS. Multilevel DcSS (odds ratio (OR) 6.12 (95% CI 3.97 to 9.42); p < 0.001) and male sex (OR 4.06 (95% CI 2.55 to 6.45); p < 0.001) were predictors of developing DCM.

Conclusion

This is the first MRI-based study for defining DcSS with multilevel canal narrowing. Level-specific cut-off canal diameters for DcSS can be used for early identification of individuals at risk of developing DCM. Individuals with DcSS at ≥ three levels and male sex are recommended for close monitoring or early intervention to avoid traumatic spinal cord injuries from stenosis.

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Introduction

Developmental cervical spinal stenosis (DcSS) is a congenital condition associated with genetic disturbance with pre-existing narrowing of the cervical spinal canal.[1-3] DcSS is considered as an important risk factor for degenerative cervical myelopathy (DCM),[1,2,4-9] which can result from various forms of degenerative pathologies including cervical spondylosis, posterior longitudinal ligament ossification, and ligamentum flavum hypertrophy.[10] Patients with DcSS are more susceptible to DCM, as the narrowed dimension of cervical spinal canal predisposes patients to spinal cord compression even with a mild degree of degeneration, whereas individuals without canal narrowing may not develop DCM with degeneration of the same extent.[1,2,8,11] Cervical canal narrowing of DcSS can be found on medical imaging even before the onset of symptoms. Therefore, it is ideal to identify these patients with a high risk of spinal cord

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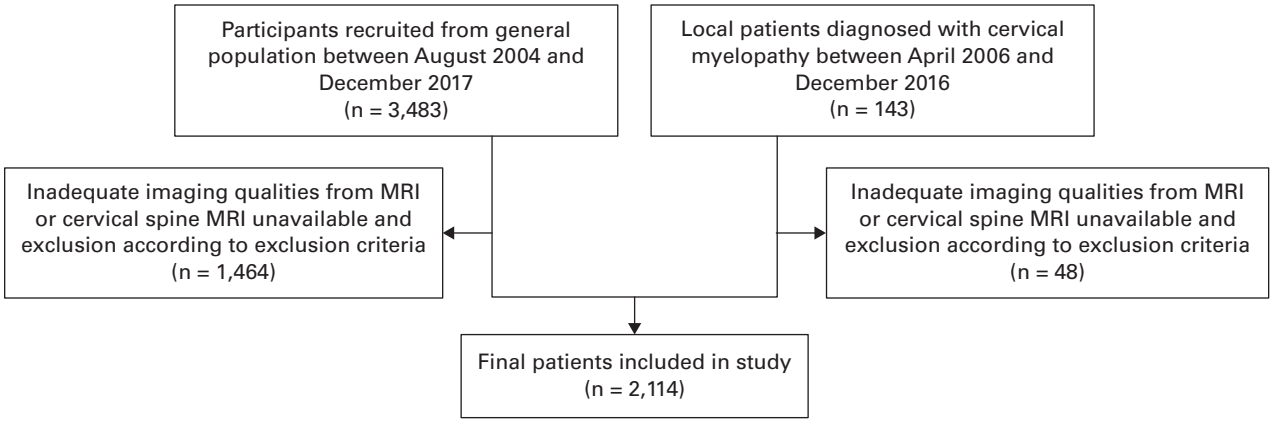

Fig. 1

Flowchart of patient recruitment.

compression early, for consideration of prophylactic surgery or posterior canal widening in order to prevent severe cord injury.[12]

Currently, there is a lack of image-based definition of DcSS representing the multilevel characteristics of developmental spinal stenosis. Generalized narrowing of the spinal canal from developmental spinal stenosis has implications for the likelihood of developing symptoms and early surgery.[13,14] Lai et al[13,15–17] showed that in the lumbar spine, developmental spinal stenosis led to multilevel stenosis because the abnormal spinal canal development affected multiple vertebral levels rather than a single level. Given that these anomalies occur during neural tube development, these phenotypes should also be identified in the cervical spine, but existing DcSS definitions have not taken into consideration the nature of multilevel involvement of vertebral stenosis.[1,8,18-20] MRI is the gold-standard imaging modality for DCM, as both osseous structures and soft-tissues are clearly seen, thereby enabling direct sagittal diameter measurement of the cervical spinal canal, vertebral body, and spinal cord, as well as assessment of ligamentum hypertrophy and any associated intervertebral disc herniation.[2,6,10] Several studies have reported normal MRI cervical spine morphology in population cohorts,[2,21-25] while some attempted to define DcSS based on generalized but not level-specific measurement at individual vertebral levels.[2,8] Among those studies proposing DcSS cut-off values, study populations were heterogeneous with various methodological and imaging methods, ranging from cadaveric studies to lateral radiograph assessment, and from CT to MRI.[4,8,18,19,23,26-30] There is, however, a lack of consensus on the definition of DcSS, with clinical implications for the management of patients with DCM.[31-33]

This study aims to: define the developmental narrowing of the cervical spinal canal based on MRI, and its multilevel characteristics; assess how common cervical developmental canal narrowing is in the local general population; and evaluate the presence of multilevel DcSS in predicting the development of DCM which requires surgical intervention. The study provides population-based cut-off values of spinal canal diameter for detecting DcSS in the Chinese population.

Methods

The study included a total of 2,114 individuals, consisting of 95 patients who underwent surgery for DCM from March 2009 to December 2016 at a single tertiary spine centre and 2,019 individuals openly recruited from the local general population (Figure 1). All individuals included had to be aged 18 years or above, and of Chinese ethnicity. The patients with DCM were diagnosed by spinal surgeons based on clinical assessment of symptoms along with MRI evidence. Clinical information and MRI of the DCM patients were retrieved from the local hospital database. Patients with cervical spine fractures or tumour, infection, rheumatoid arthritis, congenital cervical spinal deformities, previous cervical spine surgery, spinal cord injury due to other causes including trauma or traffic accidents, hyperflexion, or hyperextension were excluded. For the population-based cohort, individuals were openly recruited via news articles and emails, with the invitation to undergo MRI and clinical assessment at the time of recruitment for the screening of genomics in relation to degenerative skeletal disorders (Theme-based Research Scheme (T12-708/12 N) and Area of Excellence Scheme (AoE/M-04/04)). Individuals with a diagnosis or history of cervical myelopathy, cervical spine fractures, tumours, infections, congenital pathologies, or previous cervical spine surgeries were excluded. Exclusion criteria also included MRI images of poor quality. Ethical approval from the local institutional review board and informed consent from participants were obtained.

MRI protocol. For both DCM patients and population-based cohort participants, 3-Tesla HD MRI machines were used for imaging. For DCM patients, only preoperative MRI scans were used for measurement. These scans were taken with slice thickness and slice spacing of 3 mm and 0 mm, respectively. Field of view was 24 cm × 24 cm. The imaging matrix was 512 × 512. The repetition time and echo time were 3,000 to 4,000 ms and 80 ms to 90 ms, respectively. For MRI of the general population cohort, the field of view was 30 cm × 30 cm, with 4 mm slice thickness and 0.4 mm slice spacing. The imaging matrix was 448 × 336. The repetition time and echo time were 3,000 to 4,000 ms and 80 ms to 120 ms, respectively.

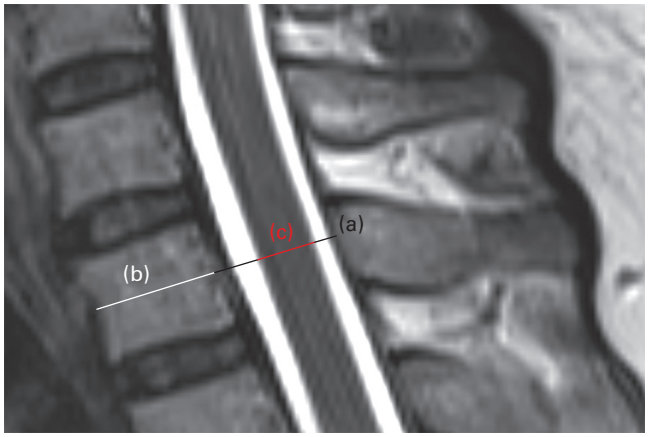

Fig. 2

Measurement on T2-weighted sagittal image: a) anteroposterior (AP) diameter of cervical spinal canal; b) mid-vertebral AP diameter of vertebral body; c) AP diameter of cervical spinal cord (measured on the same line for a)).

MRI measurement. A standardized method of measurement was used by the two investigators (JHML, VWYL) who performed the measurement independently, and they were blinded to all clinical information. T2-weighted sagittal slices of the cervical spine were selected for measurements. All measurements were performed on the median slice with the apparent largest spinous process, using eUnity Diagnostic Viewer v. 6.10.2 (Canada) and Philips DICOM Viewer R3.0-SP15 (Philips, Netherlands).

The anteroposterior (AP) diameter of the cervical spinal canal, vertebral body, and spinal cord was measured at mid-vertebral level from C3 to C7. The AP diameter of the cervical spinal canal was measured by a line perpendicular to the anterior surface of the spinal cord connecting the midpoint of the superior and inferior endplate of the posterior surface of the vertebral body to the spinolaminar line. The AP diameter of the cervical spinal cord was measured by the same line used for measuring the AP diameter of the cervical canal. The AP diameter of the vertebral body was measured by a line from the midpoint of the anterior and posterior margin of the vertebral body (Figure 2).[34] To represent the relationships between the cervical spinal canal, vertebral body, and spinal cord, the canal-body ratio (AP diameter of cervical spinal canal divided by AP diameter of cervical vertebral body), space available for cord (AP diameter of cervical spinal canal minus AP diameter of cervical spinal cord), cord-canal ratio (AP diameter of cervical spinal cord divided by AP diameter of cervical spinal canal), and cord-vertebral body ratio (AP diameter of cervical spinal cord divided by AP diameter of cervical vertebral body) were calculated.[8,21]

Inter- and intrarater reliabilities were assessed by Cronbach α analysis. The first and second rounds of measurement of randomly selected MRI slices with 50 measurements per parameter were performed four weeks apart. An α value of 0.90 to 1.00 and 0.80 to 0.90 indicated excellent and good reliability, respectively.[35] Good to excellent inter-rater reliability (α = 0.84 to 0.97) and excellent intrarater reliability (α = 0.91 to 0.99) were found.

Statistical analysis. Descriptive and frequency statistics were presented for demographics and spine morphological measurement (AP diameter of cervical spinal canal, spinal cord, vertebral body, canal-body ratio, space available for the cord, cord-canal ratio, cord-vertebral body ratio). Data normality was tested.

In order to represent the extent of cervical canal narrowing resulting in the development of DCM, spinal canal sizes of the cohort of DCM patients (n = 95) were used as reference for assessing whether stenotic vertebral levels were present in an individual. At each vertebral level of C3 to C7, the median AP spinal canal diameter of DCM patients was first found, and this was considered appropriate for defining a vertebral level as stenotic, since the median value reflected the narrowest 50% AP spinal canal diameter of DCM patients. Each individual in the general population cohort (n = 2,019) was then examined if their spinal canal diameter was below the level-specific median value at each vertebral level. To address the nature of multilevel involvement, a composite score for DcSS was established for each population-based individual with a full score of 5, consisting of a score of 1 for each stenotic level. A composite score of ≥ 3, meaning the AP spinal canal diameter was narrower than the DCM median values at three or more vertebral levels, indicated the individual was likely to have multilevel pre-existing bony canal narrowing. This definition also relates to the surgical relevance of a two-level decompression corresponding to three vertebral levels. This stratified the general population cohort into DcSS versus non-DcSS, with prevalence rate reported in percentage.

This differentiation of population-based cohort between DcSS and non-DcSS was examined through intergroup comparison of cervical spine morphologies using Mann-Whitney U tests. Receiver operating characteristic (ROC) analysis was performed to determine the optimal cut-off AP spinal canal diameter at each level from C3 to C7 for detecting DcSS, with the highest Youden's Index, sensitivity, and specificity at each vertebral level.[36] An area under the curve (AUC) of 0.7 to 0.8, 0.8 to 0.9, or ≥ 0.9 was considered acceptable, excellent, or outstanding, respectively, while 0.5 indicated no discriminating power.[37] Multivariable logistic regression was used for the prediction of developing DCM requiring surgical intervention with the presence of DcSS (Yes/No, based on canal diameter less than the newly defined cut-off values at ≥ 3 levels) as a factor, together with patient demographic data.

A p-value < 0.05 was considered statistically significant. All statistical analyses were performed by SPSS Statistics v.28 (IBM, USA) and G*Power v.3.1.9.7. (Heinrich-Heine-Universität Düsseldorf, Germany).

Results

A total of 2,114 individuals were studied, comprising 95 DCM patients (68 males and 27 females) and 2,019 cohort participants (780 males and 1,239 females), with a mean age of 64.6 years (SD 11.9) and 50.1 years (SD 9.6) for males and females, respectively. Baseline characteristics of the DCM patients and population-based cohorts are presented in Table I. The causes of

Table I. Characteristics of the general population and degenerative cervical myelopathy cohorts.

Parameters	General population cohort			DCM cohort		
	Total	Male	Female	Total	Male	Female
Sex, n (%)	2,019	780 (38.6)	1,239 (61.4)	95	68 (71.2)	27 (28.4)
Mean age at recruitment, yrs (SD)	50.1 (9.6)			64.6 (11.9)		
Mean height, m (SD)		1.70 (0.06)	1.57 (0.06)		1.66 (0.06)	1.54 (0.04)
Mean age at surgery, yrs (SD)	N/A			64.9 (11.9)		
Operated levels, n (%)						
C3 to 4	N/A			12 (12.6)		
C3 to 5	N/A			5 (5.3)		
C3 to 6	N/A			39 (41.1)		
C3 to 7	N/A			5 (5.3)		
C4 to 5	N/A			13 (13.7)		
C4 to 6	N/A			6 (6.3)		
C4 to 7	N/A			1 (1.1)		
C5 to 6	N/A			13 (13.7)		
C6 to 7	N/A			1 (1.1)		
Mean AP diameter of cervical spinal canal, mm (SD)						
Vertebral level						
C3	13.7 (1.3)	13.6 (1.2)	13.8 (1.4)	12.0 (1.2)	11.7 (1.2)	12.1 (1.1)
C4	13.3 (1.4)	13.3 (1.4)	13.3 (1.4)	11.4 (1.1)	11.2 (1.1)	11.4 (1.1)
C5	13.6 (1.5)	13.5 (1.5)	13.6 (1.5)	11.8 (1.2)	12.0 (1.1)	11.8 (1.3)
C6	14.1 (1.6)	14.0 (1.6)	14.1 (1.6)	12.7 (1.6)	12.9 (1.5)	12.7 (1.6)
C7	14.9 (1.5)	14.9 (1.5)	15.0 (1.5)	14.2 (1.2)	14.2 (1.2)	14.2 (1.2)
Mean mid-vertebral AP diameter of vertebral body, mm (SD)						
C3	14.7 (1.5)			16.2 (1.6)		
C4	14.5 (1.7)			16.3 (1.7)		
C5	14.2 (1.9)			16.3 (1.7)		
C6	14.4 (1.8)			16.5 (1.8)		
C7	14.4 (1.6)			16.1 (1.7)		
Mean AP diameter of cervical spinal cord, mm (SD)						
C3	7.5 (0.6)			6.2 (0.8)		
C4	7.2 (0.6)			6.1 (1.0)		
C5	7.0 (0.6)			5.9 (0.9)		
C6	6.8 (0.5)			5.8 (0.8)		
C7	6.4 (0.5)			5.5 (0.6)		
Mean canal-body ratio (SD)						
C3	0.94 (0.13)			0.75 (0.12)		
C4	0.92 (0.11)			0.71 (0.11)		
C5	0.96 (0.13)			0.73 (0.12)		
C6	0.99 (0.13)			0.78 (0.14)		
C7	1.05 (0.12)			0.89 (0.11)		
Mean space available for cord, mm (SD)						
C3	6.1 (1.4)			5.8 (1.2)		
C4	6.1 (1.4)			5.3 (1.2)		
C5	6.5 (1.6)			5.9 (1.3)		
C6	7.2 (1.6)			7.0 (1.6)		
C7	8.6 (1.5)			8.8 (1.2)		
Mean cord-canal ratio (SD)						
C3	0.56 (0.07)			0.52 (0.07)		
C4	0.55 (0.07)			0.54 (0.09)		
C5	0.53 (0.07)			0.50 (0.08)		
C6	0.49 (0.07)			0.46 (0.08)		
C7	0.43 (0.05)			0.39 (0.04)		

Continued

Table I. Continued

Parameters	General population cohort			DCM cohort		
	Total	Male	Female	Total	Male	Female
Mean cord-vertebral body ratio (SD)						
C3	0.52 (0.07)			0.38 (0.06)		
C4	0.50 (0.07)			0.38 (0.07)		
C5	0.50 (0.08)			0.36 (0.07)		
C6	0.48 (0.07)			0.35 (0.06)		
C7	0.45 (0.06)			0.34 (0.05)		

AP, anteroposterior; DCM, degenerative cervical myelopathy; N/A, not applicable.

Table II. Composite score distribution and multilevel canal narrowing in the general population-based cohort.

Vertebral level	C3	C4	C5	C6	C7
DCM cohort					
Mean spinal canal diameter, mm (SD)	12.0 (1.2)	11.4 (1.1)	11.8 (1.2)	12.7 (1.6)	14.2 (1.2)
Median spinal canal diameter, mm (IQR)	12.0 (11.3 to 12.7)	11.2 (10.6 to 12.1)	11.8 (10.9 to 12.6)	12.7 (11.4 to 13.9)	14.1 (13.5 to 15.1)
General population cohort below median DCM values, n (%)	176 (8.7)	119 (5.9)	233 (11.5)	374 (18.5)	563 (27.9)
Distribution of composite scores in general population cohort, n (%)*					
0	1,345 (66.6				
1	279 (13.8)				
2	148 (7.3)				
3	117 (5.8)				
4	111 (5.5)				
5	19 (0.9)				
Location of consecutive multilevel narrowing, n (%)					
C5 to C7	233 (11.5)				
C4 to C6	119 (5.9)				
C3 to C5	19 (0.9)				

*i.e. number of narrow canals.
DCM, degenerative cervical myelopathy.

DCM were: ossification of the posterior longitudinal ligament (n = 18), yellow ligament thickening with and without disc-osteophyte complex (n = 2), and cervical spondylotic myelopathy (n = 75, which consisted of soft disc with or without disc bulging (n = 2), ligamentum flavum hypertrophy (n = 17), and disc bulging/extrusion/protrusion, disc herniation, disc prolapse, or disc-osteophyte complex (n = 56)). In Table II, the median AP canal diameters for DCM patients were: 12.0 mm for C3, 11.2 mm for C4, 11.8 mm for C5, 12.7 mm for C6, and 14.1 mm for C7. By using these median values for screening, 12.2% (247 of 2,019) had a composite score of ≥ 3. At the individual level, 27.9% of the general population cohort had canal narrowing at C7, and 18.5% at C6. C5 to C7 was the cervical segment with highest percentage of consecutive multilevel canal narrowing (11.5%, 233 of 2,019) (Table II).

Given the comparable age and sex of individuals with and without DcSS, intergroup comparison revealed that the DcSS group had a significantly smaller AP canal diameter than the non-DcSS group at all measured levels (all $p < 0.001$) (Table III). The DcSS group had a smaller canal-body ratio at C4 to C7 (all $p < 0.001$) and less space available for the cord at C3 to C7 (all $p < 0.01$), while the spinal cord AP diameters were similar, at C5 to C7 (all $p > 0.05$) in particular. DcSS had a significantly larger cord-canal ratio (C3: $p = 0.041$; C4 to C7: $p < 0.001$). Cut-off values of AP canal diameters were defined for DcSS as follows: C3 12.9 mm, C4 11.8 mm, C5 11.9 mm, C6 12.3 mm, C7 13.3 mm (Table IV). The C3 cut-off value had the worst sensitivity (73.8%) and specificity (41.7%), whereas each level of C4 to C7 cut-off values had excellent sensitivity (98.5% to 98.6%) and specificity (96.8%).

Based on the newly defined cut-off values of spinal canal diameter and narrowing at ≥ three levels, 13.0% of the population-based cohort (262 of 2,019) and 47.4% of the DCM patients (45 of 95) had DcSS. Logistic regression reveals that the presence of DcSS at ≥ three levels was a significant predictor of developing DCM requiring surgical intervention, with an odds ratio (OR) of 6.12 (95% CI 3.97 to 9.42; $p < 0.001$), together with sex (OR 4.06 (95% CI 2.55 to 6.45); $p < 0.001$) (Table V). We can interpret this as showing that an individual with multilevel cervical canal narrowing is six times more likely to develop DCM compared to those with canal narrowing at less than three levels or without narrowing, and that males are four times more likely to have DCM than females.

Discussion

By using MRI, this study has defined level-specific cut-off values of AP cervical spinal canal diameter for DcSS, importantly incorporating the multilevel characteristic of pre-existing

Table III. Comparisons of imaging parameters between developmental cervical spinal stenosis (DcSS; composite score ≥ 3) and non-DcSS (composite score 2 or less) individuals in the general population-based cohort.

Parameters	DcSS group	Non-DcSS group	Post-hoc power (effect size)	p-value
Patients, n	247	1,772		
Mean age, yrs (SD)	51.4 (9.0)	49.9 (9.6)	0.58 (0.16)	0.087*
Sex, n			0.79 (0.06)	0.370†
Male	89	691		
Female	158	1,081		
Mean AP diameter of cervical spinal canal, mm (SD)				
C3	13.3 (1.5)	13.7 (1.3)	0.98 (0.30)	< 0.001*
C4	11.1 (0.6)	13.6 (1.1)	> 0.99 (2.38)	< 0.001*
C5	11.0 (0.7)	13.9 (1.2)	> 0.99 (2.52)	< 0.001*
C6	11.4 (0.7)	14.4 (1.3)	> 0.99 (2.41)	< 0.001*
C7	12.6 (0.6)	15.3 (1.2)	> 0.99 (2.36)	< 0.001*
Mean mid-vertebral AP diameter of vertebral body, mm (SD)				
C3	13.7 (1.1)	14.8 (1.5)	> 0.99 (0.75)	< 0.001*
C4	13.5 (1.2)	14.6 (1.7)	> 0.99 (0.67)	< 0.001*
C5	13.1 (1.3)	14.4 (1.9)	> 0.99 (0.71)	< 0.001*
C6	13.3 (1.4)	14.6 (1.8)	> 0.99 (0.74)	< 0.001*
C7	13.3 (1.3)	14.5 (1.6)	> 0.99 (0.77)	< 0.001*
Mean AP diameter of cervical spinal cord, mm (SD)				
C3	7.5 (0.6)	7.6 (0.6)	0.63 (0.17)	0.039*
C4	7.1 (0.6)	7.2 (0.6)	0.63 (0.17)	0.027*
C5	7.0 (0.5)	7.0 (0.6)	0.05 (0.00)	0.076*
C6	6.8 (0.5)	6.8 (0.5)	0.05 (0.00)	0.393*
C7	6.3 (0.4)	6.4 (0.5)	0.80 (0.20)	0.076*
Mean canal-body ratio (SD)				
C3	0.98 (0.14)	00.93 (0.13)	0.99 (0.38)	< 0.001*
C4	0.83 (0.09)	0.94 (0.11)	> 0.99 (1.02)	< 0.001*
C5	0.85 (0.10)	0.98 (0.13)	> 0.99 (1.03)	< 0.001*
C6	00.87 (0.11)	01.00 (0.12)	> 0.99 (1.09)	< 0.001*
C7	0.95 (0.10)	1.06 (0.12)	> 0.99 (0.93)	< 0.001*
Mean space available for cord, mm (SD)				
C3	5.8 (1.6)	6.2 (1.4)	0.97 (0.28)	0.004*
C4	4.0 (0.8)	6.4 (1.3)	> 0.99 (1.92)	< 0.001*
C5	4.0 (0.8)	6.9 (1.3)	> 0.99 (2.32)	< 0.001*
C6	4.6 (0.8)	7.6 (1.3)	> 0.99 (2.40)	< 0.001*
C7	6.2 (0.7)	8.9 (1.3)	> 0.99 (2.17)	< 0.001*
Mean cord-canal ratio (SD)				
C3	0.57 (0.08)	0.56 (0.07)	0.48 (0.14)	0.041*
C4	0.64 (0.06)	0.53 (0.06)	> 0.99 (1.83)	< 0.001*
C5	0.64 (0.06)	0.51 (0.06)	> 0.99 (2.17)	< 0.001*
C6	0.60 (0.06)	0.48 (0.05)	> 0.99 (2.34)	< 0.001*
C7	0.50 (0.04)	0.42 (0.04)	> 0.99 (2.00)	< 0.001*
Mean cord-vertebral body ratio (SD)				
C3	0.55 (0.07)	0.52 (0.07)	> 0.99 (0.43)	< 0.001*
C4	0.53 (0.07)	0.50 (0.07)	> 0.99 (0.43)	< 0.001*
C5	0.54 (0.07)	0.50 (0.08)	> 0.99 (0.51)	< 0.001*
C6	0.52 (0.07)	0.48 (0.07)	> 0.99 (0.57)	< 0.001*
C7	0.48 (0.06)	0.44 (0.06)	> 0.99 (0.67)	< 0.001*

*Mann-Whitney U test.
†Chi-squared test.
DcSS, developmental cervical spinal stenosis.

canal narrowing in developmental spinal stenosis. Based on the proposed criteria of defining DcSS (i.e. with canal narrowing detected at three or more levels), individuals with DcSS were successfully differentiated from those without DcSS as DcSS was demonstrated to have a narrower canal diameter, less space available for the cord, and a higher cord-canal mismatch, while spinal cord sizes were similar. The relationship between spinal cord size and canal space is crucial, as the space available for the neural bundles is the amount of leeway available for developmental spinal stenosis. Given the similar spinal cord size, less

Table IV. Receiver operating characteristics analysis of developmental cervical spinal stenosis cut-off values of anteroposterior spinal canal diameter per cervical vertebral level.

Vertebral level	Cut-off value of AP spinal canal diameter for DcSS, mm	AUC (95% CI)	Sensitivity %	Specificity %	Youden's index	p-value
C3	12.9	0.573 (0.533 to 0.614)	73.8	41.7	0.155	< 0.001
C4	11.8	0.998 (0.997 to 0.999)	98.6	96.8	0.954	< 0.001
C5	11.9	0.998 (0.997 to 0.999)	98.5	96.8	0.953	< 0.001
C6	12.3	0.998 (0.997 to 0.999)	98.6	96.8	0.954	< 0.001
C7	13.3	0.998 (0.997 to 0.999)	98.6	96.8	0.954	< 0.001

AP, anteroposterior; AUC, area under the curve; DcSS, developmental cervical spinal stenosis.

Table V. Logistic regression of developing degenerative cervical myelopathy requiring surgery. $X^2(2) = 101.403$, $p < 0.001$, correct prediction = 95.5%

Parameter	Coefficient, β (SE)	Ward X^2	Odds ratio (95% CI)	p-value
Presence of multilevel DcSS*	1.811 (0.220)	67.592	6.12 (3.97 to 9.42)	< 0.001
Male sex†	1.401 (0.236)	35.087	4.06 (2.55 to 6.45)	< 0.001

*Reference: no multilevel DcSS.
†Reference: female.
DcSS, developmental cervical spinal stenosis.

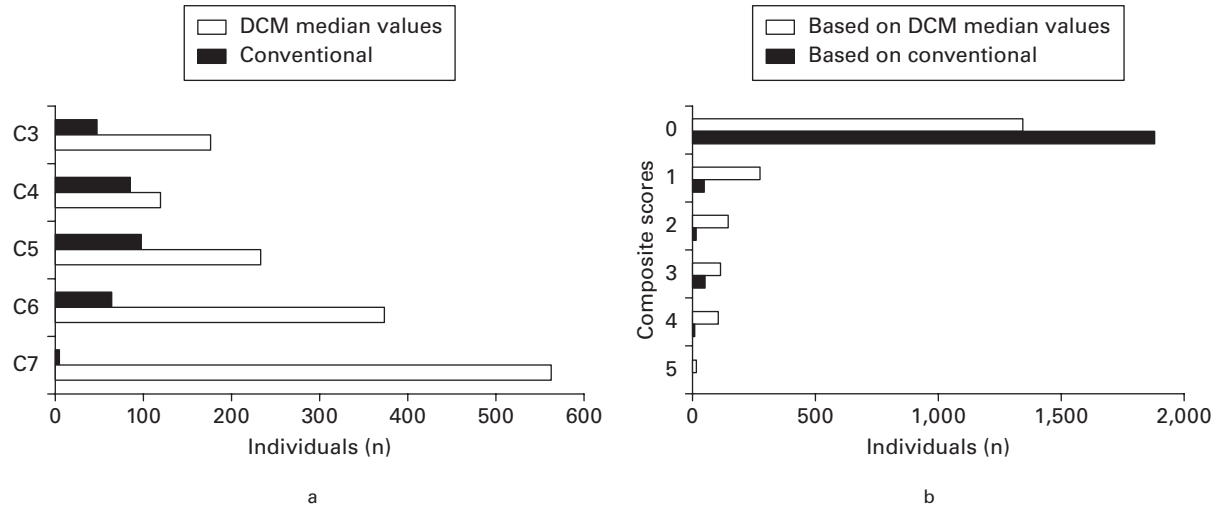

Fig. 3

a) Number of individuals with canal narrowing screened by conventional versus degenerative cervical myelopathy (DCM) median anteroposterior (AP) canal diameters. b) Composite score distributions representing the number of levels with canal narrowing.

canal space available poses a risk for neural compression. In addition, the presence of such DcSS was found to be predictive of the development of DCM that warrants surgery. This provides a set of canal size criteria for identifying patients potentially at risk of developing DCM, making image screening at an early stage possible prior to further deterioration and traumatic spinal cord compression.

With the lack of consensus on a clear definition of DcSS, it remains unclear under what criteria an individual is considered at risk of DCM. Our study has first used the local DCM cohort as a guiding reference and incorporated the characteristics of multilevel involvement of canal narrowing at three vertebral levels or more for initial screening of stenotic levels. This has revealed that cervical canal narrowing is not uncommon (12.2% of the population-based cohort, with consecutive levels of canal narrowing most common at the lower cervical segment at C5 to C7), however more customized values for DcSS screening in the general population are required. This is because we found that when the screening criteria are too stringent, as demonstrated by the conventional use of a generalized spinal canal diameter of 11 mm for screening a narrowed canal,[38] many individuals with narrowed canals as well as the multilevel characteristics are missed in comparison with using the DCM cohort level-specific median canal diameters (Figure 3). Hence, there is a need to refine the set of diagnostic criteria of cervical canal sizes, and we have derived the cut-off spinal canal diameters from the population-based cohort.

We recommend clinicians detect the presence of DcSS by examining the AP spinal canal diameter, particularly at C4 to C7 based on our level-specific cut-offs defined with high

sensitivity and specificity. The recommended AP spinal canal diameters for clinical use are: C3 < 13 mm, C4 < 12 mm, C5 < 12 mm, C6 < 12.5 mm, and C7 < 13.5 mm. Early identification of individuals with DcSS and early action are extremely important, as the traumatic spinal cord injuries from stenosis at the cervical spine can cause irreversible changes in the cord.[39] As cervical canal narrowing is a risk factor for cervical myelopathy,[24] once a patient is identified with cervical canal narrowing at any level, closer monitoring and vigilance of DCM development are mandatory. When multilevel (≥ 3) spinal canal narrowing is detected, the presence of such DcSS indicates a six-times increased likelihood of developing DCM requiring surgical intervention, compared to without DcSS. This coincides with studies by Hukuda et al[27] and Chen et al,[4] who found a smaller canal diameter (transverse and sagittal, respectively) to be a predisposing factor for cervical spondylotic myelopathy. Male sex is also associated with higher risk. These prompt the consideration of not only early intervention but also preemptive posterior canal enlargement during the silent period of stenosis or when symptoms first arise.[40] With early intervention, patients can benefit from better prognosis and faster neurological recovery.[12] Furthermore, the defined cut-off AP canal diameters can be used for screening potential DCM in cases of degeneration already detected in other segments of the spine. In order to avoid over-diagnosis of DcSS by these defined criteria, validation and long-term longitudinal follow-up studies are required to evaluate the effectiveness of applying these cut-offs in early DCM identification, and any clinical evidence for early or prophylactic decompression or canal enlargement surgery for asymptomatic DcSS.[38,41]

This study has limitations. The number of individuals in the DCM and population-based cohorts differed significantly due to the relatively lower number of DCM patients, which can affect the robustness of comparative analysis. However, the ratio of DCM and general population individuals is comparable with the prevalence (5.3%) of cervical canal compression in asymptomatic individuals in Japan.[7] Additionally, slight differences of MRI in slice thickness and spacing for DCM patient and population-based cohorts might cause small measurement errors. There is a lack of long-term follow-up to confirm the predictive value of the MRI cut-off values for DCM development, and further investigation of long-term follow-up data of the general population cohort is necessary. Moreover, the defined DcSS criteria is only applicable to the Chinese population. Future evaluation of the applicability of these cut-off values and the differences between populations is required. Similar studies need to be conducted in different countries in order to determine the prevalence of DcSS worldwide.

Based on the analyses of the MRI cervical spine morphologies of DCM patients and the general population, DcSS is defined with level-specific cervical canal diameter cut-off values with the incorporation of the characteristics of multilevel involvement. Clinical use of these DcSS canal diameter cut-offs (C3 < 13 mm, C4 < 12 mm, C5 < 12 mm, C6 < 12.5 mm, C7 < 13.5 mm) can aid in the early identification of individuals with developmental spinal stenosis at the cervical spine. Individuals with DcSS at ≥ 3 levels and of male sex are at high risk of developing DCM requiring surgery, and they are recommended for consideration of early intervention during silent stenosis or when symptoms first arise.

Take home message

- Clinically recommended cut-off anteroposterior spinal canal diameters for developmental cervical spinal stenosis (DcSS) are: C3 < 13 mm, C4 < 12 mm, C5 < 12 mm, C6 < 12.5 mm, C7 < 13.5 mm. These can be used as the criteria for detecting DcSS in individuals at risk of developing degenerative cervical myelopathy (DCM).
- Individuals with multilevel (≥ 3 vertebral levels) cervical spinal canal narrowing and of male sex are at high risk of developing DCM.
- Early intervention or prophylactic surgery can be considered for these individuals to avoid traumatic spinal cord injuries.

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