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ORIGINAL ARTICLE - SPINE DEGENERATIVE

Deep flexor sarcopenia as a predictor of poor functional outcome after anterior cervical discectomy in patients with myelopathy

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Abstract

Background Paraspinal muscle morphometry has been recognized to be a prognostic factor across various surgical conditions, but its utility in predicting disease-specific outcomes in spine surgery remains under-explored.

Methods A prospective cohort study was performed on 45 consecutive patients undergoing anterior cervical discectomy (ACD) for single-level, symptomatic cervical degenerative disc disease causing radiculomyelopathy or myelopathy. Previously described predictors of outcome such as age, gender, smoking, comorbidities, duration of symptoms, preoperative Nurick grade, extent of cord compression, and signal intensity change in the cord were recorded. Additionally, MRI-based morphometrics of the superficial and deep paraspinal muscles were recorded. Logistic regression (LR) analysis was performed using a purposeful variable selection process to identify variables that independently predicted Nurick grade improvement (NGI).

Results At a mean follow-up of 20.02 ± 8.63 months after ACD, 37 (82.22%) patients demonstrated NGI. LR analysis yielded three predictors of NGI of which two were related to the deep flexor muscles. While a worse preoperative Nurick grade negatively predicted NGI, a deep flexor area and deep flexor/deep extensor area ratio positively predicted NGI. The regression model demonstrated a good fit and was statistically significant ($\chi^2(3) = 22.18$, $p < 0.0001$). The model explained 64% of the variance in NGI and correctly classified 89% of cases.

Conclusions This study has for the first time identified the utility of paraspinal morphometrics in predicting disease-specific functional outcome after cervical spine surgery. Our results indicate that in addition to preoperative Nurick grade, an already accepted outcome predictor, the deep flexor cross-sectional area, and the deep flexor/deep extensor ratio are strong predictors of NGI following ACD for single-level, symptomatic cervical degenerative disc disease with myelopathy. Deep muscle morphometrics could be included in future risk stratification algorithms for patients with cervical disc disease.

Keywords Paraspinal muscles · Deep flexors · Predictor · Functional outcome · Anterior cervical discectomy

Abbreviations

ACD	Anterior cervical discectomy
ACDF	Anterior cervical discectomy with fusion
ACDA	Anterior cervical discectomy with arthroplasty
CSA	Cross-sectional area
CT	Computed tomography
DE	Deep extensor
DF	Deep flexor
LR	Logistic regression
MRI	Magnetic resonance imaging
NGI	Nurick grade improvement
OPLL	Ossified posterior longitudinal ligament
PSM	Paraspinal muscles
ROI	Region of interest
SE	Superficial extensor
SF	Superficial flexor
VBA	Vertebral body area

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Introduction

Sarcopenia, defined as diminished skeletal muscle mass and strength [8], has been demonstrated to be a significant predictor of adverse outcomes across various medical and surgical specialties [25, 31]. Although commonly understood to be age-related, sarcopenia can occur as a focal or generalized phenomenon in various pathological conditions. It has been postulated that smaller muscle size is a marker of a lesser biological reserve that translates to worse postoperative outcomes [26]. In the cervical spine, deep muscles have been found to be affected in various pathologies [11, 17, 20, 40, 41]. While some of the deep muscles in the above studies have been implicated in influencing postoperative sagittal outcomes [21, 38], they have not been evaluated as a potential independent predictor of disease-specific functional outcome after cervical spine surgery. Considering this gap of knowledge, the objective of our study was to evaluate the utility of cervical paraspinal muscle (PSM) morphometry in predicting Nurick grade improvement independent of the previously established risk factors for poor surgical outcome in cervical degenerative disease.

Methods

Study design and patient population

After obtaining clearance from the Institutional Review Board and Ethics Committee, a prospective cohort study was performed on 45 consecutive patients with single-level, symptomatic cervical degenerative disc disease causing radiculomyelopathy or myelopathy. Informed consent was obtained from all patients included in the study. All patients underwent anterior cervical discectomy (ACD) during the study period from July 2013 to July 2015. Exclusion criteria included recurrent disc disease, concomitant cervical and lumbar disc disease, segmental instability, and radiological evidence of degeneration at another level.

Surgical procedure

A uniform surgical protocol was adhered to by all the operating consultants in the team during the study period. Surgery was performed with the patient's neck kept extended by keeping a folded sheet under the shoulder. A modification of the Smith-Robinson technique was followed. Following a standard right-sided anterior cervical exposure using a transverse incision, the disc space was confirmed using fluoroscopy. After completion of discectomy, the posterior longitudinal ligament was incised in cases where it was thickened, or if there were disc fragments beneath it. Bone graft, plates, or cages were not used in any of the patients.

Predictive factor assessment

Previously described predictors of outcome after surgery for degenerative cervical myelopathy [32, 40] such as age, gender, smoking, comorbidities, duration of symptoms, preoperative Nurick grade, T2-weighted high signal intensity in the cord, and the extent of cord compression were recorded. The extent of cord compression was classified into two categories based on whether the dorsal subarachnoid space was obliterated ("circumferential" compression) (Fig. 1a, b) or preserved ("partial" compression) (Fig. 1c, d) [32].

In addition to the above, magnetic resonance imaging (MRI)-based morphometrics of the superficial and deep paraspinal muscles were recorded by two independent raters. The first rater was a final year neurosurgery resident (AAA) who was trained to perform the cross-sectional area (CSA) measurements on MRIs of twenty random subjects prior to the study. A neurosurgery consultant (ST) with prior experience in the CSA measurement technique functioned as the second rater.

A uniform imaging protocol was used for all patients. MR images were acquired on an HDi 1.5 Tesla magnet (GE Signa, Milwaukee, WI, USA) using a standard NV coil. The measurement parameters that were used for the study were the following: slices 26, slice thickness and space 3.7 mm, FOV 180 × 188 mm, TR 4360 ms, TE 98.2 ms, matrix size 1.60/256, number of excitations 1.5, and flip angle 90 degrees. The MRI measurement slab was manually positioned from the base of the occiput through the upper portion of the C7 vertebral body. The axial MR slices were aligned parallel to the C2/3 intervertebral disc.

CSA measurement of the PSMs was performed on digital images of the cervical spine MRI using the software in the hospital radiographic system (Synapse, Fujifilm Health Systems, USA). The CSA measurement method was based on a previously standardized and clinically reliable technique described in other studies on the cervical spine [9, 38]. Its pretest reliability was checked in the current study by performing an intra- and inter-rater agreement test. All the measurements as detailed below were performed on ten randomly selected subjects on two separate days. Both raters were blinded to their index measurement values. The intra- and inter-rater agreements were found to be excellent for all muscle groups.

For the area measurements, a region of interest (ROI) was drawn for each muscle bilaterally at the level of the upper vertebral endplates from C3 to C7. The measured groups included the superficial flexors (SF; sternocleidomastoid), deep flexors (DFs; longus colli and longus capitis), deep extensors (DEs; multifidus and semispinalis cervicis), and superficial extensors (SEs; semispinalis capitis, splenius capitis, and upper trapezius) (Fig. 2). Perpendicular lines from the lateral border of the facets were used as standardized lateral limits

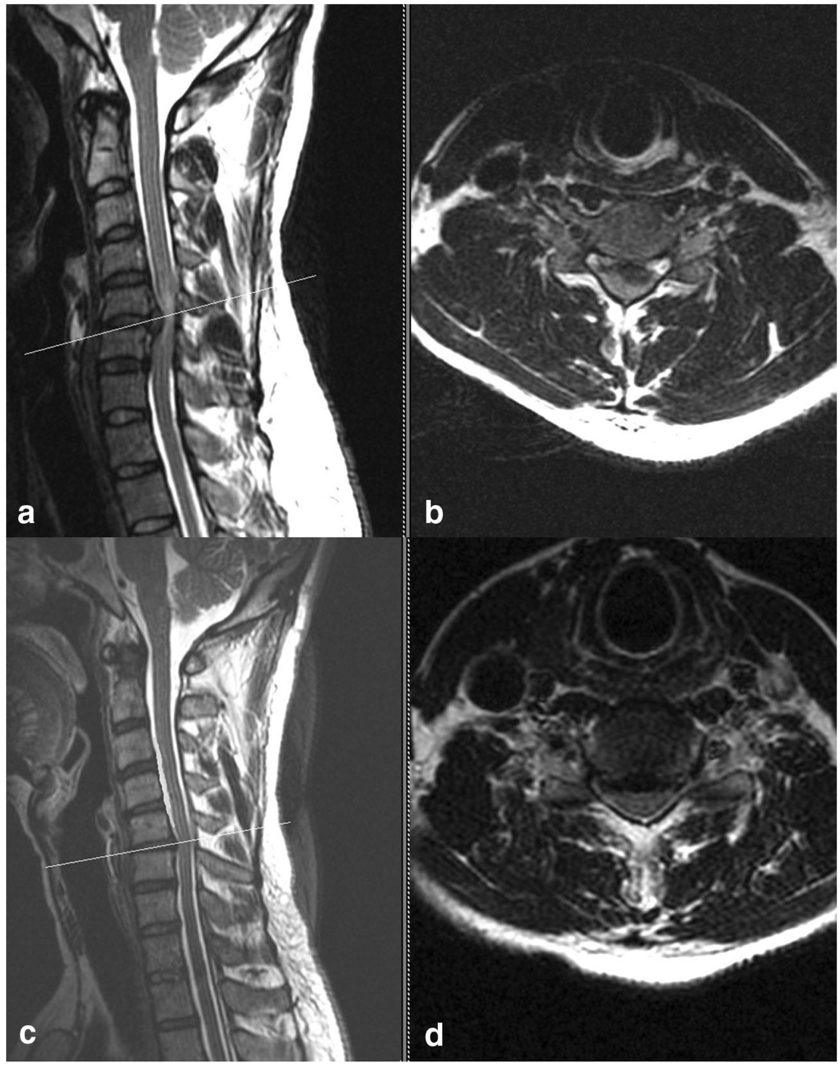

Fig. 1 **a** Sagittal and **b** axial T2-weighted MRI sequences showing a C5–6 disc prolapse causing cord compression with obliteration of the dorsal subarachnoid space ("circumferential" cord compression). MRI images of another patient. **c** Sagittal and **d** axial T2-weighted sequences showing a C5–6 disc prolapse causing cord compression but with preservation of the dorsal subarachnoid space ("partial" cord compression)

for the measurement of the SEs, as has been described previously [38].

Muscle CSA/bony CSA ratios rather than absolute muscle CSA values were used like in previous publications [37, 38] to eliminate biases due to varying builds of the patients. The vertebral body areas (VBAs) at the cuts taken for measurement of the muscle areas were used for deriving the muscle/bony CSA ratios (Fig. 2). The mean of the sum of the muscle CSAs obtained on either side at all levels and the following means of the PSM CSA/bony CSA ratios were then calculated: SF CSA/VBA, DF CSA/VBA, SE CSA/VBA, and DE CSA/VBA. The mean values of these area ratios obtained by the two raters were used for analysis.

Functional outcome assessment

Patients were followed up clinically and radiologically a year or later after surgery. Improvement in their functional status was recorded by noting the change in their Nurick grade. Although the minimal clinically important difference (MCID) of the Nurick scale has not been defined, a 1-grade change has been suggested to reflect substantial improvement in impairment [12]. For our analysis, patients were labeled to have improved functionally if they demonstrated a follow-up improvement of Nurick grade by at least 1 grade (Nurick grade improvement (NGI)).

Statistical methodology

The sample size for the study was calculated using clinically meaningful CSA values from previous studies on cervical PSMs. Using an effect size of 0.9 derived from these studies [37, 38] and a probability level of 0.05, a sample size of 45 was determined to be adequate to obtain a power of 0.9. We also applied the thumb rule of using a subject-to-variable ratio of 10:1 for a regression prediction model (i.e., the requirement

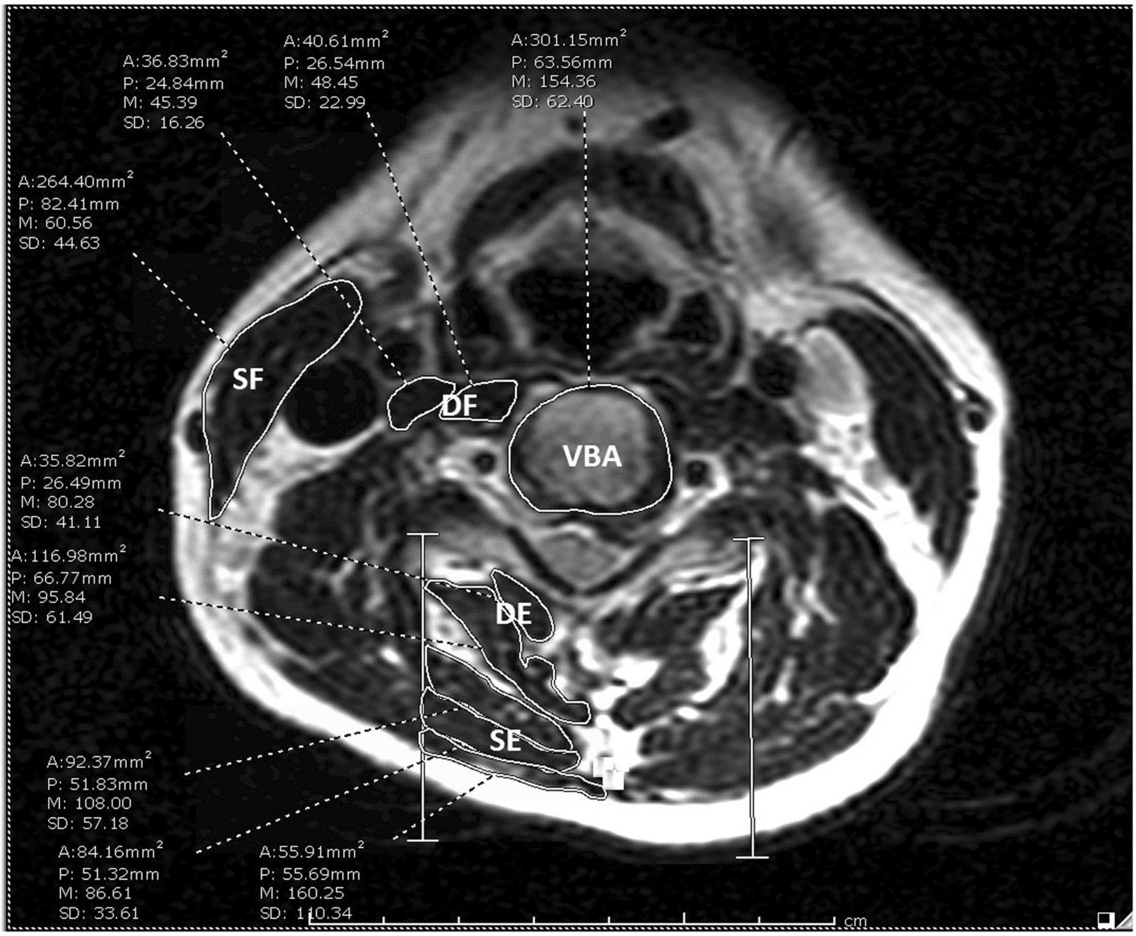

Fig. 2 T2-weighted axial MRI section demonstrating the regions of interest used in the measurement of the cross-sectional area of the paraspinal muscles. SF = superficial flexor, DF = deep flexor, SE = superficial extensor, DE = deep extensor, VBA = vertebral body area

of having at least 10 patients per variable in the final regression model). Data was analyzed using SPSS version 20. Means and standard deviations were computed for continuous variables. Intra- and inter-rater variability in the muscle area measurements was measured using Cohen's kappa coefficient (κ) and standardized ratings of agreement. Logistic regression (LR) analysis was performed to examine the relationship of the preoperative variables with NGI using a purposeful variable selection process described by Hosmer and Lemeshow [6]. Variables with a p value cut-off of 0.1 in the bivariate analysis were selected for the multivariate analysis. Covariates were removed from the model if they were non-significant and not confounders. Significance was evaluated at a 0.1 alpha level, and confounding was defined as a change of > 20% in the remaining parameter estimate as compared with the full model. Significant variables or those that made an important contribution to the model in the presence of other variables were identified, and the respective odds ratios with 95% confidence intervals were calculated (Table 3). The adjusted R^2 was used to measure the degree of variation.

Results

Demographic and clinico-radiological features

The demographic, clinical, and radiographic features of the study cohort are listed in Table 1. The cohort consisted of 40 males and 5 females with a mean age of 40.22 ± 7.81 years. While all patients complained of neck pain at presentation, 36 (80%) patients presented with radiculomyelopathy and 9 (20%) with myelopathy. A majority of the patients (88.88%) had T2-weighted high signal intensity in the cord and "circumferential" cord compression (77.77%). At a mean follow-up of 20.02 ± 8.63 months (range, 12 to 42 months) after surgery, 37 (82.22%) patients demonstrated NGI. Of the 10 patients with comorbidities, 5 had hypertension, 4 had diabetes mellitus, and 1 had asthma. One patient had a postoperative complication (transient hoarseness of voice). Follow-up data was available for all the 45 patients.

Table 1 Demographic and clinico-radiological features of the cohort

Variable		*N* (%)	
Gender			
Male		40 (88.88%)	
Female		5 (11.11%)	
Level of disc prolapse			
C3–4		6 (13.33%)	
C4–5		8 (17.77%)	
C5–6		24(53.33%)	
C6–7		7 (15.55%)	
Extent of cord compression			
Partial		10 (22.22%)	
Circumferential		35 (77.77%)	
T2-weighted change in the cord		40 (88.88%)	
History of smoking		12 (26.66%)	
Presence of comorbidities		10 (22.22%)	
		Preop	**Postop**
Nurick grade	0	0	11 (24.44%)
	1	0	17 (37.77%)
	2	12 (26.66%)	9 (20%)
	3	25 (55.55%)	5 (11.11%)
	4	8 (17.77%)	3 (6.66%)
	5	0	0
		Mean (SD)	
Age in years		40.22 (7.81)	
Duration of symptoms in months		11.76 (9.46)	
Mean follow up period in months		20.02 (8.63)	

PSM areas and correlation coefficients

The preoperative mean CSA:VBA ratios for the measured muscle groups are listed in Table 2. Figure 3 compares the mean areas of all the muscle groups in patients with and without NGI at follow-up. The intra- and inter-rater agreements for all the muscle groups were found to be excellent (intra-class correlational coefficient values of > 0.90), indicating that the CSA measurement technique used was clinically reliable.

Bivariate analysis

Bivariate analysis demonstrated age, preoperative Nurick grade, deep flexor CSA, and deep flexor/extensor CSA ratio to have significant correlations with NGI ($p = 0.01$, 0.04, 0.01, and 0.01 respectively). Preoperative T2-weighted change in the cord demonstrated weaker correlations with NGI ($p = 0.10$) while the degree of cord compression, gender, smoking, and the presence of comorbidities had the weakest correlations with NGI (p-values of 0.26, 0.99, 0.16, and 0.19, respectively).

Multivariate logistic regression

Logistic regression analysis (Table 3) using a purposeful variable selection process yielded three predictors of NGI of which two were related to the deep flexor muscles. The regression equation for the best prediction model was as follows: $19.4 \times a + 12.5 \times b - 2.6 \times c - 4.9$, where a is the deep flexor CSA/VBA, b is the deep flexor CSA/deep extensor CSA, and c is the preoperative Nurick grade. While a worse preoperative Nurick grade negatively predicted NGI, the deep flexor area and deep flexor/deep extensor area ratio positively predicted NGI. The latter two predictors contributed significantly to the regression model. The model demonstrated a good fit of the data (Supplementary material) using the Hosmer and Lemeshow test ($\chi^2 = 2.56, p = 0.92$). The overall model was statistically significant ($\chi^2(4) = 22.18, p < 0.0001$), and it explained 64% (Nagelkerke R^2) of the variance in NGI (Supplementary material). 89% of the cases were correctly classified as having NGI. Odds ratio analysis (Table 3) demonstrated that patients with larger DFs or a strong DF/DE ratio were 2.7 and 2.6 times more likely, respectively, to exhibit NGI. Residue analysis demonstrated that the residuals approximated a normal distribution.

Discussion

Outcome prediction in spine surgery

Given the growing focus on value-based care in medicine, outcome prediction is being increasingly used in spine surgery to boost the efficacy of decision-making and preoperative counseling [19]. Previously identified predictors of outcome after spine surgery include smoking [1], psychological status [3], employment status [14], and constitutional factors such as age [14], gender [30], and obesity [3]. Specific predictors of outcome after surgery for degenerative cervical myelopathy include the duration of symptoms, preoperative functional status, and a host of radiological variables related to the cord [40]. Some of the above predictors like age, gender, and obesity are associated with variations in muscle morphometry [20]. While the latter has been used as a reliable predictor of outcomes across various non-spine surgical specialties [5, 24, 25, 29, 31], its value as an independent outcome predictor in spine surgery remains under-studied.

Muscle morphometrics as a predictor of outcome

Morphometrics is the radiological measurement of muscle areas on either computed tomography (CT) or MRI [8, 41]. The psoas, quadriceps, and PSMs are amongst the frequently used muscles for assessing sarcopenia [8, 41]. Recent literature has demonstrated sarcopenia to be an independent risk

Table 2 Preoperative muscle cross-sectional area/vertebral body area ratios and the respective intra- and inter-rater agreement coefficients

Muscles	Mean value (SD)	Intra-rater agreement (κ)*	Inter-rater agreement (κ)*
SF area/VBA	1.06 (0.24)	0.95	0.91
DF area/VBA	0.38 (0.08)	0.94	0.93
SE area/VBA	0.48 (0.13)	0.92	0.90
DE area/VBA	0.51 (0.09)	0.94	0.91
DF area/DE area	0.76 (0.13)	0.91	0.90

*Cohen's kappa coefficient (κ)

SD = standard deviation, SF = superficial flexor, DF = deep flexor, SE = superficial extensor, DE = deep extensor, VBA = vertebral body area

factor in predicting outcome after spine surgery, suggesting that morphometrics is a robust proxy measure of a patient's general health and physiological reserve [4, 13, 42]. Koshimizu et al. demonstrated worse sagittal alignment and postoperative outcomes in sarcopenic patients after cervical laminoplasty [21]. In a large retrospective review of patients undergoing lumbar spine surgery, Zakaria et al. [42] found that patients with smaller psoas sizes had increased odds of postoperative complications. It thus appears that stronger muscles mitigate the degree to which the subject is affected by the disease or adverse outcomes after surgery. In the light of such findings, it has been recommended that sarcopenia should be included in the risk stratification algorithms for predicting outcome after procedures for cervical degenerative spinal pathology [20, 26].

Predictors in cervical degenerative disease

A longer duration of symptoms, greater severity of preoperative myelopathy, and older age are amongst the well-established clinical predictors of worse outcome in patients with cervical degenerative disease [35]. In addition to these predictors, a validated clinical algorithm proposed by Tetreault et al. [33, 36] demonstrated smoking, co-existent psychiatric disorders, and gait status to independently predict outcome. The significance of other factors like rapidity of disease onset and progression, various signs and symptoms,

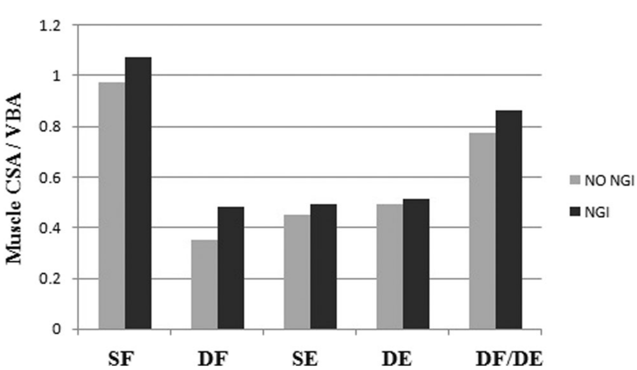

Fig. 3 Bar chart comparing the mean areas of the various muscle groups in patients with and without Nurick grade improvement at follow-up

and the presence of comorbidities has been inconsistent and of doubtful utility in predicting outcome [2, 7, 23].

Whether a surgical technique itself and its variations influence outcomes after cervical spine surgery has been a matter of debate. In this context, a recent randomized controlled trial compared outcomes after single-level cervical disc surgery in patients undergoing ACD, ACD with fusion (ACDF), and ACD with arthroplasty (ACDA) and found no significant differences at 2-year follow-up [39].

Some of the radiological predictors of outcome identified in previous studies include T1/T2-weighted signal intensity changes in the cord [34] and the extent of cord compression [32]. Ongoing studies are evaluating the predictive value of modalities like diffusion tensor imaging, functional MRI, spectroscopy, and myelin water fraction [40]. Our study has for the first time evaluated cervical PSM morphometry as a predictor of disease-specific outcome independent of some of the above-mentioned predictors.

Paraspinal muscle changes in cervical conditions

The cervical paraspinal musculature consists of superficial and deep muscles that contribute to the static and dynamic control of the head and neck. The superficial muscles assist in voluntary neck movements, while the deep muscles help in maintaining cervical posture and lordosis. PSM changes in cervical pathologies have been reported in neck pain and whiplash disorders [10], cervical spondylotic myelopathy (CSM) [38], ossified posterior longitudinal ligament (OPLL) [15], and Chiari type I malformation [37]. The types of muscle affected in these conditions differ. While patients with CSM [38] and whiplash disorders [10] reportedly suffer generalized atrophy of both the superficial and deep muscles, those with neck pain [18], Chiari type I malformation [37], and OPLL [15] demonstrate preferential changes in their deep muscles.

Deep muscle morphometrics in cervical disorders

There has been a growing interest in quantifying deep PSM deficits in patients with neck pain disorders [11, 16, 28]. Patients with neck pain demonstrate lower deep flexor (DF)

Table 3 Multivariate logistic regression analysis results

Variables in the equation

		B	SE	Wald	Df	Sig	Exp(B)	95% CI for Exp(B)	
								Lower	Upper
Step 1	Constant	−4.87	5.08	0.91	1	0.33	0.008		
	Preop Nurick	−2.61	1.42	3.40	1	0.05	0.07	0.005	1.17
	Mean DF/VBA	19.43	9.34	4.32	1	**0.04**	2.76	2.06	3.50
	Mean DF/DE	12.49	5.88	4.50	1	**0.03**	2.68	2.60	2.76

B = coefficient, SE = standard error, Df = degrees of freedom, Sig =significance, Exp(B) = odds ratio, CI = confidence interval

activation during a craniocervical flexion test [11]. A previous study in patients with CSM reported smaller DF areas to be correlated with poorer sagittal outcomes after surgery. It was suggested that a stronger deep flexor/deep extensor (DF/DE) ratio has a protective effect in maintaining segmental alignment. The present study undermines the importance of these deep muscles yet again, with stronger DF muscles and a higher DF/DE ratio being identified as independent predictors of Nurick grade recovery after ACD. The underlying physiological basis for this finding could be related to a weaker deep muscle–based proprioceptive system contributing to lesser gait recovery.

Deep cervical PSMs are predominantly comprised of type I fibers with a high density of muscle spindles which aid in the maintenance of lordosis and posture [22] and indirectly in gait stability [15]. Affection of impulses from these muscle spindles explains the disturbances in movement control, proprioception, and kinesthetic sense seen in disorders with deep PSM changes [17]. It is hence conceivable that smaller DF muscles extrapolate to a weaker cervical proprioceptive system and subsequently to poorer gait recovery in myelopathic patients. In our study, this was probably reflected in the lesser degrees of improvement in Nurick grade, a grading system based primarily on the degree of difficulty in walking.

Key findings and implications of our study

In addition to re-establishing the significance of preoperative Nurick grade in predicting outcome in cervical degenerative disease, our study has identified two novel predictors (deep flexor CSA and deep flexor/deep extensor CSA ratio) of functional recovery after ACD. These findings demonstrate that deep flexor sarcopenia can be used as a predictive factor for poor Nurick grade improvement after ACD for single-level cervical disc disease. Once externally validated, deep muscle morphometrics could be included in risk stratification algorithms for patients with cervical disc disease. An offshoot of our study would be to evaluate if focused preoperative DF muscle strengthening could alter the postsurgical clinical course in cervical disc disease. Such a "prehabilitation" approach has been demonstrated to hasten recovery after lumbar spine surgery and is reportedly more cost-effective than the standard of care [27].

Limitations of our study

Our study has several limitations. We have used only Nurick grade, a physician-centric measure as an outcome tool. Perhaps if we had used any of the patient-perceived outcome measures in addition, the results of our study may have been more meaningful. We evaluated PSM areas only preoperatively and not at follow-up. It is hence unclear at present whether postoperative changes in muscle morphometrics affect functional recovery and also whether focused postoperative physiotherapy could possibly improve outcomes. The results of our study hold good at a relatively short-term follow-up period, and it remains to be seen whether DF morphometry remains a robust predictor for long-term functional outcome after ACD. Lastly, our study focused only on patients with single-level cervical disc disease. The results of our study need validation in patients with multisegmental disease and also in different populations with larger sample sizes. It also may be cautioned that the findings of our study may not hold good for patients undergoing ACDF or ACDA, and this needs further elucidation.

Conclusions

This study has for the first time identified the utility of paraspinal morphometrics in predicting disease-specific functional outcome after cervical spine surgery. Our results indicate that in addition to preoperative Nurick grade, an already accepted outcome predictor, the deep flexor cross-sectional area, and the deep flexor/deep extensor ratio are strong predictors of NGI following ACD for single-level, symptomatic cervical degenerative disc disease with myelopathy. Deep muscle morphometrics could be included in future risk stratification algorithms for patients with cervical disc disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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