

# Clinical Equipoise and Treatment Decisions in Cervical Spondylotic Myelopathy

Michael Benatar

**ABSTRACT:** *Objective:* The primary objective of this study is to evaluate clinician attitudes towards the treatment of cervical spondylotic myelopathy (CSM) in order to determine whether clinical equipoise exists for a segment of this patient population. The secondary objective is to examine the factors that influence treatment decisions. *Methods:* Cross-sectional internet-based survey of neurologists, neurosurgeons and orthopedic surgeons. *Results:* Between 40-60% of respondents recommended surgery for (1) patients with minimal or no symptoms, but incidentally discovered increased T2 signal within the cervical cord on MRI, (2) patients with mild symptoms and indentation of the cervical cord but without increased T2 signal and (3) those with at least moderately severe clinical findings accompanied by MRI showing effacement of the thecal sac but without indentation of the cord or increased T2 signal. The severity of the radiological abnormalities most strongly influence treatment decisions. *Conclusions:* We conclude that clinical equipoise does exist for certain groups of patients with CSM, suggesting that a randomized controlled trial could be performed in this population.

**RÉSUMÉ:** *Équilibre clinique et décision de traitement dans la myélopathie cervico-arthrosique.* *Objectif :* Le principal objectif de cette étude était d'évaluer l'attitude des cliniciens concernant le traitement de la myélopathie cervico-arthrosique (MCA) afin d'établir s'il existe un équilibre clinique pour une partie de cette population de patients. L'objectif secondaire était d'examiner les facteurs qui influencent la décision de traitement. *Méthodes :* Il s'agit d'une enquête transversale par Internet auprès des neurologues, des neurochirurgiens et des orthopédistes. *Résultats :* De 40 à 60% des répondants recommandaient la chirurgie : 1) aux patients qui avaient peu ou pas de symptômes, chez qui une augmentation du signal T2 au niveau de la moelle cervicale était une découverte fortuite; 2) aux patients présentant des symptômes légers et une indentation de la moelle cervicale sans augmentation du signal T2; 3) à ceux qui avaient des manifestations cliniques modérément sévères et une IRM démontrant un effacement du sac thécal sans indentation de la moelle ou sans augmentation du signal T2. La sévérité des anomalies radiologiques influence fortement la décision de traitement. *Conclusions :* Nous concluons que l'équilibre clinique existe pour certains groupes de patients atteints de MCA et qu'un essai contrôlé, randomisé, pourrait être fait dans cette population de patients.

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Cervical spondylotic myelopathy (CSM) is a common problem that is often treated surgically despite a relative paucity of evidence regarding optimal therapy. Reliable estimates of the prevalence of CSM are lacking, but data from the Healthcare Cost and Utilization Project (HCUP) database suggest that it is an important problem that accounts for significant health care expenditure annually in the United States.<sup>1</sup> The vast majority of the literature on the treatment of CSM is retrospective and uncontrolled.<sup>2-21</sup> Several prospective uncontrolled studies<sup>22,23</sup> as well as one small randomized controlled trial<sup>24</sup> have suggested that surgery offers little benefit over a more conservative treatment strategy. Several reviews of the CSM literature over the years have reached the same conclusion and have called for a randomized controlled trial (RCT) to better define the indications for surgery in the treatment of patients with CSM.<sup>25,26</sup> There are, however, several obstacles to the design and conduct

of such a RCT, notably the bias that exists amongst treating physicians in favor of surgery. The basic premise of any RCT is the presence of clinical equipoise – the collective uncertainty amongst the medical community regarding the best approach to treatment.<sup>27</sup>

Although CSM is a clinically and radiologically heterogeneous disorder, there have been no prior efforts to

From the Department of Neurology, Emory University, The Emory Clinic, Atlanta, GA, USA.

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Reprint requests to: Michael Benatar, Department of Neurology, Emory University, The Emory Clinic, 1365A Clifton Road NE, Atlanta, Georgia, 30322, USA.

examine the attitudes towards the treatment of patients with CSM as well as the determinants of these attitudes. Here we report the results of an internet-based survey in which we have examined attitudes towards the treatment of CSM as well as the determinants of these attitudes in order to establish whether there is a population of patients with CSM for whom clinical equipoise exists regarding the indication for surgery.

#### MATERIALS AND METHODS

**Questionnaire Design.** A short questionnaire was designed that asked respondents to indicate how they would treat a series of hypothetical patients with CSM. Five short case vignettes were presented with each vignette paired with a range of cervical spine magnetic resonance imaging (MRI) abnormalities. The details of each case vignette and the radiological findings are summarized in Tables 1a and 1b. Pairing each vignette with each grade of MRI abnormalities yields 20 different clinico-radiological cases that were presented to each survey respondent.

Examples of the types of radiological abnormalities described in Table 1b are presented for illustrative purposes (Figure 1) even though these images were not available to the survey respondents.

**Study Participants.** The study was sent to members of the Cervical Spine Research Society, an organization comprising professionals (mostly orthopedic surgeons as well as some neurosurgeons and physiatrists) who have a research interest in and treat patients with disorders of the cervical spine. In order to achieve a balance in the medical and surgical specialties of the respondents, the survey was also sent to a group of neurologists mostly working at Emory University and the Beth Israel Deaconess Medical Center in Boston. The study participants were sent an email with an embedded link from which they could access an online version of the questionnaire using web software available at <http://www.questionpro.com>. The survey was sent out twice. On the second occasion it was sent only to those who did not respond to the initial invitation.

**Table 1a: Clinical features encompassed by survey case vignettes**

Clinical Grade	
Asymptomatic	Asymptomatic or minimal symptoms; MRI performed incidentally
Mild	Mild symptoms (numbness in hands/feet, stiffness in legs or urinary urgency), but without functional limitation of interference with activities of daily living; examination either normal or shows minor abnormalities such as brisk reflexes or extensor plantar response
Moderate	More prominent symptoms (urinary urge incontinence or unsteadiness of gait) that cause some functional limitation; examination shows mild spasticity without weakness, brisk reflexes, extensor plantar responses and mild dorsal column sensory loss
Severe	Progressive gait difficulty requiring walker to assist with ambulation as well as urinary urge incontinence. Examination shows moderately severe spasticity and weakness in the legs as well as moderately severe dorsal column dysfunction
Bed-bound	Progressive gait difficulty with inability to ambulate (wheelchair or bed-bound) and difficulty with tasks requiring fine motor coordination in the hands. Examination shows severe spasticity and weakness as well as severe dorsal column sensory loss.

**Table 1b: Radiological abnormalities encompassed by survey case vignettes**

MRI Grade	
Spondylosis	Diffuse spondylotic changes without effacement of the thecal sac or indentation of the cord
Effacement	Diffuse spondylotic changes with effacement of the thecal sac, but no indentation of the cord or increased T2 signal within the cord
Indentation	Diffuse spondylotic changes with effacement of the thecal sac and indentation of the cord, but no increased T2 signal within the cord
T2 signal	Diffuse spondylotic changes, effacement of the thecal sac, indentation of the cord and increased T2 signal within the cord



**Figure 1:** Examples of T2 weighted sagittal MRI scans illustrating (a) diffuse spondylotic changes with effacement of the thecal sac, but no indentation of the cord, (b) effacement of the thecal sac with indentation of the cord, and (c) indentation of the cord with associated increased T2 signal within the cord. These images are provided purely for illustrative purposes and were not available to survey respondents who based their clinical judgment about each case vignette on the verbal description of the MRI scan (Table 1b).

**Statistical Analysis.** Univariate analysis was used to evaluate survey response rates and to estimate the proportion (and 95% confidence intervals) of respondents recommending surgery for each clinical vignette. Specification was made a priori that frequency estimates of 40-60% would be taken to imply the presence of significant uncertainty regarding optimal therapy. The potential for bias due to the relatively low response rate was evaluated using the ‘continuum of resistance model’.<sup>28</sup> The underlying assumption behind this approach is that every subject in the study population has a position on the response continuum that ranges from ‘will always respond’ to ‘will never respond’. Non-respondents will be concentrated on the side of ‘will never respond’ and subjects who require more reminders before they respond would have been non-responders if the study had been stopped earlier. The late respondents, therefore, most resemble the non-respondents. The proportions of early and late respondents recommending surgery for each vignette were compared using Fisher’s exact test. A p-value of <0.01 was used in order to accommodate multiple comparisons.

Multivariate unconditional logistic regression analysis was then used to determine which factors most strongly influenced respondents’ decisions to recommend surgery. Since the severity of both the clinical manifestations and radiological features were graded using ordinal scales (Table 1), dummy variables were created with the mildest clinical and radiological grades used as the reference groups. Dummy variables were similarly created for the medical or surgical specialty of the survey respondent.

## RESULTS

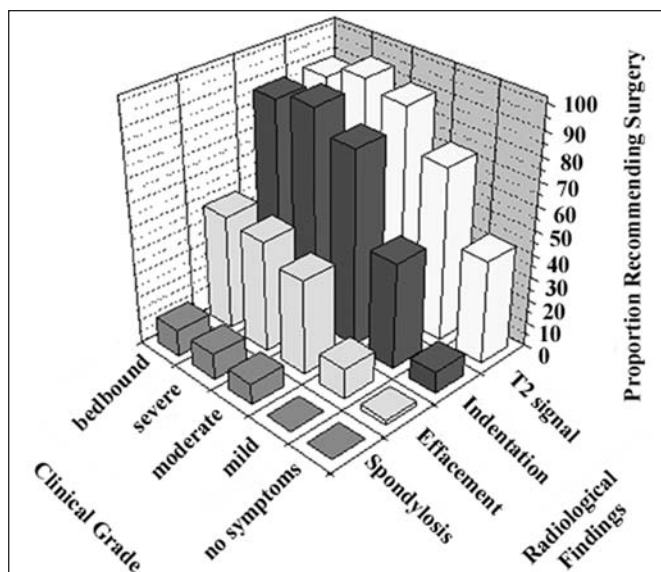
The survey was sent via email to 344 members of the Cervical Spine Research Society as well as 52 neurologists, for a total of 396 surveys. The email was not deliverable to 59 addresses (either because of errors in the email addresses or because the email was intercepted by the recipients’ spam filtering process), resulting in a total of 337 surveys being delivered. The web based interface used to send out the questionnaire indicated that

179 subjects responded to the email by accessing the questionnaire. One hundred and sixty three responses were received. The overall response rate, therefore, was 48%, but was substantially higher (91%) amongst those who accepted the email invitation to respond to the survey. Of the responses returned, 140 were complete (86%) and these form the basis of the analysis presented here.

The study population included 75 orthopedic surgeons, 42 neurologists, 21 neurosurgeons, 1 physiatrist and 1 person who identified himself as a spine surgeon. The frequency with which the respondents recommended surgery is shown in Figure 2, with responses stratified according to the clinical and radiological characteristics described in the series of case vignettes. The frequency with which respondents recommended surgery was between 40-60% for four groups of patients:

1. Patients with minimal or no symptoms but increased T2 signal on cervical spine MRI (45%, 95% CI 35-52%)
2. Patients with mild symptoms and indentation of the cervical cord without increased T2 signal (47%, 95% CI 40-56%)
3. Patients with moderately severe symptoms and MRI showing effacement of the thecal sac but without indentation of the cord or increased T2 signal within the cord (41%, 95% CI 33-50%)
4. Patients with clinical grades of severe or bed-bound together with effacement of the thecal sac but without indentation of the cord or increased T2 signal within the cord (49%, 95% CI 39-59%)

The finding that respondents were approximately evenly split with regard to the indication for surgery in these groups of patients suggests that these are the patients for whom clinical equipoise exists. For all other patients there was much greater agreement, either in favor of conservative management or in favor of surgery, suggesting that such patients could not be included in a randomized controlled trial of surgery versus conservative therapy.



**Figure 2:** Frequency tabulation of respondents' recommendations regarding surgery stratified by clinical severity and radiological findings.

There were no significant differences between the early and late respondents with respect to the proportions recommending surgery for these four groups of patients. In fact the only significant difference was that a greater proportion of late respondents (22.5% vs 5%) recommended surgery for patients with moderately severe clinical symptoms with diffuse spondylotic changes ( $p=0.004$ ). This difference was not clinically meaningful as even the higher estimate (among the late respondents) did not reach the threshold for defining the presence of equipoise within this group.

The results of multivariate logistic regression analysis are shown in Table 2. Compared to orthopedic surgeons, neurosurgeons were slightly more likely to recommend surgery whereas neurologists were significantly less likely to recommend surgery (OR 0.4,  $p < 0.0001$ ). In general, the probability that a respondent would recommend surgery increased with advancing clinical grade and severity of radiological findings. The probability that a respondent would recommend surgery was more strongly influenced by the radiological findings than by the severity of the clinical symptoms and signs. This was true irrespective of the specialty of the respondent (data not shown).

## DISCUSSION

Degenerative disease of the cervical spine, also known as cervical spondylosis, is an extremely common accompaniment of aging and is present in over half of the population over the age of 40.<sup>29</sup> Magnetic resonance imaging evidence of cervical cord indentation and compression is found respectively in 20% and 7% of asymptomatic subjects undergoing MRI for reasons unrelated to the cervical spine.<sup>30</sup> Although there are no reliable estimates of the prevalence of symptomatic CSM or the frequency with which these patients are treated surgically, data from the HCUP National Inpatient Sample database indicate that between 15,000-20,000 patients are hospitalized each year in the United States for treatment of CSM at an annual cost of several hundred million dollars.<sup>1</sup> These estimates likely reflect the frequency and cost of surgical treatment of CSM as it would be extremely unusual for a patient with CSM to be admitted for conservative therapy.

The surgical treatment of CSM is predicated on the idea that the cause of the syndrome is mechanical compression of the cord by the spondylotic process. It has been argued that without surgery, the disorder is inexorably progressive and clinical experience indicates that patients improve after surgical decompression. However, very little is known about the natural history of CSM<sup>5,14</sup> or the prognosis of conservatively treated

**Table 2: Determinants of recommendation in favor of surgery for CSM**

	OR <sup>1</sup>	95 % CI	p-value
Neurosurgeon <sup>2</sup>	1.6	1.2 – 2.1	0.002
Neurologist <sup>2</sup>	0.4	0.3 – 0.5	< 0.0001
Clinical grade – mild <sup>3</sup>	0.8	0.6 – 1.0	0.02
Clinical grade – moderate <sup>3</sup>	3.0	2.3 – 4.1	< 0.0001
Clinical grade – severe <sup>3</sup>	4.4	3.4 – 6.0	< 0.0001
Clinical grade – bed-bound <sup>3</sup>	3.7	2.7 – 5.0	< 0.0001
Radiological grade – effacement <sup>4</sup>	18.2	12.9 – 25.8	< 0.0001
Radiological grade – indentation <sup>4</sup>	36.2	25.4 – 51.6	< 0.0001
Radiological grade – T2 hyperintensity <sup>4</sup>	85.1	58.5-123.8	< 0.0001

<sup>1</sup> Odds ratio of recommendation in favor of surgery compared to no surgery; <sup>2</sup> Compared to orthopedic surgeon;

<sup>3</sup> Compared to clinical grade – asymptomatic; <sup>4</sup> Compared to radiological grade – diffuse spondylosis.

CSM and the available evidence supporting the benefits of surgery is almost entirely retrospective and uncontrolled. This retrospective literature is vast and characterized by serious methodological limitations such as the absence of control data and the failure to use defined criteria for evaluating the severity of disease and the response to treatment. As a result this literature is almost uniformly unhelpful in terms of providing evidence for the relative benefits of surgery and conservative therapy for CSM. There have, however, been two prospective cohort studies<sup>22,23</sup> as well as a single small randomized controlled trial<sup>24</sup> that have compared outcome amongst conservatively and surgically treated patients. The results of the prospective studies were conflicting, with one suggesting some benefit from surgery in terms of functional status as well as work and social activities<sup>23</sup> whereas the second showed no consistent benefit of surgery over conservative therapy.<sup>22</sup> The small randomized controlled trial similarly showed no benefit of surgery over conservative therapy at two<sup>24</sup> or three<sup>31</sup> years follow-up. The results of these studies tend more to support than to undermine the statement that the benefits of surgery over conservative therapy for patients with CSM remain unproven.

It is against this background that we have taken the first step towards the design of a randomized controlled trial of surgery versus conservative therapy for the treatment of CSM. By surveying 140 clinicians with experience in the evaluation and management of patients with CSM, we have determined the clinical and radiological features that define those patients with CSM for whom clinical equipoise exists regarding appropriate therapy. With equipoise defined on the basis of survey respondents being approximately equally divided with regard to recommending surgery for a particular patient, these results suggest that equipoise is present for three groups of patients: (1) those with minimal or no symptoms, but incidentally discovered increased T2 signal within the cervical cord on MRI, (2) those with mild symptoms and indentation of the cervical cord but without increased T2 signal and (3) those with at least moderately severe clinical findings accompanied by MRI showing effacement of the thecal sac but without indentation of the cord or increased T2 signal within the cord. We do not know what proportion of all patients with CSM are accounted for by these categories of patients, but this is the subject of an ongoing investigation.

One potential limitation of this study is the relatively low response rate of 48%. Given the internet-based nature of the survey, however, with potential respondents being solicited by email, there is some doubt about whether all of the surveys sent out were received. The response rate of 91% is much better amongst those subjects who acknowledged receipt of the survey by following the link to the survey embedded within the email solicitation. The true overall response rate probably lies somewhere between these two estimates. It should be noted that a low response rate implies the potential, but not necessarily the presence, of bias. It would have to be assumed that there is some systematic difference in the attitudes of respondents between those who did and those who did not respond to the questionnaire, in order for bias to be present. In an effort to address this issue we have utilized the 'continuum of resistance model' in which late responders (in this instance, those who completed the survey after a second request) are compared to

early responders (in this instance, those who completed the survey after the first request). The essential concept behind this approach is that the late responders are most similar to the non-responders in that they would have been classified as non-responders had the second request to complete the questionnaire not been made. The fact that we found no significant differences between the early and late responders gives us some confidence that the study population is not systematically different from the non-responders. It should be noted, however, that even if we are mistaken and there is some systematic difference between these two groups, this may be of limited relevance to the proposal to undertake a RCT comparing surgery to conservative therapy in CSM. It might be argued, for example, that those subjects who responded to the questionnaire represent the group most likely to participate in such an RCT, and the presence of equipoise within this population argues for the feasibility of such a trial.

The strength of this study lies in the fact that the responses of both surgeons (orthopedic and neurological) and neurologists were sought and that the study population largely comprised subjects with an explicit interest in the management of patients with CSM. The nature of the data collected also permitted an analysis of the factors that determine clinicians' recommendations regarding therapy, with the findings suggesting that MRI abnormalities play a relatively stronger role than symptoms and the findings on neurological examination.

In conclusion, therefore, we would venture that clinical equipoise does exist for a subset of patients with CSM and that this is the population in whom a randomized controlled trial of surgery versus conservative therapy could ethically and practically be considered.

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