

Change in Impairment Following Operative Treatment of Degenerative Cervical Myelopathy: A Systematic Review and Meta-Analysis

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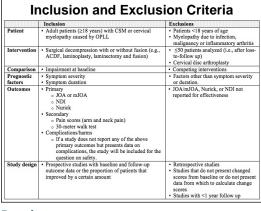


Introduction

The objective of this study was to conduct a systematic review to (1) summarize outcomes following surgical intervention for degenerative cervical myelopathy (DCM); (2) evaluate whether outcomes are dependent on preoperative disease severity or duration of symptoms; and (3) to define the safety profile of surgery.

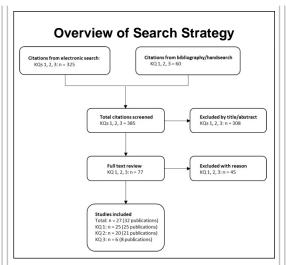
Methods

A systematic search was conducted in Embase, PubMed, and the Cochrane Collaboration for articles published between January 1, 1950 and February 9, 2015. Studies were included if they were prospective and if they evaluated clinical (mJOA, Nurick) disability (Neck Disability Index) or pain (Visual Analog Scale) outcomes in patients undergoing surgery for DCM. Studies were also included if they analyzed complications associated with surgical intervention. The quality of each study was evaluated using the Newcaste-Ottawa Scale and the strength of the overall body of evidence was rated using guidelines outlined by the GRADE Working Group.



Results

Thirty-two studies satisfied the inclusion criteria. Sample sizes ranged from 52 to 479 patients, mean ages ranged from 46 to 65 years and males comprised between 34% and 94% of the sample.



Part I: Meta-analyses indicated that surgical intervention results in significant and clinically meaninful improvements in functional impairment (mJOA and Nurick scores), disability (NDI scores) and pain (VAS scores).

A Meta-analysis Summarizing mJOA Outcomes following Surgery

Study or Subgroup		t Sco			Scor		Weight	Std. Mean Difference IV. Random, 95% CI				ference 95% CI	
Chibbaro 2009	14.9		268		2.2	268	10.2%	3.68 [3.40, 3.96]		,			+
Fehlings 2013	15.7	1.4	260	12.9	2.2	260	10.3%	1.52 [1.32, 1.71]				-	
Fehlings 2015	14.9	1.4	479	12.5	2.2	479	10.4%	1.30 [1.16, 1.44]				•	
Hirai 2011	13.6		86	9.8	3	86	10.0%	1.37 [1.04, 1.70]				-	
Hu 2014	14.7	1	55		1.6	55	8.6%	4.76 [4.02, 5.51]					-
Kimura 2014		1.4	116	11.1		116	10.1%	1.57 [1.27, 1.86]				-	
Lian 2010	13.3	2	105		2.6	105	10.1%	1.85 [1.52, 2.17]				-	
Moussellard 2014	13.4	2.2	67	11.5		67	10.0%	0.78 [0.43, 1.14]			- 1 -	-	
Ohashi 2014	14.7		121	11.6		121	10.2%	1.32 [1.05, 1.60]				+	
Ying 2007	16.2		140	12.9		140	10.2%	1.46 (1.20, 1.73)				-	
Total (95% CI)			1697			1697	100.0%	1.92 [1.41, 2.43]				•	
Heterogeneity: Tau ² =	0.64: 0	hi² -	332.2	4. df =	9 (P	< 0.00	001): 2 =	97%	-	-	-	-	-
Test for overall effect:	Z = 7.3	9 (P	< 0.00	001)					-4	-2	0	2	4
. 13-36 month													
. 15-50 month													
Study or Subgroup		t Sco	re Total		Scor		Weight	Std. Mean Difference IV, Random, 95% CI		Std. Me IV, Rar		ference	
Bapat 2008		1.5	129	10.4	3.3	129	8.3%	2.10 (1.80, 2.41)		10, 100.	1	+	
Fehlings 2015		2.2	479	12.5	3.3	479	9.0%	0.91 [0.78, 1.04]					
Hirai 2011	14.2		86	9.8	3	86	8.1%	1.59 [1.24, 1.93]				-	
Lian 2010		2.2	105	9.0	3	105	8.2%	1.89 [1.57, 2.22]				-	
Machino 2013	13.6		520	10.4		520	9.0%	1.20 [1.07, 1.34]					
Moussellard 2014	12.7		67	11.5		67	8.1%	0.46 [0.12, 0.80]			-		
Nakashima 2014	12.7		90		2.6	90	8.1%	1.39 [1.06, 1.72]				_	
Ohashi 2014	14.8		121	11.6		121	8.4%						
Setzer 2009	11.5		60	10.3		60	7.9%	1.37 [1.09, 1.65]			_	-	
Tanaka 2006				9.9	3.6	62	7.7%	0.42 [0.06, 0.78]				_	
	14.2		152			152	8.4%	1.62 [1.22, 2.03]				_	
Wang 2015					3.1			2.23 [1.94, 2.51]					
Zong 2014	12.3	2.7	396	7.4	3.4	396	8.9%	1.59 [1.43, 1.75]					
Total (95% CI)			2267				100.0%	1.40 [1.12, 1.67]				٠.	
Heterogeneity: Tau ² = Test for overall effect:					11 (< 0.0	0001); 1	= 94%	-4	-2	ó	ź	4
. >36 months													
		t Sco			Scor			Std. Mean Difference				ference	
Study or Subgroup							Weight	IV, Random, 95% CI		IV, Rar	dom,	95% CI	
Chen 2013	13.5		60		1.4	60	13.9%	2.34 [1.87, 2.81]				+	
Cheung 2008	12.4		55		3.5	55	14.2%	0.71 [0.32, 1.10]			-	-	
Chibbaro 2009	16.2		268		2.2	268	14.4%	3.94 [3.64, 4.23]					+
Hirai 2011		2.6	86	9.8	3	86	14.3%	1.45 [1.12, 1.79]				-	
Suzuki 2009	14.3	2	98	11.1	4	98	14.4%	1.01 [0.71, 1.31]				-	
Wang 2015	14.9	1.8	71	9	2.9	152	14.3%	2.26 [1.91, 2.61]				+	
Yoshida 2013	12.7	1.9	369	9.2	2.2	369	14.6%	1.70 [1.53, 1.87]				•	
Total (95% CI)			1007			1088	100.0%	1.92 [1.14, 2.69]				•	
Heterogeneity: Tau ² =	1.06: 0	hi² -	278.6	6. df =	6 (P	< 0.00	001): I ² =	98%	-4	-2	-	-	+

The Impact of Duration of Symptoms on Outcomes

Author Symptom Duration		(95% CI or ±SD)	(95% CI)	
	n	(95% CI of ±SD)	(93% CI)	(%)*
Short-term F/U (12 mos.)				
Karpova 2013				
<12 months	NR		3.1† (2.5, 3.7)	
>12 months	NR	11.9†	2.6† (2.0, 3.2)	
Suzuki 2009‡				
<12 months	65	11.2 ±3.0	3.4 (2.1, 4.7)	
>12 months	33	11.1 ±3.0	2.8 (1.4, 4.2)	
Medium-term F/U (24-36 mos.)				
Suzuki 2009				
<12 months	65	11.2 ±3.0	3.4 (2.4, 4.6)	
>12 months	33	11.3 ±3.0	2.7 (1.2, 3.8)	
Suri 2003				
<12 months	86			58.1%
12-24 months	31			71.0%
>24 months	29			51.7%
Long-term F/U (54-60 mos.)				
Suzuki 2009				
<12 months	65	11.2 ±3.0	3.4 (2.4, 4.6)	
>12 months	33	11.2 ±3.0	2.4 (1.2, 3.8)	
Cheung 2008				
<6 months	NR	8.6 ±3.4	2.9	
6-12 months	NR	10.3 ±3.9	3.1	
>12 months	NR	10.6 ±3.6	1.0	

Part II: Patients were more likely to achieve a "successful" outcome if they had a shorter duration of symptoms and less severe myelopathy preoperatively. Furthermore, patients were less likely to improve by 2 or more points if they had a worse baseline severity score.

The Impact of Preoperative Myelopathy Severity on Outcomes

Author	n	mJOA change score (95% CI)	Improved mJOA (%)	NDI change score (95% CI)	Nurick change score (95% CI)
Short-term F/U (12 mos.)					
Fehlings 2013					
Mild (mJOA ≥15)	78	1.29 (0.70, 1.87)		12.05 (7.76, 16.34)	1.54 (1.22, 1.86)
Moderate (mJOA 12-14)	105	2.58 (2.07, 3.09)		9.79 (5.90, 13.68)	1.51 (1.22, 1.81)
Severe (mJOA <12)	77	4.91 (4.34, 5.49)		12.53 (8.05, 17.02)	1.74 (1.41, 2.08)
Long-term F/U (96 mos.) Chibbaro 2009					
Moderate (mJOA 10-13)	90		86.7		
Severe (mJOA 5-9)	178		86.5		

Part III: Incidence of complications was low

Incidence of Surgical Complications

Complications	No. of studies	n/N	Cumulative incidence	95% CI
Axial pain	322,31,46	33/585	5.6%	3.8%, 7.5%
Laryngeal nerve injury/dysphagia	817,20,22,24,30,31,44,46	26/1182	2.2%	1.4%, 3.0%
Instrumentation/graft complication	917,18,21,22,25,31,36,44,46	28/1411	2.0%	1.3%, 2.7%
C-5 radiculopathy/palsy	1517,20-22,24-26,28,29,31,32,34,37,41,44	50/2661	1.9%	1.4%, 2.4%
Pseudarthrosis	717,18,22,24,31,35,46	17/954	1.8%	0.9%, 2.6%
Infection (deep and superficial)	1070-22,25,28,30-32,34,44	32/2074	1.5%	1.0%, 2.1%
Adjacent segment disease (symptomatic)	217,22	6/404	1.5%	0.3%, 2.7%
Reoperation/revision	720,22,24,30,31,33,36	13/943	1.4%	0.6%, 2.1%
Dural tear/CSF leak	1120,22,25,28,29,31-34,44,46	26/1893	1.4%	0.8%, 1.9%
Worse myelopathy	221,22	10/781	1.3%	0.5%, 2.1%
Hematoma	721,22,25,31,33,44,46	11/1237	0.9%	0.4%, 1.4%
Radiculopathy/palsy (not C5)	322,37,44	4/464	0.9%	0.0%, 1.7%
Neurologic deterioration/new deficit	317,22,12	9/969	0.9%	0.3%, 1.5%
Delayed wound healing/dehiscence	222,33	3/369	0.8%	0.0%, 1.7%
Dysphonia	321,22,24	6/867	0.7%	0.1%, 1.2%
Post-operative deformity	217,22	2/404	0.5%	0.0%, 1.2%
Death	617,18,21,22,31,33	3/1162	0.3%	0.0%, 0.5%
Stroke/transient ischemic attack	322,32,44	3/873	0.3%	0.0%, 0.7%
Esophageal injury	224,31	0/191	0.0%	0.0%, 2.9%
Other	717,20-22,24,33,44	51/1382	3.7%	2.7%, 4.7%
Cardiopulmonary	122	10/302	3.3%	1.3%, 5.3%
Fracture	128	3/141	2.1%	0.0%, 4.5%
Bed sore	117	1/129	0.8%	0.0%, 2.3%
Spinal cord injury	125	0/55	0.0%	0.0%, 0.0%
Any complication*	122	40/283	14.1%	10.1%, 18.29

Summary of the Body of Evidence using GRADE

Preoperative Durati	on of Symptoms		
Success (mJOA ≥16)	1 study (N=272) F/U 12 months	Low	The odds of a "successful" outcome following surgical intervention depend on preoperative duration of symptoms. The odds of achieving a mJOA ≥16) decreased by 22% when a patient moves from a shorter to longer duration of symptoms group (≤3; >3, ≤6; >6, ≤12; >12, ≤24; >24 months).
Preoperative Myelop	oathy Severity		
JOA improvement	1 study (N=260) F/U 12 months	Moderate§	Change in neurological status following suspical intervention depends on preoperative disease severity. Less improvement on the mIOA was observed among patients with milder symptoms at presentation (recoperative mIOA ≥15: mean improvement 1.29 (95% CI 0.70, 1.87); preoperative mIOA 12-15: 2.58 (2.07, 3.09); propoperative mIOA (2.24.34) (4.34, 5.49)).
Success mJOA ≥16 at F/U; 2-point improvement in mJOA	2 studies (N=332) F/U 12 months	Low	The odds of a "successful" outcome following surgical intervention depends on preoperative disease severity. The odds of achieving a $mJOA \geq 16$ were 1.22 times greater for every 1-point increase in preoperative $mJOA$ score.

key Question 1.	What are the expected it	inctional, disab	ility and pain outcomes following surgical intervention for DCM?
JOA/mJOA	6-12 months 10 studies (N = 1697) 13-36 months 12 studies (N = 2267) ≥ 36 months 7 studies (N = 1088)	Moderate*	Surgical Intervention resulted in improved JOA/ns/OA scores at all time points assessed. Pooled standardized mean differences showed a large effect for improvement in function from baseline at short-term (10 studies SMD 1.92), medium-term (12 studies, SMD 1.40), and long-term (7 studies, SMD 1.92).
Nurick	6-12 months 2 studies (N = 739) 13-36 months 4 studies (N = 758)	Low	Surgical intervention resulted in improved Nurick scores at short-term and medium-term assessments. Pooled mean differences showed clinically meaningfu improvement in disability from baseline at short-term (2 studies, MD 1.42) and medium-term (4 studies, MD 1.06).
Pain (VAS 100- point scale)	6-12 months 4 studies (N = 646) 13-36 months 6 studies (N = 1097) ≥ 36 months 1 study (N = 268)	Moderate* 6-12 months Very Low† 13-36 and ≥36 months	Surgical Intervention resulted in improved pain scores at all time points assessed. Pooled mean differences showed clinically meaningful improvement in pain from baseline at short-term (4 statides, MD 32.7), medium-term (6 studies, MD 32.5), and long-term (1 study, MD 40.0).

Key Ouestion 3: W	hat are the complicati	ons associated v	with surgical intervention?
C5 radiculopathy or palsy	15 studies (N = 2661)	Low	Pooled cumulative incidence of C5 radiculopathy or palsy is 1.9% (95% CI; 1.4 2.4%).
Infection	10 studies (N = 2074)	Low	Pooled cumulative incidence of infection is 1.5% (95% CI; 1.0%, 2.1%)

Summary of the Body of Evidence: Based on moderate quality evidence, surgical intervention results in significantly and clinically important improvements in JOA/mJOA in both the shortand long-term. Furthermore, surgery is associated with significant gains on the Nurick and NDI (low to very low quality of evidence). Patients with a shorter duration of symptoms have increased odds of achieving a score =16 on the mJOA. With respect to safety, pooled cumulative incidences were low for C5 radiculopathy or palsy (1.9%), infection (1.5%), reoperation (1.4%), dural tear/cerebrospinal fluid leak (1.4%), worsening of myelopathy (1.3%), death (0.3%) and pseudoarthrosis or implant complications (2.1%)

Conclusions

Surgical intervention is an appropriate treatment strategy for the management of DCM as it results in significant improvements in clinical status and is associated with a low rate of perioperative complications. Further prospective research is required to determine the impact of duration of symptoms and myelopathy severity on outcomes.