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# Survivorship Analysis of Clinical Adjacent-Segment Pathology After Single-Level Cervical Fusion

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**Background:** Clinical adjacent-segment pathology (CASP) is an important problem after anterior cervical surgery. The purpose of this study was to predict prevalence of CASP and determine the possible risk factors for CASP after single-level anterior cervical discectomy and fusion surgery.

**Material/Methods:** We retrospectively reviewed a series of patients who underwent single-level cervical discectomy and fusion surgery (ACDF). Both basic and radiographic data of patients were collected. Life-table method and Kaplan-Meier analysis were used to calculate prevalence of CASP and disease-free survival rate. Cox analysis was performed to determine the predictive factors for it.

**Results:** A total of 256 patients were included in this study. The mean length of follow-up was 70.64 months. Among them, 31 patients were diagnosed as having CASP during follow-up. Nineteen of them were at the cephalad adjacent segment, and the other 12 were at the caudal segment. After ACDF procedures, 10.01% of patients developed new symptoms of CASP within 5 years, and the incidence increased to 23.89% after 10 years. The incidence rate of CASP was an average of 2.46% per year. Multivariate Cox regression analysis showed that congenital stenosis (hazard ratio [HR], 3.250; 95% confidence interval [CI], 1.538–6.867) and degeneration of adjacent segment (HR, 2.681; 95% CI, 1.259–5.709) were correlated with the incidence of CASP.

**Conclusions:** Patients with congenital stenosis and pre-existing degenerative changes of adjacent segments had a higher risk of developing CASP after single-level anterior cervical discectomy and fusion.


**MeSH Keywords:** **Cervical Vertebrae • Postoperative Complications • Retrospective Studies • Risk Factors**

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## Background

Anterior cervical discectomy and fusion (ACDF) is a standard surgical procedure in the treatment of symptomatic cervical radiculopathy and myelopathy. Since its initial description and application by Robinson and Smith [1], ACDF procedure has shown excellent outcomes based on long-term results. However, in spite of the successful outcomes of this procedure in relieving the symptoms of cervical lesions, subsequent development of degenerative disc disease adjacent to fused discs is a matter of grave concern [2,3]. Clinical adjacent-segment pathology (CASP), which is defined as the development of new symptoms of radiculopathy or myelopathy arising from segments adjacent to the site of previous anterior cervical fusion, has been reported to affect more than one-fourth of all patients within 10 years after the index surgery [2].

The pathogenesis of CASP still remains a matter of debate [4–6], but previous studies have been performed to determine the risk factors. Several factors have been found to be associated with the development of CASP, such as age, smoking history, sagittal alignment, the number of fusion segments, and pre-existing degenerative changes of adjacent segments [7–11]. However, the majority of the studies on this topic involved relatively small numbers of patients or did not statistically control confounding variables with multivariate analyses. Although CASP is a time-dependent disease after cervical procedures, survival analysis is rarely performed to identify the potential predictive factors.

In the current study, we tried to fill some of these research gaps by analyzing patients who had only undergone single-level cervical spine procedures. As insufficient sample size and loss to follow-up is inevitable in such clinical research, we used the life-table method and Kaplan-Meier analysis to calculate the prevalence of adjacent segments. We further performed multivariate Cox analysis to determine the predictive factors for CASP.

## Material and Methods

This study was approved by the Research and Ethics Committee of the Third Hospital of Hebei Medical University, and all patients gave written informed consent for their information to be stored in the database of this hospital and used for research.

### Patient population

In this study, we reviewed a series of patients who underwent single-level cervical arthrodesis between January 2006 and December 2015. The inclusion criteria were adult patients with radiculopathy, myelopathy, or myeloradiculopathy from

degenerative single-level cervical disc disease confirmed by correlating magnetic resonance imaging (MRI) findings, and no response to non-operative treatment for at least 3 months. Those with non-degenerative disease, such as trauma, infection, tumor, deformity, or inflammation, or undergoing any prior cervical spine operation, were excluded. Those showing herniated nucleus pulposus with or without neural compression on adjacent segments based on MRI were also excluded [2].

### Operative procedure

In this study, all patients underwent anterior cervical decompression and fusion procedures. After general anesthesia, the patient was placed supine with mild cervical extension. A standard right-sided approach through a transverse incision used to expose the targeted level. After that, the compressive materials were removed, including osteophytes, herniated disc, and posterior longitudinal ligament, and then a polyetheretherketone cage filled with excised osteophytes was inserted between vertebral bodies. All procedures in this study were performed by the same surgeon. A soft cervical collar was used for 8 weeks postoperatively.

### Data collection

Antero-posterior, lateral, and flexion/extension lateral plain radiographs, as well as MRI, were obtained pre-operatively. Radiographic data were also collected postoperatively at 6 weeks, at 3, 6, and 12 months, and then annually. Patients who developed additional cervical radiculopathy or myelopathy symptoms during follow-up were advised to go back to the clinic at their earliest convenience, and MRI was performed for confirmation and further evaluation.

CASP is defined as a new development of radiculopathy, myelopathy, or myeloradiculopathy symptoms, and a newly developed compressive lesion of spinal cord or nerve root in the segments adjacent to the fusion level, which is radiologically confirmed by MRI.

Basic data included age at surgery, sex, body mass index (BMI), diabetes mellitus, history of smoking and alcohol, neurological diagnosis, and fusion level. Postoperative radiographs at the 6-month follow-up were assessed to determine the congenital stenosis, curve pattern of C2–C7, Cobb angle of fused vertebrae, ROM of C2–C7, and T1 slope.

The spinal canal diameter was evaluated by measuring the Pavlov ratio. The Pavlov ratio was related to antero-posterior diameter of the spinal canal to the antero-posterior diameter of the vertebral body at the C5 level [12]. The presence of congenital stenosis was defined as a Pavlov ratio less than 0.80; the Cobb angle from C2 to C7 was defined as the angle

**Table 1.** Proportion of patients with CASP in different interval time by life-table method.

Interval time (months)	No. of patients entering interval	No. of patients with CASP	Proportion of patients with CASP (%)	Cumulative proportion surviving (%)
0–12	256	1	0.39	99.61
12–24	255	3	1.18	98.43
24–36	249	1	0.42	98.01
36–48	222	5	2.36	95.70
48–60	196	5	2.69	93.12
60–72	171	8	5.42	88.07
72–84	116	1	0.86	87.31
84–96	115	2	1.91	85.64
96–108	92	2	2.65	83.37
108–120	57	3	6.74	77.75

CASP – clinical adjacent-segment pathology.

formed by the inferior endplates of C2 and C7 in standing lateral radiographs. An alignment of C2–C7 Cobb angle more than 0 was defined as lordosis, and an alignment of C2–C7 Cobb angle of 0 or less was defined as kyphosis. The Cobb angle of fused vertebrae was formed by the upper endplate of cranial vertebral body and lower endplate of caudal vertebral body in the operated level. The C2–C7 range of motion (ROM) was defined as the sum of the absolute value of C2–C7 Cobb angle during flexion and extension lateral radiographs [10]. T1 slope was measured as the angle between a horizontal line and the superior endplate of T1 on standing lateral radiograph [9]. Two blinded observers independently interpreted the radiological findings twice and the mean values were used.

Pre-existing degenerative changes of adjacent segments was assessed by 2 independent authors according to preoperative radiographs and MRI based on Hilibrand definitions [2]. Patients with moderate or severe degeneration of adjacent segment were not included in this study. The existence of mild degeneration of adjacent segment was recorded as a potential risk factor.

### Statistical analysis

The incidence of CASP for each year was calculated by life-table method. Kaplan-Meier analysis was used to calculate disease-free survival rate for adjacent segments. Univariate Cox proportional hazards models of association between each of the exposures of interest and the outcome were built. Hazard ratios (HRs) along with 95% confidence intervals (CIs) are reported. All variables found to be potentially associated with the outcome ( $P < 0.10$ ) were entered into the Cox proportional

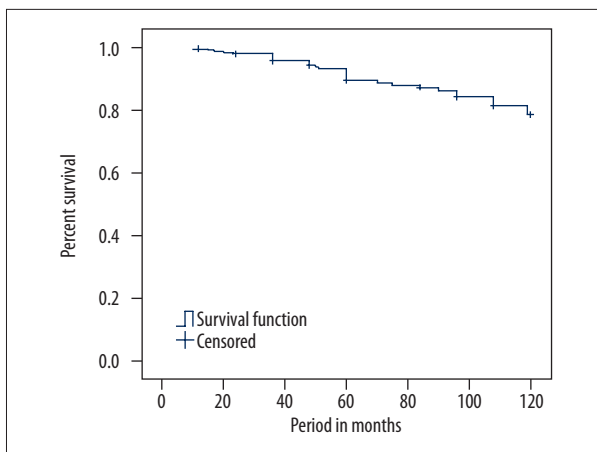
hazards regression model to analyze their relative importance. Statistical analysis was performed with the Statistical Package for Social Sciences software (version 17.0; SPSS Inc., Chicago, IL, USA), and probability value less than 0.05 was considered statistically significant.

### Results

A total of 256 patients undergoing single-level cervical spine surgery were included in this study. Among these patients, 137 were male and 119 were female. The mean age at the time of index surgery was  $50.1 \pm 6.8$  years. There were 167 patients diagnosed with radiculopathy, 42 had myelopathy, and 47 had myeloradiculopathy. During surgery, 234 patients were fixed with internal plates and the other 22 were not. The length of follow-up was  $70.64 \pm 32.46$  months. Most segments that underwent ACDF were at the C5–C6 spinal level, followed by the C6–C7, C4–C5, and C3–C4 levels in descending order of frequency.

During follow-up, 31 patients were diagnosed with CASP. Nineteen of them were at the cephalad adjacent segment, and the other 12 were at the caudal segment. Based on life-table analysis, the incidence rate of CASP was an average of 2.46% per year. The proportion of patients with CASP at different time points is listed in Table 1.

Kaplan-Meier analysis showed an 89.99% disease-free survival rate for adjacent segments (95% CI, 85.88% to 94.10%) at 5 years and 76.11% (95% CI, 66.47% to 85.74%) at 10 years (Figure 1). In terms of the prevalence of adjacent-segment pathology, these



**Figure 1.** Overall Kaplan-Meier survivorship curve for clinical adjacent segment pathology after single-level anterior cervical discectomy and fusion.

results suggested that 10.01% (95% CI, 5.90% to 14.12%) of patients would develop new symptoms of CASP within 5 years, and 23.89% (95% CI, 14.26% to 33.52%) by 10 years.

In the analysis of the association between patient basic data (Table 2), as well as radiographic data (Table 3) and the incidence of CASP, we found that involvement of C5–C6 level ( $P=0.084$ ), congenital stenosis ( $P=0.067$ ), degeneration of adjacent segment ( $P=0.033$ ), and curve pattern of C2–C7 ( $P=0.027$ ) were 4 potential risk factors, while age, sex, BMI, history of smoking or alcohol, diabetes mellitus, preoperative diagnosis, internal fixation, Cobb angle of fused vertebrae, ROM of C2–C7, and T1 slope were not ( $P>0.10$ ). In the further multivariate Cox regression analysis, congenital stenosis (HR, 3.250; 95% CI, 1.538–6.867) and degeneration of adjacent segment (HR, 2.681; 95% CI, 1.259-5.709) were correlated with the incidence of CASP during follow-up (Table 4).

**Table 2.** The association between patients’ basic data and the incidence of CASP.

Characteristic	CASP (+) group (n=31)	CASP (-) group (n=225)	P value	Hazard Ratio	95% CI
<b>Age</b>					
>60 years	7	58	0.838	0.916	0.394–2.129
≤60 years	24	167		Reference	
<b>Gender</b>					
Male	14	123	0.294	0.685	0.337–1.390
Female	17	102		Reference	
<b>BMI</b>					
>25 kg/m <sup>2</sup>	11	104	0.351	0.704	0.337–1.471
≤25 kg/m <sup>2</sup>	20	121		Reference	
<b>Smoking</b>					
Yes	13	88	0.730	1.134	0.555–2.317
No	18	137		Reference	
<b>Alcohol</b>					
Yes	10	91	0.475	0.760	0.358–1.615
No	21	134		Reference	
<b>Diabetes mellitus</b>					
Yes	5	29	0.434	1.466	0.562–3.827
No	26	196		Reference	
<b>Neurological disorder</b>					
Radiculopathy	18	149	0.179	1.770	0.769–4.073
Myelopathy	8	34	0.849	1.101	0.408–2.969
Myeloradiculopathy	5	42		Reference	
<b>C5–C6 level involved</b>					
Yes	23	131	0.084	2.032	0.908–4.544
No	8	94		Reference	

CASP – clinical adjacent-segment pathology; BMI – body mass index; CI – confidence interval.

**Table 3.** The association between radiographic data and the incidence of CASP.

Characteristic	CASP (+) group (n=31)	CASP (-) group (n=225)	P value	Hazard ratio	95% CI
<b>Internal fixation</b>					
Yes	29	205	0.798	1.206	0.287–5.067
No	2	20		Reference	
<b>Congenital stenosis</b>					
Yes	18	91	0.067	1.949	0.954–3.980
No	13	134		Reference	
<b>Degeneration of adjacent segment</b>					
Yes	16	73	0.033	2.152	1.063–4.356
no	15	152		Reference	
<b>Curve pattern of C2–C7</b>					
Kyphosis	5	18	0.027	2.961	1.131–7.752
Lordosis	26	207		Reference	
<b>Cobb angle of fused vertebrae</b>					
≤4°	17	99	0.218	1.561	0.769–3.169
>4°	14	126		Reference	
<b>ROM of C2–C7</b>					
>35°	18	129	0.986	1.006	0.493–2.056
≤35°	13	96		Reference	
<b>T1 slope</b>					
>20°	19	141	0.712	0.873	0.423–1.801
≤20°	12	84		Reference	

CASP – clinical adjacent-segment pathology; ROM – range of motion; CI – confidence interval.

**Table 4.** Cox’s proportional hazards regression model for predictive factors of CASP following single-level ACDF.

	P value	Hazard Ratio	95% CI
C5–C6 level involved	0.196	2.014	0.696–5.825
Congenital stenosis	0.002	3.250	1.538–6.867
Degeneration of adjacent segment	0.011	2.681	1.259–5.709
Curve pattern of C2–C7	0.227	1.836	0.685–4.918

CASP – clinical adjacent-segment pathology; ACDF – anterior cervical discectomy and fusion; CI – confidence interval.

## Discussion

After its introduction in the treatment of degenerative cervical lesions, ACDF is widely used and is reported to produce good results. CASP is a common but serious problem in patients after this procedure, and avoiding adjacent-segment pathology is an important issue among surgeons.

The pathogenesis of adjacent-segment pathology after discectomy and fusion is not completely understood. Cervical arthrodesis has been blamed for accelerating degenerative changes at adjacent spinal segments [13]. Many researchers believed that these degenerative changes might be associated with increased segmental motion and mechanical stress [4,14,15]. Some biomechanical studies showed that the loss of mobility

at a given spinal level increased the range of motion and intra-disc pressure at both cephalad and caudal adjacent spinal segments [16,17]. However, other reports found that these degenerative changes are part of the natural aging process of the cervical spine, and they pointed out that there was a lack of definite evidence that arthrodesis increases the incidence of adjacent-segment degeneration [5,18].

The reported incidence of adjacent-segment pathology varied greatly with different lengths of follow-up [3,19]. Adjacent-segment pathology is not always symptomatic, and radiographic adjacent-segment pathology after fusion is not correlated with clinical outcome. Our study only focused on clinical adjacent-segment pathology of the cervical spine. In the present study, the results revealed that 10.01% of patients develop new symptoms within 5 years, and the incidence increases to 23.89% after 10 years. The incidence rate of CASP was an average of 2.46% per year. Several studies agree with our results. For example, in the study by Lee et al., 21.9% of patients would need secondary surgery on adjacent segments by 10 years postoperatively, and secondary surgery on adjacent segments occurred at a relatively constant rate of 2.3% per year [8]. Lawrence et al. reported the rate of development of new symptomatic degeneration in the cervical spine after ACDF was between 1.6% and 4.2% per year [20].

Identification of the predictive factors for CASP development would enable surgeons to identify patients at the greatest risk and adjust their monitoring and follow-up decisions. The present study showed that congenital stenosis and pre-existing degenerative changes of adjacent segments were 2 predictive factors that may be associated with postoperative CASP. Patients with congenital stenosis and pre-existing degenerative changes of adjacent segments in MRI had 3.2 times and 2.7 times greater risk, respectively, than those without.

Whether CASP is due to disease progression or a fusion-associated phenomenon cannot be determined yet. Previous studies have shown that pre-existing degeneration of disc is a risk factor for the development of CASP. Goffin et al. reported that additional radiologic degeneration at the adjacent disc levels was found in 92% of their patients, who are more likely to have clinical deterioration. The severity of this degeneration is also correlated with the length of time after surgery [21]. Park et al. calculated the rate of preoperative adjacent-segment degeneration in patients after anterior cervical surgery, and found that the rate of degeneration was significantly higher in patients with adjacent-segment disease than in those without (85% vs. 52.2%). They further concluded that adjacent-segment disease may be associated with a natural history of cervical spondylosis rather than arthrodesis [22]. Although the exact

pathogenesis cannot be determined based on our study, we assumed that the pre-existing degenerative disease may act as a triggering factor for CASP.

Congenital stenosis has previously been shown to be a risk factor for degenerative disc disease [23,24], and in the present study we demonstrated it to be a predictive factor for CASP. The mechanism for this phenomenon is not very clear. Morishita et al. [25] found that a congenitally narrow canal had different effects on cervical kinematics, which means that subjects with a congenitally narrow cervical canal may be exposed to heavy mechanical loading at the cervical spine. In a recent study, Eubanks et al. reviewed a total of 635 patients retrospectively, and concluded that congenital stenosis appears to increase the incidence of radiographic adjacent-segment disease, but it does not appear to predict symptomatic adjacent-segment disease [26]. In their study, patients only had a median follow-up time of 36.2 months. We assumed that congenital narrowing is associated with a greater degree radiographic degeneration at the adjacent level initially, and it will translate into clinically significant symptoms with longer follow-up time.

Several limitations need to be considered in the present study. First, the incidence of CASP was not high; although we tried to collect all eligible patients, the sample size was relatively small, and this may weaken this study in the assessment of predictive factors. Second, were collected prospectively, but the study was retrospective in nature. We believe that a prospective, multicenter study involving a large population and long-term follow-up is needed to confirm our results.

## Conclusions

In conclusion, after ACDF procedures, 10.01% of patients are predicted to develop new symptoms of CASP within 5 years, and the incidence increases to 23.89% after 10 years. The incidence of CASP is an average of 2.46% per year. Congenital stenosis and pre-existing degenerative changes of adjacent segments were 2 independent predictive factors that may be associated with postoperative CASP.

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## Conflicts of interest

None.



## References:

1. Smith GW, Robinson RA: The treatment of certain cervical-spine disorders by anterior removal of the intervertebral disc and interbody fusion. *J Bone Joint Surg Am*, 1958; 40-A: 607-24
2. Hilibrand AS, Carlson GD, Palumbo MA et al: Radiculopathy and myelopathy at segments adjacent to the site of a previous anterior cervical arthrodesis. *J Bone Joint Surg Am*, 1999; 81: 519-28
3. Robertson JT, Papadopoulos SM, Traynelis VC: Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: A prospective 2-year study. *J Neurosurg Spine*, 2005; 3: 417-23
4. Bydon M, Xu R, Macki M et al: Adjacent segment disease after anterior cervical discectomy and fusion in a large series. *Neurosurgery*, 2014; 74: 139-46
5. Song KJ, Choi BW, Jeon TS et al: Adjacent segment degenerative disease: Is it due to disease progression or a fusion-associated phenomenon? Comparison between segments adjacent to the fused and non-fused segments. *Eur Spine J*, 2011; 20: 1940-45
6. Harrod CC, Hilibrand AS, Fischer DJ, Skelly AC: Adjacent segment pathology following cervical motion-sparing procedures or devices compared with fusion surgery: A systematic review. *Spine (Phila Pa 1976)*, 2012; 37: S96-112
7. Katsuura A, Hukuda S, Saruhashi Y, Mori K: Kyphotic malalignment after anterior cervical fusion is one of the factors promoting the degenerative process in adjacent intervertebral levels. *Eur Spine J*, 2001; 10: 320-24
8. Lee JC, Lee SH, Peters C, Riew KD: Risk-factor analysis of adjacent-segment pathology requiring surgery following anterior, posterior, fusion, and non-fusion cervical spine operations: survivorship analysis of 1358 patients. *J Bone Joint Surg Am*, 2014; 96: 1761-67
9. Park MS, Kelly MP, Lee DH et al: Sagittal alignment as a predictor of clinical adjacent segment pathology requiring surgery after anterior cervical arthrodesis. *Spine J*, 2014; 14: 1228-34
10. Song JS, Choi BW, Song KJ: Risk factors for the development of adjacent segment disease following anterior cervical arthrodesis for degenerative cervical disease: comparison between fusion methods. *J Clin Neurosci*, 2014; 21: 794-98
11. Faldini C, Pagkrati S, Leonetti D et al: Sagittal segmental alignment as predictor of adjacent-level degeneration after a cloward procedure. *Clin Orthop Relat Res*, 2011; 469: 674-81
12. Pavlov H, Torg JS, Robie B, Jahre C: Cervical spinal stenosis: Determination with vertebral body ratio method. *Radiology*, 1987; 164: 771-75
13. Matsumoto M, Okada E, Ichihara D et al: Anterior cervical decompression and fusion accelerates adjacent segment degeneration: Comparison with asymptomatic volunteers in a ten-year magnetic resonance imaging follow-up study. *Spine (Phila Pa 1976)*, 2010; 35: 36-43
14. Matsunaga S, Kabayama S, Yamamoto T et al: Strain on intervertebral discs after anterior cervical decompression and fusion. *Spine (Phila Pa 1976)*, 1999; 24: 670-75
15. Maiman DJ, Kumaresan S, Yoganandan N, Pintar FA: Biomechanical effect of anterior cervical spine fusion on adjacent segments. *Biomed Mater Eng*, 1999; 9: 27-38
16. Eck JC, Humphreys SC, Lim TH et al: Biomechanical study on the effect of cervical spine fusion on adjacent-level intradiscal pressure and segmental motion. *Spine (Phila Pa 1976)*, 2002; 27: 2431-34
17. Hwang SH, Kayanja M, Milks RA, Benzel EC: Biomechanical comparison of adjacent segmental motion after ventral cervical fixation with varying angles of lordosis. *Spine J*, 2007; 7: 216-21
18. Cho SK, Riew KD: Adjacent segment disease following cervical spine surgery. *J Am Acad Orthop Surg*, 2013; 21: 3-11
19. Kong L, Cao J, Wang L, Shen Y: Prevalence of adjacent segment disease following cervical spine surgery: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore)*, 2016; 95: e4171
20. Lawrence BD, Hilibrand AS, Brodt ED et al: Predicting the risk of adjacent segment pathology in the cervical spine: A systematic review. *Spine (Phila Pa 1976)*, 2012; 37: S52-64
21. Goffin J, Geusens E, Vantomme N et al: Long-term follow-up after interbody fusion of the cervical spine. *J Spinal Disord Tech*, 2004; 17: 79-85
22. Park JY, Kim KH, Kuh SU et al: What are the associative factors of adjacent segment degeneration after anterior cervical spine surgery? Comparative study between anterior cervical fusion and arthroplasty with 5-year follow-up MRI and CT. *Eur Spine J*, 2013; 22: 1078-89
23. Yague I, Okada S, Masuda M et al: Risk factors for adjacent segment pathology requiring additional surgery after single-level spinal fusion: Impact of pre-existing spinal stenosis demonstrated by preoperative myelography. *Eur Spine J*, 2016; 25: 1542-49
24. Zhang JT, Cao JM, Meng FT, Shen Y: Cervical canal stenosis and adjacent segment degeneration after anterior cervical arthrodesis. *Eur Spine J*, 2015; 24: 1590-96
25. Morishita Y, Naito M, Hymanson H et al: The relationship between the cervical spinal canal diameter and the pathological changes in the cervical spine. *Eur Spine J*, 2009; 18: 877-83
26. Eubanks JD, Belding J, Schnaser E et al: Congenital stenosis and adjacent segment disease in the cervical spine. *Orthopedics*, 2013; 36: e1251-55