

Research Article

Adjacent Segment Pathology in the Lumbar Spine: Progressive Disease or a Product of Iatrogenic Fusion?

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Background: Lumbar spine Clinical Adjacent Segment Pathology (CASP) has an annual incidence of 2.5%, and a 10-year 22% prevalence of repeat surgery (ReopASP). The pathophysiology remains controversial, whether due to increased mechanical stress on an adjacent motion segment after iatrogenic fusion or spondylotic disease progression. We compare CASP in traumatic and spondylotic patient cohorts.

Methods: A retrospective review of patients undergoing lumbar spine fusion for traumatic instability between 2002-2008 was compared to those undergoing lumbar spine fusions for degenerative disease, allowing for at least a five-year follow-up period. Prevalence of Reoperation for Adjacent Segment Pathology (ReopASP) and evidence of Radiological Adjacent Segment Pathology (RASP) was compared between groups.

Results: There were significant baseline clinical and technical differences found between groups with respect to mean age (trauma, 38.6 years versus spondylotic, 50.0 years, $p < 0.01$), gender (trauma, 78% males versus spondylotic, 50% males, $p < 0.01$), number of levels fused (trauma, 3 versus spondylotic, 1, $p < 0.01$), and level fused (trauma, 80% thoracolumbar versus spondylotic, 0% thoracolumbar, $p < 0.01$). A significant difference was found in the proportion of patients developing ReopASP between groups (trauma, 0/40 versus spondylotic, 15/100, $p < 0.01$). Stratified analysis controlling for age and gender still revealed a significant difference ($p < 0.05$). The level of lumbar fusion could not be adjusted for as no patients in the spondylotic group underwent thoracolumbar junction fusion.

Conclusion: A higher rate of ReopASP in patients with spondylosis was found. Our findings support patient factors predisposing to progressive spondylosis as an etiology for CASP and ReopASP, rather than mechanical factors.

Keywords: Adjacent segment disease; Adjacent segment pathology; Clinical adjacent segment pathology; Adjacent segment degeneration; Lumbar spine; Lumbar fusion

Abbreviations

CASP: Clinical Adjacent Segment Pathology; DISH: Diffuse Idiopathic Skeletal Hyperostosis; PACS: Picture Archiving and Communication System; RASP: Radiological Adjacent Segment Pathology; ReopASP: Reoperation of Adjacent Segment Pathology

Introduction

Symptomatic lumbar stenosis can have a significant impact on an individual's quality of life resulting in decreased ambulation and functioning due to pain and/or neurological deficits. It has been suggested that patients undergoing treatment for lumbar spinal stenosis can have a comparable long-term improvement in health related quality of life to those undergoing total hip and total knee arthroplasty [1]. This improvement in quality of life following surgery has potentially overshadowed long-term complications such as Clinical Adjacent Segment Pathology (CASP) requiring reoperation (ReopASP) and its radiographic correlate (RASP). However, these

phenomena have been the subject of more rigorous investigation over the past decade. 2 CASP has been reported to range between 13% at 5 years and 22% at 10 years with a mean annual incidence of 2.5% per year [3-8]. Reoperation rates for CASP development have been found to range from 7.7% at 2 years to 16.5% at 5 years. This rate has been found to be similar in fusion and non-fusion lumbar spine patient cohorts alike [7]. While a multitude of studies have been completed investigating different clinical, technical, and radiographic risk factors for CASP development [2-6,9-19], evidence remains controversial as to the role of lumbar fusion in adjacent segment pathology. Current studies suggest that adjacent segment pathology is a multi factorial process with fusion procedures likely acting to accelerate the progression of natural degeneration [2]. In light of the continued controversy, we sought to investigate this question further by comparing the prevalence of CASP in a traumatic patient cohort undergoing lumbar fusion due to mechanical instability and in a spondylotic patient cohort.

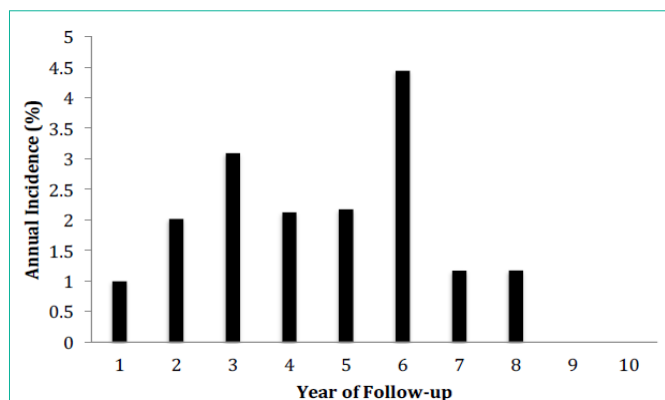


Figure 1: Bar graph showing the annual incidence of CASP development in the degenerative patient cohort.

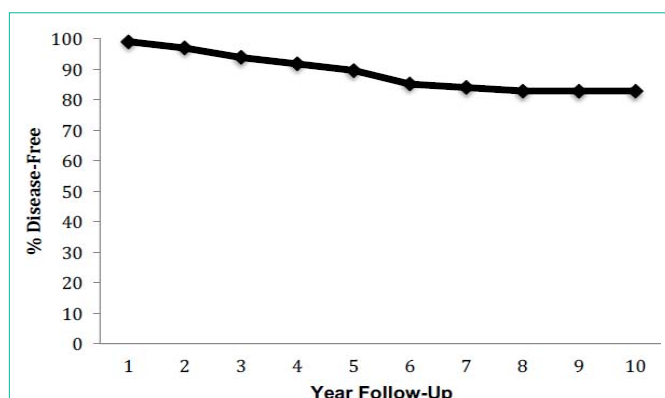


Figure 2: Kaplan-Meier survivorship curve. Each data point represents the total percentage of degenerative patients who entered a given year of follow-up without clinical adjacent segment pathology.

Materials and Methods

Ethics approval for the completion of this study was received from the local institutional Health and Research Ethics Board. Institutional operative records and operative billing codes were searched for all patients having undergone lumbar fusion procedures between 2002-2008 to allow for at least five years of follow-up. Chart review and an electronic medical database were used to collect patient clinical and demographic information including: patient age, gender, date of operation, operation performed, and operative indication. The Picture Archive and Communication System (PACS) were used to gather all pre-operative and post-operative radiological data for each case from plain radiographs (XR) of the lumbar spine including: disc space height, end-plate sclerosis, and osteophytosis. Patients under 18 years old and patients with a pathological fracture (related to metabolic, neoplastic or infectious etiologies), ankylosing spondylitis, or Diffuse Idiopathic Skeletal Hyperostosis (DISH) were excluded. Patients were divided into two cohorts for comparison based on the initial operative indication, either traumatic instability or elective decompression and fusion due to radiculopathy and/or claudicating.

For the purposes of this retrospective analysis, ReopASP was defined as a patient requiring a repeat operation for the recurrence of radiculopathy/clauding symptoms referable to an adjacent lumbar level. Occurrence of RASP was quantified using

a radiographic assessment scale previously shown to be a valid, reliable, and objective tool for assessing lumbar degenerative disease. This scale has also been shown to be experience independent, and as such no inter-rater analysis was completed [20]. The use and assessment of disc space height, extent of osteophyte formation, and degree of endplate sclerosis is a common and established method of quantifying degenerative disease among published grading systems [20-23]. Lumbar spine radiological adjacent segment degeneration was classified as none, mild, moderate, or severe [20]. Only patients demonstrating a two-grade increase in degeneration were classified as having RASP; patients with moderate degeneration prior to surgery required only a one-grade increase to be classified as having RASP. A Fisher's exact test was used to detect a statistically significant difference between the two cohorts for: prevalence of ReopASP, prevalence of lumbar spine RASP, the levels fused, and gender. A t-test was used to compare age and follow-up period. Statistical significance was set at a p-value of less than 0.05.

The incidence and prevalence of ReopASP were calculated for each year using a life-table method and construction of a Kaplan-Meier survivorship curve [24-26] (Figures 1 and 2). The prevalence of ReopASP was defined as the proportion of patients who developed CASP requiring reoperation over the given follow-up period. The annual incidence was defined as the proportion of patients requiring reoperation for CASP in any individual year.

Results

Forty traumatic lumbar fusion patients were identified. Baseline clinical and technical characteristics are outlined in (Table 1). The majority of patients were male (31/40, 77.5%), and the average age was 38.6-years old. The average length of follow-up was 7.6 years. A total of 58 procedures were completed (18 procedures in addition to the index operation for each patient for mechanical stabilization). Fourteen of these 18 procedures were to remove spinal instrumentation post-fusion; three were for repeat instrumentation and fusion due to pseudoarthrosis, and one for wound debridement post-infection. No additional operations were required due to lumbar CASP development. The majority of trauma patients had multiple levels fused (median of three levels fused). Moreover, the majority (32/40, 80.0%) of traumatic spine patients were fused at the thoracolumbar junction. Thirty-four patients (85.0%) had follow-up radiological imaging completed at a mean 29.4 months post-operatively. No patients had developed RASP.

One hundred consecutive patients undergoing elective lumbar spine fusion for spondylotic disease between 2002-2008 (50 male and 50 female) were included. Baseline clinical and technical characteristics for these patients are outlined in (Table 1). The mean age was 49.7-years old, and the average follow-up was 7.2 years. A total of 126 procedures were completed (26 procedures in addition to the index operation for each patient). Six of these procedures were for pseudoarthrosis, 1 was for wound debridement post-infection, and one was for removal of a retained drain-tube. Eighteen of these procedures were due to CASP development in 10 different patients. The median number of levels fused in the degenerative cohort of patients was 1 motion segment. In contrast to the traumatic cohort, no patients had fusion of their thoracolumbar junction. Almost all patients (99/100, 99.0%) had radiological imaging completed at a

Table 1: Baseline clinical and technical characteristics from traumatic and degenerative patients.

Factor	Traumatic Patients (%)	Degenerative Patients (%)	P-value
Gender			
Male	31/40 (78%)	50/100 (50.0)	<0.01
Female	9/40 (22%)	50/100 (50.0)	<0.01
Age (years)	38.6	50	<0.01
Clinical follow-up (years)	7.6	7.2	0.38
Radiological follow-up (months)	29.4	31.1	0.73
Number of levels fused	3	1	<0.01
Level fused (thoracolumbar)	32/40 (80%)	0/100 (0%)	<0.01

Table 2: Univariate analysis assessing rates of reoperation for CASP and RASP development following lumbar fusion.

Factor	Traumatic Cohort (%)	Degenerative Cohort (%)	P-value
Repeat operation for CASP	0/40 (0)	15/100 (15)	<0.01
Radiological progression (RASP)	0/34 (0)	14/99 (14)	0.01

mean 31.1 months post-operatively, and 14/99 (14%) demonstrated RASP.

Many baseline factors between the two groups of patients were found to be significantly different. There were a significantly higher proportion of males in the trauma group of patients than the degenerative group (78% versus 50%, p-value < 0.01). The degenerative group was also found to be significantly older than the traumatic group undergoing lumbar fusion (49.7-years old versus 38.6-years old, respectively, p-value < 0.01). Furthermore, the traumatic cohort had a higher number of motion segment levels fused (3 versus 1, p-value < 0.01), and number of patients undergoing thoracolumbar fusion (80.0% versus 0.0%, p-value < 0.01) compared to the degenerative cohort. Importantly however, there was no significant difference found between the two groups with respect to clinical follow-up (7.6 years in the traumatic group versus 7.2 years in the degenerative group, p-value=0.38), nor radiological follow-up (29.4 months versus 31.1 months, respectively, p-value=0.73).

A significantly higher proportion of patients in the degenerative cohort required a second operation for CASP development as compared to the traumatic cohort of patients (15/100 versus 0/40, respectively, p-value < 0.01) as shown in (Table 2). Moreover, more patients in the spondylotic cohort were also found to have radiological progression of their degenerative disease as compared to the traumatic patients (14/99 versus 0/34, respectively, p-value=0.01). Upon stratifying for both age and gender, a statistically significant difference in ReopASP was still found between the two cohorts (both p-values <0.01) as shown (Table 3). Other baseline differences between the two groups of patients included the median number of levels fused and the number of thoracolumbar fusions completed between the two groups. However, as previous studies have not shown a definitive relationship between the number of levels fused and ReopASP, this was not corrected for [3-5,8,27-32]. Furthermore, there were no patients in the degenerative cohort that had undergone thoracolumbar fusion, and as such it was also not possible to correct for this difference.

Table 3: Univariate analysis of stratified age and gender requiring reoperation for CASP.

Factor	Traumatic Cohort (%)	Degenerative Cohort (%)	P-value
Age (≥25 years)	0/34 (0)	14/99 (14)	0.01
Gender (male)	0/31 (0)	8/50 (16)	<0.01

Discussion

Spinal arthrodesis as a treatment for lumbar spine pathology was first described over 100 years ago by Albee for Pott's disease and Hibbs for spinal deformity correction [33,34]. Since that time, lumbar spine decompression and instrumented fusion has become commonplace, and has been shown to be an excellent treatment option for degenerative spondylolisthesis [1,25,35]. Its high rate of success with respect to improving patient symptomatology has, in many cases, overshadowed long-term complications such as adjacent segment pathology. CASP refers to the development of symptoms and signs that correlate with radiological evidence of degeneration adjacent to a previous fusion construct (RASP) [36]. Similarly, RASP refers to evidence of degeneration on imaging at spinal levels adjacent to a previous fusion. Awareness of CASP and RASP has become increasingly more important over the past decade due to a growing elderly population and an increased number of lumbar spine fusion procedures taking place [25]. Despite the importance of CASP and RASP, a detailed understanding of their etiology and pathophysiology is currently lacking. Explanations for the development of CASP have been based mainly on patient propensity for degenerative spinal changes and altered biomechanical forces at motion segments adjacent to a previous fusion. The best available evidence to date suggests that adjacent segment pathology is likely multifactorial, with fusion procedures accelerating an already progressing underlying disease process [2]. We have recently shown that ReopASP occurs more frequently in cervical spine fusion of spondylotic patients than trauma patients [37], with a hypothesis that patients presenting with biomechanical instability following trauma represent a generally healthier population, and are thereby less susceptible to degeneration of senescence [38]. The objective of this study was to further explore this issue by examining CASP development following lumbar spine fusion in traumatic and spondylotic patient cohorts.

Clinical adjacent segment pathology

The prevalence of CASP after fusion is highly variable with a reported range between 1.9-30.3% at 5 years and a mean annual incidence of 2.5% per year [3-8,27]. In our study, we found a prevalence of ReopASP of 15% at a mean 7.2 years. This represents the reoperation rate for CASP, and as such may underestimate the actual prevalence of CASP which would include patients treated successfully non-operatively. However, reported rates of reoperation for CASP have been found to range from 7.7% at 2 years to 16.5% at 5 years and 36.1% at 10 years [3-5,13]. Our findings are slightly lower than what has been reported. Several explanations could explain this difference, including differing practice patterns locally and elsewhere. For example, local spine surgeons may be more conservative in managing patients re-presenting with CASP. Furthermore, ascertainment bias may also explain this difference. Patients treated locally may have moved elsewhere and undergone treatment for CASP development (and as such were not captured in our electronic database search encompassing all patients within the province).

Several hypotheses exist explaining the development of CASP. For example, it has been proposed that increased biomechanical stress on spinal motion segments adjacent to a fusion construct result in accelerated degenerative change at those levels [7,25]. Furthermore, simulated biomechanical studies of lumbosacral fusion have demonstrated increased intra-discal pressures and increased motion at levels adjacent to fused segments [25,39]. Animal models of lumbar spine fusion have also shown increased facet loading and an accelerated degenerative process adjacent to a previous fusion. Other mechanical theories suggest that, in concert with the above, that open dissection accelerates the degenerative process due disruption and loss of the integrity of bony and ligamentous supporting structures [7,40]. Although not definitively proven, the latter would then lend itself to the belief that minimally invasive approaches to lumbar fusion should lower the incidence of CASP [7,41-44]. In contrast, others believe CASP simply represents a natural history and progression of spondylotic disease. In support of this are population and twin-based genetic studies showing a relationship between spondylosis and patient relatedness. Moreover, these patients also have a propensity to degenerative change elsewhere in the spine [41,45,46], and some studies report a similar rate of CASP development regardless of fusion [7,47-51]. In our study, we compare the prevalence of ReopASP in traumatic and degenerative groups of patients. There was a significantly higher prevalence of ReopASP in the degenerative group compared to the traumatic group of patients. Both groups have undergone lumbar spine arthrodesis for different indications—the traumatic group for mechanical instability and the degenerative group for symptoms and signs of spondylosis. If CASP development (and subsequent ReopASP) were more related to iatrogenic fusion and altered biomechanics at the adjacent fusion levels, then it would be expected that there would be at least some cases of ReopASP in the traumatic cohort of patients. This was not observed; in fact, there were no cases of ReopASP in the traumatic cohort.

However, there were baseline differences between the two cohorts that could also be biasing these results. For example, there was a difference in the mean age of the two groups at the time of their initial operation. It could be that given a longer follow-up that the traumatic group of patients may go on to develop CASP and require ReopASP. While some studies have identified age as a risk factor for CASP development [27,52,53], many studies have not, and age as a risk factor remains controversial [3,11,13,54]. Even upon stratifying for age in our study, there remained a difference found between the two cohorts in ReopASP.

There were also technical differences between groups potentially explaining the difference in ReopASP found, including the number of levels fused and specific spinal levels fused. Significant controversy exists pertaining to the association of these technical factors with adjacent segment pathology [4,7,17,27,29,30,32,55-59]. Some argue that a longer fusion simply incorporates adjacent levels likely to undergo degeneration and thus is protective, while others claim that a longer fusion increases the biomechanical strain placed on adjacent levels due to a longer lever arm. At least two *in vivo* studies have shown an increased risk for adjacent segment pathology with an increase in number of levels fused. This should theoretically increase the presence of adjacent segment pathology in our trauma cohort, a finding which we did not identify [27,59]. The difference

in specific levels incorporated into the fusion construct between the two groups could also explain the difference in ReopASP between them. How this difference would bias our results, however, is unclear. Some studies have found that spondylosis has a propensity to develop in the lower segments of the lumbar spine [7,60], whereas more proximally instrumented vertebrae being associated with an increased risk of adjacent segment pathology has also been suggested [27]. Unfortunately, it was not possible to stratify our analysis and account for this difference as no patients from the degenerative cohort underwent thoracolumbar fusion.

Radiographic adjacent segment pathology

Similarly to CASP and ReopASP, reported rates of RASP are also quite variable with a range between 8-100% being previously found [6,13]. The wide range of reported rates of RASP is likely related to the heterogeneity of studies with respect to criteria classifying and grading RASP, as well as differing lengths of follow-up. Among these grading systems, factors such as disc height, sclerosis, and osteophytosis are some of the most common criteria used to judge the extent of degeneration. The grading scale used in this study is also based on these three factors, and has been previously shown to be an objective and reliable tool for grading RASP. The rate of RASP found here was 14% in the degenerative cohort. Although a wide range in the literature exists, this is still at the lower end of what has been reported. The differing length of radiological follow-up in our study in comparison to other studies could explain this difference. Previous studies have included both longer and shorter follow-up periods resulting in both lower and higher reported rates of RASP, respectively [6,13]. Finally, there was also a significant difference between the two cohorts in our study with respect to RASP progression. The degenerative group of patients demonstrating a higher rate of RASP progression, importantly, however, the length of radiological follow-up did not differ between the two groups.

Limitations

This is a retrospective study and as a result, is prone to innate biases. Moreover, it is a single institution, single-observer study. In comparing the two cohorts of patients, technical differences existed that were not accounted for upon analysis. For example, neither the number of levels fused, nor the specific lumbar spine level fused were controlled for. As previously discussed, although the former factors relationship to CASP and ReopASP remains controversial, the specific levels fused between the two patient groups likely does represent a limiting factor in our analysis. Furthermore, additional clinical and technical factors that may affect ReopASP in our study are not accounted for including smoking status, type of instrumentation, and ascertainment bias. Accounting for these factors with identification of independent risk factors through multivariate analysis would be ideal, however difficult with no cases of ReopASP being identified in the traumatic patient group. Large sample sizes and/or increased effect size would be required to perform this kind of statistical analysis.

Conclusion

Lumbar spine arthrodesis for spondylotic disease is a common treatment strategy with many patients demonstrating excellent outcomes. An ageing population and broadening surgical indications for arthrodesis will likely only lead to more patients

undergoing spinal fusion. As a result, complications such as CASP and subsequent ReopASP are going to become more prevalent and require management. Although the etiology and pathophysiology of CASP remains poorly understood, here, we found a higher rate of ReopASP in a spondylotic group of patients undergoing elective lumbar spine fusion compared to a traumatic group undergoing fusion for mechanical instability. Even allowing for study limitations, our findings support the belief that CASP is related more to patient propensity for developing degenerative change than altered biomechanical forces post-fusion.

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