Quality of life and slip progression in degenerative spondylolisthesis treated non-operatively

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Abstract

**Study Design:** Prospective cohort study of consecutive patients.

**Objective:** Determination of the quality of life (QoL) and prevalence of slip progression in patients with degenerative lumbar spondylolisthesis managed non-operatively.

**Summary of Background Data:** Lumbar spinal stenosis secondary to degenerative lumbar spondylolisthesis is a common radiographic diagnosis associated with chronic back pain and radicular symptoms. There is limited evidence as to the clinical course in terms of validated QoL measures, and the extent of slip progression in patients with this condition treated non-operatively.

**Methods:** Validated disease specific and generic QoL metrics including SF12 physical and mental scores (SF12-PCS and SF12-MCS), Oswestry Disability Index (ODI), and numeric scales for back and leg pain as well as radiographic assessment of slip extent were evaluated at initial consultation (baseline) and at a minimum of 5 years after the baseline assessment. Slip progression was defined by a >5% increase in slip percentage.

**Results:** Thirty-nine of 160 (24.4%) patients elected to switch to operative management, despite no slip progression on preoperative radiographs. Seventy spondylolisthetic levels in 66 participants were assessed after a minimum of 5 years of non-operative management. Twenty-one participants (31.8%) had slip progression. SF12-PCS, ODI, and leg pain improved similarly in both groups (p<0.05). SF12-MCS did not change significantly in either group. Back pain improved only in the non-progressing group.

**Conclusions:** The majority of cases of low grade spondylolisthesis do not progress over 5 years with non-operative management. Regardless of whether there was progression or not, the mean PCS, ODI, and leg pain improved from baseline, although symptoms remained and a significant number elected to switch to surgical management before 5 years. Back pain improved with non-operative treatment only in those without progression.
**Key Words:** degenerative spondylolisthesis, non-operative, natural history, slip progression, quality of life

**Level of Evidence:** 2
Introduction

Degenerative spondylolisthesis of the lumbar vertebrae is an acquired displacement of a vertebra on the adjacent caudal vertebra associated with common degenerative changes in the spinal column rather than a defect in the vertebral ring seen in other varieties of spondylolisthesis\textsuperscript{1}. It is most common among women, in those over 50 years of age, and occurs most frequently at L4-5, although any lumbar level may be involved\textsuperscript{2,3}. It is classically associated with chronic back pain and radicular symptoms but may also occur in absence of symptoms and there is no recognized association between radiographic findings and the degree of symptomology\textsuperscript{2-5}. The natural history of this condition is not well defined and the optimal treatment, especially in low grade cases, remains controversial despite the increasing frequency of the diagnosis\textsuperscript{6}.

Both operative and non-operative treatment regimens have been associated with symptomatic improvement in some individuals and the cost effectiveness of different options is debated\textsuperscript{6-8}. Several studies have examined spondylolisthesis for progression and clinical outcomes but these have generally been short term, involved few patients, and/or did not use validated outcome measures\textsuperscript{2,4,7,9}. The evidence-based clinical guideline development committee of the North American Spine Society conducted a systematic review of the available literature in 2008 and recommended better studies with validated outcome measures\textsuperscript{1}. Therefore, we set out to describe the natural history of this condition in a prospective cohort of cases of lumbar degenerative spondylolisthesis followed for a minimum of 5 years. This is the first study to our knowledge that assesses these outcomes with commonly used, validated, health related quality of life measures.

Materials and Methods

All patients presenting to a university tertiary hospital with lumbar degenerative spinal stenosis and degenerative spondylolisthesis between February 2006 and June 2010 were invited to participate in a prospectively followed clinical cohort. Participants were recruited by one of three fellowship trained
orthopaedic spine surgeons at their initial consultation. All had initial MRI or CT to diagnose pathological level. Patients having the following criteria were included: non-operative management, lumbar radiculopathy or neurogenic claudication from lateral or central degenerative stenosis between L1 to S1 levels, and degenerative spondylolisthesis of Meyerding grade I-II (i.e. <50% slip of a vertebra on the caudal vertebra)\(^9\). Exclusion criteria were lumbar scoliosis >10°, previous lumbar surgery, pregnancy or planned pregnancy, progressive neurological deterioration or Cauda Equina Syndrome requiring urgent surgery, and an inability to comply with the study plan or give informed consent. Treatment was tailored to the needs of the individual patient and included activity modification, analgesics, physiotherapy, and epidural injections as indicated.

Patients were assessed at their initial consultation with the surgeon (baseline), and again a minimum of 5 years after their baseline assessment. At each visit patients completed quality of life metrics (QoL) including SF-12 version 2\(^{11,12}\), Oswestry Disability Index (ODI)\(^{11,13}\), and the numeric rating scale (NRS) for back and leg pain intensity\(^{11}\). Slip progression measurements were made on upright lateral radiographs taken at the initial consultation and at the 5-year follow-up visit using a dedicated electronic PACs workstation (GE Centricity RA1000, v3.2.2). Percentage of slip was the amount of anterior translation of the rostral vertebra on the caudal vertebra divided by the anterior-posterior depth of the caudal superior endplate (Fig. 1). Progression was defined by a greater than 5 percent increase in slip percentage\(^9\). This project was approved by our institutional research ethics board.

Participants could have more than one level with degenerative listhesis. Therefore, a participant was categorized as progressed if at least one level met the progression criteria of >5% increase in slip percentage. Initial QoL metrics and patient characteristics such as age, gender, and body mass index (BMI) were assessed to see if they were associated with later progression. Statistics were calculated using R (v 3.1.3, 2015; R Foundation for Statistical Computing, Vienna). Student’s t-tests were used...
for parametric variables, Wilcoxon signed-rank tests for nonparametric variables, and Chi-squared tests for categorical variables. Paired tests were used for assessment of baseline to follow-up differences within individuals. Change in outcome measure was calculated as score at 5 years minus score at baseline. Positive scores for PCS and MCS indicate improvement, and negative values indicate improvement for ODI and back and leg pain. An alpha of 0.05 was considered significant and all tests were two tailed.

Results

A total of 160 patients met the inclusion and exclusion criteria within the recruitment window (Fig. 2). Fifty-three participants were lost to follow-up including: 5 that passed away from causes unrelated to treatment, 1 with malignancy who felt too ill to continue attendance, 5 who withdrew for undeclared reasons, and 2 that moved to another province. Thirty-nine crossed over to operative management after a mean of 26 months (range 12-23 months) and were not included in the analysis. Final radiographs were not obtainable for 2 patients to allow assessment for progression. Therefore, 66 participants were available for analysis after a minimum of 5 years of non-operative management. This included 19 males and 47 females. Mean age at inclusion was 66.3±9.4 [SD] years for men and 66.2±8.7 [SD] years for women. The mean follow-up period was 73 months (range 60-102 months). Mean BMI was 29.1 kg/m² (95% CI 27.2-30.9 kg/m²). BMI data was not available for 4 participants. Four participants had >1 levels with degenerative listhesis. The slip was at L3-4 in 6 levels, L4-5 in 59 levels, and L5-S1 in 5 levels.

The participants that were lost to follow-up did not differ in terms of age (p = 0.12), gender (p = 0.44), BMI (p = 0.43), or involved level (p = 0.33) when compared to the participants included in the current study (Fig. 2). Additionally, participants that crossed over to surgery and were excluded for having operative management before they reached their 5-year follow-up visit (n=39) did not differ from those who were included in the current study in terms of age (p = 0.75), gender (p = 0.10), BMI (p = 0.76), or...
extent of initial slip (p = 0.62). There were fewer L4-5 levels and a larger proportion of L3-4 and L5-S1 levels in the patients that crossed over to surgical management (p = 0.04). Patients that crossed from non-operative to surgery did so due to intolerance of symptoms of spinal stenosis (i.e. neurogenic claudication/radiculopathy). These patients that crossed over to surgery did not have any slip progression before surgery; comparison between their preoperative radiographs and initial baseline radiographs did not differ in the amount of slip (p=0.99). None developed cauda equina syndrome nor neurologic deterioration.

Mean percent slip increased significantly from 18.5% (95% CI17.0-20.0%) at baseline to 22.0% (95%CI20.4-23.6%) at final the follow-up visit (Table 1; p = 0.002). However, this represents a mean increase of only 3.5%. Only 21 participants (31.8%) had a 5% increase in slip defined as progression. Only one participant with multilevel involvement had progression (at 1 of 2 levels). Among those who did progress, the mean increase in slip was 8.9% and the maximum increase was 16.4%. The levels that progressed had a smaller mean slip of 16.5% (95% CI 14.2-18.8%) at the baseline assessment compared to the baseline 20.2% (95% CI 18.2-22.1%) in non-progressing levels (p=0.02).

All the levels that progressed were at L4-5 except for two at L5-S1. Although there appeared to be a higher proportion of male participants who had progression (8 out of 19; 42.1%) compared to female participants (13 out of 47; 27.7%), this was not significant (p=0.4). There was a trend toward a younger mean age in participants who progressed (63.4±8.8[SD] years) compared to those who did not (67.5±8.5[SD] years) but this was not significant (p=0.08). A larger proportion of the participants who progressed (61.9%) were obese (BMI>30) compared to those who did not progress (26.8%; p=0.02).

There was no difference in follow-up duration between progressing (74.4 months [95% CI 68.3-76.3 months]) and non-progressing (72.3 months [95% CI 67.8-81.0 months]) participants (p=0.60).

Quality of life metrics at baseline and at the 5-year follow-up visit are shown in Table 2, and the mean change in score for each measure is shown in Figure 3. Baseline measures were not different between
patients who progressed and those who did not progress for any outcome measures (Table 2; p>0.05 for all measures). Patients in both groups saw a significant improvement in physical functioning (PCS) at the 5-year follow-up visit compared to baseline (Table 2; p<0.001). However, the mean change in score between the no progression and slip progression groups revealed that the amount of improvement was not different between groups (Fig. 3A; PCS, p=0.18). Mental functioning was not different from baseline at the 5-year follow-up visit for either group (Table 2; p>0.05 for both groups). Accordingly, the mean change in MCS score did not differ between groups (Fig. 3B; p=0.15). Compared to baseline ODI improved significantly at the 5-year follow-up visit in the slip progression group (p=0.02), but it only reached borderline significance in the non-progressing patients (p=0.05). The amount of improvement (mean change) was not different between groups (Fig. 3C; p=0.44). Compared to baseline, the intensity of back pain at the 5-year follow-up decreased in the non-progressing group (p=0.006) but not the progressing (p=0.82) group. Accordingly, the improvement in back pain (mean change) was less in patients who had a slip progression than for non-progressing patients (Fig. 3D; p=0.02). Leg pain intensity decreased significantly in both groups (p<0.001 and p=0.008, respectively), and the reduction in the intensity of leg pain (mean change) was not different between groups (Fig. 3E; p=0.87).

**Discussion**

After at least 5 years of non-surgical management, the majority of cases of degenerative lumbar spondylolisthesis did not progress. Thirty percent of spondylolisthionic levels progressed more than 5%, which is similar to that demonstrated in previous studies in degenerative spondylolisthesis of the lumbar spine\(^4,9\), although higher than the rate of progression reported for degenerative cervical slips\(^14\). As found by Matsunaga et al., those who went on to progress had a smaller initial slip and a tendency towards a younger initial age, supporting the theory that as the slip progresses it attains eventually greater stability\(^9\). Consistent with the previously reported higher rates of both degenerative spondylolisthesis and degenerative spine disease in post-menopausal women, the majority of cases
were in women > 50 years of age. However, there does not appear to be any difference in tendency to progress between men and women. Although one might expect a more rapid deterioration after menopause if loss of gonadotropins was involved in the higher rate of spondylolisthesis among women, there was no significant difference in age between men and women.

Quality of life improved similarly over 5 years in both those who progressed and those who did not when measured using SF-12 PCS, ODI, and leg pain. Using a different metric, the Assessment of Surgical Treatment of Low Back Pain scale of the Japanese Orthopaedic Association (JOA Score), a similar conclusion has been described by Matsunaga et al. Our study confirms the lack of association between progression and QoL but with more commonly used and validated QoL metrics. Additionally, patients who eventually crossed over to surgical management, presumably due to failure of non-operative management, did not have an increase in their slip before the decision to change treatment approach. The SF-12 MCS score did not change, consistent with the lack of any specific mental health component to the treatment regime employed here.

It has been suggested that the leg pain and QoL improvements seen in those that progressed may indicate that as the slip progresses it may actually become more stable and thus less symptomatic. However, in our cohort, the improvements are very similar in both progressing and non-progressive groups suggesting a similar mechanism of improvement in QoL and leg pain or a similar response to the non-operative technique deployed. Although all patients recruited to this study presented with similar symptoms of spinal stenosis, the extent of progression of the pathologic process may have been different, as suggested by the smaller initial baseline slip in the group that had slip progression compared to the group that did not. Additionally, the subset of patients that progressed did not exhibit the same improvement in back pain seen in the non-progressing majority implying that either there is not sufficient spontaneously acquired stability or this back pain is not due to instability per se.

Regardless of any stability that may be acquired, other factors, such as greater underlying facet
osteoarthritis, may simply be present in those who progress with associated greater pain and this may not be addressed to the same extent by the non-operative management employed.

The lack of direct correlation between radiographic findings of anterolisthesis in general and symptoms has been described previously\textsuperscript{2,4,5,9}. The exception found in our study was that patients with slip progression did not have the improvement in back pain seen in the non-progressing group. Again, this may simply indicate that the underlying disease in the progressing group is still progressing and may later develop a similar decrease in back pain as it becomes more stable. The clinical significance in the link between back pain and progression remains unclear.

Limitations to this study include the possibility that the cases that remained in the non-operative group represented those with less symptomatic or less progressive disease and there may be different pathology in those who were lost to follow-up or crossed over into operative treatment. These factors cannot be eliminated from the research plan due to patient autonomy; however, there was no apparent demographic difference between those who were included in the final analysis and those who were not. The exception is that participants who crossed over to surgery had a smaller proportion of L4-5 level involvement; however, the relevance of this apparent level difference is unclear at this time. Those patients who chose to switch out of this non-operative cohort and received surgery did not have progression of their slip but were unable to tolerate their symptoms.

This study represents one of the larger cohorts in the literature and appears to have the most validated and clinically useful outcome measures. Low grade degenerative spondylolisthesis did not progress over 5 years in the majority of cases. Regardless of whether there was progression or not there was a similar improvement in quality of life and leg pain with non-operative management. The cases that did have progression, however, did not have the significant improvement in back pain seen in those who did not progress suggesting that this subgroup may need some degree of alternative management. Despite the low rate of slip progression and overall mean improvements in pain and quality of life in those patients able to tolerate a conservative approach, our data indicates that
degenerative lumbar spondylolisthesis should not be mistaken for a benign condition; patients after 5 years still had residual symptoms and disability, and a significant subset of patients elected to switch to surgical management.
References


Figure Legends

Figure 1: Representative sagittal MRI image of L4 and L5 vertebral levels demonstrating a measurement technique for amount of spondylolisthesis slip. Percentage of slip was the amount of anterior translation of the rostral vertebra (red line) divided by the anterior-posterior depth of the superior endplate of the caudal vertebra (Blue line).
Figure 2: Flowchart describing disposition of non-operatively treated patients with degenerative lumbar spondylolisthesis enrolled in a longitudinal prospective cohort followed for a minimum of 5 years.

<table>
<thead>
<tr>
<th>Initial enrollment: 160</th>
</tr>
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<tbody>
<tr>
<td>Lost to follow-up: 53</td>
</tr>
<tr>
<td>• Deceased: 5</td>
</tr>
<tr>
<td>• Stopped Attending clinic/Unable to contact: 40</td>
</tr>
<tr>
<td>• Too ill to attend further clinics: 1</td>
</tr>
<tr>
<td>• Moved to another city: 2</td>
</tr>
<tr>
<td>• Withdrew from study: 5</td>
</tr>
<tr>
<td>Crossed over to surgical management: 39</td>
</tr>
<tr>
<td>Radiographs unavailable for progression analysis: 2</td>
</tr>
<tr>
<td>Available for analysis: 66</td>
</tr>
</tbody>
</table>
Figure 3: Changes in multiple quality of life metrics in non-operatively treated patients with degenerative lumbar spondylolisthesis followed for at least 5 years who either demonstrated slip progression (yes) or no progression (no). There was no statistical difference in change in SF-12 Physical Component Score (A; PCS), Mental Component Score (B; MCS), Oswestry Disability Index (C; ODI), or leg pain (E) between the two groups. Improvement in back pain was significantly less in patients who had a slip progression compared to those who did not (D). *p=0.02.
Table 1: Change in the percentage of slip in patients with degenerative spondylolisthesis that had slip progression compared to those that had no slip progression.

<table>
<thead>
<tr>
<th></th>
<th>No progression</th>
<th>Slip progression†</th>
<th>Average slip progression</th>
<th>p-value (comparison between slip groups)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 45</td>
<td>n = 21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline, %, mean ± SD</td>
<td>20.2±6.4</td>
<td>16.5±5.0</td>
<td>18.5±6.2</td>
<td>0.020</td>
</tr>
<tr>
<td>5 Year, %, mean ± SD</td>
<td>21.5±6.4</td>
<td>25.4±5.3</td>
<td>22.0±6.3</td>
<td>0.014</td>
</tr>
<tr>
<td>Change in slip, %, mean (95% CI)</td>
<td>1.3 (0.61)</td>
<td>8.9 (1.6)</td>
<td>3.5 (0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>p-value (comparison between time)</td>
<td>0.310</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

† Slip progression is defined as a >5% increase in slip percentage
Table 2: Comparison of quality of life measures at baseline and the 5-year follow-up visit within slip progression groups.

<table>
<thead>
<tr>
<th>Variable, mean ± SD</th>
<th>No progression n=45</th>
<th>5 year</th>
<th>p-value†</th>
<th>Slip progression‡ n=21</th>
<th>Baseline</th>
<th>5 year</th>
<th>p-value¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF12 PCS</td>
<td>29.5±9.2</td>
<td>34.5±11.5</td>
<td>&lt;0.01</td>
<td>26.6±4.1</td>
<td>35.1±9.7</td>
<td>&lt;0.001</td>
<td>0.173</td>
</tr>
<tr>
<td>SF12 MCS</td>
<td>50.7±11.0</td>
<td>50.2±9.9</td>
<td>0.82</td>
<td>46.6±12.3</td>
<td>50.7±11.1</td>
<td>0.11</td>
<td>0.179</td>
</tr>
<tr>
<td>ODI</td>
<td>36.2±14.1</td>
<td>31.2±17.4</td>
<td>0.05</td>
<td>38.3±11.7</td>
<td>30.1±14.3</td>
<td>0.02</td>
<td>0.555</td>
</tr>
<tr>
<td>Back pain</td>
<td>5.6±2.4</td>
<td>4.0±2.7</td>
<td>&lt;0.01</td>
<td>5.3±2.3</td>
<td>5.1±3.1</td>
<td>0.82</td>
<td>0.633</td>
</tr>
<tr>
<td>Leg pain</td>
<td>6.4±2.6</td>
<td>4.2±3.1</td>
<td>&lt;0.001</td>
<td>7.2±2.6</td>
<td>4.9±2.7</td>
<td>&lt;0.01</td>
<td>0.249</td>
</tr>
</tbody>
</table>

‡ Slip progression is defined as a >5% increase in slip percentage

†P values compare baseline and 5 year values within each group.

¶P values compare baseline scores between groups.