Do Preoperative Corticosteroid Injections Increase the Risk for Infections or wound healing problems after Spine Surgery? A Swiss Prospective Multicenter Cohort Study

Farshad, Mazda; Burgstaller, Jakob M; Held, Ulrike; Steurer, Johann; Dennler, Cyrill

Abstract: STUDY DESIGN Prospective multi-center cohort study. OBJECTIVES This study evaluates the risk for surgical site infections (SSI) or wound healing problems (WHP) in patients who underwent corticosteroid injection prior to lumbar decompression surgery. SUMMARY OF BACKGROUND DATA Corticosteroid injections are often used for the treatment of the degenerated spine. However, their well-known immunosuppressive effects could increase the risk for local infections, particularly if a surgical intervention follows the injection rapidly. METHODS The Swiss Lumbar Stenosis Outcome Study (LSOS), which is a prospective multicenter cohort study of patients with symptomatic lumbar spinal stenosis, was used as database. Of 743 patients, 422 patients underwent surgery and were eligible for the study. Ten patients (2.4%) were revised for either surgical site infections (n = 6) or wound healing problems (n = 4). A control group (n = 19) was constructed matched according to age, sex, diabetes and BMI. Odds ratios were calculated by using a conditional logistic regression model to quantify the risk of SSI or WHP after pre-operative corticosteroid injection. Subgroup analysis was performed for patients with injection within 0-3 months before surgery, 0-6 months before surgery or any injection at all before surgery. RESULTS Within this cohort, no significant association could be found between preoperative corticosteroid injection and postoperative SSI or WHP in patients with corticosteroid injections within 0-3 months before surgery (OR = 0.36, 95% CI 0.04-3.22), 0-6 months before surgery (OR = 0.69, 95% CI 0.14-3.49) or any time before surgery (OR = 0.43, 95% CI 0.04-3.22). CONCLUSIONS Within the here investigated cohort, the risk of surgical site infections or wound healing problems following lumbar spinal decompression surgery seems not highly associated with preoperative corticosteroid injections. However, the safe time interval between corticosteroid infiltrations and surgery remains unknown, should not be decreased incautiously and is subject of further research. LEVEL OF EVIDENCE 2.

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Do Preoperative Corticosteroid Injections Increase the Risk for Infections or wound healing problems after Spine Surgery? A Swiss Prospective Multicenter Cohort Study.

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Abstract

**Study design:** Prospective multi-center cohort study.

**Objectives:** This study evaluates the risk for surgical site infections (SSI) or wound healing problems (WHP) in patients who underwent corticosteroid injection prior to lumbar decompression surgery.

**Summary of Background Data:** Corticosteroid injections are often used for the treatment of the degenerated spine. However, their well-known immunosuppressive effects could increase the risk for local infections, particularly if a surgical intervention follows the injection rapidly.

**Methods:** The Swiss Lumbar Stenosis Outcome Study (LSOS), which is a prospective multicenter cohort study of patients with symptomatic lumbar spinal stenosis, was used as database. Of 743 patients, 422 patients underwent surgery and were eligible for the study. Ten patients (2.4%) were revised for either surgical site infections (n=6) or wound healing problems (n=4). A control group (n=19) was constructed matched according to age, sex, diabetes and BMI. Odds ratios were calculated by using a conditional logistic regression model to quantify the risk of SSI or WHP after pre-operative corticosteroid injection. Subgroup analysis was performed for patients with injection within 0-3 months before surgery, 0-6 months before surgery or any injection at all before surgery.

**Results:** Within this cohort, no significant association could be found between preoperative corticosteroid injection and postoperative SSI or WHP in patients with corticosteroid injections within 0-3 months before surgery (OR = 0.36, 95% CI 0.04-3.22), 0-6 months before surgery (OR = 0.69 95% CI 0.14-3.49) or any time before surgery (OR = 0.43, 95% CI 0.04-3.22).

**Conclusions:** Within the here investigated cohort, the risk of surgical site infections or wound healing problems following lumbar spinal decompression surgery seems not highly associated with preoperative corticosteroid injections. However, the safe time interval between corticosteroid infiltrations and surgery remains unknown, should not be decreased incautiously and is subject of further research.

**Key Words:** spinal stenosis; surgical wound infection; surgical decompression; spinal fusion; epidural injections; spinal injections; glucocorticoid

**Level of Evidence:** 2
Introduction

The most common reason for spinal surgery in elderly people is lumbar spinal stenosis (LSS) with increasing rates by aging of the population.\textsuperscript{1,2} The natural history of mild and moderate LSS is favorable in one-third to half of the patients.\textsuperscript{3} First-line treatment options of LSS are usually non-surgical. A potential effect of physical therapy, orthotics, rehabilitation, exercise, pain killers/NSAIDs, education, heat and cold applications and electrical nerve stimulation or alike find low evidence.\textsuperscript{4} Epidural injections of a corticosteroid (ESI) seem however to provide short-term (two weeks to six months) symptom relief in patients with neurogenic claudication or radiculopathy but with conflicting evidence regarding the long-term efficacy.\textsuperscript{3} The number of epidural injections being performed is increasing although the potential of severe adverse effects is not to be neglected.\textsuperscript{5-7} According to the US Food and Drug Administration (FDA), the administration of corticosteroids in the epidural space is considered off-label use and its use should carefully follow guidelines.\textsuperscript{3,8-10} Surgical decompression usually follows failed conservative treatment and provides a long-term pain relief in a large percentage of patients.\textsuperscript{3,11} The perioperative morbidity, despite the advanced age of the average patient, seems relatively low.\textsuperscript{12,13} One of the potentially serious complications of spinal surgery is infection with an incidence of 0.7-12\%.\textsuperscript{14,15} Compared to that, the infection rate after spinal injections is reported to be 1-2\% but still with possible devastating consequences for the patient.\textsuperscript{7,16} The immunosuppressive effect of corticosteroids is well known.\textsuperscript{17-20} Although frequently used in the treatment of LSS, ESI prior or even during surgery has not been sufficiently acknowledged or investigated as a potential risk factor for a postoperative SSI.\textsuperscript{21,22} Yang et al. published very recently a retrospective analysis of a database with 18'931 patients; the patients were assigned to one of the following groups: Lumbar epidural steroid injections within 0-1 month, 1-3 months, 3-6 months or 6-12 months between injection and surgery.\textsuperscript{21} They identified patients with injection 0-1 and 1-3 months before surgery at higher risk for postoperative infections. However, as the retrospective analyses originate form data of a large heterogeneous database, the potential of indication and selection bias is considered high and more clinically granular research was suggested by the editors.

The aim of this study was to evaluate the risk for surgical site infections (SSI) or wound healing problems (WHP) in patients who received a local corticosteroid injection prior to lumbar decompression surgery with or without fusion using a very detailed prospectively established national multicenter database. If so, the minimal time interval between injection and surgical intervention could be defined to minimalize the risk of surgical site infections or wound healing problems.
Methods

The Lumbar Stenosis Outcome Study (LSOS), an ongoing, prospective, multicenter cohort with patients recruited from several hospitals in Switzerland, was used. This multi-center cohort study was conducted in compliance with all international laws and regulations as well as any applicable guidelines. Written informed consent to participate in the study has been obtained from participants. The study was approved by the independent Ethics Committee of the Canton Zurich (KEK-ZH-NR: 2010-0395/0). Inclusion criteria for the cohort were symptomatic LSS with unilateral or bilateral neurogenic claudication, age of 50 years or older and radiographically verified spinal stenosis (CT or Magnetic Resonance Imaging). Further, the life expectancy had to be more than one year and the patients had to be available for follow-up during at least one year. Exclusion criteria for the cohort were a cauda equina syndrome requiring urgent surgery, acute fracture, infection or significant deformity (>15° lumbar scoliosis) and a clinically relevant peripheral arterial disease. A database query was performed on 743 patients to identify the case group with patients with a surgical site infection (SSI) or a wound healing problem (WHP) after primary decompression and/or fusion for LSS who underwent revision surgery for that reason. These patients of the case group were matched to a control group according to age and sex, and the presence of risk factors for postoperative infections in spine surgery like diabetes and BMI. According to a recent meta-analysis, a match for smoking status was abandoned as it was not shown as an independent risk factor for SSI in spinal surgery.

The number of corticosteroid injections and time interval to surgery was determined. Injections to different regions or different levels on the same date (e.g. to the facet joints and epidural) were not discriminated. Intraoperative application of corticosteroid in surgical treatment of LSS is considered obsolete in Switzerland and therefore this potential bias was not monitored.

In addition, established clinical outcome scores such as Symptom Severity Scale (SSM), Roland Morris Disability Scale (RMDQ), Pain numeric rating scale (NRS) and EuroQol-5D (EQ-5D) were determined for each of the subgroups at baseline and the last visit after 24 months.

The SSM, an instrument specifically developed and validated for spinal stenosis patients by Stucki et al., targets to measure severity of symptoms and quantifies disability of the lumbar spinal stenosis population. It consists of three different subscales; the symptom severity subscale, the physical function subscale and the satisfaction with treatment results subscale with score ranges from 1-5 and 1-4 (best-worst). The Roland and Morris Disability Questionnaire is a back pain specific, self-rated physical disability questionnaire developed by Roland and Morris in 1983. The maximum number of points is 24 and indicates severe disability. The EQ-5D-3L is an assessment tool to measure health-related quality of life with five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) which can be calculated as a sum score (score range 0-100, worst-best).
Statistical analyses

The software “R” was used for the statistical analysis. Descriptive statistics are reported as mean and standard deviations (SD) for continuous variables and numbers and percentages of total for the categorical variables. A matched case-control study design was employed to address the influence of pre-operative epidural injections on the rare event of SSI or WHP. Patients with infections or wound healing problems were defined as “cases”. Control patients were matched to the cases, if the variables age (±2 years), gender, BMI (≥ 30 kg/m²), and diabetes were identical. A conditional logistic regression approach was used with the advantage that all available control patients could be included, i.e. resulting in either one or more control patients for each case. Odds ratios were calculated to quantify the effect of pre-operative epidural injections on SSI or WHP; either overall, or within specified time periods up to three or six months before surgery. A p-value of <0.05 was defined as statistically significant.

Results

Of 743 patients included in the Lumbar Stenosis Outcome Study (LSOS) cohort, 422 patients (57%) were treated with spinal surgery (Figure 1). Of those, a total of ten patients (2.4%) underwent revision surgery either for SSI (n=6) or WHP (n=4) (Table 1).

Patients who were revised for a SSI had a mean age of 70.7 (standard deviation (SD) 10.5) years, a mean BMI of 29.5 (SD 4.3) kg/m² and one-third were females. Only one of the patients (16.7%) had a reported diabetes mellitus. Four of the six patient (66%) with SSI had injections prior to surgery (a total of 15 injections).

Patients who were revised for a WHP had a mean age of 65 (SD 4.2) years, mean of BMI 33.8 (SD 1.9) kg/m² and three (75%) of the patients were female. Two (50%) of the patients had a reported diabetes mellitus. Only one patient (25%) had corticosteroid injections before surgery (a total of two injections) (Table 1).

The control group was constructed with all 19 patients out of the 412 remaining surgical patients who were matched (mean age of 71 (SD 8.54) years, four (21%) females, mean BMI 29.7 (SD 5.3) kg/m², one (5.3%) patient with diabetes) according to the above-mentioned criteria. Fourteen of these 19 patients (73.7%) had an injection before surgery (Table 1).

Combining the SSI and WHP subgroup, the total amount of injections in the combined case group was 5 of 10 patients (50%) compared to 14 injections in 19 control patients (74%) (p=0.73). No significant association could be found between preoperative corticosteroid injection and postoperative surgical site infections or wound healing problems in patients with corticosteroid injections within 0-3 months before surgery (odds ratio (OR) = 0.36, 95%
confidence interval (CI) 0.04-3.22), 0-6 months before surgery (OR = 0.69, 95% CI 0.14-3.49) or any injection at all before surgery (OR = 0.43, 95% CI 0.04-3.22) (Table 2).

Neither the values of the symptom severity scale (SSM), nor those of the Roland and Morris Disability Questionnaire, the pain intensity scale (numeric rating scale NRS) or the EuroQol-5D (EQ-5D-3L) scores were significantly different between the combined case group (SSI und WHP) compared to the matched control group (Table 3).

Discussion

We aimed to illuminate whether local corticosteroid injection prior to lumbar decompression surgery is potentially a clinically relevant independent risk factor for postoperative surgical site infection (SSI) or wound healing problems (WHP) and to determine the minimal safe time interval between injection and surgery. Potential confounding factors were limited to a minimum through use of a large prospective multicenter national cohort and a matched case-control study design.

We found no statistical difference in the calculated odds ratios between the group of patients who developed a SSI or WHP compared to the matched control group, no matter if the injections were made within 3 months, 6 months or at any time point before surgery.

It is known that aseptic surgical techniques and prophylactic preoperative antibiotics are the most important measures to prevent surgical site infections.\(^{34,35}\) Further, several patient associated risk factors have been identified for SSI including diabetes and obesity. Other risk factors such as smoking are debatable.\(^{24}\) It is questionable how strong local steroids would be a relevant risk factor for SSI or WHP, although the anti-inflammatory as well as the immunosuppressive effects of cortisone are well known.\(^{17–20}\) This lack of information is even more surprising knowing that the systemic use of corticosteroids increases the rate of wound healing problems.\(^{36}\)

Intraoperative administration of epidural cortisone has been suggested to improve postoperative pain and to decrease the average length of hospital stay, however, an increase of postoperative epidural abscess formation after intraoperative epidural cortisone administration has been reported and therefore limits the advantages of the procedure.\(^{37–40}\)

Our results concerning injections within 3 months before surgery are in concordance with the recent report by Seavey et al of a large sample size\(^{41}\), but indiscordance of those reported by Yang et al. who clearly have found associations between time-interval of corticosteroid injections and the increase of surgical site infections.\(^{21}\) This might be because of several differences in the study designs and populations, such as a much smaller sample size in our cohort or inclusion of patients over 50 vs. 65 years. However, the here presented results are based on a database with meticulous prospective data gathering methodology focusing on patients with a lumbar spinal stenosis on a multi-institutional level compared
to the large but less detailed database in the study of Yang et al. A major limitation of both studies is the definition of SSI. It is known that such can affect the reported rate of surgical site infections substantially.\(^{42-48}\) In our study, we clearly focused on SSI or WHP severe enough to undergo surgery. But again, the indication for such a revision surgery was not standardized in the here used multi-center cohort. The here presented results have therefore to be interpreted in respect to this prominent limitation and also other kind of limitations. First, the relatively small number of patients who actually developed SSI or WHP might limit the statistical power, but since a rare event is being investigated, this limitation cannot be easily eliminated. We tried to account for this limitation by reduction of the potential confounding factors with the matched case-control design and by using the largest possible national cohort in our country with maximal accuracy of the available data and a reasonable follow up time of 24 to 36 months. It is certainly not excluded, rather plausible, that a statistical difference could be found with larger numbers. However, such a potential difference would probably not be clinically relevant enough, considering that corticosteroid infiltrations are established as a cornerstone of conservative treatment of LSS to be performed before indicating a surgical procedure. However, further research could focus on potential associations and the safest time interval between corticosteroid injections and surgery. Second, the injection technique per se could carry different risks of injections theoretically, although rates of infections after corticosteroid injections of the spine are very low (level of case reports). Further, with the same type of corticosteroids in all centers and the matched case control design of this multicentered national study, this potential bias can be considered to be diluted, if at all present. Third, other potential confounding factors such as intake of other immunosuppressive medication or surgical aspects such as time of surgery and amount of blood loss are not considered here since the sample size of the rare event of infections is too small for stratification.

With respect to the mentioned limitations, we conclude that the risk of surgical side infections or wound healing after lumbar spinal decompression surgery seems not significantly correlated to preoperative corticosteroid infiltrations.
References


26. Tuli SK, Yerby SA, Katz JN. Methodological approaches to developing criteria for


40. Lowell TD, Errico TJ, Eskenazi MS. Use of epidural steroids after discectomy may


Figure 1: Flow chart of study groups
SSI = surgical site infections; WHP = wound healing problems; BMI = body mass index

Patients recruited into the study:
$n = 743$

Patients who underwent surgical decompression ± fusion:
$n = 422$

Cases:
SSI: $n = 6$ (4 with infiltrations)
WHP: $n = 4$ (1 with infiltration)
Total: $n = 10$ (5 with infiltrations)

Controls:
Matched for age, sex, BMI, diabetes
Total: $n = 19$ (14 with infiltrations)
Table 1: Baseline Demographics of the study groups. BMI: Body Mass Index, SD: Standard Deviation

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Surgical site infection (SSI)</th>
<th>Wound healing problem (WHP)</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>6</td>
<td>4</td>
<td>19</td>
</tr>
<tr>
<td>Age, mean (SD), years</td>
<td>70.7 (10.5)</td>
<td>65.00 (4.2)</td>
<td>71 (8.5)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>2 (33)</td>
<td>3 (75)</td>
<td>4 (21)</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>29.5 (4.3)</td>
<td>33.8 (1.9)</td>
<td>29.7 (5.3)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>1 (16.7)</td>
<td>2 (50)</td>
<td>1 (5.3)</td>
</tr>
<tr>
<td>Number of patients with a preoperative corticosteroid injection, n (%)</td>
<td>4 (66)</td>
<td>1 (25)</td>
<td>14 (73.7)</td>
</tr>
</tbody>
</table>
Table 2: Odds-ratios and confidence Intervals reflecting the ratio of odds for SSI or WHP in patients with corticosteroid infiltrations as compared to patients without.

<table>
<thead>
<tr>
<th>Exposition</th>
<th>Odds-ratio</th>
<th>95%- Confidence-Interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection at any time point before surgery</td>
<td>0.43</td>
<td>0.40 – 3.22</td>
</tr>
<tr>
<td>Injection within 6 month before surgery</td>
<td>0.69</td>
<td>0.14 -3.49</td>
</tr>
<tr>
<td>Injection within 3 month before surgery</td>
<td>0.36</td>
<td>0.04-3.22</td>
</tr>
</tbody>
</table>

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Table 3: Clinical outcome scores of patient with a SSP or WHP compared to the matched control group. SSI: Surgical Site Infection, WHP: Wound Healing Problem SSM: Symptom Severity Scale

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>24 month</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSM (SSM symptom severity scale): Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI + WHP</td>
<td>3.4</td>
<td>2.3</td>
<td>0.84</td>
</tr>
<tr>
<td>Controls</td>
<td>3.3</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td><strong>SSM (SSM physical function subscale): Function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI + WHP</td>
<td>2.6</td>
<td>1.4</td>
<td>0.23</td>
</tr>
<tr>
<td>Controls</td>
<td>2.4</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td><strong>SSM (SSM symptom severity scale): pain domain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI + WHP</td>
<td>3.9</td>
<td>2.4</td>
<td>0.74</td>
</tr>
<tr>
<td>Controls</td>
<td>3.8</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td><strong>SSM (SSM symptom severity scale): neuroischemic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI + WHP</td>
<td>3</td>
<td>2.2</td>
<td>0.92</td>
</tr>
<tr>
<td>Controls</td>
<td>2.7</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td><strong>Roland and Morris Disability Questionnaire</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI + WHP</td>
<td>13.3</td>
<td>9</td>
<td>0.33</td>
</tr>
<tr>
<td>Controls</td>
<td>12.6</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td><strong>Pain Intensity Scale (numeric rating scale NRS)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI + WHP</td>
<td>7.1</td>
<td>3.2</td>
<td>0.86</td>
</tr>
<tr>
<td>Controls</td>
<td>6.9</td>
<td>3.5</td>
<td></td>
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<tr>
<td><strong>EuroQol-5D (EQ-5D-3L)</strong></td>
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<td></td>
<td></td>
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<tr>
<td>SSI + WHP</td>
<td>67</td>
<td>86.7</td>
<td>0.73</td>
</tr>
<tr>
<td>Controls</td>
<td>65.8</td>
<td>82.3</td>
<td></td>
</tr>
</tbody>
</table>

* p-value from independent samples Wilcoxon test of the changes from baseline to 24 months between SSI+WHP and controls.