Gender Differences in Pre-operative Opioid Use in Spine Surgery Patients: A Systematic Review and Meta-analysis

Chung-Wang Lee, MSc¹; Sharmila Devi, MBBS²; Yu Tung Lo, MBBS, BSc²; Yookyung Seo¹⁺;
Angela Simon, Pharm D, MS¹; Kelsey Zborovancik, PharmD, MBA¹;
Mona Y. Alsheikh, PharmD, MSc, PhD³; Nayan Lamba, MD²; Timothy R. Smith, MD, PhD, MPH²;
Rania A. Mekary, PhD, MSc, MSc¹,²; Linda S. Aglio, MD, MS²,⁴

*Presenting Author

Affiliations:

1. School of Pharmacy, MCPHS University, Boston, MA, USA.
2. Computational Neuroscience Outcomes Center, Department of Neurosurgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA.
3. Clinical Pharmacy Department, School of Pharmacy, Taif University, Taif, Saudi Arabia.
4. Brigham and Women’s Hospital, Department of Anesthesia, 75 Francis St, Boston MA 02115
Disclosure

• The authors report no funding sources or conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
Introduction

• Women have been demonstrated to have greater incidence of pain compared to men due to biological and psychosocial mechanisms.

• Despite the difference in the prevalence of chronic pain between men and women and negative outcomes related to pre-operative use in spine surgery, gender differences in the utilization of opioids prior to spine surgery have not been established.

• The objective of this study is to evaluate gender differences in the prevalence of pre-operative use of opioids in spine surgery.
Methods

- **Inclusion criteria**
  - Randomized clinical trials, retrospective or prospective observational studies which reported pre-operative opioid utilizations and pain score.
  - Studies with population≥18 years of age.
  - Sample size of at least 5 patients with reported data on opioid use.

- The random-effects model based on the method of DerSimonian and Laird was utilized to calculate the overall pooled prevalence and pooled relative risk (RR) estimates and their 95% confidence intervals (CI).

- Cochran’s Q test (P<0.10) and I² were utilized to assess heterogeneity among studies and measure the proportion of total variation due to the heterogeneity, respectively.

- When feasible, results were explored using subgroup analyses by categorical covariates including surgery type (traditional open spine surgery or minimal invasive surgery), surgery location (cervical or lumbar) and study duration (≤5 years or >5 years).
Results

• Four non-overlapping studies and a total of 11468 patients were included in the meta-analysis.

• Those four studies included only traditional open spine surgeries.

• The proportion of women ranged between 24% to 59%.

• The mean age of participants in studies ranged between 40.1 to 51.2 years.

• None of the included studies demonstrated that there was a statistically significant difference in pre-operative opioid use between men and women.
Results

• The meta-analysis also demonstrated that no significant difference in pre-operative opioid use between men and women existed. The pooled RR using the random-effects model was 0.99 (95% CI, 0.97-1.01; I²=22.0%; P-heterogeneity=0.28) (Figure 1)

• The result was consistent in subgroup analyses. No significant gender differences in pre-operative opioid use were detected when the data were stratified by surgical location and study duration.
  • Surgical location (Figure 2)
    • Cervical: pooled RR, 1.0; 95% CI, 0.99-1.02; I²=0%, P-heterogeneity=0.90 vs. Lumbar: pooled RR, 0.97; 95% CI, 0.94-1.00; I²=0%, P-heterogeneity=0.37; P-interaction comparing cervical to lumber=0.08
  • Study length (Figure 3)
    • ≤5 years: pooled RR, 1.00; 95% CI, 0.99-1.02; I²=0%, P-heterogeneity=0.90) vs. >5 years: pooled RR, 0.97; 95% CI, 0.94-1.00; I²=0%, P-heterogeneity=0.37; P-interaction comparing ≤5 years to >5 years=0.08
Results

<table>
<thead>
<tr>
<th>Model</th>
<th>Study name</th>
<th>Risk ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kelly MP, 2015</td>
<td>1.00</td>
<td>0.99</td>
<td>1.02</td>
</tr>
<tr>
<td></td>
<td>O’Donnell JA, 2018</td>
<td>0.88</td>
<td>0.69</td>
<td>1.11</td>
</tr>
<tr>
<td></td>
<td>Adogwa O, 2018</td>
<td>0.97</td>
<td>0.95</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Gerling MC, 2018</td>
<td>1.01</td>
<td>0.88</td>
<td>1.17</td>
</tr>
<tr>
<td>Random</td>
<td></td>
<td>0.99</td>
<td>0.97</td>
<td>1.01</td>
</tr>
</tbody>
</table>

**Figure 1.** Forest plot comparing opioid use before spinal surgery of men vs. women in observational studies. The solid squares represent the point estimate of each study; the size of the solid squares is proportional to the weight of the study; horizontal lines denote 95% confidence intervals (CIs); the black diamonds represent the pooled estimate for each subgroup. The Risk ratio for the four observational studies which use the random model was 0.99 (95% CI: 0.97, 1.01; I²: 22.0%; P-heterogeneity: 0.28).
Results

Figure 2. Forest plot for subgroup analysis for Surgical location comparing men and women opioid use before spinal surgery.\textsuperscript{4,5}
Subgroup analysis by surgical location revealed the following pooled RR for cervical: 1.0; 95% CI: 0.99 to 1.02; P: 0%; P-heterogeneity: 0.90; 2 studies;\textsuperscript{4} vs. lumbar: pooled RR: 0.97; 95% CI: 0.94 to 1.00; 2 studies; P: 0% P-heterogeneity: 0.37; (p-interaction comparing cervical to lumbar: 0.08).\textsuperscript{4,5}

Figure 3. Forest plot for subgroup analysis for Length of study comparing men and women opioid use before spinal surgery.\textsuperscript{4,5}
Subgroup analysis by study length revealed the following pooled RR for \textless{}=5 years: 1.00; 95% CI: 0.99 to 1.02; 2 studies; P: 0%; P-heterogeneity: 0.90) vs. \textgreater{}5 years (RR: 0.97; 95% CI: 0.94 to 1.00; 2 studies; P: 0% P-heterogeneity: 0.37); (p-interaction comparing \textless{}=5 years to \textgreater{}5 years: 0.08).\textsuperscript{4,5}
Discussion

• Preoperative opioid use is considered to be a significant risk factor for a long-term postoperative opioid utilization, but no study which compared the prevalence of opioid use before and after surgery stratified by gender has not been identified.

• Strengths
  • Relatively high quality of included studies (NOS scores of all studies>5)
  • Large insurance claims databases and registries representing a broad, general population

• Limitations
  • Inclusion of studies with any duration of preoperative use of opioids as a paucity of articles quantified long-term use of opioids (for more than 90 days)
  • Use of opioid prescription data as a surrogate for actual opioid consumption without the consideration of PRN (as needed) dosing.
Summary Points

• The meta-analysis of four studies did not show any significant differences in pre-operative opioid use between men and women in spine surgery despite potential gender-specific differences in pain perception and behaviors.