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Gender Disparities in Outpatient Management of Postlaminectomy Syndrome

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ABSTRACT

Introduction: Postlaminectomy syndrome (PLS), also known as failed back surgery syndrome, is the persistence of radicular pain in the face of surgical intervention. Despite its prevalence in 10 to 40% of spine surgery patients, outpatient pharmacologic and interventional management remains poorly characterized.

Methods: The 2007 to 2016 National Ambulatory Medical Care Survey (NAMCS) was utilized to include all outpatients diagnosed with PLS. For each visit, documented pain medications (opioids, nonsteroidal anti-inflammatory drugs [NSAIDs], neuropathic agents, etc) as well as patient demographics and comorbidities (sex, age, race, insurance coverage, and medical history) were recorded. The association between medication class and rate of prescription relative to sex was assessed in the population-weighted cohort, using propensity score matching to control for potential confounders.

Results: A total of 70,343 PLS patients were identified, including 36,313 (51.6%) women. After accounting for baseline demographics and comorbidity differences between male and female patients, men were 2 to 3 times more likely to be prescribed opioids (OR: 2.38; 95%CI: 2.30–2.46) and procedural interventions for PLS compared to the female cohort, while women utilized neuropathic agents (OR: 0.53; 95%CI: 0.51–0.55) and NSAIDs (OR: 0.68; 95%CI: 0.65–0.70) more frequently.

Conclusion: Pain management in outpatients presenting with PLS-related pain consisted of higher opioid utilization for men and higher neuropathic agents and NSAIDs utilization for the female patients.

Clinical Relevance: This article is the first to shed light on disparities in pain management among patients with postlaminectomy syndrome.

Level of Evidence: 3.

Complications

Keywords: PLS, postlaminectomy syndrome, pain, opioid, spine surgery

INTRODUCTION

Postlaminectomy syndrome (PLS), also known as failed back surgery syndrome, is a major cause of chronic pain in patients having undergone spinal surgery; it occurs in up to 10% to 40% of surgical spine patients.[1,2] Patients who suffer from PLS experience persistent low back or leg pain despite successful surgery to address anatomical or radiographic abnormalities.[3] PLS is a fairly common condition that results in a significant reduction in the patient's quality of life (QoL) and reduced capacity for activities of daily living (ADLs).[4] Patients experiencing chronic pain from PLS are reported to have a higher work disability rate when compared to other chronic pain condition, highlighting the need to further investigate viable long-term treatment options for this patient population.[3]

Management of this often-debilitating condition involves physical therapy, behavioral modifications, pharmacological (ie, opioid narcotics, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, and intraspinal injections), and interventional and/or surgical management (eg, steroid injections, spinal cord stimulation, and reoperation).[4,5] Previous studies have reported no significant improvement in pain and disability scores, via Oswestry Disability Index, when comparing reoperation to nonsurgical interventions, except in the case of spinal cord stimulation.[4] Many patients use nonsurgical treatment options with unknown long-term improvement in QoL and functioning in ADLs. A recent systematic review by Petzke et al noted clinically relevant pain relief from use of opioids, with little to no improvement in function within short and intermediate-term randomized controlled trials.[6]

Despite a comparable incidence and prevalence of spine disorders across the world, the United States ranks higher in the number of spine surgeries performed each year.[7] The rise in the rate of surgeries has increased patient's need for access and use of opioids in the immediate postoperative period. Particularly in

the case of PLS, reliance on opioids for persistent pain control poses the risk for potential for opioid abuse. This potential for abuse in the backdrop of the opioid epidemic has become an increasingly concerning public health crisis with mounting overdose, abuse, and mortality rates. Despite growing research on this issue, current literature often neglects gender differences in opioid prescriptions within various classes of analgesics, particularly in PLS.[8] Furthermore, few studies have investigated such disparities in outpatient settings, rather largely focusing on emergency departments and inpatient care.[8] This study investigates gender-related disparities in opioid prescriptions pertaining to PLS in a large national survey of ambulatory clinic visits.

METHODS

Patient Selection

The National Ambulatory Medical Care Survey (NAMCS) was queried for years 2007 to 2016 for all outpatients who carried a diagnosis of PLS. The NAMCS is a random sampling of office visits across the United States conducted by the Centers for Disease Control and Prevention, established as a nationally representative sample of clinic visits and outpatient management. This outpatient database has been validated as an accurate representation of office-based practice for a wide array of conditions.[9] It contains data on patient characteristics (eg, age, sex, race, and ethnicity) as well as visit characteristics, such as reason for visit, diagnoses, services ordered or provided, and treatments, including medication therapy. Visits in the survey are also assigned a population-based weight, which can be utilized to adjust for the prevalence of certain clinical presentations in accordance with the general population.

The NAMCS public use data file was queried for all patients who carried a diagnosis containing the term "postlaminectomy syndrome." Each row in the resulting unweighted cohort was then multiplied by a fraction (1/100th) of its corresponding population-adjusted weight in order to generate a larger, population-based weighted patient sample with greater statistical power. This fraction was selected due to memory and processing limitations on our research computers.

Data and Endpoints

Other than sex, demographic information collected for each visit included patient age, race, insurance coverage (Medicare, Medicaid, or private insurance), and comorbid conditions (history of cancer, chronic kidney disease, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease, depression, diabetes, hypertension, and/or substance abuse). Current antibiotic use was also noted as a proxy for bacterial infections, whether postsurgical, hospital- or community-acquired, since the inflammatory response of the body to infection can amplify existing pain.

Documented medications associated with each visit were also searched and recorded by drug class—prescription opioid narcotics, methadone, NSAIDs, and/or neuropathic agents. Opioids were defined as those whose documented prescription category was denoted as "narcotics," and NSAIDs were tracked using category "NSAIDs." Methadone therapy referrals were tracked using the search term "methadone." Because neuropathic agents comprise a wide range of medications and were not documented as a searchable category in NAMCS, these medications were searched by individual generic and brand names, and included gabapentin (Neurontin), pregabalin (Lyrica), tricyclic antidepressants (searched for using suffixes "-tryptyline" and "-ipramine"), and topiramate (Topamax). Spinal corticosteroid injections administered during the visit were also noted.

Other variables included in the study included time (in minutes) spent with physician and referrals for spinal cord stimulation for pain refractory to medical management.

Statistical Analysis

Using the weighted patient cohort, baseline variables were compared using χ^2 tests. Those found to be statistically different between male and female groups were then factored into a 1:1 propensity-matched multivariate analysis for study endpoints, which included prescription for opioids, methadone, antineuropathic agents, NSAIDs, spinal cord stimulation, and intraspinal injections, as well as time spent with the physician. In this study, variables controlled for with propensity scoring included age, race, insurance status, and all comorbid conditions. A 2-tailed P value of <0.05 was utilized in the determination of statistical significance using R version 3.5.2.

RESULTS

Patient Demographics

Baseline characteristics of men and women with PLS are summarized in Table 1. The population-based weighted patient sample included 70,333 patients, with 34,020 men (48.4%) and 36,313 women (51.6%). These groups were statistically different at the following baseline metrics: age, race, insurance coverage, and comorbidities. Among the male and female population, African Americans comprised a statistically significant higher percentage of men

Table 1. Baseline characteristics of patients.

Characteristics[a]	Men (*N* = 34,020)	Women (*N* = 36,313)	*P* Value of Difference
Age, y, mean (SD)	55.44 (11.25)	57.16 (11.42)	<0.001
Race, *n* (%)			
White/Caucasian	26,085 (76.68)	27,235 (75.00)	<0.001
Black/African American	4293 (12.62)	2656 (7.31)	
Other	3642 (10.71)	6422 (17.69)	
Insurance coverage, *n* (%)			
Medicare	10,501 (30.87)	13,227 (36.42)	<0.001
Medicaid	2416 (7.10)	5433 (14.96)	
Private insurance	13,330 (39.18)	16,640 (45.82)	
History of, *n* (%)			
Cancer	0 (0.00)	1041 (2.87)	<0.001
Chronic kidney disease	140 (0.88)	305 (1.48)	<0.001
Chronic obstructive pulmonary disease	1618 (4.76)	0 (0.00)	<0.001
Congestive heart failure	100 (0.29)	0 (0.00)	<0.001
Coronary artery disease	1707 (10.72)	246 (1.19)	<0.001
Current antibiotic use	495 (1.46)	1083 (2.98)	<0.001
Depression	8675 (25.50)	15,107 (41.60)	<0.001
Diabetes mellitus	599 (3.31)	2469 (15.73)	<0.001
Hypertension	9907 (29.12)	9761 (26.88)	<0.001
Substance abuse/dependence	2623 (16.47)	0 (0.00)	<0.001

[a]Percentages calculated from number of patients for whom value for particular variable was known.

than women with PLS (12.62% vs 7.31%; $P < 0.001$). Men with PLS also had significantly lower rates of insurance coverage across all providers ($P < 0.001$) of Medicare (30.87% vs 36.42%), Medicaid (7.10% vs 14.96%), and private insurance (39.18% vs 45.82%). Men and women also differed significantly in a number of comorbidities at baseline such as cancer (0.00% vs 2.87%; $P < 0.001$), chronic obstructive pulmonary disease (4.76% vs 0.00%; $P < 0.001$), coronary artery disease (10.72% vs 1.19%; $P < 0.001$), depression (25.50% vs 41.60%; $P < 0.001$), and substance abuse (16.47% vs 0.00%; $P < 0.001$). While the difference between all other baseline characteristics was also statistically significant and was factored into propensity matching, the negligible difference in rates was not deemed to be clinically significant.

Gender Disparities in Postlaminectomy Syndrome Management

Interventions offered to patients with PLS including opioids, methadone maintenance therapy, neuropathic agents, NSAIDs, referral for spinal cord stimulation, and intraspinal injection, as well as time spent with physicians were summarized in Table 2. Male patients with PLS had significantly higher rates of opioid (OR: 2.38; 95%CI: 2.30–2.46) and methadone maintenance therapy (OR: 6.38; 95%CI: 5.64–7.24) prescription compared to female patients. Conversely, men were significantly less likely to be prescribed neuropathic agents (OR: 0.53; 95%CI: 0.51–0.55) and NSAIDS (OR: 0.68; 95%CI: 0.65–0.70) compared to women with PLS. Men were also more likely to be referred for spinal cord stimulation (1.83% vs 0.00%; $P < 0.001$) and given intraspinal injections (3.19% vs 0.98%; $P < 0.001$).

DISCUSSION

PLS is a complex and clinically heterogeneous condition that can result in poor outcomes in up to 10 to 40% of surgical spine patients. A number of etiologies have been hypothesized for this poorly understood condition, including postsurgical adhesions, scarring, inflammation, and/or chronic compression and injury of sensory nerve

Table 2. Gender disparities in management of postlaminectomy syndrome, propensity-matched.[a]

Characteristic of Intervention	Men (*N* = 34,020)	Women (*N* = 34,020)	OR (95%CI)	*P* Value
Prescription opioids, *n* (%)	27,010 (79.39)	21,026 (61.80)	2.38 (2.30–2.46)	<0.001
Methadone maintenance therapy, *n* (%)	1827 (5.37)	300 (0.88)	6.38 (5.64–7.24)	<0.001
Neuropathic agents, *n* (%)	6220 (18.28)	10,076 (29.62)	0.53 (0.51–0.55)	<0.001
NSAIDs, *n* (%)	5581(16.41)	7641 (22.46)	0.68 (0.65–0.70)	<0.001
Referral for spinal cord stimulation, *n* (%)	623 (1.83)	0 (0.00)	–	<0.001
Intraspinal injection, *n* (%)	1084 (3.19)	332 (0.98)	–	<0.001
Time spent with physician, min, mean (SD)	21.42 (9.49)	21.20 (9.49)	–	<0.001

Abbreviation: NSAIDs, nonsteroidal anti-inflammatory drugs.
[a]Propensity matching was based on the following baseline variables: age, race, insurance coverage, and all listed comorbidities.

fibers. A large proportion of these patients have been noted to suffer from worsened postoperative pain in comparison to their preoperative state.[10] Similarly, treatment options for this population continue to lack clear evidence and efficacy, with both conservative and interventional options proposed. Interventional procedures range from adhesiolysis in the case of suspected arachnoiditis, epidural steroid injections for nerve root inflammation, spinal cord stimulators for pain of unknown etiology, and further repeat spinal surgery in cases of residual or recurrent surgical pathology.[11] Sclafani et al[12] noted that 14% of patients undergoing minimally invasive transforaminal lumbar interbody fusion in a prospectively collected database were operated on for PLS.[12] Although surgical considerations are evaluated on case by case basis, with careful consideration regarding repeat decompression and potential fusion, the data are in support of spinal cord stimulator over that of repeat surgery. The unclear evidence for interventional and surgical options to improve the QoL in these challenging patients is further compounded by a lack of literature regarding conservative pain management options aside from narcotics. Due to the difficulties in managing their chronic pain condition, many of these patients seek treatment at pain clinics and frequently employ polypharmacy with limited overall benefit.[13] A review by Desai et al[2] noted that patients are typically maintained on not only chronic opioid medications but also NSAIDs, muscle relaxants, antidepressants, anti-anxiolytics, and antiepileptics; however, the evidences behind these treatment regimens are largely inconclusive, only noting that chronic opioids such as oxycodone are the most frequently employed on a long-term basis.[2] Furthermore, despite the success of spinal cord stimulation in pain control within the PLS patient population, the stringent clinical criteria along with limited insurance approval of this procedures deter patients and clinicians from widely utilizing this procedures.

Population-based studies investigating opioid use in susceptible populations such as PLS patients are critical in managing risk factors and clarifying outcomes. The current study serves as the first retrospective investigation of gender disparities in this especially at-risk population in regard to outpatient management. In this retrospective cohort analysis of PLS patients, men were significantly more likely to be prescribed opioids than their female counterpart. This finding contrasts much of the current literature, which reveals a higher rates of prescription opioid use among women.[8] Current research states that women are less likely to achieve radicular pain relief following laminectomy, which may be attributed to sex differences in brain sensitivity, interpretation, and response to pain.[14] Consistent higher pain prevalence in women is not well understood and may be attributed to biological differences in pain sensitivity and pain relief from opioid use.[15] Previous studies have noted higher rates of opioid-related side-effects in women, suggesting gender-related differences in bodily experiences associated with opioid use. This trend may be due to female population's increased willingness to report more somatic symptoms and pain.[15] Women also tend to undergo laminectomies at more advanced stages of their pathologies, which may result in a worse prognosis.[16] Psychosocial factors relating to both the patient and clinician's views on gender roles may contribute to a more disabled functional status in women before surgery.[17] This trend may be the cause of women having an equal or greater improvement in functional status postoperation.[17] From a clinical perspective, provider bias has been shown to favor opioid prescriptions for women.[15] Despite these physiologic and psychosocial differences, this study noted that men were significantly more likely to be prescribed opioids for PLS as outpatients.

As the first study to address disparities in opioid prescriptions between men and women with PLS, this paper does not explain the etiology of this disparity and serves to draw attention to the fact that such disparity exists. The findings of this study may represent an overprescription of opioids in men, increasing their risk of addiction and death. Conversely, one may interpret the same results as an underprescription of opioids in women, diminishing QoL due to physical and mental burdens of chronic pain. Further research is needed to strike a balance between judicious opioid use and adequate pain management in PLS.

Limitations

This study contains innate limitations in utilization of an outpatient database that offers limited datapoints on each patient's condition. Furthermore, the retrospective nature and lack of randomization of this study limit the strength of its findings. Other potential limitations of this study include a lack of information about factors requiring longitudinal data such as interventions tried prior to opioid prescription and the type and number of operations that resulted in PLS. Furthermore, data regarding length of provider experience, clinic factors, stage of the disease at time of laminectomy, postsurgical complications, reason for opioid prescription, and opioid dosages were not available through NAMCS. Further prospective, randomized investigations are needed to examine how PLS pain manifests differently in men and women, as well as biases in patient evaluation. The impact of these disparities on patient outcomes should also be evaluated.

Because our study cohort is a population-weighted one derived from a much smaller, unweighted sample (N = 222), the prevalence of comorbid conditions may be underestimated by the multiplication of each unweighted row by a weight multiplier. For example, because there were no female patients with congestive heart failure or chronic obstructive pulmonary disease in the original 222-person cohort, the weighted cohort had the appearance of having a 0% prevalence of these conditions among 36,313 female patients. The same can be said for male patients with cancer and female patients with substance use disorders. Nonetheless, we were able to propensity match and control for each of these comorbidities. However, because of the underrepresentation of certain major comorbidities, we caution against the overextrapolation of our study results.

CONCLUSION

Despite similar baseline characteristics, men with PLS are significantly more likely to be prescribed opioids compared to their female counterparts. This novel finding, which contrasts with established trends noting the contrary, may be the result of physician biases and/or differing manifestations of PLS pain in men and women.

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