

Sex Differences in Patient-Rated Outcomes After Lumbar Spinal Fusion for Degenerative Disease

A Multicenter Cohort Study

Olga Ciobanu-Caraus, MD,^a Alexandra Grob, MD,^a Jonas Rohr, MD,^a Vittorio Stumpo, MD,^a Luca Ricciardi, MD, MSc,^b Nicolai Maldaner, MD,^a Hubert A.J. Eversdijk, MD,^c Moira Vieli, BMed,^a Antonino Raco, MD,^b Massimo Miscusi, MD, PhD,^b Andrea Perna, MD,^{d,e} Luca Proietti, MD,^{e,f} Giorgio Lofrese, MD,^g Michele Dughiero, MD,^g Francesco Cultrera, MD,^g Marcello D'Andrea, MD,^g Seong B. An, MD,^h Yoon Ha, MD, PhD,^h Aymeric Amelot, MD, PhD,^{i,j} Jorge B. Cadelo, MD,^k Jose M. Viñuela-Prieto, MD,^k Maria L. Gandía-González, MD,^k Pierre-Pascal Girod, MD,^l Sara Lener, MD, PhD,^m Nikolaus Kögl, MD, MSc,^m Anto Abramovic, MD,^m Christoph J. Laux, MD,ⁿ Mazda Farshad, MD, MPH,ⁿ Dave O'Riordan, BSc,^o Markus Loibl, MD,^p Fabio Galbusera, PhD,^o Anne F. Mannion, PhD,^o Alba Scerrati, MD,^q Pasquale De Bonis, MD,^q Granit Molliqaj, MD,^r Enrico Tessitore, MD,^r Marc L. Schröder, MD, PhD,^m Martin N. Stienen, MD,^s Giovanna Brandi, MD,^t Luca Regli, MD,^u Carlo Serra, MD,^a and Victor E. Staartjes, MD, PhD^a

Study Design. Heterogeneous data collection through a mix of prospective, retrospective, and ambispective methods.

Objective. To evaluate the effect of biological sex on patient-reported outcomes after spinal fusion surgery for lumbar degenerative disease.

Summary of Background Data. Current literature suggests sex differences regarding clinical outcome after spine surgery may exist. Substantial methodological heterogeneity and limited comparability of studies warrants further investigation of sex-related differences in treatment outcomes.

Materials and Methods. We analyzed patients who underwent

Received for publication May 23, 2024; accepted September 3, 2024.

From the ^aMachine Intelligence in Clinical Neuroscience and Microsurgical Neuroanatomy (MICN) Laboratory, Department of Neurosurgery, Clinical Neuroscience Center, University Hospital Zurich, University of Zurich, Zurich, Switzerland; ^bDepartment of NES-MOS, Azienda Ospedaliera Universitaria Sant'Andrea, Sapienza University, Rome, Italy; ^cDepartment of Neurosurgery, Bergman Clinics Amsterdam, Amsterdam, The Netherlands; ^dDepartment of Orthopedics Foundation Casa Sollievo Della Sofferenza IRCCS, San Giovanni Rotondo (FG), Italy; ^eDepartment of Geriatrics and Orthopedics, Sacred Heart Catholic University, Rome, Italy; ^fDepartment of Aging, Neurological, Orthopedic and Head-Neck Sciences, IRCCS A. Gemelli University Polyclinic Foundation, Rome, Italy; ^gDepartment of Neurosciences, Neurosurgery Division, "M.Bufalini" Hospital Cesena, Italy; ^hDepartment of Neurosurgery, Spine and Spinal Cord Institute, Severance Hospital, College of Medicine, Yonsei University, Seoul, Korea; ⁱDepartment of Neurosurgery, La Pitié Salpêtrière Hospital, Paris, France; ^jNeurosurgical Spine Department, University Hospital of Tours, Tours, France; ^kDepartment of Neurosurgery, Hospital Universitario La Paz, Madrid, Spain.; ^lDepartment of Neurosurgery, Vienna Healthcare Network/Landstrasse Municipal Hospital, Vienna, Austria; ^mDepartment of Neurosurgery, Medical University of Innsbruck, Innsbruck, Austria; ⁿUniversity Spine Center, Balgrist University Hospital, University of Zurich, Zurich, Switzerland; ^oDepartment of Teaching, Research and Development, Spine Center Division, Schulthess Klinik, Zurich, Switzerland; ^pDepartment of Spine Surgery, Schulthess Klinik, Zurich, Switzerland; ^qDepartment of Neurosurgery, University Hospital Sant'Anna, Ferrara, Italy; ^rDepartment of Neurosurgery, HUG

Geneva University Hospital, Geneva, Switzerland; ^sDepartment of Neurosurgery and Spine Center of Eastern Switzerland, Cantonal Hospital St. Gallen and Medical School of St.Gallen, St. Gallen, Switzerland; and ^tInstitute for Intensive Care Medicine, University Hospital Zurich, Zurich, Switzerland.

The study was approved by the appropriate national and local authorities at the initiating study site (Medical Research Ethics Committees United, Registration Number: W18.004) and at all participating centers.

The data that support the findings of this study are available from the corresponding author, V.E.S., upon reasonable request.

The authors report no conflicts of interest.

Address correspondence and reprint requests to Victor E. Staartjes, MD, PhD, Machine Intelligence in Clinical Neuroscience & Microsurgical Neuroanatomy (MICN) Laboratory, Department of Neurosurgery, University Hospital Zurich Clinical Neuroscience Center, University of Zurich Frauenklinikstrasse 10, Zurich 8091, Switzerland; E-mail: victoregon.staartjes@usz.ch

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.spinejournal.com.

Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/BRS.0000000000005183

spinal fusion with or without pedicle screw insertion for lumbar degenerative disease included within a multinational study, comprising patients from 11 centers in seven countries. Absolute values and change scores (change from preoperative baseline to postoperative follow-up) for 12-month functional impairment [Oswestry disability index (ODI)] and back and leg pain severity [numeric rating scale (NRS)] were compared between male and female patients. Minimum clinically important difference (MCID) was defined as >30% improvement.

Results. Six-hundred sixty (59%) of 1115 included patients were female. Female patients presented with significantly baseline ODI (51.5 ± 17.2 vs. 47.8 ± 17.9 , $P < 0.001$), back pain (6.96 ± 2.32 vs. 6.60 ± 2.30 , $P = 0.010$) and leg pain (6.49 ± 2.76 vs. 6.01 ± 2.76 , $P = 0.005$). At 12 months, female patients still reported significantly higher ODI (22.76 ± 16.97 vs. 20.50 ± 16.10 , $P = 0.025$), but not higher back (3.13 ± 2.38 vs. 3.00 ± 2.40 , $P = 0.355$) or leg pain (2.62 ± 2.55 vs. 2.34 ± 2.43 , $P = 0.060$). Change scores at 12 months did not differ significantly among male and female patients in ODI ($\Delta 1.31$, 95% CI: -3.88 to 1.25 , $P = 0.315$), back ($\Delta 0.22$, 95% CI: -0.57 to 0.12 , $P = 0.197$), and leg pain ($\Delta 0.16$, 95% CI: -0.56 to 0.24 , $P = 0.439$). MCID at 12 months was achieved in 330 (77.5%) male patients and 481 (76.3%) female patients ($P = 0.729$) for ODI.

Conclusion. Both sexes experienced a similar benefit from surgery in terms of relative improvement in scores for functional impairment and pain. Although female patients reported a higher degree of functional impairment and pain preoperatively, at 12 months only their average scores for functional impairment remained higher than those for their male counterparts, while absolute pain scores were similar for female and male patients.

Key Words: predictive analytics, outcome prediction, spinal fusion, neurosurgery, clinical prediction model

(*Spine* 2025;50:924–931)

Lumbar degenerative disease (LDD) is a leading cause of severe disability on a global scale.¹ Increasing evidence suggests that sex-related differences may play a role in the pathophysiology, presentation, and clinical course of LDD.^{2–4} However, conflicting data in the literature make it difficult to ascertain the existence of or effect size for sex differences in postoperative outcome.

Several studies proposed that female patients experience a higher degree of functional impairment, which may be due to anatomic-physiological differences,⁵ increased pain perception⁶ and a heightened inflammatory response.^{7,8} Consistent with that, female sex has frequently been identified as a predictive factor for worse postoperative pain, higher disability, and inferior quality of life.^{9–13} A recent review by MacLean *et al.*¹⁴ concluded that 80% of studies found that females had worse absolute postoperative scores measuring pain, disability or quality of life, and about 73% of studies reported an equivalent or greater degree of improvement between genders. Problematically, the majority of these studies were retro-

spective single-center analyses and therefore represented level IV evidence. According to this review, nine thematically relevant prospective studies have been published so far, all of which were single-center studies apart from one that analyzed the data of two centers in one country. However, effect sizes might vary substantially across different populations, health systems, and surgical procedures which renders it difficult to draw valid and generalizable conclusions from single-center analyses studying a single procedure.

Quantifying the effect of sex on postoperative outcome after spinal fusion surgery could inform clinical decision-making and optimize treatment strategies. In this study, we therefore aimed to analyze the effect of sex on patient-reported outcomes in patients undergoing spinal fusion surgery for LDD in a large multinational, multi-center cohort.

MATERIALS AND METHODS

Patient Population

A data set of a multinational study comprising patient data from 11 centers in seven countries (FUSE-ML¹⁵) was analyzed. Four centers (484 patients) provided prospective data, five centers (455 patients) retrospective data, and two centers (176 patients) mixed data. Patients who underwent spinal fusion with or without thoracolumbar pedicle screw placement, for degenerative pathologies [one or multiple of the following: spinal stenosis, spondylolisthesis, degenerative disc disease, disc herniation, failed back surgery syndrome (FBSS), radiculopathy, pseudarthrosis] were included. Exclusion criteria encompassed: surgery as the primary indication for infections, vertebral tumors, traumatic and osteoporotic fractures or deformity surgery for scoliosis or kyphosis; moderate or severe scoliosis (Coronal Cobb angle >30 degrees/Schwab classification sagittal modifier + or ++); surgery spanning more than six vertebral levels; missing endpoint data at 12 months; lack of informed consent; age below 18 years.

Data Collection

Data in each center were extracted retrospectively, from a prospective registry, or collected in a prospective registry and supplemented (S1, Supplemental Digital Content 1, <http://links.lww.com/BRS/C549>) by retrospectively collected variables, with 12-month follow-up. The following data were collected: age, biological sex, surgical indication, index level(s), height, weight, BMI (body mass Index), smoking status, American Society of Anesthesiologists (ASA) Score, preoperative use of opioid pain medication, bronchial asthma as a comorbidity, prior thoracolumbar spine surgery, race/ethnicity, surgical approach, pedicle screw insertion and minimally invasive technique. Patient-reported outcome measures (PROMs) were evaluated at baseline and at 12 months follow-up and encompassed Oswestry disability index (ODI) (scaled from 0 to 100) or core outcome measures index (COMI) for multidimensional subjective functional impairment, mo-

mentary numeric rating scale (NRS) for back pain severity, and NRS for leg pain severity.^{16,17} COMI scores were converted into ODI scores according to a previously published function.¹⁸ This study was approved by their local institutional review board (IRBs) at each study site, and data sharing statements were provided by all centers. Depending on the regulation of the local IRB, patients either provided written informed consent (in the case of prospective data collection), or the need for informed consent was waived (for retrospective data collection of pre-existing data).

Primary Endpoint Definitions

Clinically relevant improvements in ODI or NRS back and leg pain were dichotomized using the minimally clinically important difference (MCID) according to the validated threshold by Ostelo *et al.*¹⁶ (improvement in ODI and NRS pain severity by 30% from baseline to 12 mo postoperatively).

Statistical Analysis

Data were analyzed using R, version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).¹⁹ Due to the low number of missingness, complete case analysis was performed. Continuous and categorical variables were reported as means (SDs) and absolute frequencies (percentages), respectively. Student *t* test and χ^2 test were performed to test for intergroup differences. Change scores were defined as the degree of improvement from baseline up to 12 months. We controlled for age, smoking status, ethnicity, indication for surgery, minimally invasive surgery, pedicle screw insertion by including them as independent variables in multivariable logistic regression for sex, with MCID as the dependent variable. *P*-values <0.05 on two-sided tests were considered statistically significant.

RESULTS

Patient Cohort

Overall, data from 1115 patients were provided by 11 participating centers in total. Of them, 660 (59%) patients were female. Baseline demographic and disease-specific characteristics are displayed in Table 1. Female patients were significantly older (61.9 ± 12.1 vs. 59.2 ± 12.8 , $P < 0.001$), were more frequently nonsmokers (61.4% vs. 44.4%, $P < 0.001$), of Asian ethnicity (12.1% vs. 5.7%, $P = 0.002$) and operated for spondylolisthesis (58.9% vs. 46.2%, $P < 0.001$). Operative parameters stratified by sex are shown in Table 2. Male patients underwent minimally invasive surgery significantly more often than females (31.2% vs 25.5%, respectively; $P = 0.041$) and less frequently had pedicle screws inserted (95.4% vs 98%, respectively; $P = 0.019$).

Absolute Outcome Measures

Absolute and relative patient-reported outcome measures are shown in Table 3. Female patients presented with significantly higher functional impairment at baseline in terms of ODI (51.5 ± 17.2 vs. 47.8 ± 17.9 , $P < 0.001$), as

TABLE 1. Baseline Patient Characteristics Stratified by Sex

Parameter	Overall (n = 1115), n (%)	Sex, n (%)		<i>P</i>
		Male (n = 455)	Female (n = 660)	
Age, mean \pm SD (yr)	60.80 \pm 12.45	59.2 \pm 12.8	61.9 \pm 12.1	< 0.001
Smoking status				< 0.001
Active smoker	306 (27.4)	148 (32.5)	158 (23.9)	
Ceased smoking	192 (17.2)	101 (22.2)	91 (13.8)	
Never smoked	607 (54.4)	202 (44.4)	405 (61.4)	
No. missing	10 (0.9)	4 (0.9)	6 (0.9)	
Opioid analgesic use	364 (32.6)	152 (33.4)	212 (32.1)	0.863
No. missing	102 (9.1)	37 (8.1)	65 (9.8)	
Bronchial asthma	63 (5.7)	22 (4.8)	41 (6.2)	0.351
No. missing	101 (9.1)	36 (7.9)	65 (9.8)	
BMI, mean \pm SD (kg/m ²)	26.58 \pm 4.61	25.8 \pm 3.0	25.1 \pm 3.7	0.228
Race/ethnicity				0.002
Caucasian	861 (77.2)	375 (82.4)	486 (73.6)	
Black	30 (2.7)	14 (3.1)	16 (2.4)	
Asian	106 (9.5)	26 (5.7)	80 (12.1)	
Others	16 (1.4)	5 (1.1)	11 (1.6)	
No. missing	102 (9.1)	35 (7.7)	67 (10.2)	
Prior thoracolumbar surgery	257 (23.0)	112 (24.6)	145 (22.0)	0.175
No. missing	100 (9.0)	51 (11.2)	49 (7.4)	
Indication				< 0.001
LDH	202 (18.1)	92 (20.2)	110 (16.7)	
Lumbar spinal stenosis	618 (55.4)	243 (53.4)	375 (56.8)	
Spondylolisthesis	599 (53.7)	210 (46.2)	389 (58.9)	
Radiculopathy	323 (29.0)	130 (28.6)	193 (29.2)	
No. missing	101 (9.1)	36 (7.9)	65 (9.8)	
Discogenic CLBP/DDD	457 (41.0)	200 (44.0)	257 (38.9)	
Pseudarthrosis	56 (5.0)	28 (6.2)	28 (4.2)	
No. missing	100 (9.0)	35 (7.7)	65 (9.8)	
FBSS	47 (4.2)	20 (4.4)	27 (4.1)	
No. missing	100 (9.0)	35 (7.7)	65 (9.8)	
ASA class				0.367
Class I/II	791 (70.9)	330 (72.5)	461 (69.8)	
Class III/IV	324 (29.1)	125 (27.5)	199 (30.2)	
No. missing	17 (1.5)	7 (1.5)	10 (1.5)	

Statistical significance ($P < 0.05$) values are in bold.

ASA indicates American Society of Anesthesiologists; BMI, body mass index; CLBP, chronic low back pain; DDD, degenerative disc disease; FBSS, failed back surgery syndrome; LDH lumbar disc herniation.

well as pain in terms of NRS back (6.96 ± 2.32 vs. 6.60 ± 2.30 , $P = 0.010$) and leg pain scores (6.49 ± 2.76 vs. 6.01 ± 2.76 , $P = 0.005$; Fig. 1). At 12 months follow-up, female patients still reported significantly higher ODI (22.76 ± 16.97 vs. 20.50 ± 16.10 , $P = 0.025$), but not higher NRS back (3.13 ± 2.38 vs. 3.00 ± 2.40 , $P = 0.355$) or leg pain scores (2.62 ± 2.55 vs. 2.34 ± 2.43 , $P = 0.060$) compared with male patients.

Relative Outcome Measures

The change scores at 12 months were not significantly different among male and female patients in terms of ODI ($\Delta 1.31$, 95% CI: -3.88 to 1.25, $P = 0.315$),

TABLE 2. Operative Parameters Stratified by Sex

Parameter	Overall (n = 1115), n (%)	Sex, n (%)		P
		Male (n = 455)	Female (n = 660)	
Surgical index level				0.711
T12-L1	39 (3.5)	14 (3.1)	25 (3.8)	
L1-L2	24 (2.2)	8 (1.8)	10 (1.5)	
L2-L3	126 (11.3)	34 (7.5)	47 (7.1)	
L3-L4	305 (27.4)	74 (16.3)	130 (19.7)	
L4-L5	657 (58.9)	179 (39.3)	280 (42.4)	
L5-S1	401 (36.0)	88 (19.3)	114 (17.3)	
No. missing	100 (9.0)	46 (10.1)	54 (8.2)	
Surgical technique				0.842
TLIF	373 (33.5)	153 (33.6)	220 (33.3)	
PLIF	449 (40.3)	192 (42.2)	257 (38.9)	
ALIF	7 (0.6)	4 (0.9)	3 (0.5)	
Lateral	73 (6.5)	30 (6.6)	43 (6.5)	
No. missing	213 (19.1)	76 (16.7)	137 (20.8)	
Minimally invasive surgery	310 (27.8)	142 (31.2)	168 (25.5)	0.041
Pedicle screw insertion	1081 (97.0)	434 (95.4)	647 (98.0)	0.019

Statistical significance ($P < 0.05$) values are in bold.

ALIF indicates anterior lumbar interbody fusion; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion.

NRS back ($\Delta 0.22$, 95% CI: -0.57 to 0.12, $P = 0.197$), and leg pain ($\Delta 0.16$, 95% CI: -0.56 to 0.24, $P = 0.439$). Achievement of MCID at 12 months did not differ significantly between sexes for functional impairment [481 (76.3%) vs. 330 (77.5%), $P = 0.729$], or for back pain severity [500 (77.2%) vs. 336 (75.0%), $P = 0.451$], or for leg pain severity [475 (73.8%) vs. 332 (74.4%), $P = 0.855$].

Multivariable Logistic Regression Analyses

Detailed results of the multivariable logistic regression analyses for MCID achievement for ODI, NRS leg, and back pain are displayed in Table 4.

Ceased smoking (OR: 1.880, 95% CI: 1.150–3.140, $P = 0.013$), Asian ethnicity (OR: 0.563, 95% CI: 0.360–0.921, $P = 0.020$), and minimally invasive surgery (OR: 1.743, 95% CI: 1.175–2.637, $P = 0.007$) were identified as independent predictors of achievement of MCID for ODI. Female sex was not associated with MCID achievement measured by ODI (OR: 1.020, 95% CI: 0.734–1.414, $P = 0.903$), NRS back pain (OR: 1.339, 95% CI: 0.979–1.830, $P = 0.067$), or NRS leg pain (OR: 0.852, 95% CI: 0.626–1.155, $P = 0.305$).

DISCUSSION

Clarifying the relationship between sex and postoperative outcome after surgical treatment of LDD could help guide clinical decision-making process, identify patients who are risk of unfavorable postoperative outcome and enable more individualized patient care.

Several studies report female sex to be associated with an inferior preoperative clinical status,⁴ postoperative outcome in terms of more impaired quality of life,²⁰ more surgery-related complications,¹¹ less chances to return to work²¹ and an overall higher likelihood of reaching an

unsatisfactory outcome.²² The reasons for this observed discrepancy remain unclear but may be manifold:²³ as indicated by a previous study by Katz *et al.*²⁴, female patients tend to get operated at a more advanced stage of the disease. In an analysis of over 250,000 patients with LDD from a US national inpatient sample, Al Jammal *et al.*¹¹ concluded that female patients had 20% reduced odds of receiving surgery compared with male patients. Similarly, Taylor *et al.*²⁵ found that sex and ethnicity influenced the preoperative workup and surgical management of patients with LDD. While females were more likely to receive imaging tests, they were 52% less likely to have surgery offered.²⁵ This observation suggests an effect of sex-specific bias in clinical decision-making but may also be due to patient preference, as females have been previously shown to be less inclined to take surgical risks.²⁶ As a consequence, various studies previously reported female sex to be associated with an inferior clinical status at presentation,^{4,20,27,28} which is further supported by the higher preoperative ODI, NRS back, and leg pain scores of female patients in our study.

The underlying anatomic and physiological causality between sex and pain perception have been explored in numerous clinical and laboratory studies.^{3,29} However, the results have not produced a clear and consistent pattern.³ Whereas some authors reported no sex differences with regard to pain perception,³ the majority of studies concluded that healthy females and female patients with LDD had decreased heat and pressure pain thresholds, an increased radicular pain perception and were more likely to verbalize pain compared with men.^{30–32} These findings are supported by human and animal studies that showed an association between estrogen receptor polymorphisms and the perception of back pain in female patients with LDD.^{33,34} Psychosocial factors may also contribute to pain perception, although there is no clear evidence showing a higher rate of depression in female patients with radiculopathy.³⁵ As the reason for the sex-specific differences at presentation are still not entirely understood, future studies should aim to clarify the underlying reasons for the worse preoperative pain and disability status of female patients at baseline.

Analyzing 1115 patients from a multinational, multicenter data set of the FUSE-ML¹⁵ cohort, our study identified that female patients experienced a higher absolute degree of functional impairment preoperatively and postoperatively although they experienced a similar relative improvement in functional impairment (change scores, MCID achievement) from surgery compared with male patients. Similarly, preoperative pain scores appeared higher for female patients, although 12-month absolute scores as well as relative improvement was the same for female and male patients.

Lending support to our results, Strömquist *et al.*²⁸ reported the outcomes of 11,237 patients from a prospective registry of the Swedish National Spine Surgical Register and concluded that female patients experienced inferior postoperative clinical status due to higher preoperative functional impairment. Differences in postoperative improvement

TABLE 3. Absolute and Relative Patient-Reported Outcome Measures Stratified by Sex

Parameter	Overall (n = 1115)	Sex		P
		Male (n = 455)	Female (n = 660)	
Absolute score				
ODI				
Baseline	50.20 ± 17.54	47.8 ± 17.9	51.5 ± 17.2	< 0.001
12 months	21.84 ± 16.65	20.50 ± 16.10	22.76 ± 16.97	0.025
NRS back pain				
Baseline	6.81 ± 2.32	6.60 ± 2.30	6.96 ± 2.32	0.010
12 months	3.08 ± 2.39	3.00 ± 2.40	3.13 ± 2.38	0.355
NRS leg pain				
Baseline	6.29 ± 2.32	6.01 ± 2.76	6.49 ± 2.76	0.005
12 months	2.51 ± 2.50	2.34 ± 2.43	2.62 ± 2.55	0.060
Change score				
ODI	-28.12 ± 20.83	-27.34 ± 20.92	-28.65 ± 20.77	0.315
NRS back pain	-3.72 ± 2.81	-3.59 ± 2.88	-3.82 ± 2.76	0.197
NRS leg pain	-3.78 ± 3.29	-3.69 ± 3.46	-3.85 ± 3.16	0.439
MCID				
ODI	811 (76.8)	330 (77.5)	481(76.3)	0.729
No. missing	60 (5.4)	29 (6.4)	31 (4.7)	
NRS back pain	836 (76.3)	336 (75.0)	500 (77.2)	0.451
No. missing	19 (1.7)	7 (1.5)	12 (1.8)	
NRS leg pain	807 (74.0)	332 (74.4)	475 (73.8)	0.855
No. missing	25 (2.2)	9 (2.0)	16 (2.4)	

Statistical significance ($P < 0.05$) values are in bold. Values are provided as absolute numbers (%) and mean ± SD. MCID indicates minimally clinical important difference; NRS, numeric rating scale; ODI, Oswestry disability index.

between the sexes has been inconsistently reported among various studies.^{10,27,28} Some authors noted a similar or greater improvement in female patients compared with men.^{12,24,27,36} In our study, the multivariable analysis demonstrated that female sex did not significantly predict the achievement of MCID in terms of ODI, NRS back pain, and NRS leg pain. Siccoli *et al.*¹⁰ analyzed 3279 patients from a single-center prospective registry and reported similar results: female patients reported worse symptoms preoperatively and

postoperatively but experienced the same degree of improvement/benefit as male patients. Triebel *et al.*³⁶ investigated the two-year follow-up of 4780 patients using a multivariable analysis and reported that females had worse preoperative functional status but improved more and had similar postoperative outcomes compared with men. In a retrospective analysis of the preoperative and 12 months postoperative COMI scores of 1518 patients undergoing discectomy for different spinal pathologies, Pochon *et al.*²³

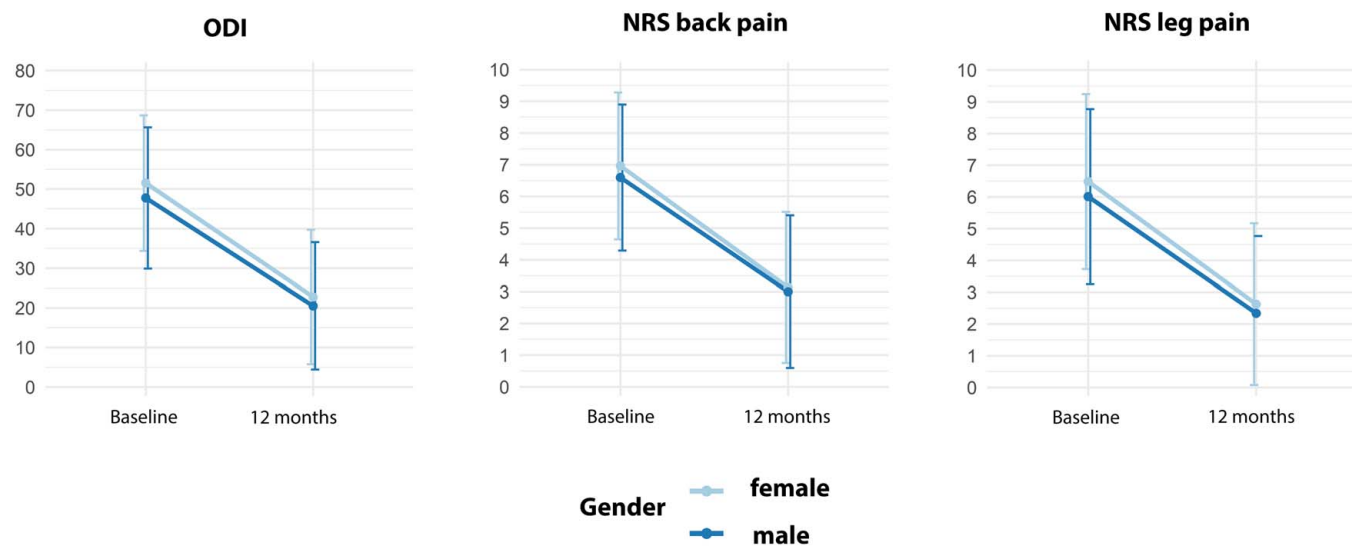


Figure 1. Graphic representation of ODI, NRS back pain, and NRS leg pain. Error bars represent 95% CI. NRS indicates numeric rating scale; ODI, Oswestry disability index.

TABLE 4. Multivariable Logistic Regression Models With MCID Achievement for Pain Measured by ODI, NRS Back Pain, and NRS Leg Pain as Dependent Variables

Variable	ODI MCID		NRS back pain MCID		NRS leg pain MCID	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Sex						
Male	1		1		1	
Female	1.020 (0.734–1.414)	0.903	1.339 (0.979–1.830)	0.067	0.852 (0.626–1.155)	0.305
Age	0.995 (0.982–1.008)	0.453	0.996 (0.983–1.009)	0.525	0.985 (0.973–0.998)	0.022
Smoking status						
Active smoker	1		1		1	
Ceased smoking	1.880 (1.150–3.140)	0.013	1.524 (0.937–2.520)	0.094	1.344 (0.872–2.087)	0.184
Never smoked	1.345 (0.924–1.954)	0.106	0.856 (0.592–1.228)	0.402	1.362 (0.956–1.937)	0.086
Ethnicity						
Caucasian	1		1		1	
Black	1.001 (0.417–2.787)	0.998	1.764 (0.662–6.115)	0.305	3.906 (1.140–24.51)	0.067
Asian	0.573 (0.360–0.921)	0.020	0.935 (0.580–1.543)	0.788	1.501 (0.878–2.690)	0.153
Others	0.570 (0.199–1.866)	0.315	0.375 (0.135–1.080)	0.059	0.174 (0.058–0.483)	0.001
Minimally invasive surgery						
no	1		1		1	
yes	1.743 (1.175–2.637)	0.007	1.331 (0.936–1.912)	0.116	0.643 (0.466–0.889)	0.007
Pedicle screw insertion						
no	1		1		1	
yes	0.245 (0.039–0.832)	0.057	0.461 (0.134–1.212)	0.157	2.078 (0.992–4.293)	0.049

Statistical significance ($P < 0.05$) values are in bold.

CLBP indicates chronic low back pain; DDD, degenerative disc disease; FBSS, failed back surgery syndrome; LDH, lumbar disc herniation; NRS, numeric rating scale; ODI, Oswestry disability index; OR, odds ratio.

noted that woman experienced the same degree of improvement postoperatively and that gender did not influence the probability of reaching a favorable outcome in the multivariable analysis.

One interesting point that is inconsistently corroborated by the literature²⁴ is the differential sex influence on different dimensions of outcome, particularly for subjective outcome measures. For example, in our study, we found that female patients demonstrated higher preoperative scores for both subjective functional impairment and for pain, but postoperatively, only impairment was still significantly higher than in their male counterparts, whereas pain scores were similar between the sexes. It appears that different dimensions of outcome assessment are differentially influenced by sex.²⁴ In the end, physiological differences among sexes are still poorly understood and diverging disease susceptibility, response to inflammation and analgesia, as well as hormonal and psychological factors may be responsible.^{3,30,37} In addition, the differential effect of sex differences on various outcome measures can be partially explained by the psychometric properties of questionnaires.^{10,30} It is conceivable that objective outcome measures, such as the five-repetition sit-to-stand test, may be less prone to such confounders.^{27,38} For the timed-up-and-go test, it has been shown that it may be an appropriate test to overcome sex bias as there were no differences regarding the presence and degree of ODI measured using age-adjusted and sex-adjusted cutoff values.⁴

In summary, it is important to recognize that our study along with the vast majority of previously published evidence suggests that female patients benefit from spinal fusion in degenerative disease to the same extent as male

patients. In this sense, female sex should not simply be regarded as a predictor for worse outcomes after spine surgery since female patients tend to report higher absolute functional impairment and pain scores for various reasons as outlined above. Rather, our results allow for a more nuanced conclusion: while absolute scores are an adequate measure to quantify the magnitude and severity of functional disability and pain, they may be biased by various influences including sex. Therefore, the use of relative measures of improvement such as 12-month change scores or MCID, adjusted for baseline characteristics, may be preferred when analyzing treatment effects.

Strengths and Limitations

Our study evaluated a large multinational cohort of patients, although some centers collected at least part of the data retrospectively. While the majority of studies in the current literature were restricted to the population of one country, our study evaluated a broader population of a total of 11 international centers and encompassed a variety of indications for spinal fusion surgery. Thus, the data in this study may be more generalizable. On the other side, this aspect also contributed to the heterogeneity of the data in our study, which may complicate drawing conclusions of subpopulations or separate indications based on the results provided herein. Moreover, the follow-up duration in the present study was only 12 months. However, it has been previously suggested that 12-month PROMs allow for appropriate evaluation of clinical outcome after spinal fusion.^{39,40} Our study was limited in the number of included variables and did not report any data on relevant comorbidities, psychosocial aspects, reoperation, complication rates, return to work, preoperative

nonopioid analgesia use, preoperative duration of symptoms, use of steroid injections, use of allied health care providers or other nonsurgeon physician resources (e.g. pain specialists), the impact of mental health status, or operative parameters that related to surgical invasiveness (e.g. estimated blood loss), which may have been potential confounders. Furthermore, we did not account for study design. Several articles demonstrated that considering both sex and gender are crucial to be able to disentangle biological from social determinants of health.^{41,42} To date, few studies reported treatment outcomes after spinal fusion specifically stratified by gender.^{2,23,43–45} While sex and gender are two different notions, we did not collect any gender-related variables and investigated only the effect of sex on patient-reported outcomes, which does not allow to draw conclusions about the effect of gender and is a significant limitation of the present study. Future studies should be designed to incorporate such gender-related factors in their data collection.

CONCLUSION

Female patients experienced a similar benefit from surgery in terms of the relative improvement in scores for functional impairment and pain compared with male patients. Although female patients on average reported a higher degree of functional impairment and pain preoperatively, at 12 months only their mean scores for functional impairment remained higher than those of their male counterparts, while absolute pain scores were similar for female and male patients. While absolute scores remain an important measure to quantify the magnitude and severity of functional impairment and pain, our study indicates that relative measures (such as change scores or MCID) should be preferably used to account for baseline symptom severity when evaluating treatment effects.

➤ Key Points

- ❑ Female patients reported higher functional impairment and pain preoperatively.
- ❑ Both sexes experienced similar relative improvement in scores for functional impairment and pain.
- ❑ At 12 months, only mean scores of female patients for functional impairment remained higher than those for their male counterparts, absolute pain scores were similar for female/male patients.

ACKNOWLEDGMENTS

The authors thank the patients whose anonymized data were used for this research.

References

1. Ravindra VM, Senglaub SS, Rattani A, et al. Degenerative Lumbar Spine Disease: Estimating Global Incidence and Worldwide Volume. *Global Spine J.* 2018;8:784–794.
2. Salamanna F, Contartese D, Tschon M, et al. Sex and gender determinants following spinal fusion surgery: A systematic review of clinical data. *Front Surg.* 2022;9:983931.
3. Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choinière M. A systematic literature review of 10 years of research on sex/gender and experimental pain perception - part 1: are there really differences between women and men? *Pain.* 2012; 153:602–618.
4. Gautschi OP, Corniola MV, Smoll NR, et al. Sex differences in subjective and objective measures of pain, functional impairment, and health-related quality of life in patients with lumbar degenerative disc disease. *Pain.* 2016;157:1065–1071.
5. Melchior M, Poisbeau P, Gaumont I, Marchand S. Insights into the mechanisms and the emergence of sex-differences in pain. *Neuroscience.* 2016;338:63–80.
6. Wiesenfeld-Hallin Z. Sex differences in pain perception. *Gen Med.* 2005;2:137–145.
7. Rosen S, Ham B, Mogil JS. Sex differences in neuroimmunity and pain. *J Neurosci Res.* 2017;95:500–508.
8. Gregus AM, Levine IS, Eddinger KA, Yaksh TL, Buczynski MW. Sex differences in neuroimmune and glial mechanisms of pain. *Pain.* 2021;162:2186–2200.
9. Strömqvist F, Strömqvist B, Jönsson B, Gerdhem P, Karlsson MK. Predictive outcome factors in the young patient treated with lumbar disc herniation surgery. *J Neurosurg Spine.* 2016;25:448–455.
10. Siccoli A, Staartjes VE, de Wispelaere MP, Schröder ML. Gender differences in degenerative spine surgery: Do female patients really fare worse? *Eur Spine J.* 2018;27:2427–2435.
11. Al Jammal OM, Shahrestani S, Delavar A, et al. Demographic predictors of treatments and surgical complications of lumbar degenerative diseases: An analysis of over 250,000 patients from the National Inpatient Sample. *Medicine (Baltimore).* 2022;101: e29065.
12. Chan AK, Bisson EF, Bydon M, et al. Women fare best following surgery for degenerative lumbar spondylolisthesis: a comparison of the most and least satisfied patients utilizing data from the Quality Outcomes Database. *Neurosurg Focus.* 2018;44:E3.
13. Staartjes VE, Vergroesen PA, Zeilstra DJ, Schröder ML. Identifying subsets of patients with single-level degenerative disc disease for lumbar fusion: the value of prognostic tests in surgical decision making. *Spine J.* 2018;18:558–566.
14. MacLean MA, Touchette CJ, Han JH, Christie SD, Pickett GE. Gender differences in the surgical management of lumbar degenerative disease: a scoping review. *J Neurosurg Spine.* 2020;32:799–816.
15. Staartjes VE, Stumpo V, Ricciardi L, et al. FUSE-ML: development and external validation of a clinical prediction model for mid-term outcomes after lumbar spinal fusion for degenerative disease. *Eur Spine J.* 2022;31:2629–2638.
16. Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine (Phila Pa 1976).* 2008;33:90–94.
17. Fekete TF, Haschtmann D, Kleinstück FS, Porchet F, Jeszenszky D, Mannion AF. What level of pain are patients happy to live with after surgery for lumbar degenerative disorders? *Spine J.* 2016;16(4 Suppl): S12–S18.
18. Mannion AF, Elfering A, Fekete TF, et al. Development of a mapping function (“crosswalk”) for the conversion of scores between the Oswestry Disability Index (ODI) and the Core Outcome Measures Index (COMI). *Eur Spine J.* 2022;31:3337–3346.
19. *R Core Team R: A language and environment for statistical computing* [computer program] Vienna, Austria: R Foundation for Statistical Computing; 2022.
20. Strömqvist F, Strömqvist B, Jönsson B, Karlsson MK. Gender differences in patients scheduled for lumbar disc herniation surgery: a National Register Study including 15,631 operations. *Eur Spine J.* 2016;25:162–167.

21. Coric D, Zigler J, Derman P, Braxton E, Situ A, Patel L. Predictors of long-term clinical outcomes in adult patients after lumbar total disc replacement: development and validation of a prediction model. *J Neurosurg Spine*. 2021;36:1–9.
22. Peul WC, Brand R, Thomeer R, Koes BW. Influence of gender and other prognostic factors on outcome of sciatica. *Pain*. 2008;138:180–191.
23. Pochon L, Kleinstück FS, Porchet F, Mannion AF. Influence of gender on patient-oriented outcomes in spine surgery. *Eur Spine J*. 2016;25:235–246.
24. Katz JN, Wright EA, Guadagnoli E, Liang MH, Karlson EW, Cleary PD. Differences between men and women undergoing major orthopedic surgery for degenerative arthritis. *Arthritis Rheum*. 1994;37:687–694.
25. Taylor BA, Casas-Ganem J, Vaccaro AR, Hilibrand AS, Hanscom BS, Albert TJ. Differences in the work-up and treatment of conditions associated with low back pain by patient gender and ethnic background. *Spine (Phila Pa 1976)*. 2005;30:359–364.
26. Hawker GA, Wright JG, Coyte PC, et al. Differences between men and women in the rate of use of hip and knee arthroplasty. *N Engl J Med*. 2000;342:1016–1022.
27. Gautschi OP, Smoll NR, Corniola MV, et al. Sex differences in lumbar degenerative disc disease. *Clin Neurol Neurosurg*. 2016;145:52–57.
28. Strömquist F, Strömquist B, Jönsson B, Karlsson MK. Inferior Outcome of Lumbar Disc Surgery in Women Due to Inferior Preoperative Status: A Prospective Study in 11,237 Patients. *Spine (Phila Pa 1976)*. 2016;41:1247–1252.
29. Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choinière M. A systematic literature review of 10 years of research on sex/gender and pain perception - part 2: do biopsychosocial factors alter pain sensitivity differently in women and men? *Pain*. 2012;153:619–635.
30. Robinson ME, Riley JL III, Myers CD, et al. Gender role expectations of pain: relationship to sex differences in pain. *J Pain*. 2001;2:251–257.
31. Wise EA, Price DD, Myers CD, Heft MW, Robinson ME. Gender role expectations of pain: relationship to experimental pain perception. *Pain*. 2002;96:335–342.
32. Tschugg A, Löscher WN, Hartmann S, Neururer S, Wildauer M, Thomé C. Gender Influences Radicular Pain Perception in Patients with Lumbar Disc Herniation. *J Womens Health (Larchmt)*. 2015;24:771–776.
33. Roh HL, Lee JS, Suh KT, et al. Association between estrogen receptor gene polymorphism and back pain intensity in female patients with degenerative lumbar spondylolisthesis. *J Spinal Disord Tech*. 2013;26:E53–E57.
34. Park YS, Suh KT, Shin JK, Lee JS. Estrogen receptor gene polymorphism in patients with degenerative lumbar scoliosis. *Br J Neurosurg*. 2017;31:63–66.
35. MacDowall A, Skeppholm M, Lindhagen L, Robinson Y, Olerud C. Effects of preoperative mental distress versus surgical modality, arthroplasty, or fusion on long-term outcome in patients with cervical radiculopathy. *J Neurosurg Spine*. 2018;29:371–379.
36. Triebel J, Snellman G, Sandén B, Strömquist F, Robinson Y. Women do not fare worse than men after lumbar fusion surgery: Two-year follow-up results from 4,780 prospectively collected patients in the Swedish National Spine Register with lumbar degenerative disc disease and chronic low back pain. *Spine J*. 2017;17:656–662.
37. Legato MJ, Johnson PA, Manson JE. Consideration of Sex Differences in Medicine to Improve Health Care and Patient Outcomes. *Jama*. 2016;316:1865–1866.
38. Stienen MN, Ho AL, Staartjes VE, et al. Objective measures of functional impairment for degenerative diseases of the lumbar spine: a systematic review of the literature. *Spine J*. 2019;19:1276–1293.
39. Staartjes VE, Siccoli A, de Wispelaere MP, Schröder ML. Patient-reported outcomes unbiased by length of follow-up after lumbar degenerative spine surgery: Do we need 2 years of follow-up? *Spine J*. 2019;19:637–644.
40. Fekete TF, Loibl M, Jeszenszky D, et al. How does patient-rated outcome change over time following the surgical treatment of degenerative disorders of the thoracolumbar spine? *Eur Spine J*. 2018;27:700–708.
41. Johnson JL, Greaves L, Repta R. Better science with sex and gender: Facilitating the use of a sex and gender-based analysis in health research. *International Journal for Equity in Health*. 2009;8:14.
42. Valeria R, Colleen MN, Uri B, et al. Identification and inclusion of gender factors in retrospective cohort studies: the GOING-FWD framework. *BMJ Global Health*. 2021;6:e005413.
43. Ayhan S, Yuksel S, Nabiye V, et al. The Influence of Diagnosis, Age, and Gender on Surgical Outcomes in Patients With Adult Spinal Deformity. *Global Spine J*. 2018;8:803–809.
44. Elsamadicy AA, Freedman IG, Koo AB, et al. Influence of gender on discharge disposition after spinal fusion for adult spine deformity correction. *Clin Neurol Neurosurg*. 2020;194:105875.
45. Parrish JM, Jenkins NW, Massel DH, et al. The Perioperative Symptom Severity of Higher Patient Health Questionnaire-9 Scores Between Genders in Single-Level Lumbar Fusion. *Int J Spine Surg*. 2021;15:62–73.