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Leveraging machine learning to ascertain the implications of preoperative body mass index on surgical outcomes for 282 patients with preoperative obesity and lumbar spondylolisthesis in the Quality Outcomes Database

Nitin Agarwal, MD,[1] Alexander A. Aabedi, MD,[1] Andrew K. Chan, MD,[1] Vijay Letchuman, MD,[1] Saman Shabani, MD,[1] Erica F. Bisson, MD, MPH,[2] Mohamad Bydon, MD,[3] Steven D. Glassman, MD,[4] Kevin T. Foley, MD,[5] Christopher I. Shaffrey, MD,[6,7] Eric A. Potts, MD,[8] Mark E. Shaffrey, MD,[9] Domagoj Coric, MD,[10] John J. Knightly, MD,[11] Paul Park, MD,[12] Michael Y. Wang, MD,[13] Kai-Ming Fu, MD, PhD,[14] Jonathan R. Slotkin, MD,[15] Anthony L. Asher, MD,[10] Michael S. Virk, MD, PhD,[14] Regis W. Haid Jr., MD,[16] Dean Chou, MD,[1] and Praveen V. Mummaneni, MD, MBA[1]

[1]Department of Neurological Surgery, University of California, San Francisco, California; [2]Department of Neurosurgery, University of Utah, Salt Lake City, Utah; [3]Department of Neurologic Surgery, Mayo Clinic, Rochester, Minnesota; [4]Norton Leatherman Spine Center, Louisville, Kentucky; [5]Department of Neurosurgery, Semmes-Murphey Neurologic and Spine Institute, University of Tennessee, Memphis, Tennessee; Departments of [6]Neurosurgery and [7]Orthopedic Surgery, Duke University, Durham, North Carolina; [8]Department of Neurological Surgery, Goodman Campbell Brain and Spine, Indianapolis, Indiana; [9]Department of Neurosurgery, University of Virginia, Charlottesville, Virginia; [10]Neuroscience Institute, Carolina Neurosurgery & Spine Associates, Carolinas Healthcare System, Charlotte, North Carolina; [11]Atlantic Neurosurgical Specialists, Morristown, New Jersey; [12]Department of Neurosurgery, University of Michigan, Ann Arbor, Michigan; [13]Department of Neurological Surgery, University of Miami, Florida; [14]Department of Neurological Surgery, Weill Cornell Medical Center, New York, New York; [15]Geisinger Health, Danville, Pennsylvania; and [16]Atlanta Brain and Spine Care, Atlanta, Georgia

OBJECTIVE Prior studies have revealed that a body mass index (BMI) ≥ 30 is associated with worse outcomes following surgical intervention in grade 1 lumbar spondylolisthesis. Using a machine learning approach, this study aimed to leverage the prospective Quality Outcomes Database (QOD) to identify a BMI threshold for patients undergoing surgical intervention for grade 1 lumbar spondylolisthesis and thus reliably identify optimal surgical candidates among obese patients.

METHODS Patients with grade 1 lumbar spondylolisthesis and preoperative BMI ≥ 30 from the prospectively collected QOD lumbar spondylolisthesis module were included in this study. A 12-month composite outcome was generated by performing principal components analysis and k-means clustering on four validated measures of surgical outcomes in patients with spondylolisthesis. Random forests were generated to determine the most important preoperative patient characteristics in predicting the composite outcome. Recursive partitioning was used to extract a BMI threshold associated with optimal outcomes.

RESULTS The average BMI was 35.7, with 282 (46.4%) of the 608 patients from the QOD data set having a BMI ≥ 30. Principal components analysis revealed that the first principal component accounted for 99.2% of the variance in the four outcome measures. Two clusters were identified corresponding to patients with suboptimal outcomes (severe back pain,

ABBREVIATIONS ASA = American Society of Anesthesiologists; BMI = body mass index; MCID = minimal clinically important difference; NRSBP = numeric rating scale for back pain; ODI = Oswestry Disability Index; PRO = patient-reported outcome; QOD = Quality Outcomes Database; SVA = sagittal vertical axis.

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increased disability, impaired quality of life, and low satisfaction) and to those with optimal outcomes. Recursive partitioning established a BMI threshold of 37.5 after pruning via cross-validation.

CONCLUSIONS In this multicenter study, the authors found that a BMI ≤ 37.5 was associated with improved patient outcomes following surgical intervention. These findings may help augment predictive analytics to deliver precision medicine and improve prehabilitation strategies.

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KEYWORDS machine learning; spondylolisthesis; obesity; Quality Outcomes Database; lumbar

Low-back pain is a well-documented leading cause of global disability, leading to a heavy economic burden on society with an estimated annual direct medical cost greater than $250 billion.[1] Degenerative lumbar spondylolisthesis is a major cause of low-back pain with a prevalence of up to 13.6% in the US.[2] With appropriate selection of surgical intervention, patients experience a significant clinical and functional benefit, but identifying the optimal surgical candidate remains an iterative process. *The New England Journal of Medicine* recently published two randomized controlled trials that aimed to evaluate the role of surgical fusion in addition to decompression for patients with lumbar spondylolisthesis, but disparate conclusions were noted.[3,4] Using the Quality Outcomes Database (QOD), Bisson et al. investigated patient-reported outcomes (PROs) following decompression with fusion for patients with grade 1 degenerative lumbar spondylolisthesis and reported superior outcomes with fusion compared with decompression alone.[5] Diagnostic heterogeneity, operative techniques, and outcome measures may account for ongoing variability in study results.[2,5–7] While the optimal management paradigm for spondylolisthesis continues to evolve, an increased emphasis has been placed on achieving optimal outcomes when surgical intervention is used as part of the therapeutic strategy. To achieve this goal, a substantial effort has been put forth to identify subgroups of patients with spondylolisthesis who may benefit most from surgery. Chan et al. recently employed machine learning techniques to identify distinct clinical presentation phenotypes of patients with lumbar spondylolisthesis and ultimate postoperative outcomes, using PRO measures.[2]

In this effort to identify the "ideal" surgical candidate, the role of patient body mass index (BMI) has been explored extensively in the context of spine surgery.[8] Previous studies have established that patients with a higher BMI are at an increased risk of complications following spine surgery.[8,9] In 2019, a study investigated the relationship between BMI and the sagittal vertical axis (SVA) change. While BMI did not affect the achievable SVA change at 1-year follow-up, a preoperative BMI ≥ 30 kg/m^2 was correlated with worse outcomes as measured by Oswestry Disability Index (ODI) scores.[8] In a preliminary study focused on spondylolisthesis, our group evaluated this threshold in the QOD database for patients with grade 1 degenerative lumbar spondylolisthesis and revealed that patients with BMI ≥ 30 still benefited from surgical intervention at the 12-month postoperative time point but had worse leg pain metrics and quality-of-life outcomes compared with patients with preoperative BMI < 30.[10] Additional clarity is required to determine a more precise preoperative BMI threshold for patients undergoing surgical interventions for degenerative lumbar spondylolisthesis.

This study aimed to use machine learning to leverage the prospectively collected, multicenter QOD spine registry and the focused lumbar spondylolisthesis data set to identify an optimal BMI threshold for patients with Meyerding grade 1 lumbar spondylolisthesis undergoing surgical intervention. This threshold may allow surgeons to reliably identify ideal surgical candidates or enroll those exceeding established BMI parameters in a prehabilitation protocol to optimize preoperative characteristics.

Methods

Patient Selection

A total of 608 patients undergoing single-segment surgery for grade 1 degenerative spondylolisthesis were prospectively enrolled by the Spine Collaboration for Outcomes Research (CORe) team as part as the multicenter QOD registry. From this cohort, the subset of patients with preoperative BMI ≥ 30 was selected, leading to a final cohort size of 282 patients.

Outcome Measures

Several validated outcome measures were collected at baseline and at 12 months postoperative follow-up from each patient. These measures included the EuroQoL-5D (EQ-5D), patient satisfaction index, numeric rating scale for back pain (NRSBP), and ODI. The EQ-5D is rated on a pseudocontinuous scale ranging from –0.11 to 1.00, with higher values indicating a better quality of life. The patient satisfaction index is rated on an ordinal scale ranging from 1 to 4 in discrete intervals, with higher values denoting dissatisfaction with surgery. The NRSBP is similarly rated on an ordinal scale with discrete intervals, but from 1 to 10, with higher values indicating worse back pain. Finally, the ODI indexes overall functional status on a pseudocontinuous scale ranging from 1 to 100, with higher values indicating greater disability.

Statistical Analysis

The primary aim of this study was to identify a BMI threshold among obese patients that is associated with optimal PROs after single-level surgery for grade 1 spondylolisthesis. To reduce model complexity and increase the clinical interpretability of the model predictions, a composite 12-month outcome was generated from the four PROs (EQ-5D, patient satisfaction index, NRSBP, and ODI) using unsupervised machine learning algorithms. Importantly, preoperative patient characteristics were not

manually stratified a priori, as the goal of this study was to determine the characteristics associated with optimal versus suboptimal outcomes in a cohort of patients with obesity via unsupervised learning. First, principal components analysis was conducted to collapse this multidimensional vector space into 2 dimensions (principal components). Each patient was subsequently projected onto this reduced space, and k-means clustering (via Hartigan and Wong's technique[11]) was performed to identify statistically distinct subpopulations of patients with varying degrees of composite postoperative disability, satisfaction, pain, etc. This approach has been used previously to stratify patients by operative outcomes and determine the factors associated with each.[12,13] The ideal number of clusters (subpopulations) to divide the patients into was determined by maximizing the silhouette score across cluster sizes ranging from 1 to 10 and was confirmed by visual inspection.[14]

Next, random forests were generated with 10,000 iterations to determine the most important variables among 25 preoperative characteristics (Supplementary Table 1) in predicting cluster assignment.[15] Hyperparameters were left at the default settings (node size of 1, sampling with replacement, five variables randomly sampled at each split), and overfitting was managed by minimizing the "out-of-bag" error in a randomly held-out subset of one-third of the patient cohort. Variable (feature) importance was determined by excluding variables from the model in an iterative fashion and then measuring the average reduction of the model's Gini coefficient achieved in predicting cluster assignment after reintroduction of that variable. Furthermore, the proportions of patients achieving the minimal clinically important difference (MCID) on the EQ-5D and ODI postoperatively were compared to assess the clinical relevance of these findings.

Finally, to generate a clinically intuitive BMI threshold predictive of outcomes, recursive partitioning was implemented with the following parameters: cost of 1, minimum split of 20, and complexity of 0.01.[16] To prevent model overfitting, the final trees were pruned, and the one that minimized the cross-validation error was selected. Analyses were conducted using R software (version 4.0.5). Random forests were generated using the randomForest package (version 4.6-14) and recursive partitioning using the rpart package (version 4.1-15) for R. Median values with interquartile ranges (IQRs) were reported throughout.

Results

Baseline Characteristics

Baseline patient characteristics are summarized in Table 1. The median age was 62 (IQR 52.3–68.3) years. Of 282 patients, 164 (58.2%) were female. The median height was 168 (IQR 160–178) cm, the median weight was 99.8 (IQR 89.9–113) kg, and the median BMI was 34.5 (IQR 32.0–38.1) kg/m^2. Sixty-seven patients (23.8%) had diabetes at baseline, 36 (12.8%) had coronary artery disease, and 14 (5.0%) had osteoporosis. Sixty-eight patients (24.1%) reported depression at baseline, while 58 (20.6%) reported anxiety. The median postoperative change in spondylolisthesis was –2.0 (IRQ –4.0 to 0) mm. Regarding baseline PROs, 8 patients (2.8%) were readmitted to the hospital within 90 days of their index procedure.

TABLE 1. Study cohort demographic characteristics (n = 282)

Characteristic	Value
Median age (IQR), yrs	62 (52.3–68.3)
Females, n (%)	164 (58.2)
Median height (IQR), cm	168 (160–178)
Median weight (IQR), kg	99.8 (89.9–113)
Median BMI (IQR), kg/m^2	34.5 (32.0–38.1)
Comorbidities, n (%)	
Diabetes	67 (23.8)
Coronary artery disease	36 (12.8)
Osteoporosis	14 (5.0)
Depression	68 (24.1)
Anxiety	58 (20.6)
Median postsurgical spondylolisthesis reduction (IQR), mm	–2.0 (–4.0 to 0)
MCID achievement, n (%)	
EQ-5D only	
Suboptimal, n = 72	45 (62.5)
Optimal, n = 130	100 (76.9)
ODI only	
Suboptimal, n = 72	32 (44.4)
Optimal, n = 130	112 (86.2)
EQ-5D and ODI	
Suboptimal, n = 72	24 (33.3)
Optimal, n = 130	90 (69.2)
90-day readmission rates, n (%)	8 (2.8)

Component and Cluster Analysis

The goal of this study was to identify a statistically rigorous BMI threshold among patients with baseline obesity that is associated with more optimal PROs after surgery for grade 1 spondylolisthesis. Therefore, we first generated a composite outcome consisting of four validated measures (EQ-5D, patient satisfaction index, NRSBP, and ODI; Fig. 1). Spearman rank correlations were computed between each pair of outcome metrics, revealing statistically significant relationships between all pairs ($p < 0.001$; Fig. 1A). To facilitate accurate clustering based on these four PROs, principal components analysis was subsequently performed to reduce the dimensionality of the data set (Fig. 1B). The first principal component captured 99.2% of the variance in the data set, and the outcome metric that loaded most heavily on this principal component was the ODI. Next, k-means clustering was conducted over this subspace (Fig. 2A). The silhouette method identified an optimal cluster size of 2 (Supplementary Fig. 1), consisting of patients with optimal and suboptimal outcomes. Cluster assignment can be further visualized in Fig. 2B, which demonstrates that patients assigned to the "optimal" cluster have lower back pain ratings (NRSBP), have lower disability indices (ODI), report better quality of life (EQ-5D), and express greater

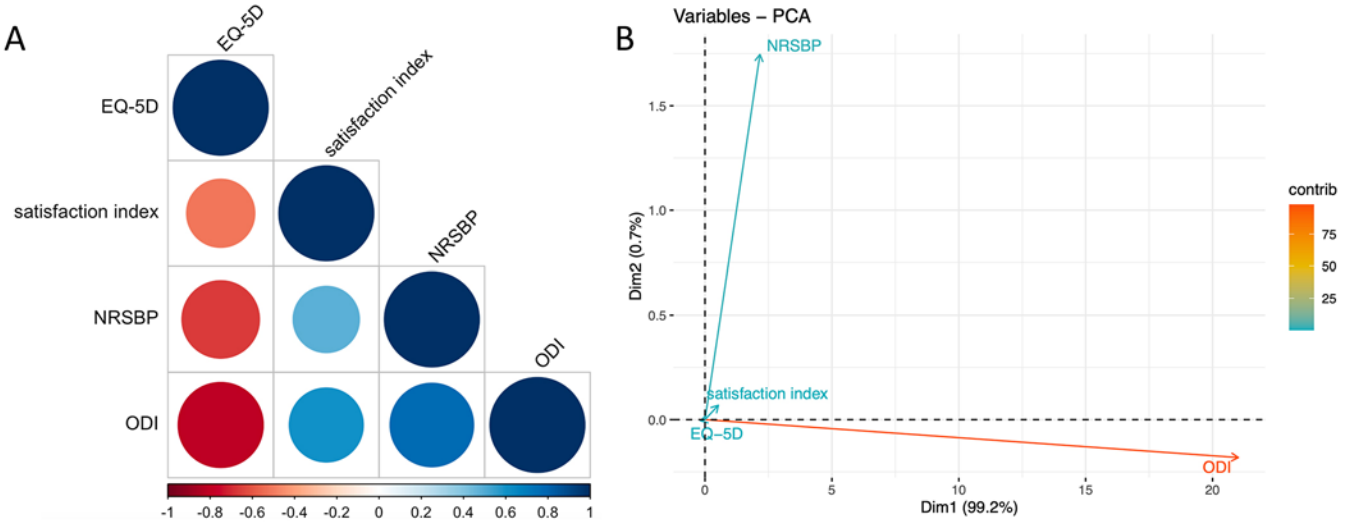

FIG. 1. Patient outcomes in obese patients (BMI ≥ 30) and subsequent clustering based on outcome metrics. **A:** Correlation matrix demonstrating statistically significant relationships between each of the four standardized patient outcome metrics. **B:** Principal components plot with loadings for each of the four outcome metrics. contrib = contribution; Dim1 = dimension 1; Dim2 = dimension 2; PCA = principal components analysis. Figure is available in color online only.

satisfaction with their surgery (patient satisfaction index). Overall, the clustering algorithm appeared to accurately partition patients into those with satisfactory and unsatisfactory outcomes. Whereas 1 patient in the optimal cluster had a 12-month NRSBP of 9, 47% of the patients in the optimal cluster had NRSBPs between 0 and 3, compared with just 5% in the suboptimal cluster. The mean BMI in the optimal outcome cluster was 34.9 ± 4.4 compared with 37.9 ± 6.0 in the suboptimal outcome cluster. Using a conservative estimate of 0.08 for the EQ-5D and 15 for the ODI based on the existing literature, we determined that 33.3% (24/72) compared with 69.2% (90/130) achieved the MCID across both measures in the suboptimal and optimal outcome clusters, respectively. This difference in proportions was statistically significant ($\chi^2 = 22.9$, $p < 0.0001$).

Machine Learning Algorithms

Next, tree-based supervised machine learning algorithms were implemented to 1) identify the factors that are most relevant in predicting whether a given patient will have an optimal or suboptimal outcome, and 2) determine whether a BMI threshold exists that is associated with optimal outcomes. Twenty-five preoperative characteristics were included in the random forest model used to predict cluster assignment (Supplementary Table 1). The top 10 variables that were most important in reducing the model's error are depicted in order of descending importance in Fig. 3. The random forest model had an out-of-bag error accuracy rate, an averaged performance metric on a held-out or unseen set of data, of 77.7%. Age and BMI emerged as the two most important variables, whereas inclusion of the remaining 8 variables provided modest improvements to model performance. To provide an estimate of the effect of these variables on the likelihood of achieving an optimal outcome, univariate logistic regression models were generated. The odds ratio (OR) was 0.89 for BMI (95% CI 0.83–0.94, $p < 0.001$) and 1.04 for age (95% CI 1.01–1.07, $p = 0.003$). Comorbidities including smoking (OR 0.30, 95% CI 0.10–0.80, $p = 0.021$), higher American Society of Anesthesiologists (ASA) class (OR 0.43, 95% CI 0.25–0.72, $p = 0.002$), and baseline anxiety (OR 0.48, 95% CI 0.25–0.96, $p = 0.037$) were additionally associated with a lower likelihood of an optimal outcome.

Multiple Regression and Recursive Partitioning

The interaction between age and BMI in terms of cluster assignment is further explored in Fig. 4. Multivariate logistic regression revealed that older patients with lower BMIs were more likely to have optimal outcomes, while younger patients with higher BMIs were more likely to have suboptimal outcomes (Fig. 4A). Older patients were also less likely to have anxiety (OR 0.97, 95% CI 0.94–0.99, $p = 0.018$) and depression (OR 0.96, 95% CI 0.94–0.99, $p = 0.017$) at baseline; anxiety was significantly associated with worse outcomes. Finally, recursive partitioning was conducted to determine whether a BMI threshold exists that would allow clinicians to rapidly assess the likelihood of optimal postoperative outcomes among patients with obesity undergoing surgery for grade 1 spondylolisthesis. This partitioning resulted in a BMI threshold of 37.5 (Fig. 4B). Patients at or below this BMI threshold had less back pain ($p = 0.005$), less disability ($p < 0.0001$), better quality of life ($p < 0.0001$), and greater satisfaction ($p = 0.007$) compared with those above this threshold 1 year after surgery.

Discussion

In this study, a k-means clustering analysis of 282 patients from the prospectively collected QOD lumbar spondylolisthesis module was leveraged to identify an optimal BMI threshold for patients with Meyerding grade 1 lum-

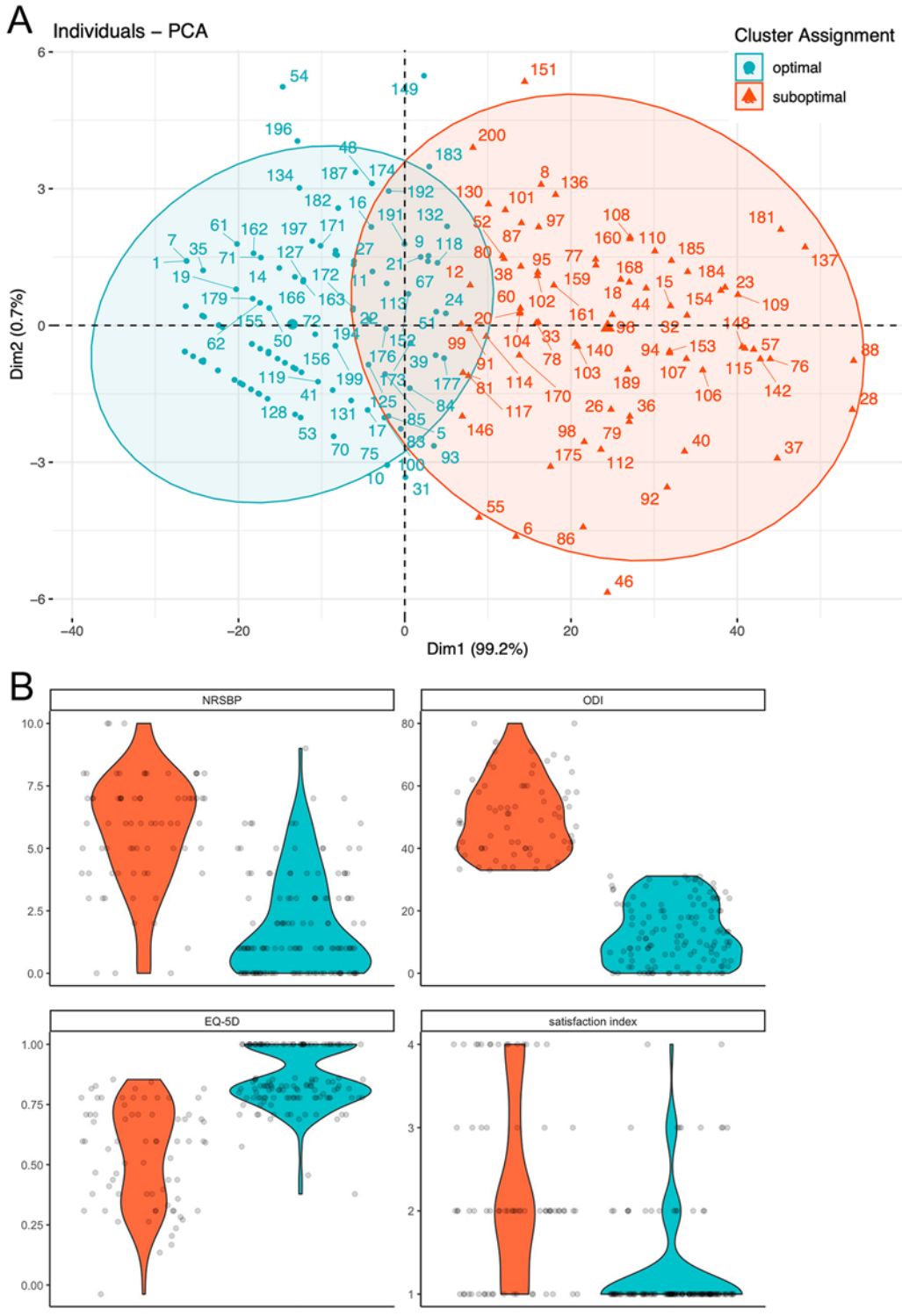

FIG. 2. A: Graph depicting k-means clustering separating patients into those with suboptimal and optimal outcomes. Labeled numbers refer to individual patients included in the study. **B:** Violin plots demonstrating differences in scoring distributions stratified by cluster. Figure is available in color online only.

bar spondylolisthesis undergoing surgical intervention. This study revealed that a BMI ≤ 37.5 kg/m^2 is associated with optimal postsurgical outcomes as measured by lower NRSBP ratings, lower ODI scores, higher quality-of-life indices, and higher satisfaction with surgery at 1-year follow-up.

With the increase in surgical interventions for lumbar spondylolisthesis, significant resources have been applied

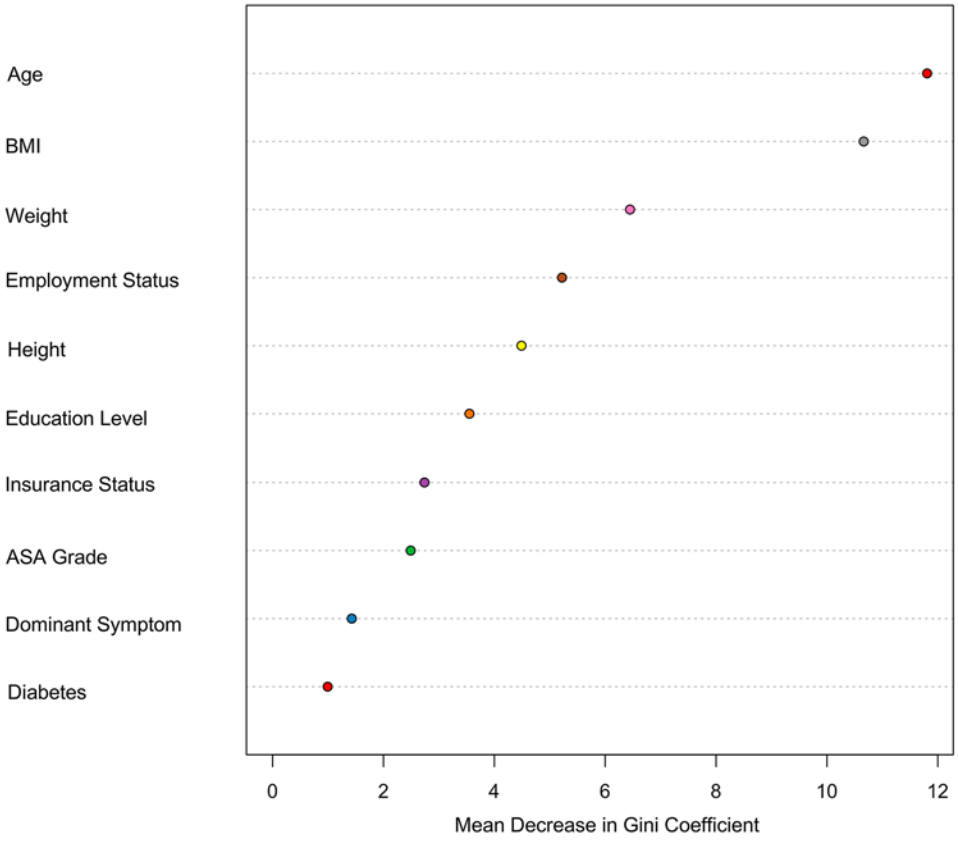

FIG. 3. Result of random forest models used to predict cluster assignment (i.e., optimal vs suboptimal outcome) based on 25 preoperative characteristics. The top 10 most important variables in decreasing the overall model error (determined via the Gini coefficient) are demonstrated. The two most important variables were age and BMI. Figure is available in color online only.

to identify ideal qualities of patients undergoing surgery.[5,6,17–31] Obesity has been linked to inferior perioperative outcomes in the postoperative period in a variety of spinal pathologies.[9,10,30,32–37] Previously, utilizing the QOD lumbar spondylolisthesis module, it was demonstrated that patients with higher preoperative disease burden were less satisfied, had lower quality of life, and had more disability, leg pain, and back pain compared with those with lower disease burdens.[10] However, this same subset of patients with high preoperative disease burden demonstrated greater degrees of improvement in functional and disability measures.[2] Given this initial clinical and postoperative phenotype, a deeper investigation into specific variables associated with optimal surgical outcomes was undertaken in this study. Previously, in an attempt to establish preoperative BMI parameters, a number of studies evaluated a litany of BMI thresholds. These studies, however, were limited by set thresholds that were not preestablished via evidence-based methodologies.[9,10]

In the context of spinal deformity surgery, it was found that while increasing preoperative BMI did not affect the ultimate postoperative SVA change, a preoperative BMI $\geq$ 30 kg/m^2 was correlated with poorer postoperative outcomes as measured by ODI scores.[8] Because a number of studies have investigated BMI dichotomously, Chan et al. in 2020 explored preoperative BMI as a continuous variable and found that as BMI increases, postoperative outcomes such as leg pain and EQ-5D scores progressively worsen.[10] Despite the increased morbidity associated with surgical interventions, obese patients still benefit from surgical intervention, although their benefit may be marginal compared with that of nonobese patients.[9]

Given the description of surgical benefit within obese patients, this study aimed to identify a BMI threshold within a cohort of obese patients who should be referred to prehabilitation services to optimize weight prior to surgical intervention. This study revealed that following surgery, patients with a preoperative BMI $\leq$ 37.5 had less back pain, less disability, better quality of life, and greater satisfaction compared with those above this threshold at 1-year follow-up. This study represents the first time an identifiable BMI threshold associated with improved postoperative outcomes has been identified for patients with grade 1 lumbar spondylolisthesis.[36] The results posited here uniquely identify a potential subset of obese patients who may benefit from a prehabilitation program to optimize preoperative risk factors and improve outcomes in the postoperative period, although more work is required in this area.

Importantly, it is crucial to recognize that obesity is not the only factor in patients with lumbar spondylolisthesis. This study showed that age and BMI are closely tied to influencing postoperative outcomes. While older patients

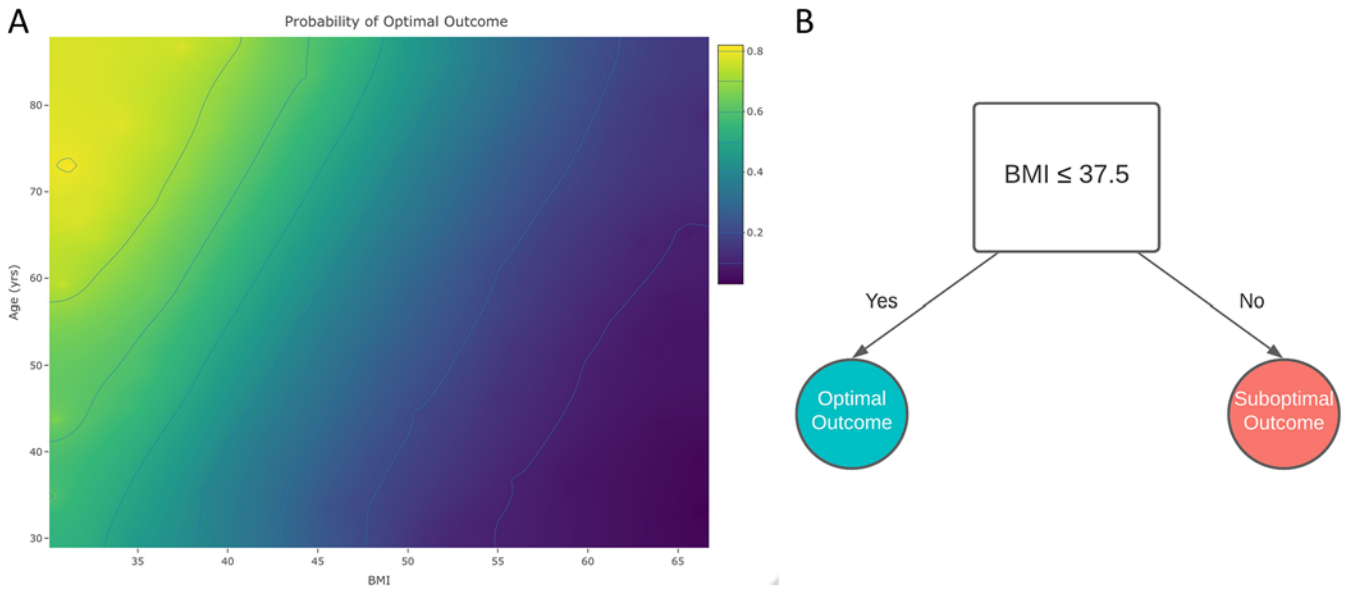

FIG. 4. Interaction between age and BMI on the probability of achieving an optimal outcome. **A:** Contour plot demonstrating the multivariate logistic regression model used to predict cluster assignment based on age and BMI. Patients with older age and lower BMI are more likely to have optimal outcomes (maximum probability > 80%). **B:** Recursive partitioning with pruning was performed to improve model generalizability. A BMI threshold of 37.5 was identified; patients at or below this threshold were more likely to have an optimal outcome. Figure is available in color online only.

are predisposed to increasing complications and poorer outcomes following surgery, in a multivariate analysis, increasing BMI was a stronger factor in suboptimal outcomes compared with age. Younger patients with higher BMIs were more likely to experience suboptimal outcomes compared with older patients with lower BMIs. While the factors driving this counterintuitive association are unclear, there appears to be an interaction with preoperative mood disorders and age: younger patients were more likely to report a baseline anxiety disorder, which was independently associated with worse outcomes.

To further explore the impact of other preoperative characteristics on postoperative outcomes following surgical interventions for lumbar spondylolisthesis, this study used k-means clustering to categorize patients into suboptimal and optimal postsurgical outcome cohorts; k-means clustering is an unsupervised machine learning method in which characteristics within a data set are identified and are grouped into distinct subgroups based on spatial clustering of nearby data points. These two distinct patient phenotypes had differing outcomes following surgery, with patients in the first cluster experiencing suboptimal postsurgical outcomes measured with higher NRSBP ratings, higher ODI scores, poorer quality-of-life indices, and less satisfaction with surgery.

Despite these findings indicating that patients with BMI > 37.5 were suboptimal surgical candidates, this result must be taken in context with the fact that prior studies have indicated that these patients still benefit from surgery. However, a preoperative diagnosis of obesity may not affect the patient's individual perception of clinical changes following surgical intervention.[38] Multiple studies have observed improved individualized patient satisfaction following surgery in obese patients, although the degree of improvement may be inferior to that in nonobese patients. In the SPORT (Spine Patient Outcomes Research Trial) study, surgical intervention was clearly associated with superior treatment effects compared with nonsurgical interventions in obese patients.[39] Interestingly, McGuire et al. found that patients with BMI > 35 had a greater improvement from baseline in regard to the mental component of the 36-Item Short Form Health Survey at 12 months of follow-up compared with nonobese patients.[40] In a prior 3- and 12-month analysis of the QOD lumbar spondylolisthesis module, it was observed that regardless of preoperative weight, patients achieved significant improvements in all domains compared with baseline.[10] In this context, it is critical to understand potential factors that are present in obese patients leading to worsened postoperative outcomes. Prior studies utilizing the same data set have shown that a higher proportion of obese patients undergo fusion procedures and therefore experience higher intraoperative blood loss and longer operative times.[10] Furthermore, other study groups have noted higher reoperation rates for obese patients compared with nonobese patients.[33] Buerba et al. identified that obese patients with BMI > 30 were more likely to develop complications following lumbar surgery, but for patients with BMI > 40, the rates of wound, urinary, and pulmonary complications were significantly higher compared with individuals with lower preoperative BMIs.[32] Given these individualistic improvements, it is crucial to not preclude well-selected obese patients from surgery, but rather use this threshold of 37.5 kg/m^2 as a guideline for selecting patients to undergo weight-loss interventions in an effort to optimize preoperative status.

Limitations

As with any large multicenter patient registry, this study is subject to the common limitations associated with these study methodologies. This study is a retrospective analysis of a prospectively collected data set, and the results must be interpreted accordingly. An important limitation to consider is the registry's patient attrition rate during the prospective data collection phase. Previous analyses of the QOD lumbar spondylolisthesis module revealed that 14.5% of patients were lost to follow-up. However, experts in evidence-based medicine have suggested that there needs to be at least a 20% attrition rate for the data to be significantly biased.[18] Therefore, while a lower attrition rate is ideal, our study data did not exhibit an unacceptable attrition rate that would unduly bias the results of the study. The second major limitation of this study is the inclusion of only Meyerding grade 1 degenerative lumbar spondylolisthesis patients who underwent surgery for the correction of their spinal pathology. This limitation results in an inclusion bias and makes these results nonapplicable to patients with higher grades of spondylolisthesis or those who are being managed with conservative therapy only. The results of this study are also not applicable to patients who are poor surgical candidates due to medical comorbidities beyond obesity. However, previous analyses of the data set utilized in this study have established the generalizability of the patient cohort.[10] Furthermore, given the observational nature of this study, direct causality between obesity and inferior outcomes cannot be confirmed. Furthermore, patients with BMI ≤ 37.5 may also benefit from weight loss prior to surgery for degenerative grade 1 lumbar spondylolisthesis, but this requires more study as few randomized prospective trials have been conducted to address this issue. Importantly, to ensure external validity of this threshold, comparison of these findings with independent data sets is necessary before specific threshold values can be implemented. Future studies with a prospective interventional prehabilitation or weight-loss arms may be warranted to determine the full impact of preoperative weight on patient perceived and measured outcome measures in the postoperative period for grade 1 lumbar spondylolisthesis.

Conclusions

In this multicenter study leveraging machine learning techniques, the authors found that a preoperative BMI ≤ 37.5 was predictive of improved patient outcomes following surgical intervention for grade 1 degenerative lumbar spondylolisthesis. Patients at or below BMIs of 37.5 prior to surgery had less back pain, less disability, better quality of life, and greater satisfaction 1 year after surgery compared with those with preoperative BMIs > 37.5. The findings posited in this study may help both augment predictive analytics to deliver precision medicine and guide prehabilitation strategies to optimize postoperative outcomes in patients undergoing surgery for grade 1 degenerative lumbar spondylolisthesis. Machine learning algorithms including recursive partitioning, random forests, and unsupervised clustering can provide novel insights into spinal outcome data sets but require continued study and validation to inform clinical decision-making.

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Author Contributions

Conception and design: Agarwal, Mummaneni. Acquisition of data: Bisson, Bydon, Glassman, Foley, CI Shaffrey, Potts, ME Shaffrey, Coric, Knightly, Park, Wang, Fu, Slotkin, Asher, Virk, Haid, Chou, Mummaneni. Analysis and interpretation of data: Aabedi, Letchuman, Chou, Mummaneni. Drafting the article: Aabedi, Agarwal, Letchuman, Mummaneni. Critically revising the article: Aabedi, Agarwal, Chan, Shabani, Bisson, Bydon, Glassman, Foley, CI Shaffrey, Potts, ME Shaffrey, Coric, Knightly, Park, Wang, Fu, Slotkin, Asher, Virk, Haid, Chou, Mummaneni. Reviewed submitted version of manuscript: Aabedi, Chan, Shabani, Bisson, Bydon, Glassman, Foley, CI Shaffrey, Potts, ME Shaffrey, Coric, Knightly, Park, Wang, Fu, Slotkin, Asher, Virk, Haid, Chou, Mummaneni. Study supervision: Mummaneni.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

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Correspondence

Alexander A. Aabedi: University of California, San Francisco, CA. alexander.aabedi@ucsf.edu.