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The influence of peri-operative depressive symptoms on medium-term spine surgery outcome: a prospective study

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Abstract

Purpose To investigate the role of depressive symptoms on clinical outcomes in patients undergoing spinal surgery up to 2-year follow-up.

Methods The study used data from an institutional spine surgery registry (January 2016, through March 2022) to identify patients (> 18 years) undergoing spine surgery. Patients with Oswestry Disability Index (ODI) < 20/100 at baseline or undergoing surgery on the cervical spine or for idiopathic spinal deformity and trauma patients were excluded. The patients were divided into two groups based on the pre-operative Mental Component Summary (MCS) score of the SF-36: depression group (MCS \leq 35) or non-depression group (MCS > 35). The ODI and MCS scores trajectory were wined over the 24-month post-surgery between groups. Additionally, a secondary subgroup analysis was conducted comparing outcomes between those with depressive symptoms (persistent-depression subgroup) and those without depressive symptoms (never-depression subgroup) at 3 months after surgery.

Results A total of 2164 patients who underwent spine surgery were included. The pre-operative depression group reported higher ODI total scores and lower MCS than the pre-operative non-depression group at all time points (P < 0.001). The persistent-depression subgroup reported higher ODI total scores and lower MCS than the never-depression subgroup at all follow-ups (P < 0.001).

Conclusion Functional disability and mental health status improve in patients with depression symptoms undergoing spinal surgery. Despite this improvement, they do not reach the values of non-depressed subjects. Over the 2-year follow-up time, patients with depression show a different trajectory of ODI and MCS. Caregivers should be aware of these results to counsel patients with depression symptoms.

Keywords Spine surgery · Mental health · Depression · Disability · Short-form 36 · Oswestry Disability Index

Introduction

Spinal disorders are considered one of the leading causes of years lived with disability worldwide [1]. In a relatively small proportion of cases, spinal surgery is the treatment of choice after assessing potential risks and benefits [2]. However, due to the inherent risks of a surgical procedure, the post-operative period, and the associated direct and indirect costs to the intervention [2], it is essential to identify those patients that benefit from spinal surgery, including the assessment of sociodemographic, physical, and psychological features [3].

Depressive symptoms are usually present in patients with back pain [4], with a prevalence of 25–40% in subjects affected by degenerative spinal disorders [5]. Besides, preoperative depressive symptoms have been suggested as a risk factor negatively affecting surgical outcomes of spinal surgery [6]. Hence, early detection of patients with signs of depression may help decision-making and the expectations

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agreement between patient and surgeon [7]. However, depression can be misrecognized or underestimated by spine surgeons in their outpatient clinics. Therefore, patientreported outcomes measures (PROMs) have been introduced to promptly identify subjects at risk, such as the Mental Component Summary (MCS) of the 36-Item Short Form (SF-36) [8, 9] or the Patient Health Questionaire-9 [10].

Previous studies have investigated the association between pre-operative mental status and clinical outcomes. On the one hand, some authors reported a correlation between pre-operative depressive symptoms and functional or pain improvement after spinal surgery [11–13]. In contrast, other authors did not find such an association [10, 14, 15]. This lack of agreement warrants the need for further investigation. Furthermore, although depressive symptoms can be prevalent after spine surgery [5], their role in medium- or long-term surgical outcomes is not well-known.

Considering the hypothesis that pre-operative and postoperative mental status can influence the medium-term outcomes after surgery, this study aims to investigate the role of peri-operative depressive symptoms on clinical outcomes up to 24-month follow-up after spinal surgery. In particular, to assess whether patients with peri-operative depressive symptoms report worse disability outcomes over time.

Methods

Study setting and population

This study was based on retrospectively compiled data from an institutional spine surgery registry—SpineReg [16]. The institutional ethics committee granted ethical permission (second amendment to the SPINEREG protocol issued on 13/04/2016), and the study complies with the Helsinki statement. The database analyzed consisted of sociodemographic and pre-and post-operative clinical variables recorded between January 2016 and March 2022. The eligibility criteria were adults (>18 years) underdoing spine surgery (i.e., spinal arthrodesis, spinal decompression, disc herniation, and degenerative spinal deformity). Exclusion criteria were a baseline disability level according to the Oswestry Disability Index (ODI) < 20/100, trauma patients and surgery on the cervical spine or for idiopathic spinal deformity. Additionally, patients were only included if at least follow-up data at the 3- or 6-month and at the 12- or 24-month were available.

Sociodemographic data and outcome measures

Baseline characteristics and clinical data included: age, sex, body mass index (BMI), smoking status, and score in the physical status classification system according to the American Society of Anesthesiologists (ASA). The independent variable for classifying patients was the pre-operative MCS of the SF-36, i.e., with pre-operative depressive symptoms (MCS \leq 35: *depression group*) or without (MCS > 35: *non-depression group*) [9]. The SF-36 was designed to assess the quality of life and different physical and mental health domains, and its scores can be reduced to two general components: physical component summary (PCS) and MCS, with final values ranging from 0 (worst health) to 100 (best health) [8].

The primary outcome was to examine the ODI score trajectory over the 24-month post-surgery between groups. The ODI is a self-report questionnaire that consists of 10 items that are rated from 0 to 5 [17]. The overall ODI score is expressed in percentage, and higher scores indicate higher disability levels [18]. The MCS score trajectory was examined over the 24-month post-surgery as a secondary outcome.

Additionally, a secondary subgroup analysis was conducted within *pre-operative depression* and *non-depression* groups comparing outcomes between those with depressive symptoms at 3-month after surgery (i.e., MCS \leq 35 at 3-month: *persistent-depression subgroup* or *new-onset depression subgroup*) and those without depressive symptoms at 3-month after surgery (i.e., MCS > 35 at 3-month: *recovered-depression subgroup* or *never-depression subgroup*).

Statistical analysis

In the case of missing data, an imputation using the nearest available observation was conducted, where the last recorded value was carried forward (backward in case of 3-months missing data). This imputation method is considered almost unbiased for missing follow-up in time [19]. Baseline characteristics were compared between groups using independent t-tests, Exact Fisher tests, or Chi-squared tests.

A two-way mixed model repeated-measures analysis of variance (RM-ANOVA) with *time* (baseline, 3-month, 6-month, 12-month, and 24-month) as a repeated factor, and *group* (*depression group* and *non-depression group*) as between factor was conducted to investigate ODI total scores and MCS. Bonferroni correction was used as a post hoc test.

The secondary analysis consisted of replicating the statistics described previously. The comparison focused on the post-operative depression group (*persistent-depression subgroup* and *new-onset depression subgroup*) and the postoperative non-depression group (*recovered-depression subgroup* and *never-depression subgroup*).

Finally, a stepwise multivariate linear regression was conducted to assess what measures interacted in predicting ODI total score at 24 months, including pre-operative ODI, pre-operative MCS, MCS at 3 months, age, sex, BMI, smoking status, ASA > 2, and PCS as independent variables. Cohen's f^2 index was calculated to determine the contribution of each variable in the predicting model, where $f^2 \ge 0.02$, $f^2 \ge 0.15$, and $f^2 \ge 0.35$ represent small, medium, and large effect sizes, respectively [20]. Statistical significance was set at P < 0.05.

 Table 1
 Baseline
 characteristics
 of
 participants
 classified
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 Mental
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| | Pre-operative depression group $n = 400$ | Pre-operative non- depression group $n = 1764$ |
|--------------------------|--|---|
| Age (years) | 56.3 [55.1–57.6] | 56.5 [55.8–57.2] |
| Female (<i>n</i> , %) | 294 (73.5%) | 993 (56.3%) |
| BMI (kg/m ²) | 25.1 [24.6-25.5] | 25.1 [24.9–25.3] |
| Smoker (<i>n</i> , %) | 75 (18.8%) | 342 (19.4%) |
| ASA≥3 (<i>n</i> , %) | 56 (14.0%) | 190 (10.8%) |
| ODI (0-100) | 59.4 [57.9-60.1] | 46.1 [45.4–46.8] |
| MCS (100-0) | 29.7 [29.3–30.1] | 49.9 [49.5–50.4] |
| PCS (100-0) | 32.3 [31.7–32.8] | 32.2 [31.9–32.6] |

Values are expressed in mean [95% confidence intervals] or n (%). *Pre-operative depression group*: MCS \leq 35 at baseline; *Pre-operative non-depression group*: MCS > 35 at baseline; *ASA* American Society of Anaesthesiologist class, *BMI* Body Mass Index, *ODI* Oswestry Disability Index, *PCS* Physical Component Summary, *MSC* Mental Component Summary. *Significant differences between groups (*P* < 0.05)

Results

A total of 2164 patients who underwent spine surgery were included in this study. Out of them, the surgery procedures rate was 60.1% (n=1332) arthrodesis, 18.0% (n=400) disc herniation, 10.2% (n=225) degenerative spinal deformity, 9.3% (n=207) decompression. The baseline characteristics of *depression* and *non-depression* groups are presented in Table 1. The *depression group* had a higher proportion of females than males and showed higher ODI and lower MCS scores at baseline than the *non-depression group*. The percentage of missing data at 3, 6, 12, and 24 months was 18%, 22%, 15%, and 31%, respectively.

Trajectory of ODI total score

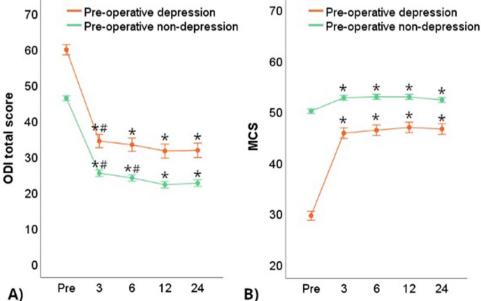
A group*time interaction was found (RM-ANOVA: $F_{4,8864} = 9.42$; P < 0.001). The pre-operative depression group reported higher ODI total scores than the pre-operative non-depression group at all time points (Bonferroni: P < 0.001). Significant lower ODI total scores were displayed in both groups at all follow-ups compared to baseline (Bonferroni: P < 0.001) (Fig. 1A).

Trajectory of MCS

A group*time interaction was found (RM-ANOVA: $F_{4,8864} = 231.9$; P < 0.001). The pre-operative depression group reported lower MCS than the pre-operative non-depression group at all time points (Bonferroni: P < 0.001). Significant higher MCS were displayed in both groups at

Fig. 1 Mean and 95% confidence intervals of the Oswestry Disability Index (ODI) and the Mental Component Summary (MCS) in the study groups according to the pre-operative scores of the Mental Component Summary (MCS) at baseline, 3-, 6-, 12-, and 24-month post-surgery. There were between-group differences at all time points (Bonferroni: P < 0.05). *Within-group differences compared to baseline (Bonferroni: P < 0.05); # Within-group differences compared to 24-month (Bonferroni: P < 0.05)





all follow-ups compared to baseline (Bonferroni: P < 0.001) (Fig. 1B).

Secondary analysis of post-operative depression subgroups

Table 2 presents baseline characteristics of the *pre-operative depression* and the *pre-operative non-depression* subgroups. On the one hand, 400 subjects belonged to the *pre-operative depression group*. At 3-month follow-up, 78 patients still maintained an MCS \leq 35 (*Persistent-depression subgroup*), and 322 patients reached an MCS > 35 (*Recovered-depression subgroup*). The *persistent-depression subgroup* showed lower MCS and PCS scores at baseline than the *recovered-depression group*. On the other hand, 1764 subjects belonged to the *pre-operative non-depression group*. At 3-month follow-up, 1680 patients still maintained an MCS > 35 (*never-depression subgroup*), and 84 patients reached an MCS \leq 35 (*new-onset depression subgroup*). The *new-onset depression subgroup* showed a lower MCS score at baseline than the *never-depression group*.

For ODI total scores in the *pre-operative depression group*, a *subgroup*time* interaction was found (RM-ANOVA: $F_{4,8864}$ =9.42; P < 0.001). The *persistent-depression subgroup* reported higher ODI total scores than the *recovered-depression subgroup* at all follow-ups (Bonferroni: P < 0.001) (Fig. 2a).

For MCS scores in the *pre-operative depression group*, a *subgroup*time* interaction was found (RM-ANOVA: $F_{4,1516}$ =54.29; *P*<0.001). The *persistent-depression subgroup* reported lower MCS than the *recovered-depression subgroup* at all time points (Bonferroni: *P*<0.002) (Fig. 2b).

For ODI total scores in the *pre-operative non-depres*sion group, a subgroup*time interaction was found (RM-ANOVA: $F_{4,6932} = 47.20$; P < 0.001). The *new-onset depression subgroup* reported higher ODI total scores than the *never-depression subgroup* at all follow-ups (Bonferroni: P < 0.001) (Fig. 2c).

For MCS scores in the *pre-operative non-depression* group, a subgroup*time interaction was found (RM-ANOVA: $F_{4,6620} = 72.10$; P < 0.001). The *new-onset* depression subgroup reported lower MCS than the *never*depression subgroup at all time points (Bonferroni: P < 0.001) (Fig. 2d).

Prediction models

Table 3 presents the factors hierarchically found to significantly predict worse ODI scores at 24-month after multivariate linear regression for the whole sample and pre-operative subgroups according to the MCS.

Considering the whole sample and the *pre-operative non-depression group*, the main predictors of worse ODI scores at 24-month were higher pre-operative ODI, lower MCS at 3-month, higher age, and lower pre-operative PCS. In contrast, the main hierarchical predictors in the pre-operative depression groups were lower pre-operative PCS, lower MCS at 3-month, higher age, higher pre-operative ODI, and reporting ASA class > 2.

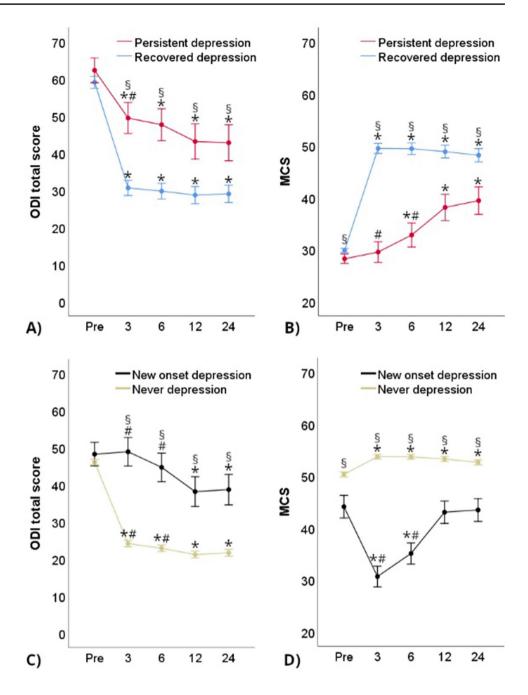
Pre-operative MCS did not contribute to predicting the outcome in any models. However, it had a small contribution to predicting ODI total score at 24-month when MCS at 3-month variable was removed from the models (Table 4).

Table 2Baseline characteristicsof participants in the pre-
operative depression and
pre-operative non-depression
subgroups classified according
to the Mental ComponentSummary (MCS) scores at
3-month post-surgery

| Pre-operative | Depression group | | Non-depression group | |
|--------------------------|---|--|--|---|
| Post-operative | Persistent depression subgroup $n = 78$ | Recovered depression subgroup $n = 322$ | New onset depression subgroup $n = 84$ | Never depression subgroup $n = 1680$ |
| Age (years) | 56.2 [53.1–59.3] | 56.4 [55.0–57.8] | 55.5 [52.5–58.6] | 56.6 [55.9–57.3] |
| Female $(n, \%)$ | 62 (79.5%) | 232 (71.8%) | 44 (53.0%) | 949 (56.5%) |
| BMI (kg/m ²) | 24.7 [23.7–25.8] | 25.1 [24.6-25.6] | 24.6 [23.5–25.7] | 25.1 [24.9–25.3] |
| Smoker (<i>n</i> , %) | 21 (26.9%) | 55 (17.1%) | 19 (22.6%) | 324 (19.3%) |
| ASA≥3 (<i>n</i> , %) | 16 (20.5%) | 40 (12.4%) | 13 (15.7%) | 177 (10.5%) |
| ODI (0-100) | 62.0 [58.6-65.5] | 58.8 [57.2-60.4] | 48.5 [45.4–51.6] | 45.9 [45.2–46.6] |
| MCS (100-0) | 28.4 [27.5–29.3]* | 30.0 [29.6–30.4] | 44.2 [42.5–45.9]* | 50.2 [49.8-50.7] |
| PCS (100-0) | 30.6 [29.4–31.9]* | 32.6 [32.0–33.2] | 31.2 [29.7–32.6] | 32.3 [32.0–32.6] |

Values are expressed in mean [95% confidence intervals] or n (%). Persistent depression subgroup: $MCS \le 35$ at 3 months with $MCS \le 35$ at baseline; Recovered depression subgroup: MCS > 35 at 3 months with $MCS \le 35$ at baseline; *New onset depression subgroup*: $MCS \le 35$ at 3 months with MCS > 35 at baseline; *Never depression subgroup*: MCS > 35 at 3 months with MCS > 35 at baseline; *Never depression subgroup*: MCS > 35 at 3 months with MCS > 35 at baseline; *Never depression subgroup*: MCS > 35 at 3 months with MCS > 35 at baseline; *Never depression subgroup*: MCS > 35 at 3 months with MCS > 35 at baseline; *Never depression subgroup*: MCS > 35 at 3 months with MCS > 35 at baseline; *Never depression subgroup*: MCS > 35 at 3 months with MCS > 35 at baseline; *Never depression subgroup*: MCS > 35 at 3 months with MCS > 35 at baseline; *ASA* American Society of Anesthesiologist class, *BMI* Body Mass Index, *ODI* Oswestry Disability Index, *PCS* Physical Component Summary, *MSC* Mental Component Summary. *Significant differences between subgroups (P < 0.05)

Fig. 2 Mean and 95% confidence intervals of the Oswestry Disability Index (ODI) and the Mental Component Summary (MCS) in the pre-operative depression and the pre-operative non-depression groups stratified according to the scores of the MCS at 3-month (Persistentdepression subgroup: MCS \leq 35 at 3 months with MCS \leq 35 at baseline; Recovered-depression subgroup: MCS > 35 at 3 months with MCS \leq 35 at baseline; New-onset depression subgroup: MCS \leq 35 at 3 months with MCS > 35 at baseline; never-depression subgroup: MCS > 35 at 3 months with MCS > 35 at baseline) displayed at baseline, 3-, 6-, 12-, and 24-month post-surgery. § Between-group differences (Bonferroni: P<0.05); *Withingroup differences compared to baseline (Bonferroni: P < 0.05); # Within-group differences compared to 24-month (Bonferroni: P < 0.05)



Discussion

This register-based study investigated the influence of peri-operative depressive symptoms on clinical outcomes in patients undergoing spinal surgery up to 24-month. We found that patients' functional disability and mental status improved after surgical treatment regardless of whether they presented pre-operative depressive symptoms. However, the secondary analysis showed that this improvement mainly happened in those patients that did not present depressive symptoms at 3-month after surgery.

Primary analysis: the role of pre-operative depression symptoms

Both groups reported the most remarkable improvement in disability during the first three months after surgery. However, patients with depressive symptoms were characterized by higher disability at baseline and all follow-ups. Nevertheless, they showed a larger improvement in ODI at all follow-ups compared to the *non-depression group*. Cushnie et al. [10] also found this pattern, which the most plausible reason may be because patients with depression, and higher disability, had a higher chance to reduce ODI scores than

Table 3 Factors predicting Oswestry Disability Index (ODI) score at24-month after multivariate linear regression of the whole sample andpre-operative group according to the Mental Component Summary(MCS)

| # | Factors | Beta [95% CI] | Р | f² |
|-----|---------------------|-------------------------|---------|------|
| Wh | ole sample n=2164 | 4 | | |
| 1 | ODI pre-op | 0.23 [0.17 to 0.30] | < 0.001 | 0.16 |
| 2 | MCS 3-months | -0.55 [-0.63 to -0.48] | < 0.001 | 0.08 |
| 3 | Age | 0.23 [0.17 to 0.29] | < 0.001 | 0.04 |
| 4 | PCS pre-op | -0.37 [-0.53 to -0.22] | < 0.001 | 0.01 |
| 5 | Female | 4.63 [2.93 to 6.33] | < 0.001 | 0.01 |
| 6 | ASA class > 2 | 6.89 [4.08 to 9.70] | < 0.001 | 0.01 |
| Pre | e-operative Depress | ion group $n = 400$ | | |
| 1 | PCS pre-op | -1.47 [-1.91 to -1.02] | < 0.001 | 0.16 |
| 2 | MCS 3-months | -0.55 [-0.73 to -0.36] | < 0.001 | 0.07 |
| 3 | Age | 0.34 [0.17 to 0.51] | < 0.001 | 0.06 |
| 4 | ODI pre-op | 0.38 [0.23 to 0.52] | < 0.001 | 0.02 |
| 5 | ASA class > 2 | 10.93 [4.07 to 17.78] | 0.002 | 0.02 |
| Pre | e-operative Non-dep | pression group n = 1764 | | |
| 1 | ODI pre-op | 0.19 [0.12 to 0.27] | < 0.001 | 0.12 |
| 2 | MCS 3-months | -0.54 [-0.63 to -0.46] | < 0.001 | 0.07 |
| 3 | Age | 0.22 [0.16 to 0.28] | < 0.001 | 0.04 |
| 4 | PCS pre-op | -0.41 [-0.58 to -0.25] | < 0.001 | 0.02 |
| 5 | Female | 4.30 [2.51 to 6.09] | < 0.001 | 0.01 |
| 6 | ASA class > 2 | 5.79 [2.72 to 8.86] | < 0.001 | 0.01 |

Pre-operative depression group: $MCS \le 35$ at baseline; Pre-operative non-depression group: MCS > 35 at baseline; ASA American Society of Anaesthesiologist class, PCS Physical Component Summary, MCS 3-month Mental Component Summary at 3-month follow-up

non-depressed subjects. The mental status, assessed through MCS, improved in both groups after surgery but remained lower in the participants with pre-operative *depressive symptoms group* throughout the whole follow-up. Other than the Δ ODI, the 3-month Δ MCS was the largest difference in the *depression group*. However, in contrast to ODI, the trajectory of the MCS score showed no further improvement after the 3-month follow-up in both groups. Overall, our results indicate that the main improvements in disability and depressive symptoms were likely to happen soon after surgery. Some trends in the non-depression group showed a continuous slight improvement over time but only in terms of ODI.

In previous studies, Lafage et al. [21] investigated the effect of mental status on ODI in patients undergoing surgery for adult degenerative scoliosis. They compared a group of patients with MCS scores below the 25th percentile (Low-MCS: \leq 35) and above the 75th percentile (High-MCS: \geq 57.3), comprising a cohort of 513 subjects. The authors found a significant improvement in ODI after surgery in both groups. However, the Δ ODI and Δ MCS between pre-operative and 2-year follow-up scores were

 Table 4
 Factors predicting Oswestry Disability Index (ODI) score at 24 months after multivariate linear regression of the whole sample and pre-operative groups according to the Mental Component Summary (MCS) without including MCS at 3 months in the models

| Factors | Beta [95% CI] | Р | f² |
|--------------------|--|--|--|
| ole sample n=216 | 54 | | |
| ODI pre-op | 0.21 [0.13 to 0.29] | < 0.001 | 0.17 |
| Age | 0.20 [0.15 to 0.27] | < 0.001 | 0.03 |
| MCS pre-op | -0.24 [-0.32 to -0.16] | < 0.001 | 0.02 |
| Female | 4.79 [3.04 to 6.54] | < 0.001 | 0.02 |
| ASA class > 2 | 7.51 [4.66 to 10.40] | < 0.001 | 0.01 |
| pression group n= | 400 | | |
| ODI pre-op | 0.23 [0.32 to 0.42] | 0.023 | 0.16 |
| Age | 0.29 [0.12 to 0.47] | 0.001 | 0.06 |
| ASA class > 2 | 9.48 [2.89 to 16.06] | 0.005 | 0.02 |
| Female | 7.55 [2.65 to 12.40] | 0.003 | 0.02 |
| MCS pre-op | -0.84 [-1.40 to -0.28] | 0.004 | 0.02 |
| PCS pre-op | -0.64 [-1.20 to -0.08] | 0.025 | 0.01 |
| n-depression group | p n = 1764 | | |
| ODI pre-op | 0.20 [0.12 to 0.29] | < 0.001 | 0.12 |
| Age | 0.18 [0.12 to 0.25] | < 0.001 | 0.03 |
| PCS pre-op | -0.51 [-0.69 to -0.32] | < 0.001 | 0.02 |
| MCS pre-op | -0.19 [-0.29 to -0.08] | < 0.001 | 0.01 |
| Female | 4.23 [2.35 to 6.04] | < 0.001 | 0.01 |
| ASA class > 2 | 6.81 [3.63 to 9.77] | < 0.001 | 0.01 |
| | ole sample n = 216 ODI pre-op Age MCS pre-op Female ASA class > 2 pression group n = ODI pre-op Age ASA class > 2 Female MCS pre-op PCS pre-op Age PCS pre-op Age PCS pre-op MCS pre-op Female | ole sample $n = 2164$ ODI pre-op0.21 [0.13 to 0.29]Age0.20 [0.15 to 0.27]MCS pre-op $-0.24 [-0.32 to -0.16]$ Female4.79 [3.04 to 6.54]ASA class > 27.51 [4.66 to 10.40]pression group $n = 400$ ODI pre-op0.23 [0.32 to 0.42]Age0.29 [0.12 to 0.47]ASA class > 29.48 [2.89 to 16.06]Female7.55 [2.65 to 12.40]MCS pre-op $-0.64 [-1.20 to -0.28]$ PCS pre-op $-0.64 [-1.20 to -0.08]$ e-depression group $n = 1764$ ODI pre-op0.20 [0.12 to 0.29]Age0.18 [0.12 to 0.25]PCS pre-op $-0.51 [-0.69 to -0.32]$ MCS pre-op $-0.19 [-0.29 to -0.08]$ Female4.23 [2.35 to 6.04] | oble sample $n = 2164$ ODI pre-op $0.21 [0.13 \text{ to } 0.29]$ < 0.001 Age $0.20 [0.15 \text{ to } 0.27]$ < 0.001 MCS pre-op $-0.24 [-0.32 \text{ to } -0.16]$ < 0.001 Female $4.79 [3.04 \text{ to } 6.54]$ < 0.001 ASA class > 2 $7.51 [4.66 \text{ to } 10.40]$ < 0.001 oression group $n = 400$ $0.23 [0.32 \text{ to } 0.42]$ 0.023 Age $0.29 [0.12 \text{ to } 0.47]$ 0.001 ASA class > 2 $9.48 [2.89 \text{ to } 16.06]$ 0.005 Female $7.55 [2.65 \text{ to } 12.40]$ 0.003 MCS pre-op $-0.84 [-1.40 \text{ to } -0.28]$ 0.004 PCS pre-op $-0.64 [-1.20 \text{ to } -0.08]$ 0.025 e -depression group $n = 1764$ 0.001 AgeODI pre-op $0.20 [0.12 \text{ to } 0.29]$ < 0.001 Age $0.18 [0.12 \text{ to } 0.25]$ < 0.001 MCS pre-op $-0.51 [-0.69 \text{ to } -0.32]$ < 0.001 PCS pre-op $-0.19 [-0.29 \text{ to } -0.08]$ < 0.001 PCS pre-op $-0.13 [2.35 \text{ to } 6.04]$ < 0.001 |

Depression group: MCS \leq 35 at baseline; non-depression group: MCS > 35 at baseline; ASA American Society of Anaesthesiologist class, PCS Physical Component Summary at baseline, MCS pre-op Mental Component Summary at baseline

greater in the Low-MCS group [21]. Consistently with our results, they showed that patients with depressive symptoms experience an improvement in mental health and disability scores after surgery similar to or even higher in absolute terms than patients without depressive symptoms. Nevertheless, they never reach the levels of non-depressed subjects. On the other hand, Cushnie et al. [10] analyzed a large cohort (2310 subjects) from the Canadian registry of spine patients, including any thoracolumbar spinal surgery. They tested the association between ODI and depressive symptoms with the Patient Health Questionaire-9. At the 2-year follow-up, the greater Δ ODI was found in patients pre-operatively categorized with severe depression. However, as previously reported by Lafage et al. [21] and consistently with our results, the post-operative ODI score remained higher in depressed patients, indicating higher levels of disability [10]. Similarly, Stull et al. [11] categorized 391 patients undergoing lumbar fusion according to two different validated cut-offs of MCS scores: 45.6 [22] and 35.0 [9, 23]. Both analyses found significant differences in baseline and 2-year ODI scores compared to non-depressed patients and a small but not significant difference in Δ ODI in favor of those

presenting depressive symptoms. However, the smaller sample of subjects, which usually implies a larger confidence interval [24], may be the reason for partial disagreements with our results.

Despite some discrepancies, our results align with previous studies to agree that patients with pre-operative depressive symptoms have a greater functional disability before and after spinal surgery than subjects without depressive symptoms. However, both their mental health and functional scores improve after surgery, and the amount of this improvement may be even greater than in non-depressed patients. These results suggest that surgeons may be confident of a gradual and steady improvement in mental status and disability, even in patients with pre-operative depressive symptoms.

Secondary analysis: the role of post-operative depression symptoms

The analysis of the trajectory of post-operative ODI provided interesting hints. In contrast to previous studies, our research further investigated the role of post-operative depressive signs (MCS \leq 35.0) at the first post-operative follow-up: 3-month. Indeed, the pre-operative depression and non-depression groups were further stratified based on 3-month follow-ups in fourth categories as shown in Table 2. In the case of post-operative depression symptoms, regardless of whether presenting pre-operative depressive symptoms or not, showed similar ODI scores at baseline if compared to the post-operative non-depressive symptoms.

In general, the *recovered-depression* and *never-depression* subgroups experienced a much greater ODI improvement at the first post-operative follow-up at 3 months if compared with *persistent-depression* and *new-onset depression* subgroups, respectively.

Prediction models

Our multivariate linear regression found pre-operative MCS to be a predictive factor of medium-term disability, which is in line with previous studies [10–13], but only when the MCS at 3-month was not included in the model. However, it is essential to highlight that the MCS at 3-month contributed much more considerably than the pre-operative MCS ($f^2 = 0.07-0.08 \text{ vs.} f^2 = 0.01-0.02$) in predicting ODI at 24-month for the whole population and subgroup analysis. Overall, these findings suggest that the presence of post-operative depressive symptoms at three months overweight the effect of pre-operative depressive symptoms in long-term disability. Therefore, the presence of depressive symptoms before undergoing spine surgery should not be considered a factor of a bad prognosis per se, but monitoring depressive levels soon after surgery may be more relevant

for post-surgery decision-making. Spine surgeons should not preclude surgical treatment for depression symptoms; instead, they should disclose realistic expectations to achieve a higher post-operative patient satisfaction rate and the estimated time needed.

In light of the results obtained, preventive interventions tackling depressive symptoms in the pre-operative period seem less relevant than immediate post-operative. However, future studies may consider interventions in the short term after surgery when the depressive symptoms are detected as persistent or newly developed.

Limitations

There are some limitations to mention. The study's retrospective design determined a potential bias in the intervention procedure chosen in each case. Furthermore, we did not record if patients were diagnosed with depression before surgery or took anti-depressant treatment, which would allow a further subgroup analysis. As previously correctly pointed out by Lafage et al. [21], using an MCS cut-off to categorize patients as depressed or not may oversimplify the identification of the depressive disorder, which is defined by specific criteria listed in the Diagnostic and Statistical Manual of Mental Disorders [25]. It is worth noting that patients with greater disability levels may be more prone to be depressed, and subjects affected by depression may perceive a greater disability compared to patients with better mental status [26]. Thus, the reciprocal influence that mental health and disability have on each other may represent a vicious cycle, which is challenging to understand and quantify.

Conclusion

Our study emphasizes the importance of assessing the mental status of patients with spinal disorders before and after surgery and shows that patients with depressive symptoms undergoing spinal surgery experience a significant improvement in ODI and MCS. However, their disability and mental health remain worse compared to non-depressed individuals. Furthermore, patients with post-operative depressive symptoms tend to improve less and slower. Therefore, physicians and surgeons should accurately screen the peri-operative mental status of their patients and discuss surgical expectations accordingly.

Author contributions B-L, FM, FL, MB-B, PB contributed to Concept and design. FM, MB-B, RB, FG, AL, CM, DV contributed to Acquisition of data. FM, FL, MB-B, RB, AL contributed to Analysis and interpretation of data. PB-L, FM, FL, RC, FG, DV, MP contributed to Drafting of the manuscript. RC, DC, CM, LS, DV, MP, PB contributed to Critical revision of paper for important intellectual content. RC, DC, CM, LS, DV, MP, PB contributed to Statistical analysis.RB, DC, FG, AL, MP contributed to Provision of study materials or patients. PB-L, CM, LS, PB contributed to Obtaining funding. PB-L contributed to administrative, technical, or logistic support. PB-L, PB contributed to Supervision.

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Data availability The datasets used and/or analyzed in the present study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest Bassani is consultant for Nuvasive—DePuy—J&J; Cecchinato is consultant for Nuvasive – Medacta; Vanni is consultant for Stryker; Berjano is consultant for Nuvasive—Medacta—Alphatec—K2M and has received research support from K2M – DePuy—J&J—Nuvasive and royalties from Nuvasive.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. The institutional ethics committee granted ethical permission (second amendment to the SPINEREG protocol issued on 13/04/2016).

Consent to participate Informed consent was obtained from all individual participants included in the institutional registry.

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