Extent of intraoperative muscle dissection does not affect long-term outcomes after minimally invasive surgery versus open-transforaminal lumbar interbody fusion surgery: A prospective longitudinal cohort study

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Abstract

Background: Minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) versus open TLIF, addressing lumbar degenerative disc disease (DDD) or grade I spondylolisthesis (DS), are associated with shorter hospital stays, decreased blood loss, quicker return to work, and equivalent short- and long-term outcomes. However, no prospective study has assessed whether the extent of intraoperative muscle trauma utilizing creatinine phosphokinase levels (CPK) differently impacts long-term outcomes.

Methods: Twenty-one patients underwent MIS-TLIF (n = 14) versus open-TLIF (n = 7) for DDD or DS. Serum CPK levels were measured at baseline, and postoperatively (days 1, 7, and 1.5, 3 and 6 months). The correlation between the extent of intraoperative muscle trauma and two-year improvement in functional disability was evaluated (multivariate regression analysis). Additionally, baseline and two-year changes in Visual Analog Scale (VAS)-leg pain (LP), VAS-back pain (BP), Oswestry Disability Index (ODI), Short-Form-36 (SF-36) Physical Component Score (PCS) and SF-36 Mental Component Score (MCS), and postoperative satisfaction with surgical care were assessed.

Results: Although the mean change from baseline in the serum creatine phosphokinase level on POD 1 was greater for MIS-TLIF (628.07) versus open-TLIF (291.42), this did not correlate with lesser two-year improvement in functional disability. Both cohorts also showed similar two-year improvement in VAS-LP, ODI, and SF-36 PCS/MCS.

Conclusion: Increased intraoperative muscle trauma unexpectedly observed in higher postoperative CPK levels for MIS-TLIF versus open-TLIF did not correlate with any differences in two-year improvement in pain and functional disability.

Key Words: Long-term outcomes, minimally invasive transforaminal lumbar inter-
body fusion, Open-transforaminal lumbar interbody fusion, Serum creatine phosphokinase

INTRODUCTION

Harms and Rolinger first described the open transforaminal lumbar interbody fusion (TLIF) technique in 1982. It was devised to improve fusion rates, maintain vertebral alignment, and relieve mechanical back pain (BP). However, as previous studies reported on the harmful effects of the extensive muscle dissection and retraction required to perform traditional open-TLIF procedures, the muscle splitting technique utilized to minimize muscle trauma was developed for minimally invasive surgery (MIS)-TLIF. Although MIS-TLIF have resulted in decreased hospital stays, shorter rehabilitation periods, and quicker resumption of daily activities, they have not resulted in statistically better functional improvement. Furthermore, although a major theoretical advantage of MIS should be the reduction of unnecessary exposure and tissue trauma, no prospective study has quantified how/whether the degree of intraoperative tissue trauma reflected in postoperative serum CPK levels should differentially impact long-term clinical outcomes for MIS-TLIF versus open-TLIF surgery.

MATERIALS AND METHODS

Patient selection
The primary aim of this two-year prospective study was to determine whether increased tissue distraction (based on the change in postoperative serum CPK levels), presumably more attributed to open-TLIF versus MIS-TLIF, would result in less improvement in pain/functional disability (change in ODI score). All patients underwent TLIF surgery by one of the two fellowship-trained spine surgeons at our institution. The institutional review board approved this study. The inclusion criteria included: (1) magnetic resonance imaging (MR) evidence of degenerative disc disease (DDD) or grade I spondylolisthesis (DS); (2) mechanical low back pain and radicular symptoms; (3) age between 18 and 70 years old; and (4) failure of at least 6 weeks of conservative therapy. The exclusion criteria included: (1) prior back surgery; (2) an extraspinal cause of back pain or sciatica; (3) an active medical or workman’s compensation lawsuit; (4) any pre-existing spinal pathology; or (5) unwillingness or inability to participate with follow-up procedures. Patients with notable associated abnormalities, such as inflammatory arthritis, or metabolic bone disease, were also excluded.

Clinical parameters
Twenty-one patients undergoing MIS-TLIF or open-TLIF between 2008 and 2009 were prospectively entered into the database, and none were excluded or lost to follow-up. The overall mean ± SD age was 47.28 ± 9.86 years (14 women and 7 men) [Table 1]. All patients presented with back pain and leg pain with associated radiculopathy and radiographic evidence attributed to MR-documented DDD in eight patients or grade I DS in 13 patients. Of the eight patients presenting with radiographic evidence of DDD, one had an extruded disc, while seven had “black discs” with associated neurological deficits. All 13 patients presenting with grade I DS had clinical and radiographic evidence of central/foraminal stenosis. The overall mean ± SD duration of symptoms was 68.90 ± 66.60 months (MIS-TLIF: 75.14 ± 75.96; open-TLIF: 56.42 ± 44.82; P = 0.48) [Table 1].

Baseline and two-year clinical outcome measures
Two-year outcomes after TLIF surgery were prospectively assessed. Baseline and two-year postoperative pain/functional disability were assessed via face-to-face interviews by an independent investigator who was not involved with the clinical care. Questionnaires administered included: the Visual Analog Scales for low back pain (BP-VAS) and leg pain (LP-VAS), the Oswestry Disability Index (ODI), the SF-36 physical component score (PCS), the SF-36 mental component scores (MCS) for the assessment of mental health status. All patients were considered to be appropriate candidates for either MIS-TLIF or open-TLIF surgery.

At presentation, the overall mean ± SD back pain-VAS and leg-pain-VAS were 6.60 ± 2.12 (MIS-TLIF: 6.80 ± 2.40; open-TLIF: 6.14 ± 1.67; P = 0.47) and 5.74 ± 2.82 (MIS-TLIF: 5.99 ± 2.61; open-TLIF: 6.07 ± 2.69; P = 0.45) [Table 1].

Table 1: Demographic and comorbidity data for patients undergoing minimally invasive-transforaminal lumbar interbody fusion versus open transforaminal lumbar interbody fusion surgery

| Measure                          | MIS-TLIF (n = 14) | Open-TLIF (n = 7) | Combined cohort (n = 21) | P value |
|----------------------------------|-------------------|-------------------|--------------------------|---------|
| Mean age (years)                 | 48.14 ± 7.02      | 47.28 ± 8.12      | 47.28 ± 6.60             | 0.86    |
| BMI (kg/m²)                      | 30.71 ± 5.58      | 33.48 ± 8.57      | 31.79 ± 6.51             | 0.45    |
| Smoker (%)                       | 3 (21.42%)        | 5 (71.42%)        | 9 (42.85%)               | 0.04    |
| Hypertension (%)                 | 9 (64.28%)        | 4 (57.14%)        | 13 (61.90%)              | 0.77    |
| Diabetes (%)                     | 1 (7.14%)         | 1 (14.28%)        | 2 (9.52%)                | 0.66    |
| Duration of pain (months)        | 75.14 ± 13.21     | 56.42 ± 9.86      | 68.90 ± 66.60            | 0.45    |
| Data expressed as the mean ± SD or number (%) |                    |                   |                          |         |
The mean baseline ODI was 21.40 ± 8.00 (MIS-TLIF: 20.50 ± 7.76; open-TLIF: 22.57 ± 9.32; P = 0.62) [Table 2].

Assessment of postoperative narcotic use, time to return to work, general satisfaction

The duration of narcotic use and the time to return to work were documented in real time as part of a standard of care protocol. Patients were also asked about their general satisfaction with their overall care, and outcomes after spine surgery. Patient satisfaction was dichotomized as either “YES” or “NO” on whether they were satisfied with their surgical outcome 2 years after surgery.

Performance of minimally invasive transforaminal lumbar interbody fusion versus open-transforaminal lumbar interbody fusion by two surgeons based on “preference”

MIS-TLIF versus open-TLIF was performed purely based on surgeon preference. All open-TLIFs were performed by one surgeon who uniformly preferred open approaches, while MIS-TLIFs were performed by a second surgeon who uniformly preferred MIS approaches. Nevertheless, both surgeons practiced similar postoperative management paradigms. In all cases, surgeons encouraged discharge from the hospital beginning 72 hours after surgery, weaned patients off narcotics beginning 2–3 weeks after surgery, and returned patients to work as soon as the patient felt capable.

Creatine phosphokinase measurements

Creatine phosphokinase (CPK) is an enzyme that is found primarily in skeletal muscle. Trauma and other conditions that damage skeletal muscle elevate serum CPK levels. To assess the significance of intraoperative muscle damage on long-term outcomes, peripheral venous blood samples were collected before surgery, and then postoperatively; days 1 and 7, and 1.5, 3, and 6 months. Serum concentrations of total CPK were measured using agarose gel electrophoresis, and the values were recorded in units/liter (U/L).

Statistical analysis

The primary aim of this study was to assess the independent effect of the extent of intraoperative muscle trauma on two-year outcomes (change in disability; ODI score) after MIS-TLIF versus open-TLIF surgery utilizing serum CPK levels. Parametric data were expressed as the mean ± standard deviation, and were compared utilizing the Student’s t-test. Nonparametric data are expressed as the median (interquartile range), and were compared utilizing the Mann–Whitney U-test. Nominal data were compared with the χ²-test. Variables trending or significantly associated with two-year ODI in univariate regression analysis (P < 0.10) were entered into a multiple linear regression model to identify the independent predictors of postoperative outcome (change in ODI score). Stepwise multiple regression was performed to identify all the variables that were independently associated with two-year ODI (P < 0.05).

RESULTS

MIS-TLIF: Shorter Surgery, Less Estimated Blood Loss and Hospital Length of Stay Versus Open-TLIF

MIS-TLIF and open-TLIF were performed at the L₄–L₅
(52%) and L₃–S₁(48%) levels, and solely involved one-level fusions. The mean ± SD duration of surgery was longer for MIS-TLIF procedures versus open-TLIF procedures (235 ± 88.36 min versus 211± 43.23, P = 0.60). The mean ± SD estimated blood loss during surgery was less for MIS-TLIF versus open-TLIF [220 ± 207.32 mL versus 280 ± 219.65, P = 0.61]. The median (inter quartile range) length of hospitalization after surgery was less for MIS-TLIF compared with open-TLIF [3.0 (3.0–4.0) versus 3.5 (3.5–4) days, P = 0.65].

**Minimal short-term postoperative complications**

Of interest, postoperatively, no patients from either surgical category developed surgical site infections, or hardware failures. There were no perioperative complications in the MIS-TLIF cohort, including the absence of cerebrospinal fluid (CSF) leaks. However, for patients undergoing open-TLIF, two exhibited incidental durotomies (CSF leaks) that were successfully repaired intraoperatively, without any subsequent complications.

**Relationship between serum creatine phosphokinase levels and duration of surgery**

CPK levels peaked higher for MIS-TLIF one day postoperatively versus open-TLIF, but both returned to comparable levels within one postoperative week. Prior to surgery, the mean ± SD CPK levels were slightly elevated for the open-TLIF (96 ± 50) versus MIS-TLIF (111 ± 130) (P = 0.68) patients. However, the peak mean ± SD serum CPK level on POD 1 was higher for MIS-TLIF (739 ± 1002) versus open-TLIF (387 ± 242; P = 0.23) [Figure 1]. At one postoperative week, both levels subsequently decreased to normal.

**Differences in postoperative creatine phosphokinase levels for men and women**

Preoperatively, there was no statistically significant difference in serum CPK levels between males and females (males: 188.33 ± 175.41 U/L; females: 73.46 ± 36.28 U/L; P = 0.17). As expected, on the first postoperative day, the total serum CPK level was significantly higher in males (1332.15 ± 1095 U/L) versus females (284.06 ± 134.85 U/L, P = 0.03) [Figure 2]. This was presumably attributed to the greater overall muscle mass dissection required in the typically larger and more muscular male patients. The total serum CPK profile stratified by gender is shown in Figure 2.

**Two-year outcomes**

Both MIS-TLIF and open-TLIF cohorts demonstrated similar improvement in back pain-VAS, leg-pain-VAS, ODI, SF-36 PCS, and SF-12 MCS. The mean two-year outcomes were significantly improved from baseline levels for VAS-BP (3.14 versus 6.14 P = 0.0001), VAS-LP (1.58 versus 6.07, P = 2.94E-05), ODI (11.95 versus 22.57, P = 0.007), SF-36 PCS (39.28 versus 27.25, P = 0.002), and SF-36 MCS (52.32 versus 37.00, P = 0.04) [Figure 3 and Table 3].

**Variables correlating with two-year improvement in pain/functional capacity**

In a univariate analysis, the baseline level of pain and
functional disability (preoperative ODI and VAS BP/LP), quality of life (preop SF-36 PCS, SF-36 MCS), BMI, estimated intraoperative blood loss (EBL), and the extent of intraoperative muscle damage (change in serum CPK level) were all associated with two-year improvement in pain and functional disability. Alternatively, patient age, comorbidities such as diabetes, HTN, MI, depression and osteoporosis, and the duration of symptoms were not associated with a two-year improvement in pain and functional disability.

### Correlation between postoperative creatine phosphokinase levels and two-year improvement in pain and functional disability

When included in a multivariate linear regression model, increasing intraoperative muscle damage (based on postoperative change in the serum CPK level) was not associated with less two-year improvement in pain and functional disability [Table 4]. Compared with patients in the bottom quartile (least intraop muscle damage; change in serum CPK levels), patients in the top quartile (most intraop muscle damage; change in serum CPK levels) experienced similar improvement in pain and functional disability (ODI change score, \(P = 0.71\)) two years after MIS-TLIF versus open-TLIF surgery.

### Correlation between postoperative change in serum cpk and patient satisfaction with care

Overall, 84% of patients reported being satisfied with their surgical outcome (MIS-TLIF: 85%; open-TLIF: 83%; \(P = 0.90\)). In a univariate analysis, baseline pain and functional disability (preop ODI and VAS BP/LP), quality of life (preop SF-36 PCS, SF-36 MCS), BMI, estimated intraoperative muscle damage (change in serum CPK level), history of depression, patient age, and gender were all associated with patient-reported satisfaction with care. When included in a multivariate linear regression model, the extent of intraoperative muscle damage (based on postoperative change in serum CPK level) was not associated with patient satisfaction [Table 5]. Independent of MIS-TLIF versus open-TLIF, patients in the top quartile (most intraoperative muscle trauma) of postoperative change in serum CPK level did not report less satisfaction with the outcome of their surgery and overall care experience compared with patients in the bottom quartile (least intraop muscle damage) (80% versus 80%).

| Variable | Coefficient | \(P\) value |
|----------|-------------|-------------|
| Patient age | 0.11 | 0.76 |
| Creatine phosphokinase (CPK) | -0.04 | 0.49 |
| Smoking | -0.16 | 0.70 |
| Depression | -2.88 | 0.83 |
| BMI | -0.45 | 0.64 |
| Preop VAS-BP | -1.88 | 0.47 |
| Preop VAS-LP | -1.11 | 0.51 |
| Pre-op SF-36 PCS | -0.46 | 0.56 |
| Preop SF-36 MCS | -0.67 | 0.20 |
| Preop ODI | -1.20 | 0.27 |

**Table 3: Two-Year Improvement in Pain and Functional Disability for Minimally invasive transforaminal lumbar interbody fusion Versus open-transforaminal lumbar interbody fusion**

|                     | MIS-TLIF \((n = 14)\) | Open-TLIF \((n = 7)\) | \(P\) value |
|---------------------|-------------------------|------------------------|-------------|
| Mean back-pain VAS  | 4.72 ± 3.31             | 1.21 ± 3.35            | 0.07        |
| Mean leg-pain VAS   | 4.08 ± 3.36             | 4.21 ± 3.77            | 0.94        |
| Mean ODI            | 11.44 ± 8.14            | 1.66 ± 14.16           | 0.15        |
| Mean SF-36 Physical health | 15.97 ± 10.13   | 12.95 ± 9.24           | 0.57        |
| Role physical       | 10.57 ± 11.32           | 4.7 ± 9.63             | 0.31        |
| Bodily pain         | 15.20 ± 12.89           | 6.0 ± 7.36             | 0.11        |
| General health      | 4.1 ± 10.15             | 2.08 ± 11.59           | 0.32        |
| Vitality            | 12.13 ± 11.97           | 4.75 ± 7.64            | 0.18        |
| Social functioning  | 12.2 ± 16.81            | 8.15 ± 6.65            | 0.54        |
| Role emotional      | 6.56 ± 11.13            | 10.55 ± 13.32          | 0.56        |
| Mental health       | 5.11 ± 10.71            | 8.33 ± 9.69            | 0.56        |
| SF-36 PCS           | 14.78 ± 11.08           | 5.13 ± 11.57           | 0.14        |
| SF-36 MCS           | 4.7 ± 10.47             | 7.18 ± 9.17            | 0.64        |

*Data expressed as the mean ± SD or number (%)*

**Table 4: Multivariate regression analysis of improvement in disability following Minimally invasive transforaminal lumbar interbody fusion versus open-transforaminal lumbar interbody fusion**

| Variable                     | Coefficient | \(P\) value |
|------------------------------|-------------|-------------|
| Patient age                  | 0.26        | 0.61        |
| Creatine phosphokinase (CPK) | 0.24        | 0.61        |
| Smoking                      | 2.14        | 0.14        |
| Depression                   | 4.26        | 0.03        |
| BMI                          | 2.17        | 0.14        |
| Gender                       | 0.53        | 0.46        |
| Preop VAS-BP                 | 0.57        | 0.45        |
| Preop VAS-LP                 | 1.44        | 0.22        |
| Preop SF-36 PCS              | 0.09        | 0.75        |
| Preop SF-36 MCS              | 0.99        | 0.31        |
| Preop ODI                    | 0.04        | 0.82        |

**Table 5: Analysis of variables associated with satisfaction after Minimally invasive transforaminal lumbar interbody fusion versus open-transforaminal lumbar interbody fusion**

| Variable                     | Coefficient | \(P\) value |
|------------------------------|-------------|-------------|
| Patient age                  | 0.26        | 0.61        |
| Creatine phosphokinase (CPK) | 0.24        | 0.61        |
| Smoking                      | 2.14        | 0.14        |
| Depression                   | 4.26        | 0.03        |
| BMI                          | 2.17        | 0.14        |
| Gender                       | 0.53        | 0.46        |
| Preop VAS-BP                 | 0.57        | 0.45        |
| Preop VAS-LP                 | 1.44        | 0.22        |
| Preop SF-36 PCS              | 0.09        | 0.75        |
| Preop SF-36 MCS              | 0.99        | 0.31        |
| Preop ODI                    | 0.04        | 0.82        |
DISCUSSION

Similar two-year outcomes for minimally invasive transfomaminal lumbar interbody fusion versus open-transforaminal lumbar interbody fusion: independent of muscle trauma

In this two-year prospective longitudinal cohort study, we assessed the clinical significance of elevated serum CPK levels on improvement in pain and functional disability 2 years after MIS-TLIF versus open-TLIF surgery. The two-year outcomes were similar, and independent of the extent of intraoperative muscle trauma. Independent of baseline levels of pain and functional disability, quality of life (preop SF-36 PCS, SF-36 MCS, BMI, and extent of surgical invasiveness, increasing serum CPK levels (a measure of muscle trauma) was not significantly or independently associated with less improvement in pain, functional disability, and patient reported satisfaction with care 2 years after MIS versus open-TLIF surgery.

Unanticipated higher creatine phosphokinase levels for minimally invasive transfomaminal lumbar interbody fusion

Although short-term (1 day) serum CPK levels were higher following MIS-TLIF procedures compared to open-TLIF procedures, no statistically significant long-term differences in postoperative serum CPK levels were found between the two. The higher one-day postoperative CPK levels found with MIS-TLIF were unexpected, as one would assume these procedures would involve “less muscle dissection”, resulting in lower serum CPK levels. One possible explanation might be the “iatrogenic compartment syndrome” that can develop around a “contained” surgical bed. The small incision and limited surgical area of MIS procedures could limit the available space that displaced muscle and blood volume may migrate into. This in turn could lead to greater endothelial cell dysfunction, increased volume in the interstitial space of the affected tissues, and consequently, increases in tissue pressure. In contrast, the open-TLIF procedures have longer incisions and wider surgical beds, which decrease intramuscular pressures, and, consequently reduce the likelihood of developing an “iatrogenic compartment syndrome.” Future randomized, prospective studies are needed to determine whether the muscle splitting technique utilized to place the tubular retractor system for the MIS-TLIF procedures result in more or less muscle trauma versus the subperiosteal detachment of the muscle from the spinous process characteristic of open-TLIF.

Comparable long-term pain and functional capacity outcomes for minimally invasive transfomaminal lumbar interbody fusion versus open-transforaminal lumbar interbody fusion

This study and others’ studies strongly suggest that both techniques (MIS-TLIF versus open-TLIF) are equally effective at relieving long-term pain, and provide similar benefits in long-term functional capacity. Peng and colleagues reported similar mean improvements in ODI and VAS, 2 years after (ODI: 16.2 versus 17.5; VAS: 10.0 versus 12.0) MIS-TLIF versus open-TLIF. Schizas and colleagues showed similar improvement in 2-year VAS and ODI scores following MIS-TLIF versus open-TLIF procedures. Ntoukas and colleagues also showed similar improvement in the 1-year mean VAS (2.0 versus 2.5) and ODI (15 versus 18) scores for MIS-PLIF versus open-PLIF approaches.

Other studies found an association between postoperative creatine phosphokinase and gender

A number of previous studies have found an association between postoperative serum CPK activity and gender. Shumate and colleagues reported that peak serum CPK levels were higher in males than in females and attributed this to the difference in muscle volume between the two. Termote and colleagues reported that the erector spinae and posterolateral muscles are larger in males than in females based on computed topographic evaluations. Analogous to these studies, we observed higher postoperative serum CPK levels in males versus females although both reported similar improvement in pain and functional disability 2 years after MIS-TLIF versus open-TLIF surgery.

Limitations of this study

Lack of Creatine phosphokinase isoenzyme measurement

The first key limitation of this study was the lack of CPK isoenzyme measurement. Creatine phosphokinase has three known isoenzymes: CPK-BB in the brain, CPK-MB in the heart, and CPK-MM in skeletal muscle. In this study, only total serum CPK concentration was measured; however, CPK-MM accounts for greater than 95% of the total CPK level. Therefore, it seems reasonable to analyze total serum CPK, although the CPK-MM is more specific for skeletal muscle injury.

Retrospective and nonrandomized study design

Another major limitation of this study is the lack of prospective randomization; one surgeon performed all open-TLIF procedures, and another performed all MIS-TLIF. These findings, therefore, may be surgeon-based/surgeon-specific and not generalizable. Nevertheless, the strength of the current study lies in the systematic postoperative evaluation of pain intensity and functional outcome in relation to serum CPK levels, and the unanticipated finding that, on postoperative day 1, more muscle trauma was associated with the longer MIS-TLIF versus open-TLIF procedures. Furthermore, the current study demonstrates that MIS-TLIF, using the tubular retractor system, was not superior to open-TLIF.
CONCLUSION

Although both MIS-TLIF and open-TLIF procedures provided comparable 2-year improvement in pain and functional capacity, contrary to expectations, MIS-TLIF was associated with greater muscular trauma reflected in higher short-term postoperative (1-day) serum CPK levels versus open-TLIF.

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