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Serum creatine phosphokinase as an indicator of muscle injury after various spinal and nonspinal surgical procedures

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Object. Muscle injury is inevitable during surgical exposure of the spine and is quantified by the release of creatine phosphokinase (CPK). No studies have been conducted on different spinal approaches and nonspinal surgery with regard to muscle injury. The present prospective cohort study was conducted to evaluate the results of postoperative serum CPK as an indicator of muscle injury in relation to various spinal and nonspinal procedures.

Methods. The authors analyzed data in 322 consecutive patients who had undergone 257 spinal and 65 nonspinal procedures. Primary procedures were performed in 264 patients and revision surgeries in 58. Spinal procedures were subdivided according to the degree of surgical invasiveness as follows: minimally invasive (microendoscopic lumbar discectomy, unilateral transflaval discectomy, and minithoracotomy), average invasiveness (bilateral lumbar discectomy, laminectomy, and anterior cervical discectomy), and extensive surgery (instrumented single or multilevel spondylodesis of the entire spinal column). Spinal localization, number of spinal levels involved, surgical approach, duration of surgery, and body mass index (BMI) were recorded. Creatine phosphokinase was measured before surgery and 1 day after surgery, and the CPK ratio (that is, the difference within one patient) was used as the outcome measure.

Results. There was a significant dose-response relationship between the CPK ratio and the degree of surgical invasiveness; extensively invasive surgery had the highest CPK ratio and minimally invasive surgery had the lowest. Thoracolumbar surgery had a significantly higher CPK ratio compared with those for cervical and nonspinal surgery. There was a slightly negative relationship between the number of spinal segments involved and the CPK ratio. The CPK ratio in revision surgery was significantly higher than in primary surgery. Posterior surgical approaches had a higher CPK ratio, and the ratios for unilateral compared with bilateral approaches were not significantly different. The duration of surgery and preoperative serum level of CPK significantly influenced postoperative CPK. There was also a significant association between CPK ratio and nonspinal surgery. Age, sex, and BMI were not significant factors.

Conclusions. Data in this study have shown a dose-response relationship between CPK and the extent of surgical invasiveness. Thoracolumbar surgery, posterior approaches, duration of surgery, revision surgery, and preoperative value of CPK were significant influencing factors for the CPK ratio. The clinical significance of the results in the present study is not known. *(DOI: 10.3171/SPI-07/09/282)*

Key Words • **creatine phosphokinase** • **muscle injury** • **spinal surgery**

During surgical exposure of the spinal column, muscle injury is inevitable, which has been demonstrated on postoperative magnetic resonance imaging.[1,7,8] Muscle trauma is quantified by the release of the enzyme CPK. Serum CPK is elevated after various lumbar spinal procedures and reaches a maximal value 1 day after surgery.[4–6,9,10,12]

Postoperative low-back pain is one of the main problems after lumbar spine surgery and may be associated with iatrogenic muscle devascularization and denervation;[11] therefore, it is important to limit muscle injury to reduce back pain. The concept of minimally invasive spine surgery refers to less tissue trauma, reduced low-back pain, shorter hospitalizations, and quicker resumption of daily activities. However, the relationship between limited muscle injury and reduced postoperative CPK elevation is controversial.[9,10] Whether an increased serum level of CPK, as a marker of muscle injury, is associated with significant postoperative low-back pain is unclear. It is not known whether postoperative CPK is related to different surgical approaches of the entire spinal column, either anterior or posterior, unilateral or bilateral, operation time, or a patient's BMI. Moreover, there is insufficient data on serum CPK samples obtained after nonspinal surgery.

Abbreviations used in this paper: BMI = body mass index; CPK = creatine phosphokinase; MED = microendoscopic lumbar discectomy.

The purpose of the present study was to determine a possible relationship between various spinal and nonspinal surgical procedures, and postoperative serum CPK levels.

Clinical Material and Methods

Study Design

Three hundred twenty-two consecutive patients, who underwent surgery between January 2004 and June 2004, were included in the present study. There were 173 male (53.7%) and 149 female (46.3%) patients with a mean age of 52.6 years (range 17–92). The patients' mean BMI was 25.9 (range 17.1–39.6). Two hundred fifty-seven spinal procedures (79.8%) and 65 nonspinal procedures (20.2%; controls) were performed; 264 cases (82%) were primary procedures and 58 (18%) were reoperations. The nonspinal procedures included craniotomy for various underlying pathological entities (41 cases), bur hole procedure for chronic subdural hematoma (nine cases), stereotactic tumor biopsy procedure (seven cases), and ventriculoperitoneal drainage (eight cases).

The spinal procedures were anatomically subdivided into cervical (46 cases), thoracic (15 cases), and lumbar surgery (196 cases). Thirty-seven patients underwent an anterior approach, 217 patients a posterior, and three patients a circumferential approach. In 105 patients the spinal column was exposed unilaterally and in 152 cases bilaterally. The number of involved spinal levels was documented as follows: one level in 176 patients, two levels in 47 patients, three levels in 13 patients, four levels in 14 patients, and more than four levels in seven patients. The median duration of surgery was 70 minutes (range 15–720 minutes). Demographic data are summarized in Table 1.

The various spinal and nonspinal surgical procedures are presented in Table 2. The spinal procedures were classified into three surgical subgroups corresponding to the degree of invasiveness as follows: minimally invasive (MED, unilateral transflaval lumbar discectomy, and minithoracotomy), average invasiveness (bilateral lumbar discectomy, laminectomy, and anterior cervical discectomy), and extensively invasive (instrumented single or multilevel spondylodesis of the entire spinal column). According to this classification, 109 patients (42.4%) were assigned to the minimally invasive group, 92 patients (35.8%) to the average invasiveness group, and 56 patients (21.8%) to the extensively invasive group.

The serum concentration of total CPK was measured before surgery (CPK1) and 1 day after surgery (CPK2). In our hospital, the normal serum CPK value in men is 25 to 200 IU/L and in women 25 to 170 IU/L.

TABLE 1

*Demographic data in 322 patients who underwent a spinal or nonspinal procedure**

Factor	No. of Patients (%)
sex	
male	173 (53.7)
female	149 (46.3)
mean age in yrs (range)	52.6 (17–92)
mean BMI (range)	25.9 (17.1–39.6)
median op time in mins (range)	70 (15–720)
spinal procedures	257 (79.8)
cervical	46 (17.9)
thoracic	15 (5.8)
lumbar	196 (76.3)
nonspinal procedures	65 (20.2)
craniotomy	41 (63.1)
bur hole	9 (13.8)
stereotactic tumor biopsy	7 (10.8)
VP drainage	8 (12.3)

* VP = ventriculoperitoneal.

TABLE 2

*Different surgical procedures and within-patient relative change in CPK**

Surgical Procedure	No. of Patients	Median CPK Ratio
spinal	257	4.02
cervical	46	2.46
ant discectomy	22	1.45
ant spondylodesis	7	3.36
laminectomy	7	2.41
pst spondylodesis	7	9.31
circumferential spondylodesis	3	4.49
thoracic	15	7.25
minithoracotomy	4	6.12
thoracotomy	3	10.82
laminectomy	4	7.12
costotransversectomy	1	5.92
spondylodesis	3	7.25
lumbar	196	4.18
MED	39	2.43
unilat discectomy	67	3.21
bilat discectomy	16	5.24
interlaminar decompression	19	4.88
laminectomy	25	5.17
spondylodesis	30	19.2
nonspinal	65	1.81
craniotomy	41	3.79
bur hole	9	1.14
stereotactic tumor biopsy	7	1.19
VP drainage	8	1.59

* The CPK ratio = CPK2/CPK1. The median CPK ratios for all procedures are shown. Abbreviations: ant = anterior; pst = posterior.

Statistical Analysis

Both CPK1 and CPK2 are nonnormally distributed and heavily skewed; therefore, all analyses were performed on the log transforms of these two variables. The log(CPK) is perfectly normally distributed. The variable of interest (dependent variable) is the CPK ratio (CPK2/CPK1), which characterizes the within-patient relative change in CPK. Given that $\log(CPK2/CPK1) = \log(CPK2) - \log(CPK1)$, the difference (being perfectly normally distributed as shown in Fig. 1) can be used as the outcome variable in a multivariable analysis of variance (regression analysis). The final regression model predicts the log(CPK ratio) using sex and type of surgery as fixed factors and age and BMI as continuous covariates. No interaction terms were studied, and all main effects were assessed in the final model. Estimates of marginal means were visualized as profile plots for prediction purposes. Statistical significance was set at the probability level of 0.05. The method of least significant differences was used for pairwise comparisons

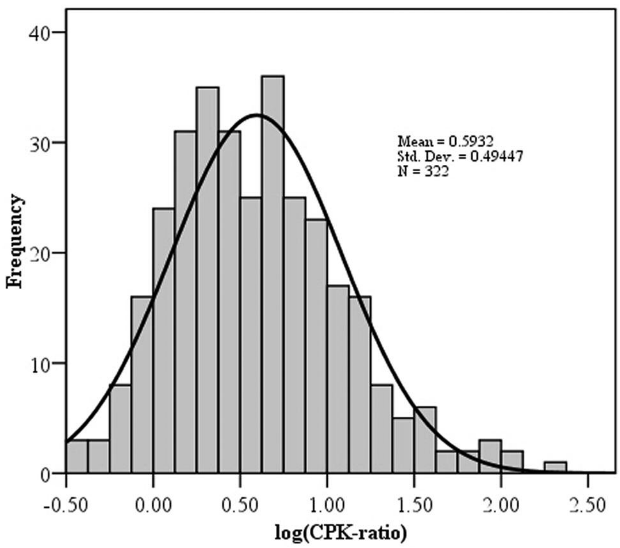

FIG. 1. Bar graph demonstrating the normally distributed within-patient CPK difference (log[CPK ratio]), which was calculated from the log transform of the heavily skewed and nonnormally distributed CPK1 and CPK2. Frequency on the y axis refers to the number of patients. N = total number of patients; Std. Dev. = standard deviation.

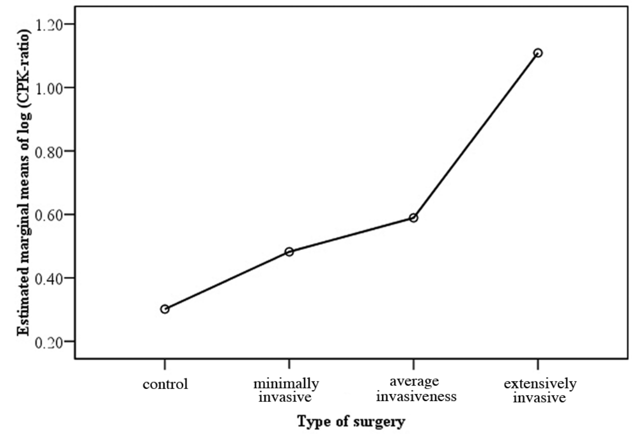

FIG. 2. Graph depicting the relationship between the invasiveness of surgery and log(CPK ratio). Note that 0.00 corresponds to a CPK ratio of 1, and 1.00 to a CPK ratio of exp(1) = 2.7. A clear monotonous dose-response relationship is shown. All groupwise comparisons were significant at the 0.01 level except for the comparison between surgery with average invasiveness and minimally invasive surgery, which was borderline significant ($p = 0.09$).

to adjust for multiple testing when analyzing a factor with more than two categories. The covariates were chosen a priori because they were assumed to be a possible risk factor (predictor) for the postoperative CPK level.

Results

Among all patients, the median CPK1 was 87.5 IU/L, the median CPK2 368.5 IU/L, and the median CPK ratio 3.59. When the spinal procedures were categorized into anatomical regions, the median CPK ratio for cervical, thoracic, and lumbar surgery was 2.46, 7.25, and 4.18, respectively. The median CPK ratios for all spinal and nonspinal (control) procedures were 4.02 and 1.81, respectively (Table 2).

There was no apparent relationship between serum CPK concentration and patient BMI and age. In men the CPK level was higher than in women, a difference that was borderline significant ($p = 0.06$). The duration of surgery and serum CPK1 were highly significant factors affecting serum CPK2 in all patients ($p < 0.001$), including those who underwent nonspinal (control) procedures.

The relation between log(CPK ratio) and the three surgical subgroups is shown in Fig. 2. In the extensively invasive group the mean log(CPK ratio) was 1.109, in the average invasiveness group 0.589, and in the minimally invasive group 0.482. The log(CPK ratio) in the control group was 0.301. These estimates were obtained for a multivariable model adjusting for sex, age, BMI, and log(CPK1). The overall effect of the surgical procedure was highly significant ($p < 0.001$) and showed a clear monotonous dose-response relationship. Adjusted for multiple testing, all groupwise comparisons were significant at the 0.01 level except for the comparison between surgery with average invasiveness and minimally invasive surgery, which was borderline significant ($p = 0.09$).

The relation between log(CPK ratio) and localization of spine surgery is shown in Fig. 3. The mean log(CPK ratio) in cervical surgery was 0.494, in lumbar surgery 0.682, in thoracic surgery 0.802, and in nonspinal surgery (controls) 0.293. After adjusting for multiple testing, all groupwise comparisons were significant ($p < 0.04$) except the comparison between thoracic and lumbar surgery ($p = 0.38$).

In a multivariable model including the factor of anterior surgery compared with posterior surgery, this factor was highly significant ($p < 0.001$) after adjusting for all other variables mentioned earlier. Whenever lumbar procedures were excluded from analysis (because all but one procedure was approached posteriorly), the CPK was significantly lower after anterior surgery than after posterior surgery ($p = 0.04$) in cervical and thoracic procedures. Obviously, the control group was excluded in the evaluation of this model.

No significant difference was shown between unilateral and bilateral muscle dissections in terms of the log(CPK ratio) after adjustment for all other factors. Regarding the extent of surgical exposure, the log(CPK ratio) was slightly negative for two-, three-, or four-level surgery compared with that for one-level exposure, but the difference was not significant ($p = 0.10$). The log(CPK ratio) in revision surgery was significantly higher than in primary surgery ($p < 0.001$).

Discussion

Muscle dissection is inevitable during surgical exposure of the spinal column. To prevent iatrogenic muscle devascularization and denervation, tissue damage should be minimized. Serum levels of CPK have been shown to be an indicator of postoperative muscle injury.[4,5] Whether CPK is related to various spinal and nonspinal surgical procedures and whether elevated serum CPK has clinical significance remain unclear. Moreover, whether less invasive surgery is related to reduced postoperative CPK levels is still debated.

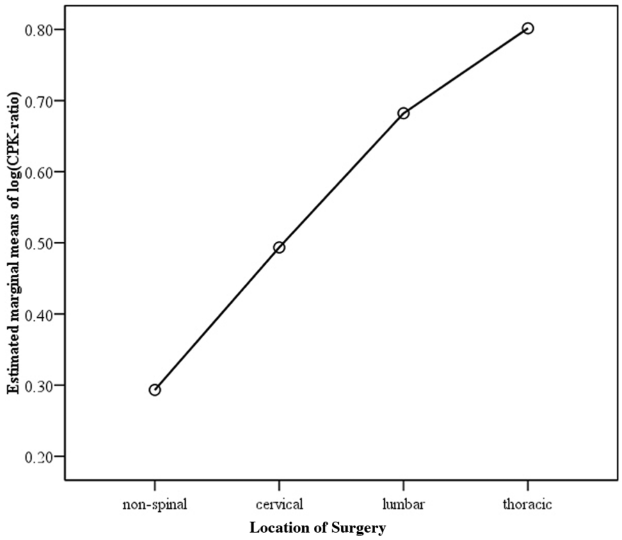

FIG. 3. Graph illustrating the relationship between the anatomical localization of surgery and log(CPK ratio). Note that 0.00 corresponds to a CPK ratio of 1, and 1.00 to a CPK ratio of exp(1) = 2.7. After adjustment for multiple testing, all groupwise comparisons were significant ($p < 0.04$) except for the comparison between thoracic and lumbar surgery ($p = 0.38$).

The results of the present study showed a highly significant relationship between the invasiveness of the surgical procedure and the postoperative CPK elevation. Extensively invasive surgery was related to a higher CPK ratio compared with minimally invasive surgery, lumbar and thoracic procedures corresponded to a higher CPK ratio compared with cervical surgery, posterior spinal approaches significantly increased the CPK ratio compared with anterior approaches, long-lasting surgery was related to a higher CPK elevation compared with short-duration surgery, and revision surgery was related to a higher CPK ratio compared with primary surgery.

Extensive exposure of the spinal column during posterior instrumented spondylodesis is inherent to bilateral dissection and retraction of the voluminous multifidus and erector spinae muscles. To keep the spine erect during standing and walking, the posterior erector spinae muscles are much more voluminous than the anterior longus colli and psoas muscles. This difference in volumes probably explains the higher postoperative CPK elevation after posterior surgery and may suggest that in terms of muscle injury anterior surgery is less invasive.

We found no significant difference between unilateral and bilateral muscle dissection. One would expect at least some difference between these two groups because twice the amount of muscle is dissected. Perhaps adequate surgical exposure in a unilateral approach requires the surgeon to open the retractor more firmly than in a bilateral approach. Greater retraction pressure may result in substantial muscle injury and the consequent release of CPK during unilateral muscle dissection.

Our results showed a negative trend with multilevel spinal surgery and CPK elevation, although not significant. Extensive spinal surgery with muscle dissection of two or more vertebral segments was found to be associated with a smaller increase in CPK levels than in single-segment exposure. Longer skin incisions and muscle dissection in multilevel surgery might be related to reduced muscle retraction pressure, which is consistent with previous results.[4] However, CPK was not reduced in longer skin incisions, and muscle injury might increase according to the extent of exposure.[4,5]

In experimental studies, it has been shown that the intermittent release of muscle retraction prevents postoperative denervation atrophy of paraspinal muscles.[3] Recently, in a comparative study of lumbar discectomy with or without retraction, Kotil et al.[6] also determined that muscle injury is related to retraction and relaxation time. In daily practice, it may be advisable to release the muscle retractor frequently during long posterior procedures to minimize muscle injury and prevent failed–back surgery syndrome.

Various confounders might be responsible for CPK elevation. In general, instrumented spondylodesis is characterized by extensive bilateral exposure of the spinal column, mostly posterior, and the surgery is very time-consuming. Therefore, the factors of surgery duration and use of the posterior approach might be responsible for the postoperative CPK increase. Note, however, that an evaluation of the duration of surgery in nonspinal intracranial procedures revealed high significance as well. As most of the spinal procedures were performed in the lumbar region and nearly all the surgeries were approached posteriorly, we excluded lumbar surgery in our analysis of the surgical approach. Thus, the serum CPK value was also significantly higher after posterior surgery than after anterior surgery. This finding is in agreement with previous results and may suggest that anterior surgery is less invasive than posterior surgery.[5]

The CPK ratio in secondary procedures was found to be significantly higher than in primary procedures. We would have expected increased muscle injury and CPK elevation in primary surgery because of the normal structure of muscle fibers and the absence of scar tissue inherent to revision surgery. However, the highly significant difference could be explained by the confounder that revision surgery usually is more invasive with extensive bilateral muscle dissection compared with primary surgery, especially when instrumented spondylodesis is performed.

Postoperative serum CPK concentration may also be related to positioning of the patient during surgery. Jourdan and colleagues[2] reported on 93 patients who underwent spine surgery in the knee–elbow position and compared them with patients who underwent intracranial neurosurgery without muscle retractors and with those who underwent abdominal surgery with the aid of retractors. Serum CPK was similarly increased in patients treated with spine surgery and abdominal surgery; therefore, the postoperative increase appeared to be related to muscle stretching rather than patient positioning. In contrast, in the present study we also found CPK elevation after intracranial neurosurgery. Even though these patients underwent surgery in the supine position, the increase in serum CPK was substantial. A possible explanation for the elevation in CPK after intracranial surgery is the duration of surgery, which was mentioned previously, or extensive dissection of the temporal muscle.

One of the rationales for minimal invasive surgery is reduced tissue injury, less back pain, quicker mobilization, and faster resumption of daily activities. Thus, in the case of lumbar disc surgery, the muscle-splitting technique of MED has gained popularity. In our opinion, conventional unilateral transflaval discectomy can be considered as minimally invasive as well, given that the fiber attachments to the spinal process and lamina are dissected exclusively and the muscle itself is preserved. Therefore, we classified both techniques as minimally invasive surgery, and both were consistently associated with a reduced CPK ratio compared with the average invasiveness and extensively invasive groups. Authors of two previous studies evaluated postoperative serum CPK after MED and conventional open discectomy separately, but their results were controversial and the number of patients was rather small.[9,10]

The key limitation of our study is the lack of clinical evaluation in relation to serum CPK. Systematic postoperative evaluation of functional outcome and pain intensity on a visual analog scale was not performed, and therefore the clinical significance of our results is not known. Note, however, that in a prospective randomized trial of lumbar discectomy with or without retraction, no significant difference in terms of long-term back pain was shown.[6] To elucidate the hypothesized cause of failed–back surgery syndrome, which is considered to be related to iatrogenic muscle injury, documentation of perioperative CPK levels could be valuable.

Another limitation of our study is the lack of CPK isoenzyme measurement. Creatine phosphokinase has three isoenzymes: CPK-MB in the heart, CPK-BB in the brain, and CPK-MM in skeletal muscle. In our study we measured only the serum concentration of total CPK; however, more than 95% of the total CPK activity is due to CPK-MM.[5,13] Thus, it seems legitimate to analyze the total serum CPK, although the CPK-MM isoenzyme is more specific for skeletal muscle injury.

Conclusions

Muscle dissection with related injury is, to some extent, inevitable during spine surgery. Our data showed a significant relationship between postoperative CPK elevation and the invasiveness of surgery, duration of surgery, spinal localization, posterior approach, revision surgery, and preoperative serum level of CPK. Age, sex, BMI, bilateral approach, and multilevel exposure were nonsignificant influencing factors. Nonspinal intracranial surgery was also associated with a CPK increase. The clinical significance of the results in terms of postoperative low-back pain is not known. Whether minimally invasive surgery is related to reduced muscle trauma and the CPK level is debatable, and further studies are necessary.

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