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RESEARCH

A standardized anesthetic/analgetic regimen compared to standard anesthetic/analgetic regimen for patients with high-risk factors undergoing open lumbar spine surgery: a prospective comparative single-center study

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Abstract

The objective of the study is to improve the results of patients undergoing lumbar spine surgery who are at high risk for anesthesia and/or surgical complications. Two independent groups were compared: the study group (SG, $n=40$) (standardized neuroanesthetic protocol with multimodal analgesia) and the control group (CG, $n=40$) (intravenous anesthesia based on propofol and fentanyl). The data were collected using prospective observation of early and long-term results of lumbar fusion. After 24 months, the level of functional state and quality of life were studied. Patients in the SG did not have statistically significant changes in intraoperative hemodynamics; the best indicators of cognitive functions were noted. The effectiveness of the SG compared with the CG was confirmed by a statistically significantly lower amount of perioperative opioid drugs required ($p=0.01$) and a minimal level of incisional pain ($p<0.05$). An intergroup comparison of the adverse effects of anesthesia revealed a significantly lower number in the SG ($n=4$) compared to the CG ($n=16$) ($p=0.004$). The number of postoperative surgical complications was comparable ($p=0.72$). Intergroup comparison showed improved ODI, SF-36, and the Macnab scale at 24 months after surgery in the SG compared to the CG ($p<0.05$). Long-term clinical results correlated with the level of incisional pain in the first three postoperative days. Our standardized neuroanesthetic protocol ensured effective treatment of postoperative incisional pain, significantly decreased the perioperative use of opioids, reduced adverse anesthesia events, and improved long-term clinical results in patients with high risk factors for anesthetic complications who undergoing open lumbar spine surgery.

Keywords Lumbar spine · Degenerative disease · Overweight · Elderly · Comorbidity · Open decompression-stabilization interventions · Surgical stress response · Ropivacaine · Dexmedetomidine · ERAS

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Introduction

Degenerative diseases of the lumbar spine remain one of the dominant causes of disability and reduced quality of life in developed countries [1]. To improve patients' functional state and restore physical activity, various decompressive and decompressive-stabilizing interventions are typically utilized [2]. The use of spinal surgical technologies may be accompanied by incisional pain of varying intensity [3]. Narcotic analgesics are generally accepted as effective for postoperative pain associated with direct soft tissue injury [4]. The long-term use of opioids, especially in high doses, has been associated with complications such as drug addiction, depression, nausea, vomiting, respiratory depression, intestinal paresis, and urinary retention [5–8]. However, inadequate pain relief in the early postoperative period lengthens the recovery period and the duration of inpatient treatment [9]. Indeed, the development of chronic pain syndrome significantly reduces quality of life, may lead to psychosomatic disorders of varying severity, and requires long-term, complex treatment [10].

Thus, the method of anesthesia [11] as well as the patient's initial physical status, anthropometric characteristics, and comorbid background [12, 13] all have an influence on the surgical outcomes of patients with degenerative diseases of the lumbar spine. As such, special care is required to optimize high-risk patients in need of neuroanesthetic care. These include older patients, those who are overweight, and patients with one or more concomitant diseases [14, 15].

Patient-tailored anesthesia method planning and anticipating and addressing possible predictors of unsatisfactory outcomes are all important for optimizing perioperative results, particularly in patients undergoing lumbar spine surgery who are at high risk of anesthesia complications [10, 13, 15].

The objective of the study is to improve the results of patients undergoing lumbar spine surgery who are at high risk for anesthesia and/or surgical complications. Project tasks: (1) reduce the perioperative need for opioids; (2) reduce the level of incisional pain; (3) decrease the number of perioperative complications; (4) improve long-term clinical outcomes.

Materials and methods

Study design

This was a prospective non-randomized comparative controlled study, conducted from January 2017 to January 2020 at the Center of Neurosurgery of the Irkutsk Railway Clinical Hospital. The study was approved by the Ethics Committee of Irkutsk State Medical University, protocol no. 1, dated January 16, 2017. Each patient gave voluntary consent to be included in the study.

Inclusion criteria:

The study included patients with.

- high-risk factors for anesthesia complications—risk according to the American Surgical Association (ASA) III–IV degree due to the presence of excess body weight, concomitant pathology, and/or age over 65 years;
- persistent radicular pain syndrome, resistant to 6–8 weeks of conservative therapy;
- no preoperative use of opioids;
- degenerative segmental instability or kyphotic deformity.

Exclusion criteria:

The criteria for exclusion from the study were.

- Minimal risk of developing anesthetic aid and surgical intervention—ASA I–II risks;
- revision surgery;
- inflammatory diseases, tumors, and traumatic injuries in the lumbar spine;
- osteoporosis;
- intolerance to administered drugs;
- preoperative dementia—Montreal Cognitive Assessment (MoCA) score less than 16 points, Frontal Assessment Battery (FAB) score less than 12 points.

One surgical team performed all of the surgical procedures, and the anesthesia protocols were alternated between the study and control patient groups. A series of surgical interventions and anesthesia benefits were analyzed in patients who were screened consecutively until 40 patients were recruited in each group.

After 24 months, 7 patients have excluded 3 patients from the first group (loss of follow-up ($n=2$), refusal to participate in the study ($n=1$)) and 4 patients from the second group (loss of follow-up ($n=2$), refusal to participate in the study ($n=1$), and death unrelated to the postoperative complications ($n=1$)). A pilot observational study was conducted to determine if there was a between-group difference and effect size. Figure 1 shows a flow chart that characterizes the study design.

Surgical and anesthesia techniques

All surgical interventions were performed by one operating team. In all cases, we performed open decompression and stabilization from a midline approach with bilateral dissection

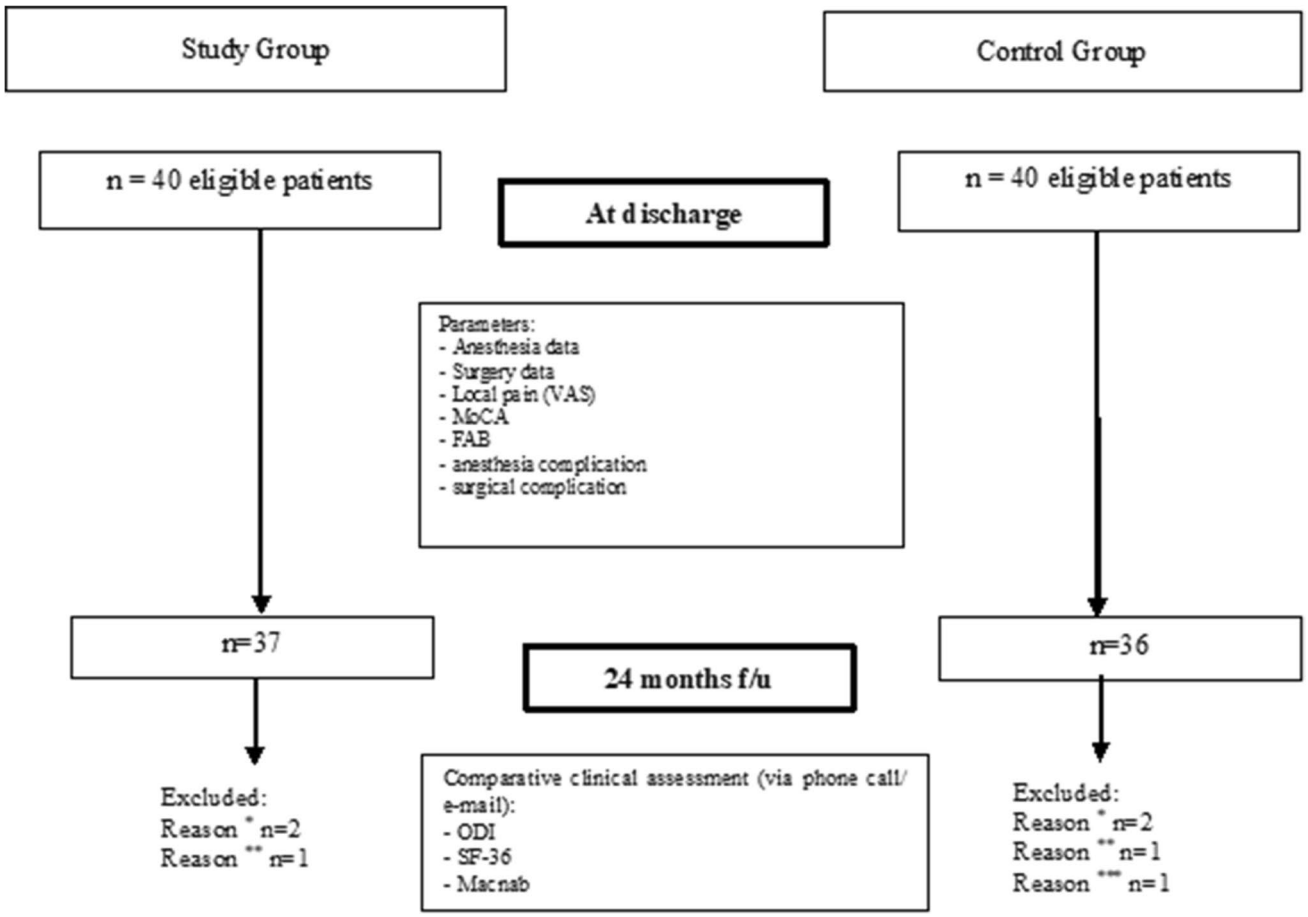

Fig. 1 Patients' study flowchart. Exclude reason: reason * = loss of follow-up; reason ** = refusal to participate in the study; reason *** = death unrelated to the operation (in these cases, there were no postoperative complications)

of the paravertebral muscles, partial or complete laminectomy, discectomy, and interbody fusion using Open-TLIF technology with bone graft in a cage, and open transpedicular fixation.

Anesthesia and perioperative follow-up of patients included in the study was carried out by one anesthesiologist. Throughout the operation, the depth of anesthesia was controlled using a bispectral index (BIS) monitor (Vista, Aspect Medical Systems, USA) and a train of four (TOF) apparatus for analyzing neuromuscular conduction (MNMB-DIAMANT, Russia). Anesthetic dosage was adjusted to achieve a BIS value between 40 and 60 from the commencement of anesthesia to the end of surgery. An audible alarm was set when the BIS number fell out of the prescribed range. Maintaining the level of anesthesia according to the BIS monitor was provided by fentanyl titration, which was done necessary to reduce the perioperative need for opioids.

In the control group ($n = 40$) (we used the anesthesia regimen standard for our medical institution), intravenous anesthesia with artificial lung ventilation was used: propofol 4–12 mg/kg per hour; for myoplegia, rocuronium bromide was used, 0.6–1.0 mg/kg; for pain relief, fentanyl 0.04–0.1 mg/kg per hour.

In the study group ($n = 40$), anesthesia based on propofol and fentanyl was also used in combination with a standardized neuroanesthetic protocol: multimodal analgesia with a preoperative intramuscular injection of ketoprofen 100 mg, infiltration of paraspinal muscles, subcutaneous fat and skin with ropivacaine 0.75%, 10 ml before incision, intraoperative dexmedetomidine 0.2–0.4 mcg/kg/h, postoperative paracetamol 1000 mg.

Outcomes of the study

For a comparative analysis, we evaluated the following:

- *Early postoperative period (during hospitalization):*

(1) Duration of anesthesia and surgery, blood loss, intraoperative amount of opioids used, dynamics of the heart rate (HR), and mean arterial pressure (MAP);

(2) length of stay in the postoperative observation ward, terms of mobilization, and inpatient treatment;
(3) severity of incisional pain according to the VAS scale (pain level was assessed every 8 h before the use of postoperative analgesia, and then the average value of VAS per day was calculated);
(4) postoperative need for narcotic drugs in the form of oral morphine equivalents (OME) using an online calculator (https://globalrph.com/medcalcs/advanced-opioid-conversions-equianalgesic-morphine-equivalents/) (access date january 2023) in the intensive care unit (ICU) per hour and in the hospital. For both study groups, the regimen of postoperative analgesia depended on the level of local pain syndrome, which was assessed every 8 h before the use of postoperative analgesia, and then the average value of VAS per day was calculated. Methods of postoperative pain relief were stratified: for VAS < 40 mm, no intervention was made; for VAS > 40 mm, the patient received 100 mg tramadol until pain intensity dropped below 40 mm (maximum dose 300 mg per day);
(5) dynamics of cognitive function before surgery and on the 5th postoperative day according to the MoCA and FAB;
(6) number of adverse effects of anesthesia verified by an anesthesiologist in the ICU;
(7) number of postoperative surgical complications verified by neurosurgeons during the hospitalization.

- *In the long-term postoperative period (after 24 months—*via *phone call or e-mail):*

(1) Functional state according to the ODI scale;
(2) quality of life according to the SF-36 questionnaire;
(3) satisfaction with the outcome of surgery on the Macnab scale.

Statistical analysis

Statistical analysis was carried out on a personal computer using the Statistica 8.0 program (TIBCO Software Inc., Palo Alto, California). Analysis of the nature of the distribution of signs showed the presence of statistically significant differences ($p < 0.05$); in this regard, the distribution was considered different from normal. In this regard, the criteria of nonparametric statistics were used to assess the significance of the differences in the samples. When using a power analysis software module, the minimum number of respondents for each group was calculated. To perform a research study with a power of 80% and a statistical significance of $p < 0.05$ with a minimum difference level of 10 points and a standard deviation of 15 ODI points, a minimum number of respondents in the group equal to 37 is a necessary condition. The obtained results are presented by the median and the values of the 1st and 3rd quartiles—Me (Q_{25}; Q_{75}). For a comparative analysis of the obtained values, the Mann–Whitney U test, the Wilcoxon signed rank test, and the χ^2 criterion for binomial signs were used. The correlation analysis was carried out using Spearman's RS rank correlation coefficient. The differences were considered significant at the level of $p < 0.05$.

Results

Patient data are presented in Table 1. A comparative intergroup analysis revealed that the two groups were statistically similar in gender, age, constitutional characteristics, degree of physical status according to the ASA, the presence of concomitant pathology, smoking status, the nature of the pathological process, or the number of operated segments. In addition, there were comparable clinical data on the level of cognitive function, functional state according to the ODI, and quality of life according to the SF-36.

An intergroup comparison of specific features of surgical interventions and early postoperative period revealed that the blood loss, duration of surgery, and anesthesia were comparable ($p > 0.05$) (Table 2). There was a significantly lower number of drugs administered for anesthesia (fentanyl 0.005%/ml/case) and the need for postoperative analgesia both in the ICU ($p < 0.05$) and during the entire hospital stay ($p < 0.05$) in the study group. It was found that 21 (52.5%) patients in the study group did not need analgesics starting from the 3rd postoperative day. The indications for discharge were a decrease in the level of postoperative pain to less than 40 mm according to VAS, learning in safe physical activity, the absence of postoperative complications, and adverse effects of anesthesia.

All patients in the study group were transferred to the neurosurgical department within 2 h after the operation, while in 21 (52.5%) patients of the control group, due to insufficient recovery of the level of consciousness after extubation and intense postoperative pain, it was necessary to extend the observation in the ICU up to 12 h. The decision to transfer the patient to the ICU was made by the anesthesiologist, who was blinded to the method of anesthesia.

Regarding cognitive function, according to the MoCA and FAB scales, there was no significant intergroup difference in preoperative parameters ($p = 0.51$), while control measurements demonstrated better mental functions in the study group ($p < 0.05$). After surgery, there were complaints of cognitive dysfunction (decreased memory and concentration, increased fatigue) in 4 (10%) patients in the study group and 22 (55%) in the control group ($p = 0.004$). During the postoperative period, 3 (7.5%) patients in the study group and 21 (52.5%) patients in the control group ($p = 0.001$) had a score of less than 16 according to the FAB method, while 2 (5%) patients from the study group

Table 1 Demographics

Criteria		Study group ($n=40$)	Control group ($n=40$)	p
Age (years), Me (Q_{25}; Q_{75})		59 (53; 71)	62 (55; 73)	0.27
Sex	Male, n (%)	29 (72.5)	27 (67.5)	0.62
	Female, n (%)	11 (27.5)	13 (32.5)	
BMI (kg/m^2), Me (Q_{25}; Q_{75})		26.9 (24.1; 29.1)	25.9 (23.9; 28.3)	0.71
ASA score, n (%)	III	36 (90)	38 (95)	0.39
	IV	4 (10)	2 (5)	
Concomitant pathology, n (%)	Diabetes mellitus	5 (12.5)	3 (7.5)	0.19
	Arterial hypertension	12 (30)	14 (35)	
	Lung disease	2 (5)	5 (12.5)	
	Kidney disease	4 (10)	1 (2.5)	
Smoking, n, %		8 (20)	9 (22.5)	0.36
Pathology, n (%)	Intervertebral disc hernia with segmental instability	7 (17.5)	8 (20)	0.57
	Spondylolisthesis	27 (67.5)	29 (72.5)	
	Local kyphotic deformity	6 (15)	3 (7.5)	
Number of operated segments, n (%)	1 segment	13 (32.5)	15 (37.5)	0.38
	2 segments	23 (57.5)	24 (60)	
	3 segments	4 (10)	1 (2.5)	
Cognitive function before surgery	MoCA score, Me (Q_{25}; Q_{75})	27.5 (27; 29.5)	28 (26.5; 30)	0.29
	FAB score, Me (Q_{25}; Q_{75})	17 (16.5; 18)	17.5 (16; 18)	0.61
Preoperative value of the functional state according to ODI score, Me (Q_{25}; Q_{75})		72 (66; 84)	70 (66; 82)	0.17
SF-36 before surgery, score Me (Q_{25}; Q_{75})	Physical component	26.99 (20.28; 35.25)	28.33 (19.65; 33.21)	0.73
	Psychological component	31.29 (18.72; 41.91)	35.58 (19.6; 40.93)	0.42

and 19 (47.5%) patients from the control group ($p=0.002$) had a score of less than 26 according to the MoCA method. Thus, the results indicate the presence of mild to moderate cognitive impairment in 6 (15%) patients in the study group and in 25 (62.5%) patients in the control group ($p=0.006$).

The intra-operative MAP in the control group patients was significantly lower compared to the study patients ($p<0.001$) during the entire follow-up period—as well as compared to their baseline value ($p<0.001$) (Fig. 2). In the study patients, there were no episodes of arterial hypotension (less than 10 mm Hg from baseline blood pressure). HR decreased significantly in the study group ($p=0.007$) and had statistically significant differences compared to the control group ($p<0.001$) during the entire follow-up period. In the study group, compared to the control group, there was a decrease in intraoperative HR by an average of 19.5% from the baseline level.

When comparing pain levels as measured on the VAS, a statistically significantly lower level of pain was found in the study group patients during the 10-day early postoperative period ($p<0.05$) (Fig. 3).

An intergroup comparison of the adverse effects of anesthesia revealed a significantly lower number in the study group compared to the control group ($p<0.05$); the number

Table 2 Comparative characteristics of intraoperative parameters and the course of the postoperative period

Criteria	Study group ($n=40$)	Control group ($n=40$)	p
Duration of surgery, min, Me (Q_{25}; Q_{75})	170 (135; 210)	175 (150; 200)	0.26
Duration of anesthesia, min. Me (Q_{25}; Q_{75})	190 (160; 215)	200 (175; 230)	0.42
Blood loss, ml, Me (Q_{25}; Q_{75})	330 (250; 500)	400 (300; 680)	0.34
The number of drugs administered for anesthesia, fentanyl 0.005%/ml/case, Me (Q_{25}; Q_{75})	15.5 (12.5; 19)	19.5 (18; 24.5)	**0.01**
OME in ICU, per hour, Me (Q_{25}; Q_{75})	2.8 (1.9; 4.4)	11.9 (8.4; 21.2)	**< 0.001**
OME in hospital, per day, Me (Q_{25}; Q_{75})	1.4 (0.6; 2.9)	46.2 (29.7; 78.1)	**< 0.001**
Terms of activation, per day, Me (Q_{25}; Q_{75})	1 (1; 2)	2 (2; 3)	**0.03**
Length of hospital stay, bed-day, Me (Q_{25}; Q_{75})	6 (4; 7)	8 (7; 10)	**0.02**

The significance of the symbol [boldface] reflected inside Table 2 is the presence of statistically significant differences

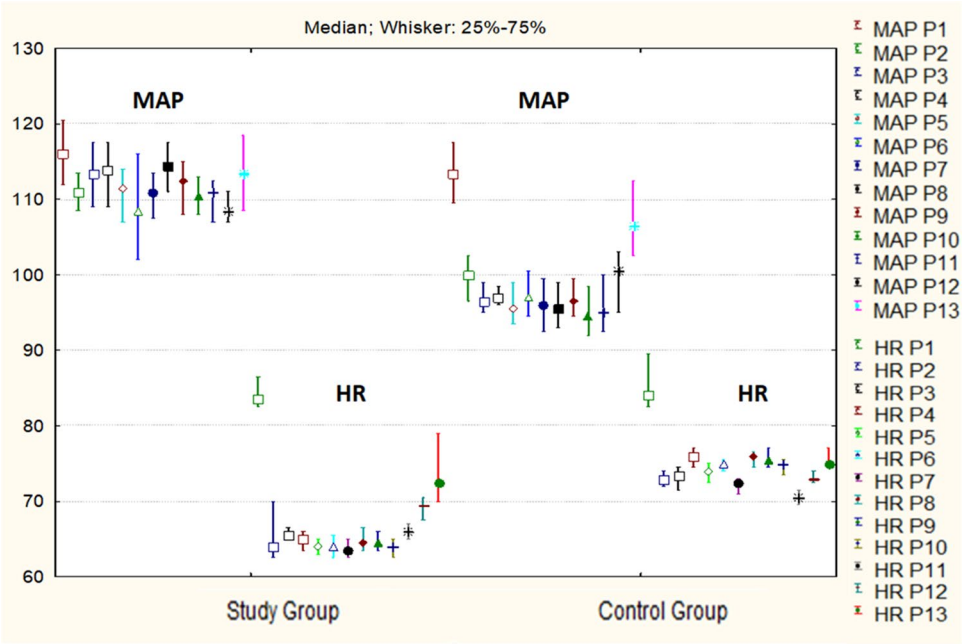

Fig. 2 Intergroup dynamics of intraoperative hemodynamic parameters. Note: Point (P) = time indicator: before induction of anesthesia (P1), during skin incision (P2), then at 25-min intervals (on average up to 200 min—P3–P10), when suturing an operating wound (P11), after extubation (P12) and 15 min after extubation (P13); mean arterial pressure (MAP, mmHg, Me (Q25; Q75)); heart rate (HR, bpm Me (Q25; Q75))

of postoperative surgical complications between the groups was comparable ($p = 0.72$) (Table 3). The assessment of motor activity and command execution was made by the anesthesiologist, who was blinded to the method of anesthesia, and was based on the restoration of the patient's consciousness and the ability to execute verbal commands.

After 24 months, information was available on 37 patients from the study group and 36 patients from the control group. The intragroup analysis revealed a significant improvement in the ODI and SF-36 scores both in the study group ($p = 0.003$ and $p = 0.008$, respectively) and in the control group ($p = 0.01$ and $p = 0.02$, respectively). At 24 months, the study group had statistically significantly better ODI and SF-36 scores, as well as greater subjective satisfaction with the outcome of surgery on the Macnab scale ($p < 0.05$) (Table 4).

A correlation analysis of long-term clinical outcomes (ODI and SF-36) with the intensity of local pain syndrome

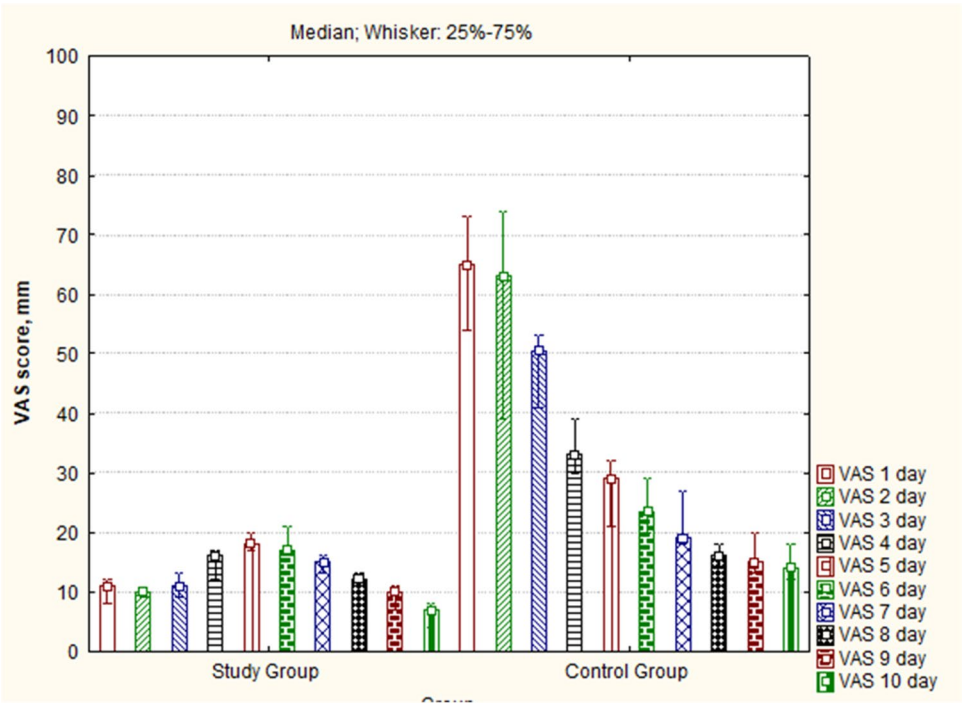

Fig. 3 Intergroup comparative analysis of the VAS surgical pain level

Table 3 Information on the adverse effects of anesthesia and surgical complications

Criterion		Study group ($n=40$)	Control group ($n=40$)	p
Adverse effects of anesthesia	Postoperative nausea and vomiting	1	5	
	Bradycardia	2	1	
	Dizziness	1	3	
	Respiratory depression with decreased saturation after extubation	-	2	
	Laryngospasm after extubation	-	1	
	Insufficient motor activity and command execution	-	4	
	Total, n (%)	*4 (10)*	*16 (40)*	***0.004***
Early surgical complications	Intermuscular hematoma	2	3	
	Surgical site infection	1	1	
	Deep vein thrombosis	1	1	
	Total, n (%)	*4 (10)*	*5 (12.5)*	*0.72*

The significance of the symbol [boldface] reflected inside Table 3 is the presence of statistically significant differences

(VAS) during the first 10-day postoperative period was carried out for the study and control groups. We did not correlate long-term clinical outcomes on the Macnab scale, due to the possible data error associated with the subjective nature of the result. There was a significant direct nonparametric correlation between the long-term outcomes of surgical treatment (according to the ODI) and a moderate inverse nonparametric correlation (according to the SF-36) with the level of pain in the first three postoperative days (Table 5).

Discussion

Degenerative diseases of the spine that require reconstructive surgery are a considerable issue facing modern healthcare [16]. Given the trend toward a sedentary lifestyle and an increase in total life expectancy, there is an increasing number of patients with high-risk factors for anesthesia complications, such as obesity, the presence of co-morbidities, and older age [17, 18]. Each of the above increases the surgical and anesthetic risk. In order to mitigate such risks, the following methods have been advocated: reducing the duration of anesthesia and surgery, reducing the amount of opioids, increasing the safety of anesthesia, as well as early mobilization and rehabilitation [19, 20]. Severe postoperative pain necessitates a high level of analgesia, increasing the risk of delirium and the need for intensive monitoring, thus increasing the duration and total cost of inpatient treatment [21]. In order to address such issues, various peri-operative protocols to optimize pain management have been proposed [22].

Over the past several years, the authors developed and utilized a multifaceted anesthesia/analgesia protocol to treat patients who are at high risk for anesthesia complications undergoing degenerative open lumbar fusion procedures. This work represents the first assessment of the early and long-term clinical results of our standardized neuroanesthetic protocol. Our results suggest that early pain severity has a significant effect on long-term clinical outcomes. This implies the need for effective antinociceptive modalities in the early postoperative period, including the use of multimodal analgesia for patients with high-risk factors for anesthesia complications. We chose patients with a high-risk

Table 4 Comparative analysis of clinical outcomes at 24 months postoperatively

Criterion		Study group ($n=37$)	Control group ($n=36$)	p
Functional state according to ODI, scale Me (Q_{25}; Q_{75})		10 (7; 14)	20.5 (18; 30)	**0.004**
SF-36 score, Me (Q_{25}; Q_{75})	Physical component	54.98 (52.86; 57.19)	39.74 (36.49; 41.69)	**< 0.001**
	Psychological component	55.84 (52.75; 58.01)	37.13 (29.2; 39.75)	**< 0.001**
Macnab, *n* (%)	Excellent	14 (37.8)	6 (16.7)	**0.002**
	Good	18 (48.7)	17 (47.2)	
	Satisfactory	5 (13.5)	11 (30.5)	
	Unsatisfactory	-	2 (5.6)	

The significance of the symbol [boldface] reflected inside Table 4 is the presence of statistically significant differences

Table 5 Correlation of the ODI and SF-36 scores at 24 months postoperatively and the level of local pain syndrome during the first 10-days postoperatively

Index	Group	Day of postoperative observation																			
		VAS 1		VAS 2		VAS 3		VAS 4		VAS 5		VAS 6		VAS 7		VAS 8		VAS 9		VAS 10	
		R	*p*	*R*	*p*	*R*	*p*	*R*	*p*	*R*	*p*	*R*	*p*	*R*	*p*	*R*	*p*	*R*	*p*	*R*	*p*
ODI	Study group ($n=37$)	**0.94**	**< 0.05**	**0.89**	**< 0.05**	**0.77**	**< 0.05**	0.05	> 0.05	0.18	> 0.05	0.10	> 0.05	0.24	> 0.05	0.27	> 0.05	0.37	> 0.05	0.06	> 0.05
	Control group ($n=36$)	**0.83**	**< 0.05**	**0.72**	**< 0.05**	**0.80**	**< 0.05**	0.11	> 0.05	0.34	> 0.05	0.20	> 0.05	0.01	> 0.05	0.03	> 0.05	0.15	> 0.05	0.02	> 0.05
SF-36, physical component	Study group ($n=37$)	**−0.63**	**< 0.05**	**−0.64**	**< 0.05**	**−0.62**	**< 0.05**	−0.01	> 0.05	−0.12	> 0.05	−0.04	> 0.05	−0.14	> 0.05	−0.15	> 0.05	−0.27	> 0.05	−0.25	> 0.05
	Control group ($n=36$)	**−0.67**	**< 0.05**	**−0.50**	**< 0.05**	**−0.47**	**< 0.05**	−0.25	> 0.05	−0.36	> 0.05	−0.24	> 0.05	−0.08	> 0.05	−0.04	> 0.05	−0.13	> 0.05	−0.02	> 0.05
SF-36, psychological component	Study group ($n=37$)	**−0.58**	**< 0.05**	**−0.46**	**< 0.05**	**−0.47**	**< 0.05**	−0.09	> 0.05	−0.02	> 0.05	−0.04	> 0.05	−0.10	> 0.05	−0.07	> 0.05	−0.35	> 0.05	−0.01	> 0.05
	Control group ($n=36$)	**−0.69**	**< 0.05**	**−0.71**	**< 0.05**	**−0.62**	**< 0.05**	−0.14	> 0.05	−0.34	> 0.05	−0.09	> 0.05	−0.07	> 0.05	−0.02	> 0.05	−0.28	> 0.05	−0.04	> 0.05

p, the confidence probability; *R*, Spearman's rank correlation coefficient. The significance of the symbol [boldface] reflected inside Table 5 is the presence of statistically significant differences

group of ASA grades III–IV and excluded grades I–II in order to obtain a homogeneous study group and to make an objective assessment of a standardized neuroanesthetic protocol in patients with significant comorbidities.

We found that our multimodal analgesia protocol made it possible to decrease postoperative pain, as well as opiate use, and allow for early mobilization. In addition, we found that the degree of pain that patients experienced in the early postoperative period was predictive of long-term physical and psychological outcomes. To our knowledge, this is the first study to evaluate the efficacy and safety of a multimodal perioperative approach to decrease early postoperative pain syndrome and to evaluate its effect on the long-term quality of life and functional state. Our results suggest that an effectively decreasing the intensity of surgical pain during the first three days is statistically correlated with better long-term status. Further, we demonstrated the beneficial effects in the most vulnerable cohort of patients—those undergoing open lumbar spine surgery who are at high risk for anesthesia complications.

One of the factors that significantly reduces quality of life is a non-specific postoperative pain syndrome in the lumbar spine [23]. The sources of pain are the soft tissues surrounding the surgical site and the paravertebral muscles [24]. The pain is thought to be mediated by mechanoreceptors and chemoreceptors (nociceptors) in the muscle tissue that responds to damaged muscle fibers [25]. While short-term stimulation of nociceptors is characterized by transient pain, repeated and severe muscle trauma can be accompanied by a constant pain syndrome [26]. Due to spasms and dysfunction of the damaged muscle, the antagonist muscle groups are overloaded, resulting in the development of reflected pain [27].

Chronic postoperative pain occurring at the surgical site or in the surrounding area is a significant problem and has been reported to exist in up to 85% of all surgical patients [9]. To prevent the development of chronic postoperative pain syndrome, effective early pain relief is required [28]. At the same time, it is advisable to rapidly mobilize patients while managing surgical pain with a minimum amount of opioids [29]. This is due to the fact that the long-term use of narcotic analgesics after spinal surgery is associated with an increase in mortality, the development of opioid addiction, and various pharmacologically adverse events [5]. The above circumstances have resulted in the introduction of multimodal analgesia as a component of the "Enhanced Recovery After Surgery (ERAS)" protocols, the goals of which are to reduce perioperative opiates, the intensity of surgical stress, intraoperative and postoperative complications, shorten the duration of inpatient treatment, promote early functional recovery, and reduce financial costs [30].

Such approaches are especially relevant when treating obese patients due to the high frequency of comorbidities, the difficulty of selecting the dose of analgesics, and the significant risk of perioperative complications [31]. They are also important for older patients due to concomitant pathology, low physical activity, and a high risk of cognitive dysfunction [32]. There are numerous studies that have advocated for various multimodal perioperative approaches to optimize anesthetic management [19, 20, 22, 29]. This indicates the ongoing search for solutions aimed at rapid recovery and avoidance of postoperative complications, especially for those at high risk for anesthesia complications.

While multi-modal analgesia has been presented in a number of spine studies in the form of various combinations of drugs, the results of their use are ambiguous. In his study, Tucker et al. [33] used multi-modal analgesia in 37 patients according to the following protocol: preoperatively—300 mg of gabapentin, 1 g of intravenous acetaminophen, and 0.5 mg/kg of intravenous ketamine before incision; intraoperatively—lidocaine with 2 mg/kg/h, dexamethasone 10 mg and magnesium sulfate 1 g, and ketorolac 30 mg for suturing a wound. Compared with the patients who did not receive multi-modal analgesia, the authors noted a significant decrease in intraoperative administration of opioids in the multimodal analgesia group (5.69 morphine milligram equivalents (MMEs) and 15.13 MMEs ($p < 0.001$), respectively, as well as postoperative oral usage of narcotic analgesics (3.21 MMEs and 6.08 MMEs ($p = 0.02$), respectively). At the same time, there was no statistical difference in the level of postoperative pain 30 and 60 min after the intervention between the groups. These findings contrasted with those by Maheshwari K. et al. [29] They used multimodal analgesia in 150 patients: once before surgery, 1 g of acetaminophen and 600 mg of gabapentin, intraoperative infusion of 5 µg/kg/min of ketamine before wound suturing, and 1.5 mg/kg/h of lidocaine with a decrease in the concentration of the latter to 1 mg/kg/h while suturing the wound and continuing its infusion in the ICU for an hour. The authors did not find clinical efficacy in the first 48 h after surgery in terms of the level of pain and the number of analgesics used in comparison to the control group. When using multimodal analgesia in 21 patients (intramuscular diclofenac, intravenous paracetamol and clonidine, and skin infiltration with bupivacaine and adrenaline), Savitha K.S. et al. [34] noted lower perioperative opioid consumption and fewer undesirable consequences of anesthesia compared with the control group. Using a combination of methadone at a dosage of 0.2 mg/kg and 250 mg of ketamine in 66 patients, Murphy G.S. et al. [35] found a significantly lower level of pain during the first 48 h after surgery with comparable adverse pharmacological consequences of anesthesia compared to the non-ketamine control group. Southerland W.A. et al., in a clinical case, noted an increase in the duration of anesthesia and a reduction in opiates during dorsal decompression-stabilizing intervention at the cervical level when intraoperative injections of ropivacaine, dexmedetomidine,

and dexamethasone were used in the erector spinae muscles [36]. In addition, good clinical efficacy in terms of the dynamics of the level of pain syndrome and functional state, and a high opioid-sparing effect with a decrease in the adverse effects of anesthesia have been proven when multimodal analgesia is combined with minimally invasive surgical technologies [37]. At the same time, Waelkens P. et al. in their systematic review and analysis of 31 randomized clinical trials determined an optimal perioperative analgesia regimen using NSAIDs, COX-2 inhibitors, ketamine, and epidural analgesia [38]. The authors did not recommend the use of gabapentin and methadone due to the high risk of undesirable drug consequences, nor the use of local anesthetics, dexmedetomidine, or glucocorticosteroids due to the lack of reliable evidence of their effectiveness.

The effectiveness of the ERAS protocols and the integrated use of multimodal analgesia is felt to be due to the opioid-sparing effect and the reduction in adverse effects associated with long-term use of narcotic analgesics [20]. In addition, there is a decrease in the overall financial cost of treatment and rehabilitation [39]. We therefore believe that our standardized neuroanesthetic protocol is useful and relevant for open surgical treatment of degenerative pathology of the spine in patients at high risk for anesthesia complications.

Limitation

The limitations of the study include the following. First, this pilot study was conducted at a single center, and patients were not randomized. However, the patients were assigned to the study or control groups in an alternating fashion, such that there was no assignment bias. Randomization was not performed due to the difficulty of blinding the surgical and anesthetic team to the proposed study design. Given our pilot study data demonstrating the effectiveness of our neuroanesthesiological protocol, we plan to carry out a randomized clinical trial on a larger number of respondents in the future. Second, multiple different analgesic/anethestic agents were studied, which does not allow us to assess the impact of individual agents on the final outcomes. But this was inherent in the design of our study in that our goal was to determine the best possible case scenario to minimize the side effects of the entire peri-operative period. ERAS protocols have been shown to be superior to standard anesthetic/analgesic protocols, and most have not identified the impact of individual agents on the final outcomes. However, to our knowledge, this is the first study evaluating the benefits of combining multimodal analgesia with a preoperative intramuscular injection of ketoprofen 100 mg, infiltration of paraspinal muscles, subcutaneous fat and skin with ropivacaine 0.75%, 10 ml before incision, intraoperative dexmedetomidine 0.2–0.4 mcg/kg/h, and postoperative paracetamol 1000 mg. Third, we did not analyze the relationship between the dynamics of postoperative pain syndrome, psychosomatic status, duration of the disease, and the history of preoperative use of opioid analgesics, as this was beyond the scope of our study. Fourth, this was an analysis of perioperative outcomes only in a cohort of patients at increased risk of anesthetic complications (ASA III–IV). Therefore, the results may not be generalizable to other ASA groups. Fifth, we did not compare various combinations and modifications of the individual components of multimodal analgesia. It is certainly possible that a superior anesthetic/analgesic regimen exists. Finally, given that we obtained clinical follow-ups from patients via phone calls or e-mail, we were unable to analyze radiographic data and the extent to which fusion had an effect on long-term outcomes. Despite all of the above limitations, the study prospectively enrolled a relatively large number of subjects using an alternating assignment protocol to eliminate bias. It demonstrated that using our standardized neuroanesthetic protocol can result in substantial improvement in patient outcomes over standard anesthetic/analgesic protocols in patients at high risk for anesthesia complications undergoing open lumbar spine surgery.

Conclusions

The use of nonsteroidal anti-inflammatory drugs (ketoprofen) before surgery, long-acting local anesthetics before incision (ropivacaine), intraoperative alpha-2-agonist (dexmedetomidine), nonnarcotic analgesic (paracetamol) during wound suturing provided a controlled depth of anesthesia without pronounced depression of the cardiovascular system at all stages of surgery. This protocol also provided a decrease in the number of perioperatively administered opioid drugs, a reduction in the incidence of postoperative cognitive disorders, and of the number of adverse effects of anesthesia compared to traditional anesthesia based on propofol and fentanyl.

Our standardized neuroanesthetic protocol for open surgical treatment of degenerative lumbar disease in patients with high-risk factors (obesity, concomitant pathology, advanced age) contributed to the effective correction of early pain syndrome that correlated with the best long-term clinical outcomes according to the ODI and SF-36 scales.

Author contribution Each author made significant individual contributions to this manuscript. VAB, VYG, AAK, and KDR were the main contributors to the drafting of the manuscript. VAB, VYG, AAK, YYP, and VVS performed the anesthesia and surgery, patient follow-up, and gathered clinical data. VYG, AAK, YYP, and VVS evaluated the data from the statistical analysis. VAB, VYG, AAK, and KDR performed the literature search and review of the manuscript and contributed to the intellectual concept of the study.

Data availability Data are available from the corresponding author (prof. Vadim A. Byvaltsev) for researchers who meet the criteria for access to confidential data.

Declarations

Ethical approval The study was approved by the Ethics Committee of Irkutsk State Medical University, protocol no. 1, dated January 16, 2017.

Competing interests The authors declare no competing interests.

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