The Efficacy and Safety of Fluid Gelatin for LSS Undergoing PE-ULBD: A Prospective, Randomized Controlled Trial

Hao Yan[1], Ruzhan Yao[2], Mingdong Yu[2], Rongsheng Dou[1], Yu Zhang[1], Huaibin Wang[1], Yulin Shi[2], Weiqiang Liu[2]*

[1]Department of Medicine, Shandong Second Medical University, Weifang, Chin

[2]Department of Spinal Surgery, Weifang People's Hospital, Weifang, Chi

Research Article

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***For Correspondence:**
Weiqiang Liu, Department of Spinal Surgery, Weifang People's Hospital, Weifang, China
E-mail: lwq01228@163.com

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ABSTRACT

Background: Absorbable fluid gelatin is a novel collagen hemostatic agent that has been validated in multiple surgical procedures. However, the effectiveness of using this hemostatic agent during Percutaneous Endoscopic Unilateral Laminectomy for Bilateral Decompression (PE-ULBD) remains controversial. Our research aims to conduct a prospective randomized controlled trial to investigate the effectiveness and safety of this hemostatic material in patients undergoing PE-ULBD for Lumbar Spinal Stenosis (LSS).

Materials and methods: From October, 2023 to May, 2024 a total of 90 patients with LSS who underwent PE-ULBD, were enrolled in this study. The 90 patients were randomly divided into two groups: Group A (45 cases, using fluid gelatin) and group B (45 cases, not using fluid gelatin). Primary outcomes included perioperative blood loss and the success rate of achieving hemostasis within 3 min. Secondary outcomes encompassed surgical time, intraoperative blood loss, length of stay and complications.

Results: The perioperative blood loss in group A was significantly less than that in group B (p=0.039), and the success rate of achieving hemostasis within 3 min in group A was significantly higher than that in group B (p=0.021). There were no statistically significant differences between the two groups in terms of intraoperative blood loss, length of stay and complications, with the sole exception that the surgical time in group A was significantly shorter than in group B (p=0.006).

Conclusion: When patients with LSS undergo PE-ULBD, the prophylactic use of fluid gelatin can reduce postoperative bleeding without any observed additional complications. Therefore, the prophylactic use of fluid gelatin in PE-ULBD is an effective and safe strategy.

Keywords: Fluid gelatin; Lumbar spinal stenosis; Hemostasis; Percutaneous endoscopic; Lumbar decompression

Abbreviations: BV: Blood Volume; Hb_i: Preoperative Hemoglobin Concentration; Hb_e: Postoperative Hemoglobin Concentration; BMI: Body Mass Index; PT: Prothrombin Time; APTT: Activated Partial Thromboplastin Time; Hb: Hemoglobin; HCT: Hematocrit; SBP: Systolic Blood Pressure; DPB: Diastolic Blood Pressure; OR: Operative Room

INTRODUCTION

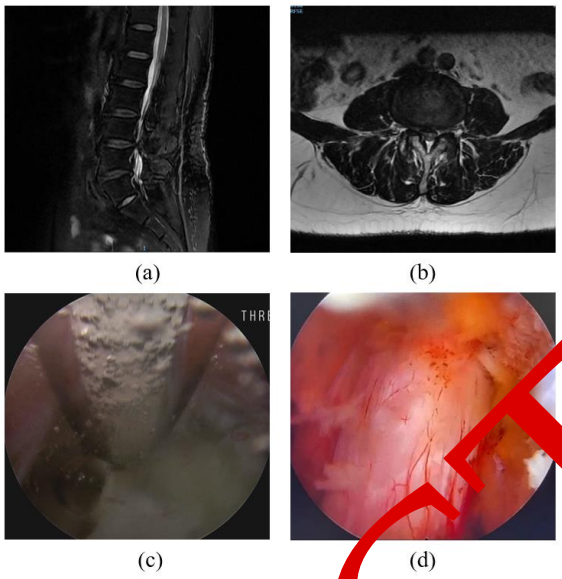
Patients with lumbar spinal stenosis often experience leg pain or numbness when standing or walking, a condition that severely threatens the quality of life and safety of elderly patients due to its association with high disability rates [1,2]. As a result, minimally invasive surgery has become the primary method for alleviating symptoms in patients with lumbar spinal stenosis [3]. Patients with LSS typically have thinner epidural venous plexus compared to normal individuals, increasing the risk of bleeding during decompression and raising the likelihood of Postoperative Epidural Hematoma (PEH) formation [4-6]. Therefore, minimizing surgical bleeding is critical for ensuring successful outcomes.

In recent years, endoscopic technology has gained widespread acceptance in the treatment of spinal diseases due to its advantages, such as reduced bleeding, minimal trauma and shorter surgical times [7]. Percutaneous Endoscopic Unilateral Laminectomy for Bilateral Decompression (PE-ULBD) is a procedure aimed at achieving bilateral decompression by removing a portion of the vertebral lamina [8]. However, due to the limited operating space compared to open surgery, a clearer surgical field is required. Additionally, because the incision for the surgical approach is smaller, it may lead to insufficient hemostasis, making hemostasis during the surgery particularly important [9,10].

In recent years, a new absorbable fluid gelatin called Surgiflo™ has gradually been used in surgical hemostasis [11]. This material is injected as a liquid into the surgical site requiring hemostasis and disperses into local irregular spaces to achieve localized hemostatic effects [12]. However, a recent randomized controlled trial conducted by Takami et al., measuring drainage and assessing postoperative MRI findings, showed that prophylactic use of fluid gelatin during microscopic endoscopic surgery did not affect PEH occurrence [13]. A study in neurosurgery by Gazzeri et al., found that using Surgiflo™ more than doubled the risk of thrombosis compared to conventional hemostatic methods [14]. Robert et al., also pointed out that Surgiflo™ may cause allergic reactions due to its extraction from animal collagen [15]. However, there are issues regarding the lack of adverse reaction data comparing fluid gelatin with other treatment modalities in spine surgery field analysis. Therefore, there is currently insufficient evidence analyzing the effectiveness and safety of fluid gelatin in percutaneous endoscopic surgery.

In this study, we conducted a clinical analysis on patients with lumbar spinal stenosis who underwent PE-ULBD surgery to evaluate the effectiveness and safety of Surgiflo™ as a hemostatic material during and after the surgical procedure. Ultimately, this study provides valuable experiential references for clinical practice (Figure 1).

Figure 1. Surgiflo™ usage during PE-ULBD. (a/b) A sagittal and axial MRI of a patient with lumbar spinal stenosis. (c) Injection of Surgiflo™ under endoscopic visualization. (d) Under endoscopic observation, Surgiflo™ has been completely cleared from around the dura mater.



MATERIALS AND METHODS

Study design

This prospective, double-blind study aims to evaluate the hemostatic efficacy and safety of a gelatin hemostatic agent (Surgiflo™, Johnson & Johnson Wound Management, Somerville, NJ) in patients undergoing PE-ULBD. During the surgery, patients were randomly divided into two groups: Group A and Group B. Prior to the commencement of the study, this protocol obtained approval from the ethics committee of our institution and was registered on the Chinese clinical trial registry website. The study has been designed to adhere to the Consolidated Standards of Reporting Trials (CONSORT) guidelines [16]. This research adheres to the Helsinki Declaration and requires each participant to sign a written informed consent form in order to ensure their rights are protected.

Inclusion criteria

We included patients aged between 18 years and 80 years who were diagnosed with single-level, LSS accompanied by corresponding clinical symptoms. These patients showed no improvement after three months of conservative treatment and provided informed consent to undergo PE-ULBD at our institution.

Exclusion criteria

Patients with blood diseases, infections, spinal tumors, requiring revision surgeries, intraoperative dural injury, or requiring the use of fluid gelatin due to inadequate hemostasis, as well as those currently participating in other clinical trials, those who have withdrawn from the study, those who have been unblinded, or any other patients deemed unsuitable for inclusion, will be excluded from this study.

Sample size determination

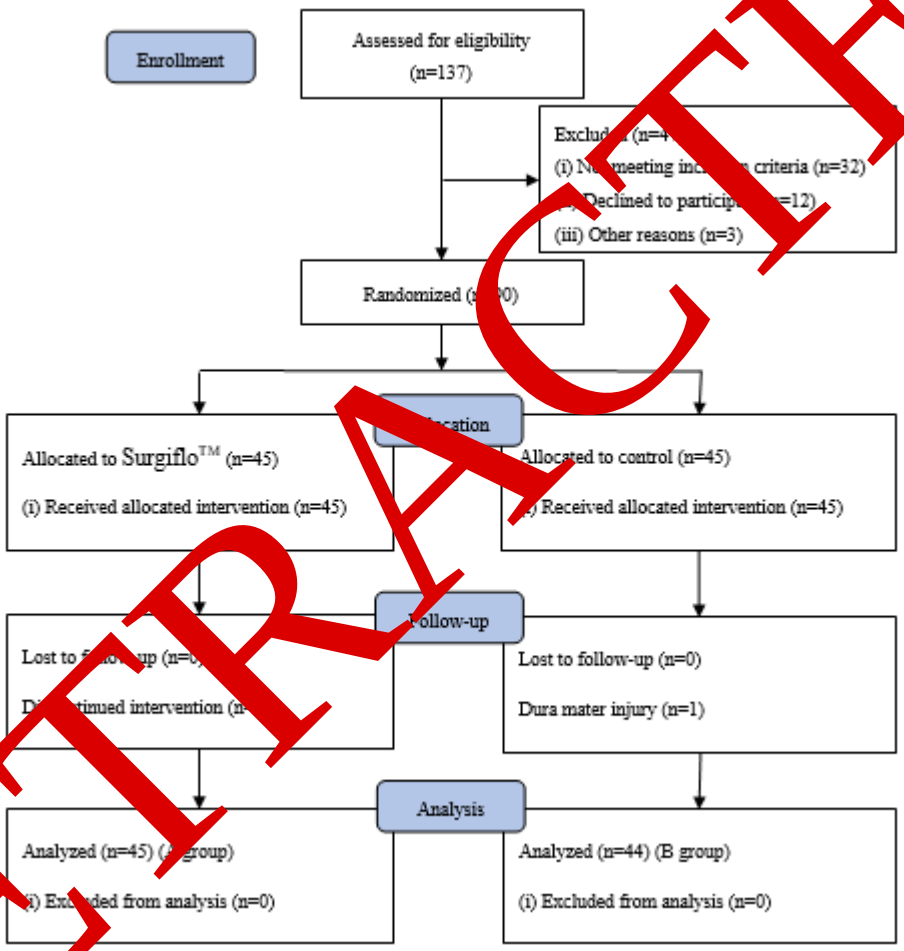
The sample size calculation is based on a prospective randomized trial conducted by Ng et al., [17]. To evaluate perioperative blood loss in PE-ULBD. Assuming an average difference of 185 milliliters or greater between the two

groups, and aiming for a statistical power of 0.90 and 'α' error rate of 0.05, each group would require 30 patients. Considering that 10% of the patients may be lost to follow-up for various reasons and there is a 10% possibility of data loss, a total of 90 participants were recruited for this study.

Randomization procedure

A nurse allocated patients in a 1:1 ratio to either group A or group B. A block size was used in the randomization. Prior to surgery, the surgeon was informed whether fluid gelatin would be used for each patient. Research assistants were responsible for data collection, and throughout the entire study process, the grouping information was kept confidential from both patients and research assistants (Figure 2).

Figure 2. Randomization flow chart.



Interventions

All patients underwent the following surgical procedure, and all surgeries were performed by the same experienced spine surgeon. After induction of general anesthesia and endotracheal intubation, the C-arm x-ray machine is used for fluoroscopy to locate the target area. The puncture point is 2 cm away from the midline. Under fluoroscopic guidance, a puncture needle and guide wire are inserted, followed by the insertion of a cannula along with the guide wire in stages. After confirming the accurate position of the cannula through fluoroscopy again, an endoscope system is inserted.

First, we exposed the spinous process, lamina, and base of the interlaminar space on one side of the surgeon. Using an electric drill, we removed part of the lamina until the border of the ligamentum flavum was exposed. Next, the electric drill was used to grind away the contralateral lamina and the medial edge of the inferior articular process, then the contralateral ligamentum flavum was addressed, followed by the contralateral lateral recess. Finally, we addressed the ligamentum flavum on the surgeon's side and performed decompression at the lateral recess. During the surgery, if bleeding occurred, local hemostasis was achieved using fluid gelatin in group A and electrocautery in group B.

After confirming adequate decompression, hemostasis was achieved using fluid gelatin in group A and conventional radiofrequency electrocautery in group B. The specific method for using fluid gelatin was as follows: First, fluid gelatin was thoroughly mixed with 2 ml of saline solution. Then the catheter tip was placed near the bleeding site. After pausing saline irrigation, an appropriate amount of fluid gelatin was injected into the bleeding site, and after 5 min, the area was rinsed clean.

In this study, we used perioperative blood loss (including intraoperative blood loss and postoperative blood loss within 2 days) as an indicator for evaluation. Perioperative blood loss refers to the total amount of bleeding from the start of surgery until 48 h after surgery. The Meunier's calculation method can estimate blood loss, which requires measuring hemoglobin levels for calculation purposes [18]. To measure blood volume, we followed the method proposed by Nadler [19]. Therefore, we conducted a blood routine examination upon admission and again 48 h after surgery. The specific procedures are as follows:

$$\text{Blood loss volume}=BV \times (Hb_i-Hb_e)/Hb_e$$

$$BV=k1 \times \text{height}(m)^3+k2 \times \text{weight}(kg)+k3$$

Note: Male: k1=0.3669, k2=0.03219, k3=0.6041; Female: k1=0.3669, k2=0.03219, k3=0.6041.

We estimated intraoperative blood loss by measuring hematocrit levels [20]. At the end of the surgery, a 10 ml sample of the irrigation fluid was collected, and its hematocrit was determined. Blood loss was then calculated using the total volume of irrigation fluid and the hematocrit of normal blood.

The specific formula is as follows:

$$V_{blood}=Hct_1/Hct_2 \times V_{rinse\ solution}$$

Note: V_{blood}: The volume of intraoperative blood loss; Hct_1: The hematocrit of rinse solution; Hct_2: The hematocrit of normal blood; $V_{rinse\ solution}$: Total volume of rinse solution.

Postoperative treatment included pain relief and antithrombotic measures. Pain relief was achieved using Non-steroidal Anti-Inflammatory Drugs (NSAIDs), while antithrombotic measures involved lower limb care and massage. On day 2 after surgery, patients can wear appropriate support devices for moderate weight-bearing activities. A blood routine examination is conducted at 48 h postoperatively before discharge when patients are able to walk steadily.

Outcome measures

The primary outcomes were perioperative blood loss, as well as the success rate of achieving hemostasis within 3 min. Secondary outcomes included surgical time, intraoperative blood loss, Length of Stay (LOS) and the occurrence of complications such as thrombosis formation, immune rejection reactions, allergic responses and delayed hematoma.

Evaluation of background factors

Based on the data of all enrolled patients from two research groups, we extracted the following relevant factors from the electronic medical record system: Age, sex, height, weight, surgical segments, presence or absence of hypertension, presence or absence of the use of anticoagulation/platelet drugs, preoperative Activated Partial Thromboplastin Time (APTT), preoperative Prothrombin Time (PT), preoperative platelet count, preoperative hemoglobin, hematocrit, systolic and diastolic blood pressure at admission, systolic and diastolic blood pressure upon return from the operative room and total volume of rinse solution.

Statistical methods

Conducting comprehensive qualitative and quantitative descriptive analyses on all collected variables, qualitative variables will be assessed using frequency and percentage distributions, while quantitative variables will be evaluated through calculations of the mean, Standard Deviation (SD), median and Interquartile Range (IQR) spanning from the 25th to 75th percentile. T-tests were used to determine differences between two groups in the demographic characteristics, preoperative clinical data, pre-operative and post-operative blood pressure, total blood loss, surgical time, intraoperative blood loss and length of hospital stay. Differences in descriptive data, including gender, hypertension preoperatively, preoperative anti-thrombotic use, the success rate of achieving hemostasis within 3 min, surgical segments and complications, between two groups were compared using the chi-square test. All analyses were performed using SPSS v27.0.1 software (IBM SPSS Statistics for Windows; IBM Corp.). When the p-value is less than 0.05, it can be considered statistically significant.

RESULTS

From October, 2023 to May, 2024 a total of 137 patients consented to participate in the clinical study. Among them, 47 individuals were excluded from the study due to reasons such as not meeting the inclusion criteria or refusing to participate. The remaining 90 patients were enrolled in a randomized controlled trial. However, one patient sustained a dura mater injury during the surgical procedure and was subsequently excluded from the analysis.

Baseline characteristics

The group A comprised 23 male patients and 22 female patients, with an average age of 52.7 years. The group B comprised 25 male patients and 19 female patients, with an average age of 53.2 years. In the statistical analysis, no significant differences were found in baseline characteristics between the group A and group B, except for the volume of irrigation fluid. The characteristics compared included age, gender, surgical segment, BMI, preoperative indices, blood pressure, and blood parameters. The data of the baseline characteristics are presented in Table 1.

Table 1. Baseline characteristics.

	Group A (n=45)	Group B (n=44)	p-value
Sex (Female/Male)	22/23	19/25	0.589
Age (years)	52.7 ± 12.8	53.2 ± 14.9	0.843
BMI (kg/m^2)	24.8 ± 3.4	25.1 ± 3.5	0.688
Surgical segments (n,%)	-	-	1.000
L3/4	2 (4.4%)	3 (6.8%)	-
L4/5	37 (82.2%)	36 (81.8%)	-
L5/S1	6 (13.3%)	5 (11.4%)	-
Preoperative PT (sec)	11.3 ± 0.9	11.5 ± 0.8	0.263
Preoperative APTT (sec)	27.2 ± 2.3	27.6 ± 3.4	0.528
Preoperative Hb (g/dl)	139 ± 16	144 ± 19	0.243

Preoperative platelet count (× 104)	230 ± 57	241 ± 48	0.298
Preoperative anti-thrombotic use (n,%)	6 (13.3%)	7(15.9%)	0.731
Hypertension preoperatively (n,%)	9 (20%)	7(15.9%)	0.615
SBP at admission (mmHg)	132 ± 20	131 ± 14	0.855
DBP at admission (mmHg)	81 ± 12	81 ± 12	0.909
SBP at return from OR (mmHg)	130 ± 21	134 ± 20	0.429
DBP at return from OR (mmHg)	82 ± 11	84 ± 12	0.347
The HCT of normal blood (%)	41.9 ± 3.6	42.3 ± 4.7	0.651
The HCT of rinse solution (%)	7.9 ± 1.9	7.2 ± 1.6	0.105
Total volume of rinse solution	6287 ± 1612	7266 ± 1443	0.00

Primary outcomes

Surgery was uneventful in the majority of patients. In terms of perioperative blood loss, the group A was 0.204 ± 0.286 liters (mean ± standard deviation), while the B group was 0.338 ± 0.317 liters. Consequently, a significant statistical difference was observed between the experimental and control groups according to the primary outcomes-perioperative blood loss (p=0.039).

The success rate of achieving hemostasis within 3 min in the group A was 86.7% and 65.9% in the group B. The experimental group and the control group showed significant differences in terms of the success rate of achieving hemostasis within 3 min (p=0.021). The data of the primary outcomes are presented in Table 2.

Table 2. Results in the primary outcomes.

	Group A (n=45)	Group B (n=44)	p-value
Perioperative blood loss (L)	0.204 ± 0.286	0.338 ± 0.317	0.039
The success rate of achieving hemostasis within 3 min (n,%)	39 (86.7%)	29 (65.9%)	0.021

Secondary outcomes

There were no postoperative complications observed in the group A. In comparison, two cases in the group B had a delayed hematoma. Additionally, neither of the two groups observed thrombosis formation, allergic responses, or immune rejection reactions. This demonstrates that there was no statistically significant difference in complications between the experimental group and the control group.

The surgical time for group A was 85 ± 19 min, while for group B, it was 97 ± 19 min. There is a significant difference in the surgical time between the two groups of patients (p=0.006). The intraoperative blood loss for group A was 11.9 ml ± 4.5 ml, while for group B, it was 12.6 ml ± 4.1 ml (p=0.431). The length of stay for group A was 7.5 days ± 1.5 days, while for group B, it was 7.9 days ± 1.6 days (p=0.237). The secondary outcomes are detailed in Table 3.

Table 3. Results in the secondary outcomes.

	Group A (n=45)	Group B (n=44)	p-value
Surgical time (mins)	85 ± 19	97± 19	0.006
Intraoperative blood loss (ml)	11.9 ± 4.5	12.6 ± 4.1	0.431
Length of Stay (LOS, days)	7.5 ± 1.5	7.9 ± 1.6	0.237
Complications	-	-	-
Thrombosis formation	0	0	-

Immune rejection reactions	0	0	-
Allergic responses	0	0	-
Delayed hematoma	0	2	0.242

DISCUSSION

Research has shown that severe stenosis of the spinal canal is a contributing factor to excessive bleeding, increasing the risk by 2.8 times [21]. Patients with LSS often experience prolonged compression, leading to thinner walls of the intra spinal veins compared to normal conditions. Decompression may stimulate vein rupture and cause bleeding [8]. Improper hemostasis can lead to hematoma formation and compression of the cauda equina or nerve roots, resulting in neurological symptoms [22]. Additionally, severe spinal canal compression can weaken blood flow return and cause issues with epidural venous filling. PE-ULBD is performed in a relatively small and confined space, requiring a clear surgical field. Theoretically, this might lead to a higher incidence of postoperative hematoma compared to open surgery [23]. Therefore, the reduction of postoperative bleeding is major.

Surgiflo™ is able to quickly cover irregular wounds during application, demonstrating excellent hemostatic effects [24]. This study found that in terms of the success rate of achieving hemostasis within 3 min, the group A was significantly superior to the group B, and the group A had significantly lower perioperative blood loss compared to the group B. Additionally, we investigated patient factors such as age, BMI, preoperative APTT, PT, PLT and found no significant differences between the two groups. Therefore, we believe that patient age, nutritional status and coagulation function have no significant impact on blood loss. Consequently, we conclude that Surgiflo™ exhibits a more significant hemostatic effect. This may be attributed to the coagulation mechanism of fluid gelatin. The fluid gelatin achieves hemostasis through the patient's intrinsic coagulation cascade mechanism. Its fluid matrix provides an environment for platelet adhesion and activation, thereby triggering platelet aggregation cascade reactions and activating both endogenous and exogenous clotting factors in the patient to promote the clotting process [25,26]. Research results indicate that the application of liquid gelatin in posterior lumbar spine surgery and transformational lumbar interbody fusion can effectively reduce intraoperative blood loss and postoperative drainage, which is consistent with our research findings [27,28].

Among the secondary outcomes in this study, the surgical time of patients in group B was significantly longer than that of group A, indicating a significant difference between these two groups. This situation may be attributed to the non-use of fluid gelatin by patients in group B, which consequently required more time for hemostasis. Additionally, the statistical difference in the volume of rinse solution was also due to the variation in surgery times. Supporting this observation is a study conducted by Ma et al., where no statistical difference was observed in surgical time between the experimental and control groups [27]. However, the experimental group had shorter surgical times compared to the control group, further indirectly confirming our proposed viewpoint. There was no statistically significant difference in intraoperative blood loss between the two groups. A possible reason is that intraoperative blood loss includes both intraspinal bleeding and soft tissue bleeding, while fluid gelatin was used only when dealing with the spinal canal. However, bleeding from muscles and other soft tissues is also an important component of intraoperative blood loss. The length of stay showed no significant difference between the two groups, however, the group A had a shorter hospital stay compared to the group B.

Additionally, some studies have suggested that the use of gelatin sponge may lead to complications such as thrombosis formation, immune rejection reactions, allergic reactions, and delayed hematoma. In this study, no delayed hematomas were found in the group A, while 2 cases of delayed hematomas occurred in the group B. However, these results were not statistically significant. A randomized controlled trial conducted by Takami et al., found no evidence to suggest that prophylactic use of fluid gelatin leads to delayed hematomas, further supporting our research findings [13]. After conducting research, it has been found that the use of fluid gelatin may potentially trigger allergic reactions and immune rejection reactions, which contradicts our research findings. Surgiflo™ is a gelatin matrix derived from pig skin and is believed to be recognized as a foreign antigen when introduced into the human body, thus possibly leading to allergic reactions [30]. No thrombus formation was observed in either group of patients in this study. However, the instructions for using surgiflo™ explicitly state that there is a risk of thromboembolism when using this product intravascularly. On one hand, it can lead to reduced blood flow, interfere with cellular metabolism, and induce local clotting enzyme aggregation. On the other hand, platelets are activated and aggregated at the site of vascular wall injury [31].

CONCLUSION

Research has found that the prophylactic use of Surgiflo™ significantly reduces perioperative blood loss and surgical time undergoing PE-ULBD, while also significantly increasing the success rate of hemostasis within 3 min. At the same time, this method does not increase the risk of complications. Therefore, we believe that the use of fluid gelatin in the surgical treatment of lumbar spinal stenosis through PE-ULBD is an effective and safe method. Future prospective, randomized, controlled studies with larger sample sizes are needed for further investigation.

LIMITATIONS

Our study has certain limitations. Firstly, the number of cases is still limited, and it is a single-center study with few observed indicators. Furthermore, the relatively short follow-up duration necessitates further in-depth exploration of the long-term incidence of thrombosis. Despite this, we still believe that our experimental data results are reliable because this study is a randomized controlled trial. Therefore, we adopted random sampling for all patients entering the study, greatly reducing the possibility of selection bias.

ETHICAL APPROVAL AND CONSENT

This study had been approved by the Ethics Committee of*** Hospital (KYLL20231027-1). All included hospitals signed informed consent.

CONFLICTS OF INTEREST DISCLOSURE

The authors had no conflicts of interest.

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