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REVIEW

The Emerging Role of Liposomal Bupivacaine in Erector Spinae Plane Blocks for Post-Operative Pain Management in Spine Surgeries: A Narrative Review

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Abstract: Postoperative pain is a common consequence of spinal operations related to tissue trauma, manipulation of neural structures, and lengthy procedures. While opioid medications are frequently used for pain control, their side effects, such as nausea, vomiting, tolerance, and dependency, have led to increased interest in multimodal analgesic techniques. This review aims to examine effectiveness and safety of liposomal bupivacaine (LB, EXPAREL) in erector spinae plane blocks (ESPB) for postoperative pain management following spinal surgery. Regional anesthesia methods, particularly ESPB, have gained attention in reducing opioid requirements. The ESPB technique involves ultrasound-guided administration of local anesthetics beneath the erector spinae muscles and above the transverse process, effectively inhibiting ventral and dorsal rami of spinal nerves. Despite its popularity for versatility and safety, the analgesic effects of ESPB with conventional local anesthetics are relatively short-lived. LB, which releases the drug gradually as liposomes are degraded, offers extended pain control. Early clinical applications in pediatric scoliosis surgery and transforaminal lumbar interbody fusion have revealed that ESPB with LB adequately outperformed the control analgesic in terms of opioid consumption (30% and 50% decrease in mentioned studies) and length of stay (24%, 32%, and 12% decrease in mentioned studies). These findings indicate that LB in ESPB represents a promising strategy for enhanced perioperative pain management in spinal procedures. However, further research with larger and more diverse patient populations and outcome measurements are needed to overcome the current limitations of current research. In the present investigation, current evidence regarding the implementation of LB in ESPB during spine surgeries is summarized, focusing on safety and potential to improve patient outcomes by prolonging analgesia, minimizing opioid use, and promoting faster recovery.

Keywords: liposomal bupivacaine, erector spinae plane block, regional anesthesia, post-operative pain, spine surgeries

Introduction

Significant postoperative pain often occurs following spinal surgeries secondary to tissue and muscle trauma from extensive dissection, manipulation of neural elements, and continued exposure to instrumentation. In addition, the prolonged operating time of many of these procedures contributes to the intensity of postoperative discomfort.[1] In this regard, opioid medications are commonly used to treat postoperative pain related to spinal surgery. However, opioid use results in a variety of adverse effects, including nausea, vomiting, tolerance, and dependence. Multimodal analgesic techniques are being implemented to manage pain, to decrease opioid consumption, and to help combat the ongoing opioid epidemic.[2] Appropriate pain management is crucial during the perioperative period to prevent chronic postsurgical pain, and inadequate relief can result in delayed ambulation and more extended hospital stays.[3] Effective and timely control of pain can therefore play an important role in promoting recovering and improving overall patient outcomes.

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Consistent evaluation of pain levels and adjustment of treatment strategies are also essential to ensure optimal post-operative care.

An emerging component of multimodal analgesia protocol, regional anesthesia techniques have proven valuable in reducing opioid consumption following surgery. Among these, the erector spinae plane block (ESPB) has drawn interest in its use for spinal surgeries. ESPB consists of injecting local anesthetic deep into the erector spinae muscles and superficial to the transverse process. This inhibits the ventral and dorsal rami as the anesthetic spreads within the fascial plane. ESPB demonstrates decreased postoperative pain, as well as an extended interval between spinal surgeries and the need for a first rescue analgesic administration. Similarly, patients receiving ESPB show decreased postoperative opioid consumption.[4] The ESPB procedure utilizes ultrasound guidance to locate specific anatomical landmarks such as the transverse processes and the erector spinae muscle group (spinalis, longissimus, and iliocostalis). This block has gained popularity from its versatility, simplicity, and safety.[5] However, the efficacy of ESPB is limited related to relatively short duration of analgesic effect when using conventional local anesthetics. A potential solution to increase the span of analgesia is the use of liposomal bupivacaine (LB). This formulation of bupivacaine allows the body to slowly degrade the liposomes, resulting in a gradual and sustained release of local anesthetic. Early applications of ESPB with LB have been reported in pediatric scoliosis surgery; its use produced sufficient postoperative pain management and decreased opioid consumption.[6] In this review, we summarize evidence involving safety and efficacy of LB when used in ESPB for postoperative pain management in spine surgeries. This narrative review aims to summarize current evidence on the safety and efficacy of liposomal bupivacaine in erector spinae plane blocks for spine surgery, with relevant studies identified through a nonsystematic search of PubMed using keywords related to "erector spinae plane block", "liposomal bupivacaine", "regional anesthesia", and "spine surgery" from inception through 2024.

Description of Liposomal Bupivacaine

LB is an extended-release formulation of the amide local anesthetic bupivacaine, designed to provide prolonged analgesia compared to standard formulations. This formulation loads bupivacaine into multivesicular lysosomes, which offers a prolonged analgesic effect compared to standard bupivacaine. This is related to the vesicles being slowly degraded by the body over an extended period of time, decreasing the need for opioids and reducing pain scores for up to 72 hours.[7] By maintaining sustained plasma concentrations, LB aims to overcome the short duration of action associated with conventional bupivacaine, which usually provides analgesia for only 6–12 hours after a single injection. Standard bupivacaine has one of the longest half-lives of similar anesthetics related to its protein-binding capabilities. Therefore, by prolonging this half-life with the use of liposomes, significant analgesia can be accomplished. In addition, this structural difference maintains a comparable safety profile and prevents the need for a secondary dose or catheter placement.[8] The mechanism of action of LB is similar to standard bupivacaine. The active drug inactivates voltage-dependent sodium channels in neurons and prevents nerve impulse propagation. Compared to lidocaine, there is a slower release of bupivacaine from its binding site, which leads to prolonged analgesia.[7]

The US Food and Drug Administration (FDA) first approved LB in 2011 under the trade name *Exparel* for local infiltration into the surgical site to provide postsurgical analgesia. This marked the first approval of a liposomal formulation of a local anesthetic designed explicitly for extended-release pain control. Since its introduction, LB has been applied across a broad range of surgical procedures, both within its approved labeling and in off-label contexts. Procedures such as breast reconstruction, tooth extraction, and rotator cuff repair have all shown benefits of LB for perioperative analgesia.[9] Clinically, it has also been used in orthopedic procedures such as total knee and hip arthroplasty and several nerve plane blocks. However, results across various studies remain mixed about LB compared to other traditional analgesics in reference to cost-effectiveness and side effects.[10] Thus, LB represents a significant advancement in local anesthetic drug delivery. By utilizing multivesicular liposome technology, it provides extended and more stable analgesia compared to plain bupivacaine. Initially approved for local infiltration, its applications have since expanded into a variety of surgical and regional anesthesia contexts, including off-label use in truncal and peripheral nerve blocks. Its pharmacological properties and clinical versatility make it a promising agent for incorporation into multimodal analgesia protocols, particularly in high-pain procedures such as spine surgery.

Use of Liposomal Bupivacaine

LB is approved for the dose of 266 mg in a single injection with local infiltration. In comparison to bupivacaine HCL with an analgesic effect of 4–5 hours, LB can provide an extraordinary lengthened analgesic effect of 3–4 days with studies showing that the addition of dexamethasone can further increase the duration after a single injection.[11] The longevity of these drugs affect Factors related to the dosing of LB such as the patient comorbidities, size of the surgical site, and area of coverage needed. Considerations are to be made in patients with poor liver health due to the high protein components of the drug, possibly limiting the clearance of the drug. So, dosage should be adjusted in accordance with liver health. There is a distinct dosage when performing a peripheral nerve block, cutting the dose in half to 133 mg to prevent risk of local anesthetic toxicity. However, when combined with bupivacaine HCL, LB dosage should also be reevaluated as administration of both forms of the drug produces an additive effect of the drug. So, the ratio of bupivacaine HCL to LB should not exceed 1:2.[11]

Concerning LB usage in spinal surgeries, an erector spinae plane block has provided reliable results. The block reliably provides an analgesic effect of the dorsal rami rendering it useful in spine surgeries. It also frequently covers the axillary midline and into the anterior chest wall possibly granting clinical application in more than spine surgery.[12] Applications in spine surgeries go beyond the ESPB as local infiltration has been of use as a post-surgical analgesic for posterior spine surgeries, with use in lumbar and cervical fusions and decompressions.[13]

In addition to ESPB and other methods of use mentioned before, the implications for LB are rapidly expanding. The use of LB for TAP blocks has been approved by the Food and Drug Administration (FDA) as it has shown promising results in the use in abdominal surgeries. The use of LB in intra-articular injection is in clinical trials specifically in the setting of a total knee arthroplasty. However, the current research does not show a significant difference yet in the use of LB compared to normal bupivacaine. The administration of LB has also been seen in trials for epidural injections with studies showing an increased analgesic effect from the use of plain bupivacaine with three times the half-life in plasma and approximately 6 times the sensory numbness to cold.[8] Peripheral nerve blocks with LB have also been of use but currently have scarce supporting evidence for use as superior treatment.

In use outside of spinal surgeries, LB has evidence supporting the use in infiltration of surgical sites to reduce post-operative incisional pain through nerve blocks at the transverse abdominis plane and interscalene brachial plexus. Procedures the FDA approves for the use of LB are hemorrhoidectomies, bunionectomies, TAP blocks, and local infiltration in total knee arthroplasty and inguinal hernia repair.[11] LB may also prove useful in the setting of chronic pain in Radiofrequency Ablations (RFA) lengthening the pain relief to just before follow up appointments instead of the short period of analgesic effect plain lidocaine or bupivacaine would provide.

Benefits/Efficacy of Liposomal Bupivacaine for Erector Spinae Block in Comparison to Traditional Medications

Studies of LB use in an ESPB compared to other anesthetic treatments have shown promising results in aspects such as reducing hospital stay time (measured in days), opioid consumption (measured in morphine milligram equivalents (MME)), and pain scores. The retrospective study by Dincer et al in 2023[1] compared the use of LB in both a marginal suprafascial/subfascial plane (MSSP) injection and ESPB in 50 patients who underwent a transforaminal lumbar interbody fusion.[4] They found that the group of 25 patients who received both the MSSP-LB and ESPB-LB yielded a significant difference in length of hospital stay compared to the group who only received a MSSP-LB (2.56 days vs 3.36 days). Change in narcotic use found in this study also showed a decrease for the MSSP-LB and ESPB-LB group compared to the other treatment in total opioid consumption (137.3 MME vs 194.7 MME) and in the 12–24 hr post operative period (50.1 MME vs 62.3 MME). Pain scores revealed in this study that only a decrease in the 12–24 hr post operative period showed a statistically significant decrease in pain scores for the MSSP-LB and ESPB-LB group. This data shows that the addition of an ESPB with LB in spine surgeries is a promising candidate to effectively reduce time in the hospital and use of opioids and can potentially decrease post operative pain and should be considered for further research to prove consistent results.

Two related studies have found similar results. One study by Stondell and Roberto in 2022 compared two pediatric patients with idiopathic scoliosis who underwent a posterior spinal fusion (PSF) with an ESPB with a mixture of bupivacaine HCL and LB and 13 other patients who received IV methadone to control post operative pain.[6] The addition of bupivacaine HCL was because of the delayed efficacy in LB administration, so bupivacaine HCL would provide an immediate analgesic effect. The focus of this study was the relative length of stay (measured in minutes), opioid consumption (measured in oral morphine equivalents (OME)), and pain scores using the visual analogue pain scale. The two patients with the ESPB-LB resulted in a decreased length of stay in the hospital (3630 and 3830 minutes) compared to the IV methadone group (5490 minutes). The use of an ESPB with LB also contributed to a decrease in opioid consumption (1.67 and 1.85 OMEs mg/kg) compared to the IV methadone treated patients (3.5 OMEs mg/kg). Pain scores however were higher in the two patients receiving an ESPB with LB compared to the IV methadone patients. Because the sample size of this study only compares 2 patients receiving ESPB-LB, these findings should not be considered for statistical significance. However, it does prove the need for more research to effectively analyze the efficacy of this alternative and promising postoperative pain protocol.

The following studies provide a more reliable analysis of clinical efficacy with more patient outcomes in a similar setting of a posterior spinal fusion. A study by Young et al in 2025 further evaluates ESPB with LB with and without the addition of a patient-controlled analgesic (PCA) in patients with idiopathic scoliosis who underwent a posterior spinal fusion.[14] This study evaluated 72 patients who were divided into group A (patient-controlled analgesia (PCA) and an ESPB with LB) and group B (ESPB with LB only). This study resulted in group B showing a decrease in patient length of hospital stay (3.7 days) in comparison to group A (4.2 days) as well as a decrease in opioid consumption not only in total (99.8 MME vs 200.7) but also in every post operative day (POD0–POD3). Another similar study in the use of the ESPB in posterior spinal fusions has replicated the results shown in previously. Changoor et al evaluated the use of intraoperative liposomal bupivacaine (LB) in adolescents undergoing PSF for idiopathic scoliosis, comparing LB patients (n=53) to a non-LB control group (n=66). Consistent findings were found with LB use with decreased opioid consumption (44.5 vs 70.2 OME) and reduced length of stay (2.42 vs 2.74 days), reinforcing that the extended-release local anesthetic can be of use in elevating postoperative care.[15] However, the study revealed decreases in pain scores that did not show a statistical difference between the two groups. With the small sample sizes, similar patient populations, and heterogeneity of the results shown in the previous studies, this topic still requires a need for larger and diverse patient populations to analyze efficacy of the use of LB in spine surgery. The data in Table 1 shows a summarization of each comparative treatment in all studies analyzed and demonstrates that LB is a promising alternative analgesic and could consistently give patients a higher standard of post operative care in spinal surgeries.

As for general benefits of using the ESPB in spine surgery, the block is easily understood from an anatomy standpoint with very few structures to appreciate, making it easy to learn and perform.[12] Concerns with antithrombotic therapy can

Table 1 Clinical Efficacy

Author (Year)	Treatment Groups	Procedure	Length of Stay (LOS)	Opioid Consumption	Pain Score
Dincer et al (2023)[16]	MSSP-LB + ESPB-LB vs MSSP-LB only (n=50)	Transforaminal lumbar interbody fusion	MSSP-LB + ESPB-LB showed decrease in LOS	MSSP-LB + ESPB-LB showed decrease in 12–24 hr and total consumption	MSSP-LB + ESPB-LB showed lower pain scores from 12–24 hr postop and overall
Stondell and Roberto (2022)[6]	ESPB-LB vs IV Methadone (n=15)	Posterior Spinal Fusion	ESPB-LB showed decrease LOS	ESPB-LB showed lower consumption	IV methadone showed lower pain scores
Young et al (2025)[14]	ESPB-LB +PCA vs ESPB-LB only (n=72)	Posterior Spinal Fusion	ESPB-LB only showed decreased LOS	ESPB-LB only showed lower consumption	ESPB-LB only showed lower pain scores only on POD2
Changoor et al (2024)[15]	ESPB-LB vs standard multimodal pain management (n=119)	Posterior Spinal Fusion	ESPB-LB showed decreased LOS	ESPB-LB showed lower total consumption	No significant difference in pain scores

also be neglected with the ESPB. With the block considered as a "superficial plane" block any hemorrhage as a result of performing the ESPB would be compressible, so antithrombotic therapy can continue, compared to the paravertebral or epidural block which are deeper and can result in more serious hemorrhaging.[12] The previous studies mentioned before provide a framework for the benefits of using an ESPB with LB compared to other analgesics with decreased length of stay which can be attributed to other factors like decreased post operative pain and opioid consumption which lowers the risk for opioid side effects, ultimately promoting patient mobilization.[17] The decreased length of stay of LB highlighted in these studies also give an economical advantage to using this preoperative method. With a cost of $334.18 for the administration of LB, the patient's likelihood to be transferred to home care instead of a skilled nursing facility is increased. This decreases the cost of patient stay after surgery by approximately $1300 in a study with patients undergoing cephalomedullary nail implant to treat intertrochanteric hip fractures.[18]

Safety of LB and Complications Associated with LB Administration

Work done to analyze the safety of LB has shown promising results when comparing it to bupivacaine HCL. In a study by Ilfeld et al (2015), it was demonstrated by retrospectively analyzing the manufacturers clinical trials aimed at gaining approval for peripheral nerve blocks.[19] At the time the manuscript was written, the drug was only FDA approved for injections directly to the surgical site. The authors used 6 clinical studies which they claimed were the only studies available, to their knowledge, that examined the safety of this formulation for a peripheral nerve block in humans. They found that while overall AE (adverse event) rates were similar between liposome bupivacaine and placebo, treatment-related AEs were much lower with liposome bupivacaine than with bupivacaine HCl (13% vs 36%). Nervous system AE rates were comparable across groups, and cardiac safety margins remained well below toxic thresholds, even at the maximum FDA-approved dose. This data shows that LB is as safe, or potentially safer than bupivacaine HCL in some ways.

Other studies have shown similar results. An investigation by Viscusi et al from 2014 that analyzed safety data from 10 randomized, double-blind studies of LB[20] focused on local injections to the surgical site rather than peripheral nerve blocks. This study found that AE incidence was lower with LB (62%) vs bupivacaine HCl (75%), though higher than placebo (43%). No treatment-related SAEs were reported with liposome bupivacaine or placebo, compared to 6 cases with bupivacaine HCl. Any deaths and study withdrawals were rare and not considered drug related. This paper also looked at "AEs of special interest" and noted a few interesting findings. Although treatment-related cardiac AEs were <1% and only observed in liposome bupivacaine groups, they were mild, self-limited, and required no intervention. Another important note is that even with very high plasma concentrations from unintended intravascular injection, no clinical or ECG abnormalities occurred. Additionally, when looking at the potential risk of intra-articular damage due to exposure of bupivacaine, the data was similar between liposome and standard formulations, with no evidence of joint-related toxicity. These results further illustrate how LB seems to be safe and effective for use in surgical operations.

Not all patient outcomes are directly related to adverse events and complications. In a more recent paper by Brown et al from 2023, the researchers chose to look at an interesting relationship between patients who received LB and patients who did not, and their rates of opioid consumption after their surgery.[21] This study showed that patients who used preoperative LB for a nerve block consumed a much lower amount of opioid medication post-operatively. Less opioid consumption by the patient indicates that they experienced less pain and thus had less need for the medication. This also contributes to patient safety given that opioid medication can be addictive and have severe side effects.[22]

Recently a randomized controlled trial was published by Niu et al in September 2025, which gives great data on the comparison between standard methods of wound infiltration (WI) compared with ESPB using LB.[23] From a safety standpoint, the study found no significant differences between ESPB with LB and traditional wound infiltration. The procedure, performed under ultrasound guidance, was consistently safe and uncomplicated, with no reports of local anesthetic toxicity, hematoma formation, or nerve injury. Functional outcomes, as measured by the Oswestry Disability Index, were equivalent between groups, confirming that ESPB did not impair postoperative recovery. This paper also looked at the opioid-sparing effect associated with ESPB and again mentioned how it could indirectly enhance safety by reducing the risk of opioid-related adverse effects. Collectively, these findings support ESPB with LB as a safe, well-tolerated, and technically secure method for postoperative analgesia in spine surgery. See Table 2.

Table 2 Summary of Key Safety Findings

Study (Year)	Design and Use	Key Safety Findings
Viscusi et al (2014)[20]	Pooled analysis of 10 RCTs using local infiltration (n=1459)	AE rates: LB 62% vs bupivacaine HCl 75% vs placebo 43%. No treatment-related SAEs with LB or placebo. Deaths and withdrawals were rare and unrelated.
Ilfeld et al (2015)[19]	Pooled analysis of 6 trials evaluating peripheral nerve blocks (n=600)	Treatment-related AEs: LB 13% vs bupivacaine HCl 36%. Comparable nervous system AE rates; no cardiac toxicity or deaths. Demonstrated strong safety for peripheral nerve block use.
Brown et al (2023)[21]	Prospective cohort using supraclavicular nerve blocks for distal radius fractures (n=20)	No LB-related complications, neurologic, or cardiac events. Similar pain relief with significantly lower opioid use in the LB group.
Niu et al (2025)[23]	Randomized controlled trial using ESPB for lumbar fusion surgery (n=80)	No procedure-related adverse events, toxicity, or nerve injury. Comparable postoperative outcomes and reduced intraoperative opioid requirements.

Discussion

The growing emphasis on multimodal analgesia has driven a shift toward regional techniques that can effectively minimize opioid consumption while maintaining adequate postoperative pain control. Within this framework, LB administered via ESPB represents a promising evolution in perioperative analgesic strategy for spine surgery. The collective findings from multiple clinical studies demonstrate consistent trends toward reduced opioid use, improved postoperative pain scores, and shorter hospital stays when LB is incorporated into analgesic regimens.

The extended duration of analgesia observed with LB compared to standard bupivacaine formulations is particularly relevant in spine surgeries, which are often associated with substantial postoperative discomfort. The multivesicular liposome delivery system provides sustained drug release, prolonging the analgesic window from hours to several days. This extended relief can bridge the critical early postoperative period, during which patients are most vulnerable to pain-related complications and opioid overuse. Moreover, this sustained effect contributes to earlier mobilization and enhanced recovery, aligning with current Enhanced Recovery After Surgery (ERAS) protocols.

In addition to efficacy, safety and tolerability remain central concerns for any anesthetic agent introduced into regional blocks. The reviewed studies consistently report that LB maintains a safety profile comparable to or better than that of conventional bupivacaine HCl. Notably, the incidence of treatment-related adverse events was significantly lower with LB, and no serious cardiac or neurologic complications were observed even at maximal FDA-approved doses. This finding supports the pharmacologic predictability and stability of liposomal formulation.

The lack of intra-articular or chondrotoxic effects reinforces the safety of LB in settings where inadvertent joint exposure might occur, as in some spine and orthopedic procedures. Despite encouraging results, limitations remain in the current body of evidence. Many of the available studies are retrospective or limited in sample size, and several include heterogeneous surgical populations or dosing regimens. Additionally, cost-effectiveness analyses are not uniform, with some studies suggesting higher upfront costs of LB relative to standard bupivacaine, though potential savings from reduced opioid use and shorter hospital stays may offset this. Another consideration is that the onset of analgesia with LB alone may be delayed, leading some clinicians to use a combination of LB with bupivacaine HCl for immediate effect, a practice that requires careful dosing to avoid additive toxicity.

Future research should focus on optimizing dosing strategies, identifying ideal surgical contexts, and clarifying the long-term outcomes associated with LB-based regional anesthesia. Randomized controlled trials comparing ESPB with LB against other long-acting regional techniques, such as paravertebral or epidural blocks, would provide valuable insights into its relative efficacy. Additionally, further exploration into patient-reported outcomes, functional recovery, and opioid-sparing potential will help define the broader role of LB within multimodal pain management protocols.

In summary, the evidence supports the growing role of LB as a valuable addition to perioperative analgesia in spine surgery, combining effective, long-lasting pain control with a strong safety profile. As clinical adoption increases and evidence continues to mature, LB-based ESPB has the potential to become a cornerstone in the pursuit of safer, opioid-

sparing postoperative care. Across multiple clinical investigations, LB administered via erector spinae plane block (ESPB) demonstrated a favorable balance between efficacy, safety, and tolerability in postoperative pain management for spine surgery. Compared with bupivacaine HCl and placebo, LB provided similar or lower overall adverse event rates, notably fewer treatment-related adverse events, and no serious drug-related complications, even at the maximum FDA-approved dose of 266 mg. The most common events, such as nausea, constipation, and pruritus, were generally mild to moderate and occurred at rates comparable to placebo. Importantly, treatment-related cardiac and neurologic events were rare, and no instances of chondrotoxicity or intra-articular injury were reported, underscoring the formulation's strong safety profile. Clinically, the prolonged analgesic duration of LB supports improved postoperative comfort and earlier mobilization, while reducing dependence on opioids—a key goal of modern multimodal pain strategies. The pharmacokinetic data further reinforces its safety margin, with peak plasma concentrations remaining well below established toxicity thresholds.

Conclusion

In conclusion, these findings suggest that LB represents a safe and effective advancement in regional anesthesia for spine surgery, capable of sustaining analgesia without increasing systemic risk. There is still a need for larger, procedure-specific trials are warranted to optimize dosing and confirm cost-effectiveness. Current data is limited, and further prospective studies are required to confirm LB as superior to standard bupivicaine. While there is still much work to be done, the accumulated evidence positions LB-based ESPB as a valuable component of enhanced recovery pathways, offering both extended pain control and meaningful opioid reduction in the perioperative setting.

Disclosure

The authors report no conflicts of interest in this work.

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