

Subarachnoid-Subarachnoid Bypass Surgery Treats Syringomyelia Through Indirect Drainage via Perivascular Spaces and Ependymal Repair: Evidence from Rat Models and Clinical Application

Can Zhang

heibei

Chenghua Yuan

Xuanwu Hospital Capital Medical University

Jun Bai

Xuanwu Hospital Capital Medical University

Shengyu Cui

Xuanwu Hospital Capital Medical University

Jinze Li

Xuanwu Hospital Capital Medical University

Sumei Liu

Xuanwu Hospital Capital Medical University

Nanding Li

heibei

Kang Li

Xuanwu Hospital Capital Medical University

Fan Yuan

Xuanwu Hospital Capital Medical University

Xiaoli Sun

heibei

Honglei Liu

heibei

Jian Guan

heibei

Fengzeng Jian

jianfengzeng@xwh.ccmu.edu.cn

heibei

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Abstract

Background

Syringomyelia is a chronic progressive disorder characterized by abnormal cerebrospinal fluid (CSF) accumulation within the spinal cord, often due to subarachnoid space (SAS) obstruction. Conventional decompression or shunt procedures yield unsatisfactory long-term outcomes, limited by inadequate decompression, arachnoid adhesions, or shunt failure.

Methods

A modified rat model of syringomyelia was created using polystyrene microspheres to obstruct the SAS. Syrx volume was assessed by 7.0T MRI, alongside behavioral, electrophysiological, and immunofluorescence analyses comparing subarachnoid–subarachnoid (S-S) bypass with decompression. CSF tracer studies evaluated postoperative dynamics, and confocal imaging quantified tight junction proteins (ZO-1, Claudin-5) and ciliary markers (Arl13b, γ -Tubulin). CSF proteomics explored underlying mechanisms. Clinically, seventeen patients with syringomyelia secondary to arachnoid adhesions underwent S-S bypass as a preliminary feasibility and safety evaluation, with MRI and neurological evaluation pre- and postoperatively.

Results

In rats, the bypass surgery significantly reduced syrinx volume compared with decompression, improving sensory and motor function. The bypass restored outward CSF flow via perivascular spaces, preserved ZO-1 and Claudin-5 expression, and enhanced ciliary markers, indicating ependymal integrity and improved clearance. Proteomics implicated mitochondrial dysfunction and neurodegenerative pathways, with Cox5a identified as a potential biomarker. Clinically, all seventeen patients showed MRI and neurological improvement, supporting the feasibility and preliminary therapeutic potential of this technique.

Conclusion

S-S bypass surgery restores physiological CSF circulation without damaging spinal cord parenchyma and preserves ependymal structure. This approach provides superior outcomes to decompression in rat models, and preliminary clinical results support its feasibility and translational potential as a novel treatment strategy for syringomyelia.

Introduction

Syringomyelia is a serious complication secondary to spinal cord injury, arachnoid adhesion, intramedullary tumor and other pathologies. It is characterized by abnormal cystic expansion within the spinal cord(1, 2). Prevailing theories attribute syrinx formation and expansion to impaired CSF circulation with resultant localized pressure elevation(3–5). Consequently, resolving CSF dynamics disturbances represents a potential therapeutic strategy.

Current clinical management primarily employs arachnolysis to achieve decompression and restore physiological CSF flow(6). After laminectomy, adherent arachnoid tissue is carefully dissected with microsurgical scissors and dissectors to relieve compression of the nerves and spinal cord. However, in many patients, decompression fails to improve outcomes due to severe adhesions or surgical trauma, and it may even lead to complications such as postoperative adhesive arachnoiditis(7–9) – consistent with our prior rodent model findings(10). Shunt procedures, diverting syrinx fluid to subarachnoid, thoracic, or peritoneal cavities, offers an alternative approach to address CSF dynamic abnormalities(11). Nevertheless, its efficacy is limited by intradural manipulation requiring spinal cord penetration for catheter placement, high shunt obstruction rates, and overdrainage complications(12, 13).

Building on shunt surgery principles, we developed a novel bypass procedure in rats and successfully applied it to patients with syringomyelia. This technique employs subcutaneous tunneling to position drainage catheters at spinal segments exhibiting CSF dynamic abnormalities, thereby restoring physiological CSF circulation without requiring manipulation of the spinal cord.

Syringomyelia progression is a chronic process spanning months to years. Clinical symptoms manifest only when syrinx expansion exceeds the spinal cord's compensatory threshold – typically coinciding with critical structural involvement or substantial volume increases that limit intervention efficacy(14). Early detection is therefore critical for prognosis improvement. This study aims to identify potential biomarkers for syringomyelia progression using proteomics, thereby providing a theoretical basis for early diagnosis and therapeutic intervention of this condition.

Methods

2.1. Animal Inclusion and Ethics Statement

A total of 46 8-week-old female Sprague-Dawley rats (200-240g; WeiTongLiHua Corp., Beijing, China) were used in this study. All rats were housed under standard conditions at the Animal Experiment Center of Xuanwu Hospital, with a 12-hour light/dark cycle and ad libitum access to food and water. All animal experiments complied with laboratory animal welfare requirements. The experimental protocol was approved by the Animal Ethics Committee of Capital Medical University (Approval No. XW-20230712-1). Rats that underwent syringomyelia induction were screened by MRI at 4 weeks. After excluding animals with a syrinx diameter < 0.5 mm or length < 3 mm (15) (thresholds below which prior studies indicate that reproducible neurological deficits may not occur), the modeling success rate was 83.33%. Eligible

rats were stratified by MRI-measured syrinx volume and randomized into groups using stratified block randomization. The specific method is as follows: 30 eligible rats were randomized by a researcher who was not involved in any subsequent experimental procedures. we first ranked all animals from smallest to largest syrinx size. The ranked list was then stratified into three tertiles: small (positions 1–10), medium (positions 11–20), and large syringes (positions 21–30). Within each stratum, we applied block randomization (block size = 3). Animals were assigned numerical codes in SPSS based on their rank order, and block allocation was generated using a random number generator (seed = 2,000,000; range 0–10). Starting from the first animal in the list, each was allocated to a treatment group according to the generated random number. The final group assignments were sealed in opaque, animal-coded envelopes. Surgeons remained blinded to all allocation information throughout the study. The final allocation included 10 rats in the Bypass group, 10 in the Decompression group, 10 in the Vehicle group (this group underwent the same anesthesia and surgical exposure as the other groups but did not receive any therapeutic procedure), and 10 in the Sham group. The detailed experimental timeline is outlined in Supplementary Fig. 1A. This study has been reported in accordance with the ARRIVE guidelines (Animals in Research: Reporting In Vivo Experiments)(16).

2.2. Surgical Procedures in rats

2.2.1. Modified Syringomyelia Induction Surgery

This method differs slightly from our previously described syringomyelia induction protocol(10), primarily by replacing sterile cotton pellets with elastic polystyrene microspheres. Briefly, rats were anesthetized via face mask with 1.5% isoflurane (RWD Life Science, Shenzhen, China). Following exposure of the T12-T13 interlaminar space, the ligamentum flavum was incised using microscissors. In contrast to our previous method using sterile cotton pellets, three sterile, elastic polystyrene microspheres (0.5 mm in diameter; Chuangxin Corp., Shandong, China) were gently inserted sequentially into the SAS. Successful SAS obstruction was defined microscopically by observable indentation of the dura mater with close apposition to the spinal cord surface (Fig. 1A). Sham group received identical procedures terminated at ligamentum flavum incision, preserving epidural integrity. Muscles and skin were closed in layers postoperatively.

2.2.2. Decompression Procedure

The original incision was reopened to expose the T12. The scar encapsulating the microspheres was incised microscopically with removal of compressive microspheres. This revealed indented dura with visible vasculature. Within minutes post-removal, expansion of the collapsed spinal cord beneath the dura mater was observed, indicating SAS reestablishment (Fig. 1B). Decompression was deemed successful upon complete resection of residual scar tissue using microscissors.

2.2.3. S-S Bypass Procedure

Following anesthesia, the spinal cord and dura mater beneath T10-L2 vertebral laminae were exposed. a thermoplastic polyurethane catheter (HuaMei Corp., Shanghai, China; ID 0.30 mm, OD 0.40 mm) was trimmed, bevel-tipped microscissorically, and fenestrated with 30-gauge needle slits within 0.5 cm of both ends; after heparinized saline immersion (100 U/mL), introducer needle delivery to L2 preceded micro-forceps-guided 0.5 cm rostral subarachnoid advancement—confirmed by sustained CSF efflux—with analogous 0.5 cm caudal placement at L2 (Fig. 1C), maintaining ventral bevel orientation and gentle insertion force to prevent parenchymal injury; the catheter was then secured followed by layered muscle and skin closure. At the end of the experiment, drainage catheters were dissected from the rats and examined for patency. All catheters were patent, and cerebrospinal fluid tracer studies further confirmed catheter patency (Supplementary Fig. 1B).

All procedures were performed by a single surgeon under surgical microscopy (OPMI Pico, Carl Zeiss, Germany; 16×). Postoperative infection prophylaxis consisted of intraperitoneal cefuroxime sodium (100 mg/kg every 8 hours for 7 days).

2.3.CSF tracer injection

To visualize CSF flow within the SAS, 2.5% Evans Blue (EB) was used as a tracer(15). Briefly, after anesthesia, animals were placed in the prone position, and a 1.5 cm midline incision was made at the cranio-cervical junction. The overlying soft tissues and muscles were bluntly dissected to expose the atlanto-occipital membrane. A 34G needle was inserted through the membrane, followed by placement of a polyethylene-10 tube (inner diameter 0.28 mm) into the cisterna magna. Laminectomies were then performed at the T10 and L2 vertebral levels to expose the underlying dura mater. A total of 150 μ L of 2.5% EB was continuously infused via the PE-10 tubing over 30 minutes using an injection pump (R462, RWD Life Science Co., Shenzhen, China). The puncture site and cannula were sealed with surgical adhesive to prevent CSF or tracer leakage. Throughout the process, a real-time imaging system (Dow Peak, Beijing, China) linked to a surgical microscope and image processing software (S-EYE, version 1.6.0.11) was used to capture high-resolution static images of the dura mater at both T10 and L2 levels.

To further assess CSF flow within the central canal (CC) and SAS, Alexa Fluor 647 and Alexa Fluor 568 (45 kDa; Thermo Fisher Scientific Inc., USA) were used as fluorescent tracers. Injections were performed using a microsyringe (Hamilton, Weike, China) fitted with a 30G needle and mounted on a stereotactic micromanipulator. Tracers (5 μ L at 25 μ g/ μ L) were slowly delivered into the cisterna magna, SAS, or syrinx over 5 minutes. Following injection, the needle was left in place for an additional 20 minutes to minimize reflux. At specified time points, animals were perfused and tissue samples collected. Confocal imaging was performed after sample preparation and sealing(17).

2.4. Animal MRI and Syrinx Volume Measurement

In vivo MRI was performed using a 7.0 Tesla scanner (PharmaScan 7T, Bruker Corp., Karlsruhe, Germany) with 400 mT/m gradient strength at the Animal Imaging Laboratory Center of Capital Medical University. An 89 mm volume coil was used for signal transmission and reception. Rats were positioned supine on the scanner bed and secured with two restraining belts to immobilize the trunk. Anesthesia was

maintained with isoflurane throughout the procedure, and physiological parameters including body temperature, heart rate, and respiration were continuously monitored. Following rapid whole-body localization scans, sagittal and axial T2-weighted images were acquired using a fat-saturated RARE sequence centered on the surgical site(18).

Syrinx volume was semi-automatically calculated from T2-weighted images using 3D Slicer software(19). Briefly, the Segment Editor module was used to apply an initial threshold range of 15,000–32,000 to roughly distinguish the hyperintense syrinx lumen from surrounding spinal cord tissue. Manual slice-by-slice correction was then performed in axial, sagittal, and coronal planes to exclude non-syrinx hyperintense regions. A three-dimensional model was subsequently reconstructed using the Model Maker function, and total syrinx volume was automatically calculated. Collection and quantitative analysis of relevant data were performed by fully blinded researchers.

2.5. Sensory and Motor Function Assessment

Sensory deficits, particularly diminished pain and thermal sensitivity are characteristic features of syringomyelia. To quantitatively assess the pain threshold, the Von Frey hair test was conducted. Rats were placed in transparent cages with metal mesh floors and allowed to acclimate for 15 minutes. Mechanical stimuli of increasing force (1.4–60 g) were applied vertically to the central plantar surface of the hind paw. Each stimulus lasted 4–6 seconds. A withdrawal, licking, or shaking response was recorded as a positive reaction. The paw threshold was calculated using the classic "up-and-down" method(20). Each hind paw was tested three times with a 10-minute interval between trials, and the average value was recorded as the result.

Thermal sensation was evaluated using the hot plate test with a hot/cold plate pain analyzer (Bioseb, France). The plate was maintained at a constant temperature of $52 \pm 0.5^{\circ}\text{C}$. The latency to pain response—defined as paw withdrawal, licking, or jumping—was recorded. If no response occurred within 50 seconds, the animal was removed to prevent tissue damage, and the test was terminated. Each animal underwent three trials, and the average latency was used for analysis.

The ladder walking test was used to assess motor coordination and fine motor skills(21). The apparatus consisted of a 1-meter-long, 15-centimeter-wide staircase with 2-centimeter steps, enclosed in a transparent tunnel and elevated 50 cm above the ground. Dark boxes were placed at both ends, with a food reward located in one. Each rat was tested in three sessions, with at least a 10-minute interval between trials. Animals were motivated to cross the stairs to reach the food reward. The test sessions were recorded and analyzed based on a detailed 0–6 point foot fault scoring system.

Collection and quantitative analysis of relevant data were performed by fully blinded researchers to ensure data reliability and minimize observer bias.

2.6. Neurological electrophysiology analysis

Rats were anesthetized with isoflurane. After shaving and disinfecting the scalp, a midline incision was made to expose the skull. Two small cranial windows (approximately 1–2 mm in diameter) were carefully drilled using a micro dental drill at 2.0 mm posterior to bregma and 2.0 mm lateral to the midline to expose the dura mater. Somatosensory evoked potentials (SEPs) were recorded using a multichannel physiological signal acquisition system (RM6240EC, Chengyi). The stimulating electrode was inserted parallel into the gastrocnemius muscle, the recording electrode was placed directly on the exposed dura over the somatosensory cortex, and the ground electrode was inserted subcutaneously into the dorsal skin. Electrical stimulation was delivered at an intensity of 10 mA and a frequency of 1 Hz to evoke SEPs. For each rat in all experimental groups, SEP latency and amplitude were analyzed: Latency: the time representing the total sensory conduction time from the peripheral stimulation site to the cortex. Amplitude: the peak-to-peak voltage reflecting the number of synchronously activated neurons along the sensory pathway. Collection and quantitative analysis of relevant data were performed by fully blinded researchers.

2.7. Collection of CSF Samples and Spinal Cord Tissues

Following anesthesia induction, rats were positioned prone with the head oriented vertically downward on a custom-made thermostatic surgical table maintained at 36°C to fully expose the foramen magnum (Fig. 7A), and the foramen magnum area was shaved and disinfected. A 30 G insulin syringe was then carefully inserted into the skin, and negative pressure was applied by slowly pulling the plunger. The needle was advanced toward the foramen magnum, and clear, transparent CSF was observed entering the syringe. CSF was collected at four time points: 1 week prior to modeling, 2 weeks post-modeling, 4 weeks post-modeling, and 4 weeks post-treatment. Approximately 100–120 µL of CSF was obtained at each collection. The samples were immediately placed in liquid nitrogen for rapid freezing and later transferred to a – 80°C freezer for storage and future analysis(22).

Following excessive inhalation of isoflurane, rats were perfused with 4% paraformaldehyde (PFA, Sigma) in PBS. The spinal cord was carefully extracted and placed in 4% PFA overnight at 4°C. The tissue was then transferred to 30% sucrose (Sigma) and incubated at 4°C overnight. For cryoprotection, the spinal cord was embedded in optimal cutting temperature (OCT) compound (Sakura Corp., Tokyo, Japan) on dry ice. Tissue sections of 20 µm thickness were cut using a cryostat microtome (CM3050 S, Leica Biosystems, Nussloch, Germany) and mounted on charged slides for subsequent analyses.

2.8. Immunofluorescence

Collected sections were first washed with 1× PBS (0.01 M) and then incubated with 5% normal donkey serum (NGS, Sigma) and 0.3% Triton X-100 (Sigma) at room temperature for 1 hour to block non-specific binding. Following this, the sections were incubated overnight at 4°C with primary antibodies. The next day, the sections were washed three times with PBS and incubated with fluorescently labeled secondary antibodies (Invitrogen) for 1 hour at room temperature. After thorough PBS washing, the sections were mounted using a DAPI-containing anti-fading mounting agent. Immunofluorescent images were then

acquired using a confocal laser scanning microscope (STELLARIS 5, Leica Corp., Wetzlar, Germany) with appropriate excitation wavelengths.

The primary antibodies used were as follows: mouse anti-Neun (Proteintech, 66836-1-Ig, 1:500), rabbit anti-Chat (Proteintech, 20747-1-AP, 1:500), mouse anti-NF200 (Sigma, N0142, 1:500), rabbit anti-MBP (Abcam, 218011, 1:500), mouse anti-CS56 (Sigma, C8035, 1:200), mouse anti-RECA-1 (Santa Cruz, 52665, 1:200), rabbit anti-GFAP (Abcam, 7260, 1:500), rabbit anti-ZO-1 (Abcam, 221547, 1:500), mouse anti-Claudin5 (Invitrogen, 35-2500, 1:500), goat anti-FOXJ1 (AF3619, 1:500), rabbit anti-ARL13b (Proteintech, 17711-1-AP, 1:500), and mouse anti- γ -Tubulin (Sigma, T6557, 1:500).

2.9 Scanning Electron Microscopy

To assess the ultrastructure of ependymal cilia lining the CC, we performed scanning electron microscopy (SEM). At the study endpoint, spinal cord segments containing the syrinx were harvested after perfusion fixation and opened along the sagittal plane to expose the canal lumen while avoiding compression of the scanning surface. Samples were fixed at room temperature in electron microscopy fixative (G1102, Servicebio, China) for 2 hours and then stored at 4°C. The ependymal surface of the CC was imaged using a QUANTA 200 scanning electron microscope (FEI, Hillsboro, USA).

2.10 CSF Proteomic Analysis

Proteins were extracted from rat CSF using SDT lysis buffer (4% SDS, 100 mM Tris-HCl, pH 7.6). Protein concentration was quantified using the BCA assay and samples were digested with trypsin following the filter-aided sample preparation (FASP) method. Peptides were desalted with C18 cartridges, lyophilized, and reconstituted in 0.1% formic acid containing iRT standard peptides. Data-independent acquisition (DIA) analysis was performed on an Orbitrap Astral high-resolution mass spectrometer (Thermo Scientific) coupled to a Vanquish Neo nanoflow liquid chromatography system. Raw data were processed using Spectronaut Pulsar X software. Differentially expressed proteins were first identified using a threshold of fold change ≥ 1.5 and $p < 0.05$, followed by Benjamini–Hochberg correction to control the false discovery rate. K-means clustering, with the optimal K determined by the elbow method, was then applied to select proteins whose expression patterns aligned with disease progression and treatment response. Subsequently, protein–protein interaction network analysis and supporting literature were used to identify proteins located at key network nodes and implicated in neurological pathology. These proteins were designated as the final candidate biomarkers. Gene Ontology (GO) annotation and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were performed using the clusterProfiler package (Version 3.8.1).

2.11 Clinical Samples and Surgical Procedure

This study included seventeen patients with syringomyelia secondary to arachnoid adhesions, treated at Xuanwu Hospital between January 2024 and June 2025. Some patients were enrolled in a prospective cohort study (ClinicalTrials.gov NCT06375759, 2024-04-16, Xuanwu Hospital, Beijing).

All patients presented with progressive neurological symptoms and underwent the S-S bypass surgery. Inclusion criteria were: (1) adhesive arachnoiditis resulting from trauma or prior intraspinal surgery; (2) progressive neurological deficits and/or pain syndrome; (3) MRI-confirmed syringomyelia without tumor recurrence, hardware loosening, or kyphotic deformity; and (4) exclusion of patients with isolated myelomalacia, intradural cysts. Motor weakness and sensory deficits were assessed using the American Spinal Injury Association (ASIA) motor and sensory scores(23). Syrinx size was evaluated by the number of vertebral segments involved and by calculating the syrinx tension index(24). All evaluations were performed by two independent specialists blinded to patient details. Written informed consent was obtained from all participants prior to surgery, and the study was approved by the institutional review board.

The surgical method is as follows(25): Under general anesthesia, the patient was placed in the prone position. Based on preoperative MRI and CT myelography, the cranial and caudal levels for the S-S bypass surgery were identified to expose normal dura. A subcutaneous tunnel was created using a tunneling device. Under an operating microscope, two 3 mm longitudinal incisions were made on each side of the midline at the cranial site to expose normal arachnoid. The arachnoid was opened, and two medical-grade silicone catheters (internal diameter 1.1 mm, external diameter 2.5 mm; Sophysa Systems Corporation) were inserted parallel to the longitudinal axis of the spinal cord into the normal SAS to a depth of approximately 5 cm. The same procedure was performed at the caudal site (Fig. 7A). Throughout the procedure, meticulous microsurgical technique was maintained to avoid inadvertent injury to the spinal cord or superficial vessels, and the bypass catheters were oriented carefully during insertion. When the catheter tip reached the normal CSF-containing region, CSF flow and air bubble movement were visible within the catheter. After one catheter was fully inserted into the SAS at both ends and the other catheter was inserted at only one end, sterile saline was injected via the unattached end to fill the dural sacs at both sites. The transparent walls of the catheters allowed visualization of fluid movement between the two ends. The dura was then closed tightly with 6 – 0 non-absorbable sutures, and the catheters were secured to both the dura and fascia.

2.12 Statistical Analysis

Quantitative data are presented as mean $\pm$ SEM. Before applying parametric tests, we systematically assessed normality using the Shapiro–Wilk test and homogeneity of variance using Levene’s test. When both assumptions were met ($p > 0.05$), group comparisons were performed using Student’s t-tests. If either assumption was violated, alternative methods were selected as appropriate, including Welch’s t-tests, Mann–Whitney U tests, or Wilcoxon signed-rank tests. Statistical significance was defined as $*p < 0.05$, $**p < 0.01$, and $***p < 0.001$. All analyses were performed using GraphPad Prism 10.2.3 (GraphPad Software, San Diego, CA, USA) and SPSS version 27.0 (IBM, Armonk, NY, USA). All sensory and motor assessments were performed with three technical repetitions to ensure data reliability.

Result

3.1 The S-S Bypass Surgery Significantly Reduces Syring Volume and Improves Neurological Function Compared to The Decompression Surgery

This study aimed to evaluate the therapeutic effects of the S – S bypass surgery and decompression surgery in the treatment of syringomyelia. MRI and 3D reconstruction were employed to assess changes in syringomyelia before (4W) and after surgery (8W) (Fig. 1B). MRI at 4 weeks post-surgery revealed a significant reduction in syrinx volume in the Bypass group (52.86%) compared to the decompression group (29.76%) (Fig. 1C). The treatment effectiveness rate, defined as a reduction in syrinx volume by more than 50%(15, 26, 27), was 80.00% in the Bypass group, significantly higher than the 40.00% rate observed in the decompression group (Fig. 1D). Syringomyelia typically leads to abnormal sensory perception, pain sensitivity, and motor dysfunction. To assess the therapeutic effects on these symptoms, we conducted a comprehensive analysis of postoperative behavior and physiological changes, utilizing Von Frey hair test, hot plate test, electrophysiological assessments, and the ladder walking test. Sensory function evaluation demonstrated the Bypass group exhibited significant improvements in sensory and pain perception compared to the Decompression group at 4 weeks post-surgery (Von Frey hair test: $p = 0.011$, Cohen's $d = -1.271$; the ladder walking test: $p = 0.042$, Cohen's $d = -0.977$) (Fig. 1E, F). Electrophysiological recordings of SEP revealed a significant improvement in the Bypass group at 4 weeks post-surgery, as reflected by changes in amplitude and latency, in contrast to the Decompression group (SEP latency: $p = 0.038$, Cohen's $d = -1.001$; SEP amplitude: $p = 0.026$, Cohen's $d = 1.084$) (Fig. 1G-I). Furthermore, results from the ladder rung walking test indicated superior recovery in the Bypass group at 4 weeks post-surgery, with a statistically significant difference when compared to the Decompression group ($p = 0.037$, Cohen's $d = 1.010$) (Fig. 1J-L). These findings suggest that the S – S bypass surgery is more effective than decompression surgery in reducing syrinx volume and improving sensory dysfunction, pain perception, and motor coordination in rats.

3.2 The S – S Bypass Surgery Confers Neuroprotection by Preserving Anterior Commissure Neurons and Myelin Integrity

The mechanical dilation occurring during the development of syringomyelia can adversely affect the neurons surrounding the spinal cord. Neuronal innervation is mediated by the excitatory neurotransmitter acetylcholine(28), and the expanding syrinx often leads to the loss of myelin sheath and the rupture of axons. Sensory dysfunction in syringomyelia is primarily caused by the invasion of the anterior junction area, and timely intervention can reverse this pathological process(15, 29). We compared the number of neurons (NeuN⁺) between the Bypass group and the Decompression group. The density of NeuN⁺ cells around the spinal cord was significantly higher in the Bypass group than in the Decompression group ($p = 0.037$, Cohen's $d = 1.578$) (Fig. 2A, E). This was further corroborated by Nissl staining, which confirmed a higher density of neurons in the Bypass group ($p = 0.012$, Cohen's $d = 2.042$) (Fig. 2B, G). Moreover, the immunoreactivity for acetylcholine (Chat⁺) was significantly higher in the Bypass group compared to the Decompression group ($p = 0.008$, Cohen's $d = 2.236$) (Fig. 2A, F), consistent with the results observed in

the ladder rung walking test. Additionally, we compared the myelin sheath (MBP⁺) and axons (NF200⁺) in the anterior junction area. The Bypass group exhibited better preservation of NF200⁺ axons ($p = 0.016$, Cohen's $d = 1.919$) (Fig. 2D, H) and MBP⁺ myelin structures ($p = 0.034$, Cohen's $d = 1.614$) (Fig. 2D, I) compared to the Decompression group. LFB staining further supported this finding, showing less myelin loss in the Bypass group ($p = 0.036$, Cohen's $d = 1.592$) (Fig. 2C, J). In addition, we performed Spearman correlation analyses between syrinx volume and key histological measures. Syrinx volume showed significant negative correlations with neuronal survival, cholinergic neuronal markers, axonal density, and myelin integrity (Supplementary Fig. 1C). These results indicate that the bypass surgery provides superior neuroprotective effects compared to decompression surgery, preventing further myelin and axonal damage.

3.3 Evaluation of CSF Circulation in the Two Surgical Methods

To explore the reasons behind the differences in therapeutic outcomes between the two surgical methods, we first employed EB as a CSF tracer, 4 weeks post-surgery. Following injection into the cisterna magna, we observed color changes in the subdural CSF at the T10 and L2 spinal segments to indirectly assess the patency of the subdural CSF pathway (Fig. 3A). Within 15 minutes, the blue color change was more pronounced in both the Bypass and Decompression groups compared to the Vehicle group, with noticeable differences in the color intensity between the Bypass and Decompression groups (Fig. 3B).

To further quantify these differences, OVA647 was used as a CSF tracer 4 weeks post-surgery, and animals were sacrificed 15 minutes later. The spinal cords from the T10, T12, and L2 were examined, and the percentage of tracer-positive area was calculated. At the T10, the Vehicle group exhibited a significantly higher percentage of tracer-positive area than the Bypass group ($p = 0.024$, Cohen's $d = -2.895$). However, no significant difference was observed between the Bypass and Decompression groups, suggesting that the Bypass and Decompression groups had similar CSF flow, while the Vehicle group had more substantial CSF obstruction. In the L2, the Bypass group showed a significantly lower percentage of tracer-positive area compared to both the Decompression group ($p = 0.041$, Cohen's $d = -2.423$) and the Vehicle group ($p = 0.011$, Cohen's $d = 3.629$) (Fig. 3C, D), indicating improved CSF patency in the Bypass group. These results suggest that the Decompression group still experience partial CSF obstruction post-surgery. To investigate this further, we examined the scar formation in the Decompression group and found partial scar formation in both transverse and longitudinal sections. These scars adhered to the SAS and were connected to the dura mater (Fig. 3E).

3.4 The Fluid Transport Mechanism in Syringomyelia and The Therapeutic Basis of the S – S bypass Surgery

3.4.1 Dynamic CT Tracing Reveals Fluid Migration via the SAS–Spinal Parenchyma Pathway

Syringomyelia ultimately results from the accumulation of fluid within the CC, yet the precise entry route of this fluid remains under debate. To investigate this, rats with MRI-confirmed syringomyelia were subjected to intraventricular injection of iohexol, followed by serial CT imaging to track the distribution of the contrast agent over time (Fig. 5A). At 30 minutes post-injection, iohexol was confined to the SAS (indicated by red arrows), with no visible enhancement in the CC. At 1 hour, the signal within the SAS began to diminish. By 2 hours, contrast intensity in the SAS had markedly decreased, while faint enhancement appeared in the CC (white dashed line). At 3 hours, subarachnoid signal was nearly absent, whereas contrast in the CC was clearly intensified (white dashed line). These observations suggest that the contrast agent migrates from the ventricular system into the SAS, and subsequently enters the CC via the spinal parenchyma.

3.4.2 PVS Mediate Fluid Transport in Syringomyelia Formation

PVS have been implicated in CSF transport and exchange(30, 31). IF analysis of tracer distribution demonstrated clear colocalization with vascular structures within the spinal cord parenchyma (Fig. 5B). Tracer accumulation was particularly prominent in the anterior median fissure region of the SAS (red arrows, Fig. 5B), suggesting CSF preferentially enter the parenchyma through the anterior median fissure. Three-dimensional confocal imaging with vascular (Reca-1) and astrocytic (GFAP) markers revealed that OVA647 was distributed along PVS bounded by Reca-1⁺ endothelia and GFAP⁺ astrocytic endfeet (red arrow, Fig. 5C). These findings support a mechanism by which CSF enters the CC from the SAS via PVS.

3.4.3 Dual-Tracer Experiment: The S – S Bypass Surgery Enhances Outward Net Flow and Reduces Syrinx Volume

Building upon the above findings, we propose a model wherein fluid exchange between the CC and the SAS is bidirectional under physiological conditions (Fig. 4D). Obstruction of CSF flow within the SAS increases local pressure, leading to a net influx of fluid into the CC and subsequent syrinx formation (Fig. 4E). The S – S Bypass surgery restores CSF circulation by introducing an alternative flow route, reversing the pressure gradient and promoting resolution of the syrinx. To test this hypothesis, dual-tracer studies were performed in rats following syringomyelia induction and bypass surgery. Tracers of identical molecular weight—OVA568 (red) and OVA647 (white)—were used to assess fluid movement (Fig. 4F). In the Vehicle group, stereotactic injection of OVA568 into the syrinx and OVA647 into the SAS revealed symmetric distribution of both tracers in the SAS and syrinx region, confirming bidirectional exchange. In contrast, animals that underwent bypass surgery (assessed on postoperative day 3) exhibited markedly different tracer behavior. OVA568 injected into the syrinx migrated into the SAS, whereas OVA647 introduced into the SAS failed to enter the syrinx and remained restricted to the spinal

parenchyma (Fig. 4G). These results indicate that the S-S bypass surgery inhibits inward flow from the SAS to the CC, thereby reducing syrinx volume through restoration of outward net flow.

3.5 The Role of Ventricular Ependymal Structural and Functional Abnormalities in Syringomyelia and the Restorative Effects of Bypass Surgery

Previous findings from our group suggest that ependymal cells (Foxj1) surrounding the CC play a key role in the development and progression of syringomyelia(29, 32). Tight junctions (TJs) between these cells act as critical barriers regulating fluid permeability(33), with proteins such as ZO-1 and Claudin-5 contributing to the maintenance of CC boundary integrity(34). Additionally, coordinated beating of ependymal cilia (Arl13b) is essential for CSF flow and exchange(35), while the presence of centrioles (γ -Tubulin) supports ciliary stability. In the syringomyelia model, we observed that TJs disruption within the CC ependymal layer is a key factor promoting syrinx expansion (Fig. 5A). Specifically, when the honeycomb structure remained continuous, CSF tracer injected into the anterior median fissure region of the SAS showed limited entry into the CC. In contrast, when honeycomb structures continuity was lost, tracer distribution within the CC significantly increased. These results indicate that loss of TJ integrity facilitates abnormal fluid entry into the CC, driving syrinx enlargement. We next assessed the integrity of TJs in the CC ependyma across the Bypass group and the Vehicle group. Both the structural continuity of ZO-1 and Claudin-5 expression were significantly preserved in the Bypass group compared to the Vehicle group (Fig. 5B–D). We further evaluated ciliary architecture and centrioles density between the Bypass group and the Vehicle group. IF staining revealed a marked increase in cilia and centrioles density in the Bypass group (Fig. 5E–G). Scanning electron microscopy confirmed these findings: in the Bypass group, cilia were well-preserved in both structure and number, while in the Vehicle group, cilia were reduced and frequently displayed significant lodging (Fig. 5H). These findings suggest that the potential mechanism of the S – S bypass surgery treatment for syringomyelia involves both repairing or preventing TJ disruption to block abnormal CSF influx, and enhancing CSF clearance by restoring ciliary motility or preventing further ciliary damage.

3.6 Analysis of Differential CSF Proteins and Identification of Candidate Biomarkers During Syringomyelia Progression

To investigate potential biomarkers and molecular pathways involved in the pathogenesis and progression of syringomyelia, we performed proteomic profiling of CSF collected from rats at distinct time points. Based on previous findings that syringomyelia formation occurs around 4–6 weeks post-induction, samples were collected at four time points: pre-modeling, 2 weeks post-modeling, 4 weeks post-modeling, and 4 weeks post-treatment. Using fold change $FC > 1.5$ and $p < 0.05$ as thresholds for significance, a total of 464 differentially expressed proteins (DEPs) were identified across the time points. A heatmap illustrated the temporal expression patterns of these DEPs between groups (Fig. 6B). To characterize the functional roles and biological processes associated with the DEPs, GO enrichment analysis was performed. In the Biological Process category, upregulated proteins were significantly

enriched in proton transmembrane transport, fatty acid β -oxidation, and positive regulation of gene expression. In the Cellular Component category, DEPs were predominantly localized to the mitochondria, mitochondrial matrix, mitochondrial membranes, and immunoglobulin complexes. In the Molecular Function category, DEPs were enriched in ATP binding, ribosomal structural constituents, RNA binding, and protein binding (Fig. 6C–E). KEGG pathway analysis further revealed that DEPs were significantly associated with metabolic pathways, ribosome function, amyotrophic lateral sclerosis, various neurodegenerative disease pathways, and Parkinson's disease (Fig. 6F). To further stratify DEPs and explore underlying protein networks, K-means clustering and protein–protein interaction (PPI) mapping were conducted (Fig. 6G). Based on these analyses and supported by literature-reported biological functions and pathway involvement, five candidate biomarkers were identified: Cox5a, Hspa5, Hnrnpa2b1, Mtco2, and Gsta3 (Fig. 6H, I), and Cox5a has been previously linked to cytotoxic edema in the spinal cord(36). These results suggest that specific CSF protein signatures may serve as candidate biomarkers for monitoring disease progression and therapeutic response in syringomyelia.

3.7 Preliminary Feasibility and Safety of S-S Bypass in Patients

In this study, 17 patients (12 men and 5 women) underwent the S-S bypass surgery for syringomyelia associated with arachnoid adhesions. Detailed patient data are provided in Supplementary Table 1. The mean age at surgery was 50.05 years (range, 27–64 years). The mean interval between symptom onset and bypass surgery was 61.89 months (range, 3–168 months). The mean follow-up duration was 13.95 months (range, 12–17 months). The mean ASIA sensory score improved from 198.82 ± 13.12 preoperatively to 201.41 ± 12.59 postoperatively ($p < 0.001$, $r = 0.824$), while the mean motor score improved from 84.18 ± 9.81 to 86.53 ± 8.99 ($p < 0.001$, Cohen's $d = -1.454$). The mean syrinx length decreased from 13.35 ± 5.88 to 11.59 ± 6.26 ($p < 0.001$, Cohen's $d = 1.138$). The postoperative syrinx tension index was also significantly reduced compared with the preoperative value ($70.06 \pm 13.18\%$ vs. $39.15 \pm 11.78\%$, $p < 0.001$, Cohen's $d = 3.157$)(Fig. 7B–E). At the final follow-up, including MRI evaluation, no patient exhibited any procedure-related complication or adverse event requiring additional intervention.

Case 1

(39-year-old female): History of lumbar spine trauma surgery 16 years prior. Presented with right lower limb weakness for 3 years and right-sided numbness for 1.5 years. Preoperative MRI showed syringomyelia above the L1 level. Myelography revealed contrast blockage at L1 level. Bypass catheters were placed at T11 and L2. Postoperative MRI demonstrated a reduction in syrinx volume, with marked improvement in right-sided numbness (Fig. 7F).

Case 2

(47-year-old male): History of lumbar fracture surgery 30 years earlier. Developed right-sided numbness for 6 years, accompanied by right hand muscle atrophy and bladder/bowel dysfunction. Preoperative MRI showed extensive syringomyelia from C1 to T12. Myelography demonstrated contrast blockage at T12. Bypass catheters were placed at T10 and T12. Postoperative MRI revealed a reduction in syrinx volume, with significant improvement in right-sided numbness (Fig. 7F).

Case 3

(27-year-old male): History of thoracic stab injury with postoperative paraplegia 10 years earlier. Eight years ago, developed right upper limb and cervicothoracic sensory loss, weakness, and poor bladder control. Preoperative MRI showed syringomyelia above T11. Myelography revealed contrast blockage at T7. Bypass catheters were placed at T4 and T9. Postoperative MRI demonstrated syrinx reduction, with improvement in right cervicothoracic sensation and decreased numbness (Fig. 7F).

Discussion

The progression of syringomyelia is closely associated with SAS obstruction. As such, relieving SAS blockage has become a primary objective of surgical interventions. While decompression and arachnolysis remain the most commonly employed procedures, clinical outcomes are often suboptimal. Reports indicate that 10% to 40% of patients experience unsatisfactory postoperative results, including persistent or recurrent syrinx formation(8, 37, 38). These limitations have prompted the search for alternative strategies that more effectively restore CSF dynamics. Shunt surgery has emerged as a viable option, particularly in patients with extensive arachnoid adhesions(39). Conventional shunting procedures—such as syringo-subarachnoid, syringo-peritoneal, and syringo-pleural shunts—typically involve direct insertion of a catheter into the syrinx to divert fluid. However, these approaches require penetration of the spinal parenchyma, introducing significant risk of neurological injury. Furthermore, diversion of CSF into extracranial syrinx may result in overdrainage and complications such as intracranial hypotension(13), ultimately compromising therapeutic efficacy and limiting widespread clinical adoption. These limitations underscore the need for surgical strategies that restore CSF dynamics while minimizing trauma and secondary scarring.

The S – S bypass technique described in this study represents a significant advancement in both surgical design and underlying therapeutic mechanism. Rather than directly draining syrinx fluid, this approach establishes a subcutaneous CSF diversion channel that bypasses the obstructed SAS segment—commonly caused by arachnoiditis or extrinsic compression—without invading the spinal cord. By preserving the integrity of the parenchyma, this method substantially reduces the risk of iatrogenic injury and simplifies the surgical procedure. More critically, the bypass technique shifts the therapeutic paradigm: instead of reducing syrinx volume by directly evacuating intralesional fluid, it relieves upstream CSF pressure by draining the SAS proximal to the obstruction. This pressure gradient promotes endogenous clearance of syrinx contents via perivascular pathways, thereby facilitating syrinx reduction through physiological routes. This mechanism not only addresses the root cause of CSF

accumulation but also avoids the complications associated with traditional shunt systems. Experimental data confirmed a significant reduction in syrinx volume following bypass surgery compared to decompression. Notably, new syrinx was observed in the Decompression group, potentially due to post-surgical adhesive arachnoiditis. Functional recovery, assessed by behavioral and electrophysiological testing, was significantly greater in the Bypass group. IF results further indicated that neuronal and myelin preservation was enhanced following the S – S bypass surgery.

Our modified rat model further clarifies why decompression often fails clinically. To address the limitations of traditional modeling techniques—such as uneven compression, incomplete decompression, and persistent arachnoiditis triggered by residual sterile cotton—we optimized the model by employing sterile polystyrene microspheres. This approach markedly improved model success rates by enabling standardized and localized SAS obstruction, highly reproducible and more complete decompression, and reliable induction of postoperative scar formation. Despite achieving technically complete decompression using this refined approach, the EB result and CSF tracer IF revealed persistent CSF flow obstruction in the Decompression group. Given the surgical precision of this model, residual obstruction is unlikely to be due to under-decompression. Subsequent IF analysis of the surgical site showed significant postoperative scar tissue regeneration, despite complete intraoperative removal of all visible adhesions. This suggests that tissue trauma and the inflammatory response inherent to surgical manipulation may be key drivers of postoperative scar(40, 41), ultimately compromising the long-term efficacy of decompression. It is important to note that the rat model used in this study shows a strong tendency to develop adhesions and fibrotic scarring after surgery, which likely contributes to the higher rate of re-adhesion observed in the decompression group during follow-up. We emphasize that this model represents a mechanistically relevant but simplified pathological scenario that enables controlled investigation of CSF flow disturbance, postoperative scarring, and treatment response. Although this response may differ from that of clinical patients, it effectively reproduces the clinical scenario encountered in individuals with unfavorable local tissue conditions—such as those with severe trauma, prior infection, or multiple previous surgeries—who are at high risk of recurrent adhesion and failure after conventional decompression. These observations are consistent with clinical reports describing similar challenges in this subset of patients. These findings align with clinical reports highlighting postoperative arachnoid adhesion as a major cause of decompression failure in human syringomyelia(42). Therefore, our findings suggest that S-S bypass may serve as an alternative surgical strategy for patients identified preoperatively as being at high risk for recurrent adhesion. This approach offers a promising solution to the persistent clinical challenge of re-adhesion and treatment failure following conventional decompression.

These findings also refine our understanding of syringomyelia pathophysiology. The classical Gardner theory proposes that pulsatile “water hammer” waves generated in the fourth ventricle during cardiac systole are transmitted through the obex into the CC, leading to syrinx formation and progressive dilatation(43). Williams further suggested that transient intracranial–spinal pressure gradients during Valsalva maneuvers drive CSF from the fourth ventricle into the CC(44). Oldfield’s “piston theory” attributes syrinx formation to caudal displacement of the cerebellar tonsils, which allegedly acts as a

piston to propagate pressure waves within the SAS(45). Although influential, these theories assume direct communication between the fourth ventricle and CC. Our findings challenge these assumptions. Dynamic CT myelography demonstrated that intraventricularly injected contrast did not directly enter the CC or the syrinx. Instead, contrast first accumulated within the SAS and only later appeared within the CC, suggesting an indirect transport pathway. This observation aligns with Milhorat's clinical data and provides experimental evidence against the notion of direct ventricular–canal continuity(46).

Further, 3D IF imaging in our rat model revealed that tracer migrated from the SAS into the CC via PVS within the spinal parenchyma. This supports the perivascular flow hypothesis proposed by Roberts(47) and is consistent with the intramedullary pulse pressure theory incorporating the Venturi effect(4, 48). Based on these findings, we propose a model of CSF dynamics in syringomyelia. Under normal conditions, CSF produced in the ventricles enters the SAS and is modulated by cardiac and respiratory pulsations as well as transient pressure fluctuations during Valsalva maneuvers. Fluid exchange between the SAS and CC occurs through PVS, maintaining equilibrium. When SAS obstruction develops, this balance is disrupted. Proximal SAS pressure rises, driving excessive fluid entry into the CC via PVS. Sustained inflow that exceeds outflow gradually enlarges the syrinx, providing a mechanistic explanation for the delayed progression often observed after spinal trauma, where chronic perivascular transport slowly transforms pressure imbalance into structural dilation. To further characterize this process, we applied a dual-tracer approach at the 2-hour time point, identified previously by Magdalena as optimal for studying spinal CSF outflow(49). In stable syringomyelia models, tracers showed bidirectional exchange between the SAS and CC via PVS. Following S-S bypass surgery, however, this pattern shifted toward net outflow from the CC to the SAS, in contrast to the Vehicle group. These findings indicate that bypass surgery reduces local pressure gradients by diverting CSF proximal to the obstruction, thereby facilitating physiological clearance of syrinx fluid through perivascular pathways. In the early postoperative period, we observed that S-S bypass surgery altered the CSF flow pattern from a bidirectional exchange between the SAS and the CC to a net outward flow from the CC into the SAS. The establishment of this outward flux represents an important initiating event that may help reverse the local pressure gradient and create a permissive environment for the progressive reduction of the syrinx over the following weeks. It is also likely that this early outward flow, together with immediate pressure equilibration and subsequent resolution of inflammation, jointly triggers a cascade of processes that drive sustained syrinx shrinkage. Repeating the dual-tracer experiment at later time points would help determine whether this pressure-driven flow pattern persists. This mechanism distinguishes it fundamentally from conventional shunting. Whereas traditional shunts achieve rapid decompression by directly draining syrinx contents through intraparenchymal catheters—often at the cost of tissue injury and syrinx collapse—the S-S bypass harnesses endogenous perivascular conduits to gradually re-establish CSF homeostasis. This indirect, pressure-driven strategy minimizes iatrogenic risk and provides a more physiological resolution.

In parallel, we observed that syrinx progression is closely associated with disruption of the ependymal barrier. Disruption of TJs within the Foxj1 + ependymal lining, particularly the loss of continuity in the ZO-1 honeycomb structure, appears to be a critical event facilitating abnormal inward CSF influx into the syrinx. We propose that increased CSF pressure proximal to the obstruction imposes mechanical stress

on the ependymal barrier, leading to structural or functional disruption of tight junctions. This interpretation is consistent with prior work by Amandine et al., showing that intact tight-junction architecture prevents Evans blue penetration, whereas discontinuities result in focal leakage(50, 51). In our model, preserved ZO-1 continuity restricted tracer entry, whereas junctional loss markedly increased intraluminal fluid accumulation, suggesting that tight-junction integrity is essential for maintaining barrier function and resisting syrinx expansion. Importantly, following S-S bypass, we observed partial recovery of ependymal integrity and ciliary architecture alongside syrinx reduction. Compared with the vehicle group, bypass-treated animals showed improved ZO-1 continuity, increased Claudin-5 expression, and enhanced ciliary organization and polarity. These findings support the interpretation that bypass surgery alleviates pathological CSF pressure by establishing an alternative drainage route, thereby relieving mechanical stress on the ependymal barrier and enabling spontaneous repair of tight junctions and cilia. This is consistent with the notion that tight junctions (limiting abnormal influx) and motile cilia (facilitating physiological clearance) function cooperatively(52). Their recovery likely reflects the dual process of pressure normalization and progressive syrinx collapse. Thus, restoration of ependymal structure and ciliary function may represent a key biological mechanism underlying the sustained therapeutic effects of S-S bypass. Future work using targeted inhibition of tight junction or ciliary function will be essential to directly test their roles in the therapeutic effects of the S-S bypass.

Complementary insights came from CSF proteomics, which revealed profound molecular changes across disease stages. We identified 464 differentially expressed proteins, pointing to dysregulation of energy metabolism, mitochondrial function, and protein homeostasis during syrinx formation and progression. Enrichment in mitochondrial components, ATP binding, and pathways linked to endoplasmic reticulum stress and unfolded protein response indicates sustained cellular stress, while KEGG analysis revealed enrichment in neurodegenerative disease pathways (amyotrophic lateral sclerosis, Parkinson's disease, and other neurodegenerative disorders), strongly suggesting shared pathological mechanisms, including oxidative stress, protein homeostasis disruption, and neuronal vulnerability. By integrating K-means clustering, protein-protein interaction networks (Fig. 7G), biomarker prediction, and literature evidence, five proteins—Cox5a, Hspa5, Hnrnpa2b1, Mtco2, and Gsta3—emerged as candidate biomarkers, and Cox5a has also been shown to act together with AQP4 in regulating cytotoxic edema of the spinal cord. Their roles in endoplasmic reticulum stress regulation, mitochondrial respiratory function, RNA processing, and detoxification highlight the central contribution of mitochondrial dysfunction and oxidative stress to syringomyelia pathogenesis. A key question is whether these protein alterations represent causal drivers or downstream consequences of disease. Based on current data, causality cannot yet be established. A plausible interpretation is that they form part of a self-reinforcing pathological cycle: initial SAS obstruction disrupts CSF dynamics and induces local hypoxia and metabolic stress; this stress triggers mitochondrial dysfunction and ER activation, reflected in altered expression of proteins such as Cox5a; subsequent impairment of these organelles likely compromises the energy supply and barrier function of ependymal cells, weakens ciliary motility, and disrupts perivascular transport, thereby exacerbating fluid imbalance and syrinx expansion.

It is essential to emphasize that these candidate biomarkers were derived from a relatively small discovery set in an animal model. Their diagnostic or prognostic value must be validated in larger animal cohorts and eventually in human CSF using orthogonal assays such as Western blotting or ELISA. Moreover, any mechanistic link between these protein changes and PVS outflow or ependymal function requires direct experimental verification. Thus, these molecules should be regarded as promising leads for future translational research rather than established clinical markers. Future studies should focus on two directions: (1) validation of these candidates in independent cohorts, and (2) functional interrogation using cell models or conditional knockout animals to define their roles in disease. Confirming their diagnostic, prognostic, and treatment-monitoring potential in human CSF will be essential for eventual clinical translation.

Finally, our clinical case series of 17 patients with syringomyelia secondary to traumatic or postoperative arachnoid adhesions provides preliminary data on the feasibility and safety of the S-S bypass procedure. Over short-term follow-up (3–6 months), postoperative MRI demonstrated a reduction in syrinx volume in all patients, accompanied by partial improvements in neurological symptoms. These findings parallel the treatment effects observed in our rat model and provide early support for the potential of S-S bypass to restore CSF dynamics in the clinical setting. Unlike the rat model, in which only a single bypass catheter was used, all clinical patients underwent S-S bypass with two parallel catheters. This approach was adopted because the longer human spinal segments and larger SAS can accommodate dual-catheter placement. The dual configuration not only reduces the risk of complete obstruction if one catheter becomes occluded but may also enhance longitudinal CSF flow, thereby improving long-term patency and stability. Given the small sample size, short follow-up duration, absence of a control group, and reliance on clinical rating scales, the conclusions drawn from this study are necessarily preliminary and hypothesis-generating. Its primary contribution lies in establishing the technical feasibility and short-term safety of the S-S bypass procedure. In recognition of these limitations, a randomized controlled trial designed to rigorously assess long-term efficacy and safety is currently underway.

Research Limitations

Although the polystyrene microsphere–induced compression model effectively improved the stability of the animal model, several limitations should be acknowledged. First, inherent anatomical and physiological differences between rats and humans, such as variations in spinal cord structure and posture, may lead to discrepancies in the rate of syrinx formation and compensatory mechanisms compared with clinical cases. Second, although the current sample size is consistent with standard designs for mechanistic studies and sufficient to detect significant intervention effects, the exclusive use of female rats may limit the generalizability of the findings. In addition, no a priori sample size or power calculation was performed. Third, while the 4-week postoperative observation period was adequate to verify short-term efficacy and elucidate key mechanisms, it was insufficient to assess long-term durability. At the molecular level, proteomic analysis suggested the involvement of mitochondrial dysfunction and neurodegenerative pathways in disease progression; however, the specific roles of key

proteins in perivascular fluid transport remain to be clarified through gene knockout or pharmacological intervention studies. Likewise, the causal mechanisms and dominant pathways underlying ependymal repair require further investigation. Future studies should therefore include both sexes, expand sample size (incorporate formal sample size and power calculations), extend follow-up duration, and incorporate genetic and pharmacological approaches to deepen mechanistic understanding and validate the long-term therapeutic potential of the S-S bypass.

In addition, the clinical data reported in this study constitute a preliminary feasibility and safety assessment. This early experience derives from a single-center, non-controlled, single-arm case series. The primary objective was to evaluate the technical feasibility and short-term safety of this novel S-S bypass procedure in patients. Although the observed reductions in syrinx volume and improvements in neurological scores are encouraging, the absence of a control group precludes direct comparison with conventional decompression surgery and does not allow conclusions that the clinical efficacy of the S-S bypass is superior to decompression alone. Furthermore, the reliance on clinical rating scales without complementary electrophysiological assessments represents an additional limitation. Accordingly, the present findings should be interpreted as evidence that the procedure can be performed safely and may offer early clinical improvement, rather than as definitive proof of clinical efficacy or superiority over standard decompression surgery. These results provide the rationale and framework for the ongoing randomized controlled trial (ClinicalTrials.gov NCT06375759, 2024-04-16, Xuanwu Hospital, Beijing), which is specifically designed to rigorously evaluate comparative outcomes.

Conclusion

This study, using an improved rat model of syringomyelia, for the first time introduces a minimally invasive and physiologically compatible alternative and demonstrates that it significantly reduces syrinx volume and improves neurological function compared with decompression surgery in rat models. Animal findings and preliminary clinical observations support the feasibility and translational relevance of this approach. The core mechanism involves reconstructing the continuity of the SAS, which promotes CSF outflow via the PVS while avoiding spinal cord parenchymal injury and postoperative scar adhesion caused by additional surgical manipulation. CSF proteomics further implicates mitochondrial dysfunction and neurodegenerative pathways in syringomyelia progression, identifying potential biomarkers and therapeutic targets. It is important to emphasize that this study is not the endpoint, but a solid starting point. The experimental platform and preliminary clinical evidence presented here lay a solid foundation for future long-term, multi-center, controlled clinical studies, which are essential for the clinical validation of this technique. These findings open new avenues for developing novel treatments for syringomyelia.

Abbreviations

CSF
cerebrospinal fluid

SAS
subarachnoid space
PVS
perivascular space
EB
Evans Blue
CC
central canal
SEPs
Somatosensory evoked potentials
OCT
optimal cutting temperature
SEM
scanning electron microscopy
DIA
data-independent acquisition
GO
Gene Ontology
KEGG
Kyoto Encyclopedia of Genes and Genomes
IF
immunofluorescence
TJs
tight junctions
DEPs
differentially expressed proteins
PPI
protein–protein interaction
ASIA
American Spinal Injury Association

Declarations

Conflicts of interest

The authors declare no conflicts of interest, financial or otherwise, that could influence the content of this work.

Ethical approval

The experimental protocol was approved by the Animal Ethics Committee of Capital Medical University (Approval No. XW-20230712-1). The human study was approved by the Xuanwu of Ethics Committee Review Board (KS2025073, Xuanwu Hospital).

Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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Datastatement

The data that support the findings of this study are available from the corresponding author on reasonable request.

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Author Contribution

C.Z.,C.Y and J.B. wrote the original draft and contributed to methodology, conceptualization, and data curation. S.C., J.L. contributed to methodology, formal analysis, data curation, and conceptualization. S.L., N.L., K.L., and F.Y. contributed to validation, methodology, and investigation. X.S. and H.L. contributed to writing – review & editing, conceptualization and supervision. G.J. and F.J. contributed to writing – review & editing, conceptualization, supervision, and resources. All authors reviewed the manuscript.

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Data Availability

The data that support the findings of this study are available from the corresponding author on reasonable request.

References

1. Blegvad C, Grotenhuis JA, Juhler M. Syringomyelia: a practical, clinical concept for classification. *Acta Neurochir (Wien)*. 2014;156(11):2127–38.
2. Milhorat TH. Classification of syringomyelia. *NeuroSurg Focus*. 2000;8(3):E1.
3. Buell TJ, Heiss JD, Oldfield EH. Pathogenesis and Cerebrospinal Fluid Hydrodynamics of the Chiari I Malformation. *Neurosurg Clin North Am*. 2015;26(4):495–9.
4. Greitz D. Unraveling the riddle of syringomyelia. *Neurosurg Rev*. 2006;29(4):251–63. discussion 64.
5. Capel C, Padovani P, Launois PH, Metanbou S, Balédent O, Peltier J. Insights on the Hydrodynamics of Chiari Malformation. *J Clin Med*. 2022;11:18.
6. Bonfield CM, Levi AD, Arnold PM, Okonkwo DO. Surgical management of post-traumatic syringomyelia. *Spine*. 2010;35(21 Suppl):S245–58.
7. Heiss JD, Suffredini G, Smith R, DeVroom HL, Patronas NJ, Butman JA, et al. Pathophysiology of persistent syringomyelia after decompressive craniocervical surgery. Clinical article. *J Neurosurg Spine*. 2010;13(6):729–42.
8. Kleindienst A, Laut FM, Roeckelein V, Buchfelder M, Dodoo-Schittko F. Treatment of posttraumatic syringomyelia: evidence from a systematic review. *Acta Neurochir (Wien)*. 2020;162(10):2541–56.
9. Tosi U, Lara-Reyna J, Chae J, Sepanj R, Souweidane MM, Greenfield JP. Persistent Syringomyelia After Posterior Fossa Decompression for Chiari Malformation. *World Neurosurg*. 2020;136:454 – 61.e1.
10. Ma L, Yao Q, Zhang C, Li M, Cheng L, Jian F. Chronic extradural compression of spinal cord leads to syringomyelia in rat model. *Fluids barriers CNS*. 2020;17(1):50.
11. Aghakhani N, Baussart B, David P, Lacroix C, Benoudiba F, Tadie M, et al. Surgical treatment of posttraumatic syringomyelia. *Neurosurgery*. 2010;66(6):1120–7. discussion 7.
12. Rothrock RJ, Lu VM, Levi AD. Syrinx shunts for syringomyelia: a systematic review and meta-analysis of syringosubarachnoid, syringoperitoneal, and syringopleural shunting. *J Neurosurg Spine*. 2021;35(4):535–45.
13. Johnson AR, Rugilo CA, Argañaraz RA. Case report: CSF hypotension secondary to a free syringo-subarachnoid-peritoneal shunt. *Child's Nerv system: ChNS : official J Int Soc Pediatr Neurosurg*. 2024;40(12):4365–8.
14. Yuan C, Du Y, Yao Q, Zhang C, Zhang L, Liu Z et al. Natural history of Chiari I malformation-syringomyelia: longitudinal cohort study. *Journal of neurology, neurosurgery, and psychiatry*. 2025.

15. Cui S, Li J, Zhang C, Li Q, Jiang C, Wang X, et al. Glial scarring limits recovery following decompressive surgery in rats with syringomyelia. *Exp Neurol*. 2025;385:115113.
16. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. *PLoS Biol*. 2010;8(6):e1000412.
17. Jiang C, Wang X, Lu C, Li Q, Ma L, Li W, et al. The Physiological Occlusion of the Central Canal May Be a Prerequisite for Syringomyelia Formation. *Neurospine*. 2023;20(4):1346–57.
18. Liu S, Ma L, Qi B, Li Q, Chen Z, Jian F. Suppression of TGF β R-Smad3 pathway alleviates the syrinx induced by syringomyelia. *Cell bioscience*. 2023;13(1):98.
19. Jian X, Xu F, Yang M, Zhang M, Yun W. Correlation between enlarged perivascular space and brain white matter hyperintensities in patients with recent small subcortical infarct. *Brain Behav*. 2023;13(9):e3168.
20. Dixon WJ. Efficient analysis of experimental observations. *Annu Rev Pharmacol Toxicol*. 1980;20:441–62.
21. Metz GA, Whishaw IQ. Cortical and subcortical lesions impair skilled walking in the ladder rung walking test: a new task to evaluate fore- and hindlimb stepping, placing, and co-ordination. *J Neurosci Methods*. 2002;115(2):169–79.
22. Han JR, Yang Y, Wu TW, Shi TT, Li W, Zou Y. A Minimally-Invasive Method for Serial Cerebrospinal Fluid Collection and Injection in Rodents with High Survival Rates. *Biomedicines*. 2023;11(6).
23. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (revised 2011). *J Spinal Cord Med*. 2011;34(6):535–46.
24. Guan J, Yuan C, Yao Q, Du Y, Fang Z, Zhang L, et al. A novel scoring system for assessing adult syringomyelia associated with CM I treatment outcomes. *Acta Neurol Belgica*. 2023;123(3):807–14.
25. Zhang C, Yuan C, Wang J, Wu H, Chen Z, Jian F et al. A novel Minimally-Invasive technique for Non-Traumatic postoperative adhesive Syringomyelia. *European spine journal: official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*. 2025.
26. Dai DW, Wang GM, Zhang TF, Wang CH, Gulberdiyev A, Qiu YM, et al. Syringo-Subarachnoid Shunt with Tube Versus T-Tube via the Dorsal Root Entry Zone Approach for Eccentric Syringomyelia. *World Neurosurg*. 2024;185:e415–20.
27. Wang Z, Wang X, Jian F, Zhang C, Wu H, Chen Z. The changes of syrinx volume after posterior reduction and fixation of basilar invagination and atlantoaxial dislocation with syringomyelia. *European spine journal: official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical. Spine Res Soc*. 2017;26(4):1019–27.
28. Zhang YT, Jin H, Wang JH, Wen LY, Yang Y, Ruan JW, et al. Tail Nerve Electrical Stimulation and Electro-Acupuncture Can Protect Spinal Motor Neurons and Alleviate Muscle Atrophy after Spinal Cord Transection in Rats. *Neural Plast*. 2017;2017:7351238.

29. Lu C, Wu X, Wang X, Xiao Z, Ma L, Dai J, et al. Single-cell transcriptomics reveals ependymal subtypes related to cytoskeleton dynamics as the core driver of syringomyelia pathological development. *iScience*. 2023;26(6):106850.
30. Barisano G, Lynch KM, Sibilia F, Lan H, Shih NC, Sepehrband F, et al. Imaging perivascular space structure and function using brain MRI. *NeuroImage*. 2022;257:119329.
31. Liu S, Lam MA, Sial A, Hemley SJ, Bilston LE, Stoodley MA. Fluid outflow in the rat spinal cord: the role of perivascular and paravascular pathways. *Fluids barriers CNS*. 2018;15(1):13.
32. Wang X, Jiang C, Lu C, Ma L, Feng Y, Cui S, et al. Impairment of Connexin 43 may initiate cilia decline in syringomyelia. *Exp Neurol*. 2023;365:114430.
33. Steed E, Balda MS, Matter K. Dynamics and functions of tight junctions. *Trends Cell Biol*. 2010;20(3):142–9.
34. Furuse M, Hirase T, Itoh M, Nagafuchi A, Yonemura S, Tsukita S, et al. Occludin: a novel integral membrane protein localizing at tight junctions. *J Cell Biol*. 1993;123(6 Pt 2):1777–88.
35. Lee L. Riding the wave of ependymal cilia: genetic susceptibility to hydrocephalus in primary ciliary dyskinesia. *J Neurosci Res*. 2013;91(9):1117–32.
36. Huang Y, Li SN, Zhou XY, Zhang LX, Chen GX, Wang TH, et al. The Dual Role of AQP4 in Cytotoxic and Vasogenic Edema Following Spinal Cord Contusion and Its Possible Association With Energy Metabolism via COX5A. *Front NeuroSci*. 2019;13:584.
37. Depreitere B, Van Calenbergh F, van Loon J, Goffin J, Plets C. Posterior fossa decompression in syringomyelia associated with a Chiari malformation: a retrospective analysis of 22 patients. *Clin Neurol Neurosurg*. 2000;102(2):91–6.
38. Matsumoto T, Symon L. Surgical management of syringomyelia—current results. *Surg Neurol*. 1989;32(4):258–65.
39. Guillaumet G, Aghakhani N, Morar S, Copaciu R, Parker F, Knafo S. Reintervention rate of arachnolysis versus shunting for nonforaminal syringomyelia. *J Neurosurg Spine*. 2021;34(4):673–9.
40. Koyanagi I, Chiba Y, Uemori G, Imamura H, Yoshino M, Aida T. Pathophysiology and surgical treatment of spinal adhesive arachnoid pathology: patient series. *J Neurosurg Case lessons*. 2021;2(16):Case21426.
41. Tu YT, Chiang YH, Lin JH. Delta Cord as a Radiological Localization Sign of Postoperative Adhesive Arachnoiditis: A Case Report and Literature Review. *Diagnostics (Basel Switzerland)*. 2023;13:18.
42. Wang YB, Wang DH, Deng SL. Symptomatic secondary spinal arachnoid cysts: a systematic review. *spine journal: official J North Am Spine Soc*. 2023;23(8):1199–211.
43. Gardner WJ, Angel J. The mechanism of syringomyelia and its surgical correction. *Clin Neurosurg*. 1958;6:131–40.
44. Williams B. The distending force in the production of communicating syringomyelia. *Lancet (London England)*. 1969;2(7613):189–93.

45. Oldfield EH, Muraszko K, Shawker TH, Patronas NJ. Pathophysiology of syringomyelia associated with Chiari I malformation of the cerebellar tonsils. Implications for diagnosis and treatment. *J Neurosurg.* 1994;80(1):3–15.
46. Milhorat TH, Kotzen RM, Anzil AP. Stenosis of central canal of spinal cord in man: incidence and pathological findings in 232 autopsy cases. *J Neurosurg.* 1994;80(4):716–22.
47. Lloyd RA, Fletcher DF, Clarke EC, Bilston LE. Chiari malformation may increase perivascular cerebrospinal fluid flow into the spinal cord: A subject-specific computational modelling study. *J Biomech.* 2017;65:185–93.
48. Heiss JD, Patronas N, DeVroom HL, Shawker T, Ennis R, Kammerer W, et al. Elucidating the pathophysiology of syringomyelia. *J Neurosurg.* 1999;91(4):553–62.
49. Lam MA, Hemley SJ, Najafi E, Vella NGF, Bilston LE, Stoodley MA. The ultrastructure of spinal cord perivascular spaces: Implications for the circulation of cerebrospinal fluid. *Sci Rep.* 2017;7(1):12924.
50. Mullier A, Bouret SG, Prevot V, Dehouck B. Differential distribution of tight junction proteins suggests a role for tanycytes in blood-hypothalamus barrier regulation in the adult mouse brain. *J Comp Neurol.* 2010;518(7):943–62.
51. Serra R, Simard JM. Adherens, tight, and gap junctions in ependymal cells: A systematic review of their contribution to CSF-brain barrier. *Front Neurol.* 2023;14:1092205.
52. Mahuzier A, Shihavuddin A, Fournier C, Lansade P, Faucourt M, Menezes N, et al. Ependymal cilia beating induces an actin network to protect centrioles against shear stress. *Nat Commun.* 2018;9(1):2279.

Figures

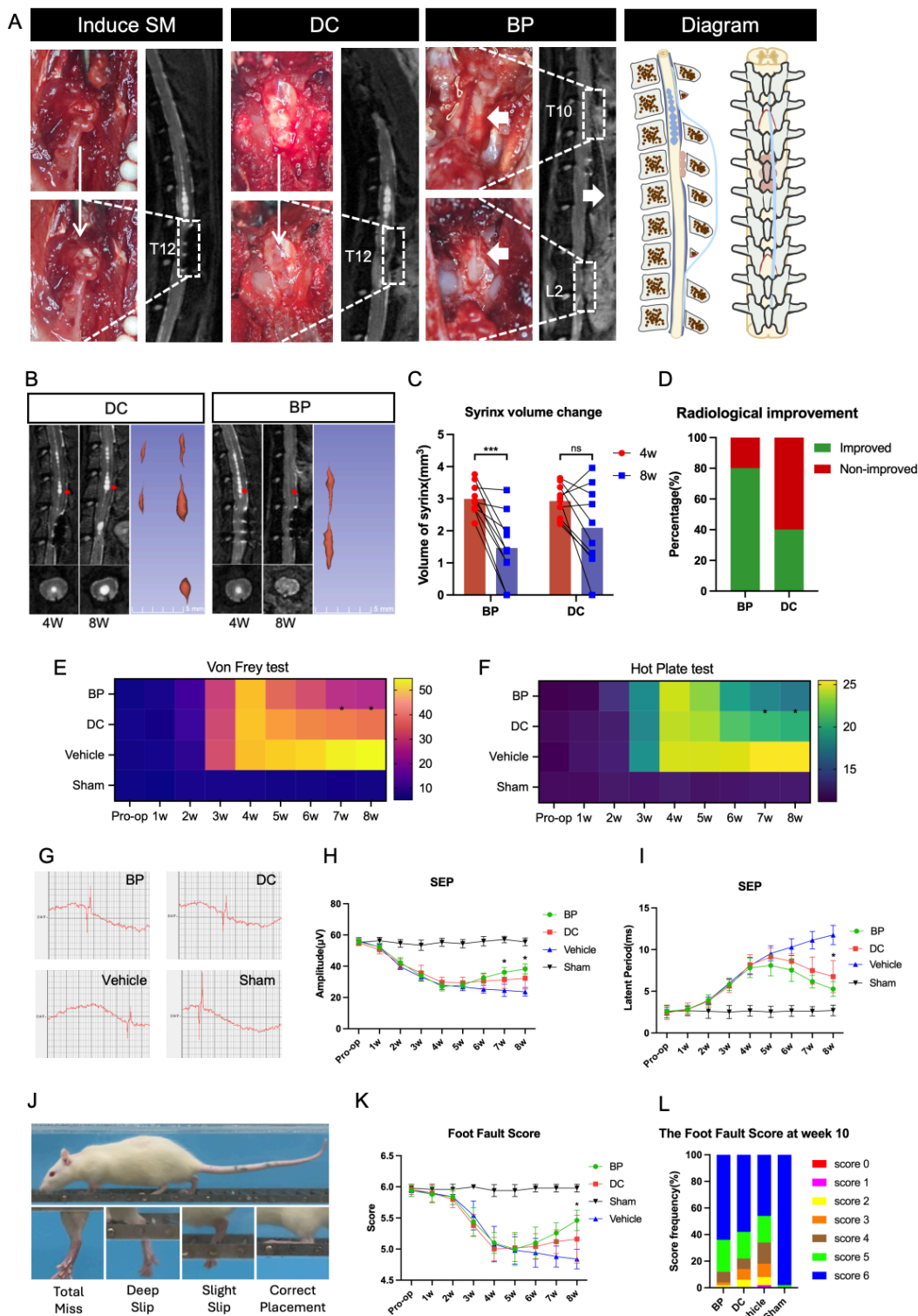


Figure 1

Intraoperative images and postoperative MRI of syringomyelia induction and two surgical treatments, along with postoperative changes in syrinx volume and neurological function.

Intraoperative images and postoperative MRI of syringomyelia induction and two surgical procedures (white arrows indicate the shunt catheter filled with cerebrospinal fluid), along with a schematic

illustration of the S-S bypass surgery. (BP: The Bypass group; DC: the Decompression group)

(B) MRI and 3D reconstructions of the syrinx before surgery (4 weeks) and after surgery (8 weeks) in both treatment groups (red arrow). Notably, in the Decompression group, new syrinx formation was observed near the surgical site (yellow arrow).

(C, D) Quantitative analysis of syrinx volume before and after surgery, and the postoperative improvement rate (n=10).

(E, F) Assessment of hind paw mechanical pain threshold (Von Frey test) and thermal sensitivity (hot plate test) at multiple time points (n=10).

(G) Representative schematic of SEP recording at 8 weeks.

(H, I) Statistical analysis of SEP amplitude and latency period across time points.

(J) Schematic of the ladder walking test used to assess locomotor coordination.

(K) Statistical results of the ladder walking test at different time points (n=10).

(L) Proportional analysis of the ladder walking test at 8 weeks (n=10).

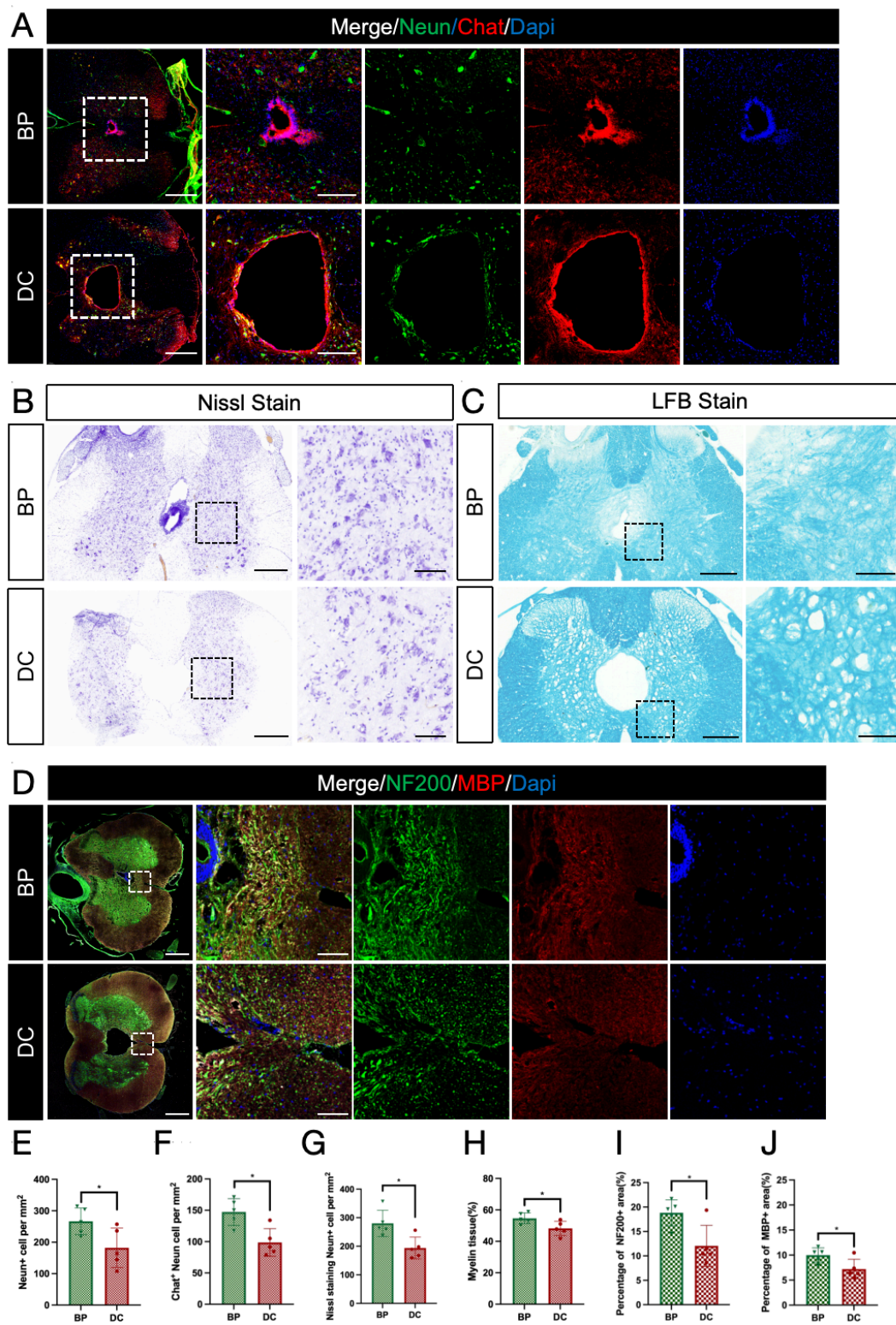


Figure 2

Postoperative Effects on Functional Neurons, Axons, and Myelin

(A) Representative IF images showing NeuN, ChAT, and DAPI staining after surgery. Scale bar: 500µm (overview); 100µm (magnified view).

(B) Representative Nissl staining images demonstrating neuronal morphology postoperatively. Scale bar: 500µm (overview); 100µm (magnified view).

(C) Representative Luxol Fast Blue (LFB) staining images of myelin integrity following the two surgical approaches. Scale bar: 500µm (overview); 100µm (magnified view).

(D) Representative IF images of the anterior commissure region showing NF200, MBP, and DAPI staining. Scale bar: 500µm (overview); 100µm (magnified view).

(E–G) Quantitative analysis of NeuN+ and ChAT+ neuronal cell counts, and Nissl-positive cell density in magnified views (n=5).

(H–J) Quantification of LFB-stained myelin content, NF200+, and MBP+ expression as percentage area in magnified views (n=5).

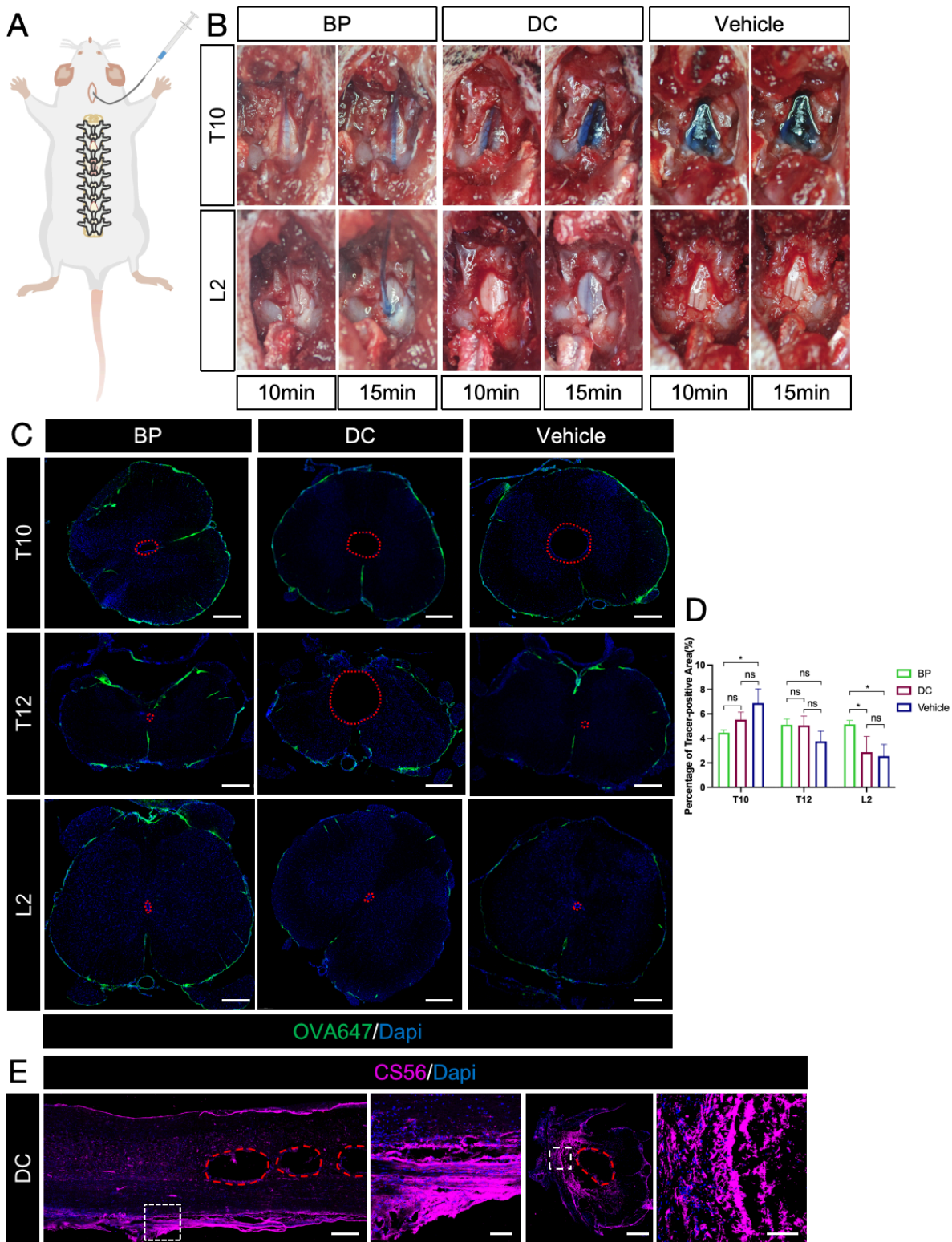


Figure 3

CSF Tracing and IF Reveal SAS Obstruction

(A) Schematic illustration of CSF tracer experiments in rats.

(B) Representative intraoperative images showing EB distribution across different time points and spinal cord segments in each group.

(C) Representative images showing OVA647 distribution within the SAS. Scale bar: 500µm.

(D) Quantitative analysis of OVA647 permeability at different stages (n=3); tracer-positive area (%) = OVA-positive area / total spinal cord area.

(E) Representative longitudinal and transverse sections showing expression of the scar marker CS56 in the Decompression group postoperatively. Scale bar: 500µm (overview); 100µm (magnified view).

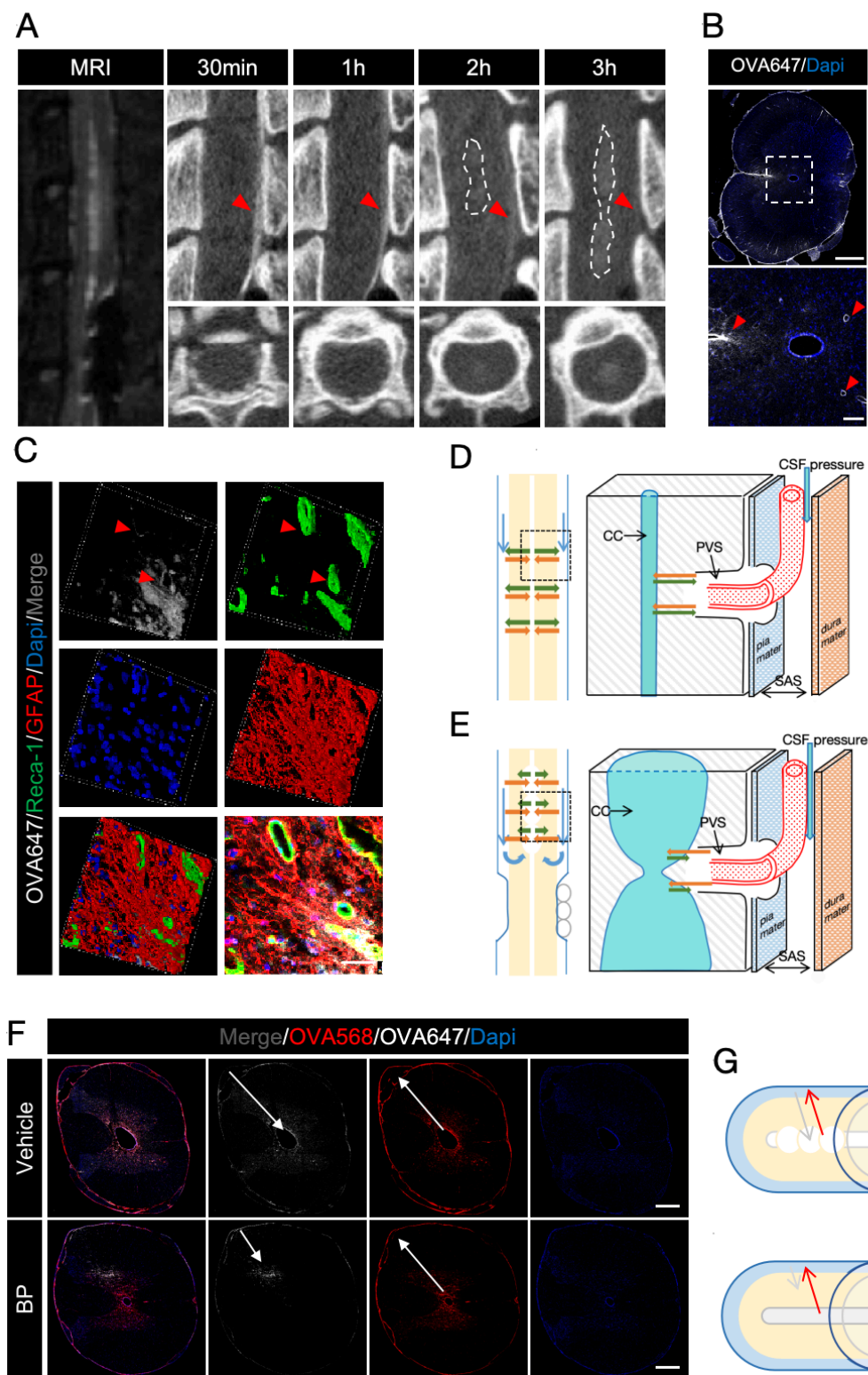


Figure 4

CSF Tracing and IF Reveal Fluid Transport Pathways in Syringomyelia and The Bypass Surgery

(A) MRI of syringomyelia in rat and corresponding CT at multiple time points following intrathecal iohexol injection. Red arrows and white dashed lines indicate tracer distribution.

(B) Tracer was predominantly localized around vascular structures and the anterior median fissure. Scale bar: 500µm (overview); 100µm (magnified view).

(C) Representative 3D IF images showing OVA647 co-localized with Recα-1 and GFAP. Scale bar: 50µm.

(D) Schematic illustration of physiological bidirectional fluid exchange between the CC and SAS; a magnified section of the spinal parenchyma is shown on the right.

(E) Schematic of disrupted SAS flow, CSF pressure increases proximal to the blockage, where net CSF influx into the CC exceeds efflux, leading to syrinx formation.

(F) Representative tracer distribution images in the Bypass and Vehicle groups following separate injection of two tracers into the SAS and syrinx, respectively. Scale bar: 500µm.

(G) Schematic illustration of comparative schematic of intraparenchymal CSF flow dynamics in the Bypass and Vehicle groups (Red arrows indicate net CSF outflow from the CC to the SAS, while gray arrows indicate net inflow from the SAS into the CC).

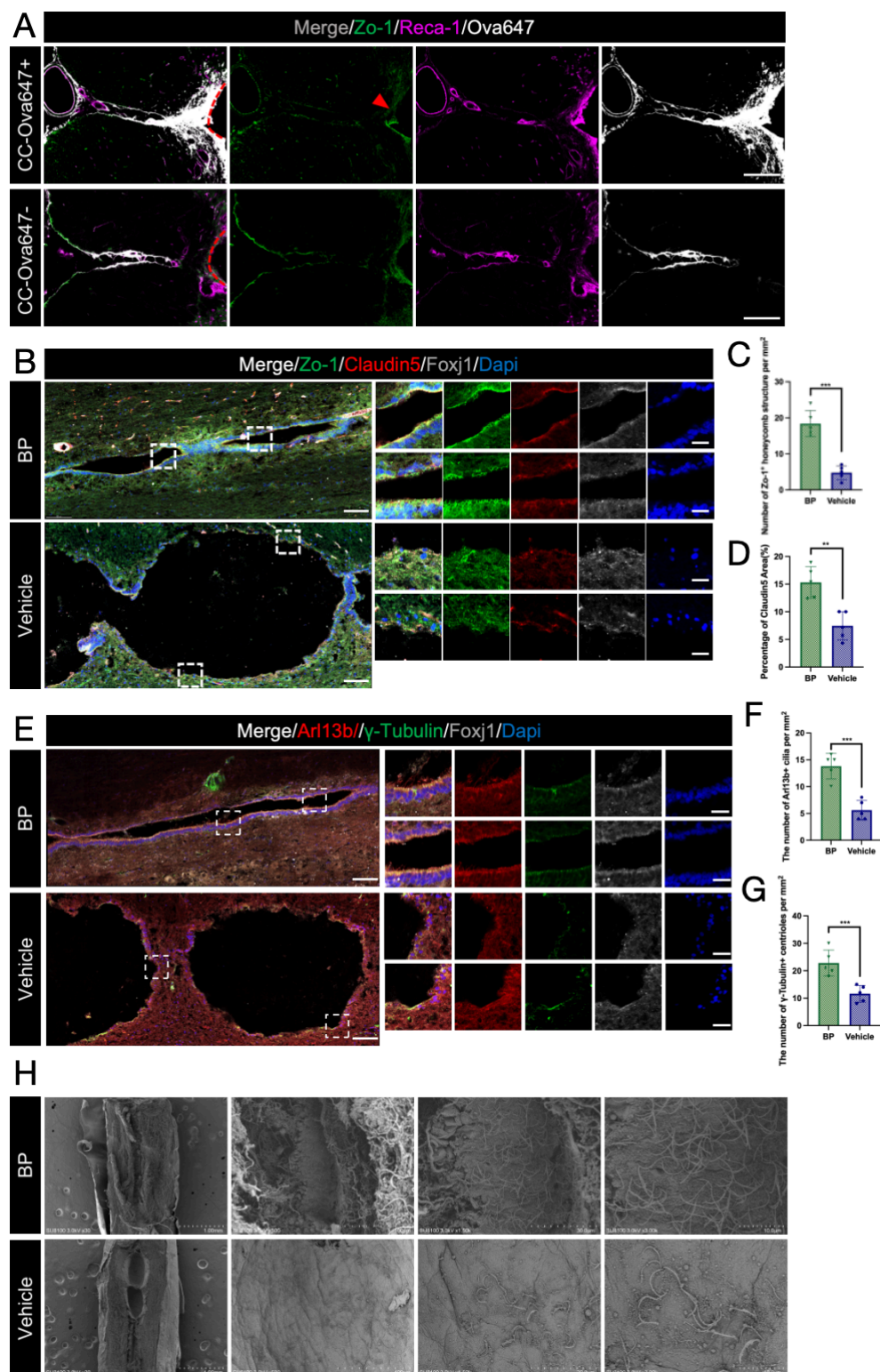


Figure 5

IF Reveals Ependymal Structural and Functional Abnormalities in Syringomyelia and the Restorative Effects of the S-S Bypass Surgery

(A) Tracer penetration patterns within the CC. Disruption of honeycomb structures continuity leads to excessive tracer influx into the CC. (red dashed lines indicate the syrinx region; red arrows mark

disrupted junctions). Scale bar: 100µm.

(B) Representative sagittal IF images showing Zo-1, Claudin-5, Foxj1, and DAPI in spinal cords following syringomyelia and bypass surgery. Scale bar: 200µm (overview); 50µm (magnified view)

(C, D) Quantification of Zo-1⁺ honeycomb structures and Claudin-5⁺ area in magnified views (n=5).

(E) Representative sagittal IF images of Arl13b, γ-Tubulin, Foxj1, and DAPI showing ciliary structures in the CC following syringomyelia and after bypass surgery. Scale bar: 200µm (overview); 50µm (magnified view).

(F, G) Quantification of Arl13b⁺ cilia number and γ-Tubulin⁺ area from magnified views (n=5).

(H) Representative SEM images showing ependymal cilia within the CC in syringomyelia and after the bypass surgery.

(B) Hierarchical clustering heatmap of differentially expressed proteins. T0, T1, T2, and T3 correspond to pre-modeling, 2 weeks post-modeling, 4 weeks post-modeling, and 4 weeks post-treatment, respectively (n=4). Red indicates upregulation; blue indicates downregulation.

(C–E) Gene Ontology (GO) enrichment analyses of differentially expressed proteins across time points. (C) Biological Process, (D) Cellular Component, and (E) Molecular Function. The x-axis represents the enrichment factor (Rich Factor), and the y-axis shows the enriched GO terms. Color intensity reflects statistical significance (p-value), with red indicating stronger enrichment. Numeric labels indicate the number of differentially expressed proteins within each GO term.

(F) Top 10 significantly enriched KEGG pathways displayed as a bubble plot.

(G) Protein–pathway interaction network constructed based on pathway enrichment results, highlighting associations between key pathways and differentially expressed proteins.

(H) Expression pattern analysis of proteins across time points using K-means clustering, illustrating representative trends within each cluster.

(I) Identification of five potential CSF protein biomarkers that align with the pathophysiological progression and therapeutic response of syringomyelia.

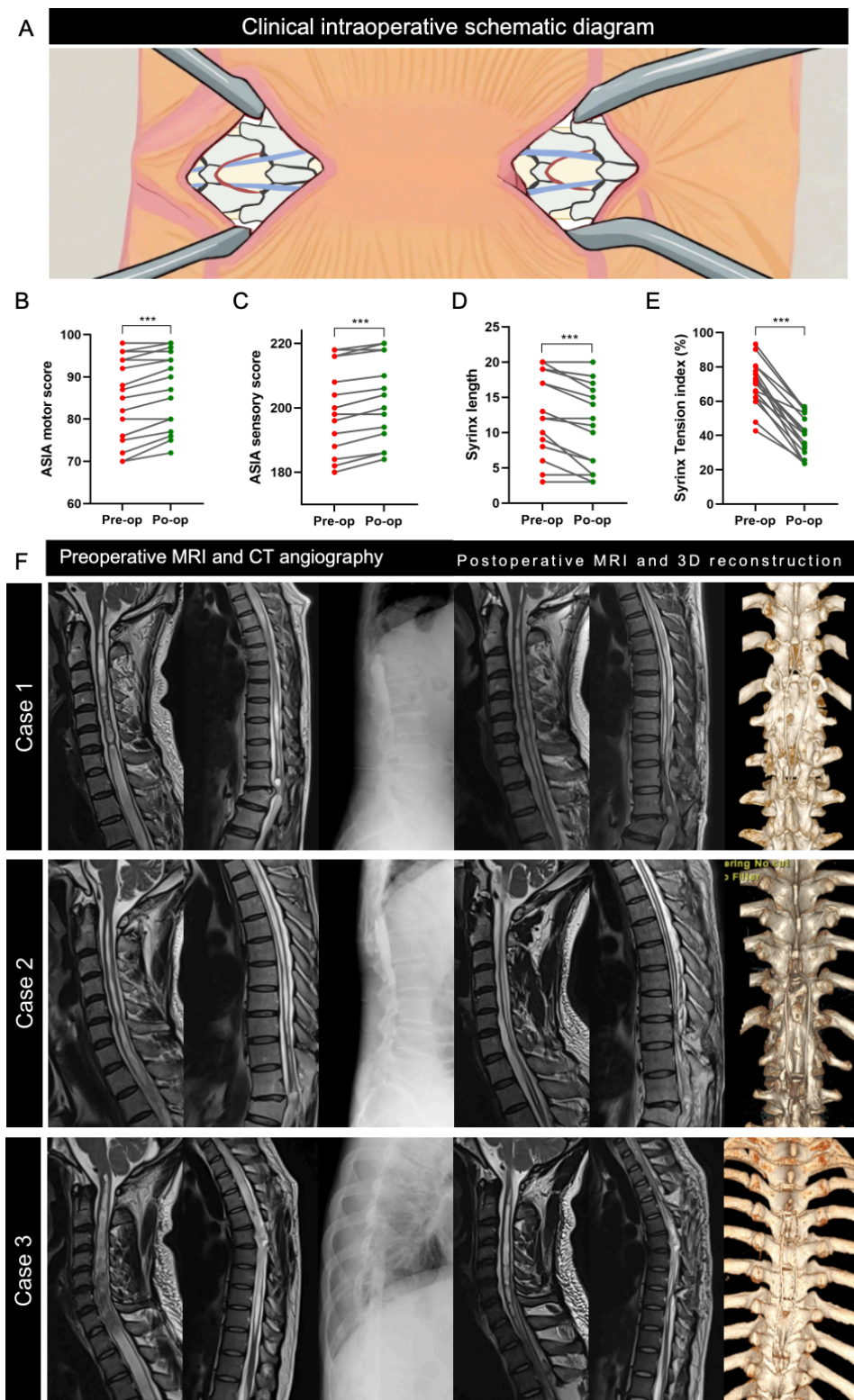


Figure 7

Intraoperative schematic of the S-S bypass procedure and postoperative clinical and imaging findings.

(A) Clinical intraoperative schematic of the S-S bypass procedure

(B-E) Changes in various indicators before and after surgery: ASIA Sensory Score (B); ASIA Motor Score (C); Syring length (D); Syring Tension index (E).

(F)Case 1: Preoperative MRI demonstrated extensive syrinx above the L1 level. Myelography showed complete contrast blockage at L1. Postoperative MRI revealed a reduction in syrinx size, and 3D reconstruction confirmed placement of the bypass catheter at T11 and L2.

Case 2: Preoperative MRI showed extensive syrinx from C1 to T12. Myelography revealed contrast blockage at T12. Postoperative MRI demonstrated marked syrinx reduction, and 3D reconstruction confirmed catheter placement at T10 and T12.

Case 3: Preoperative MRI revealed syrinx extending above T11. Myelography showed contrast blockage at T7. Postoperative MRI indicated syrinx reduction, and 3D reconstruction confirmed catheter placement at T4 and T9.

Supplementary Files

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