

Figure 1. Flowchart of Cohort Selection

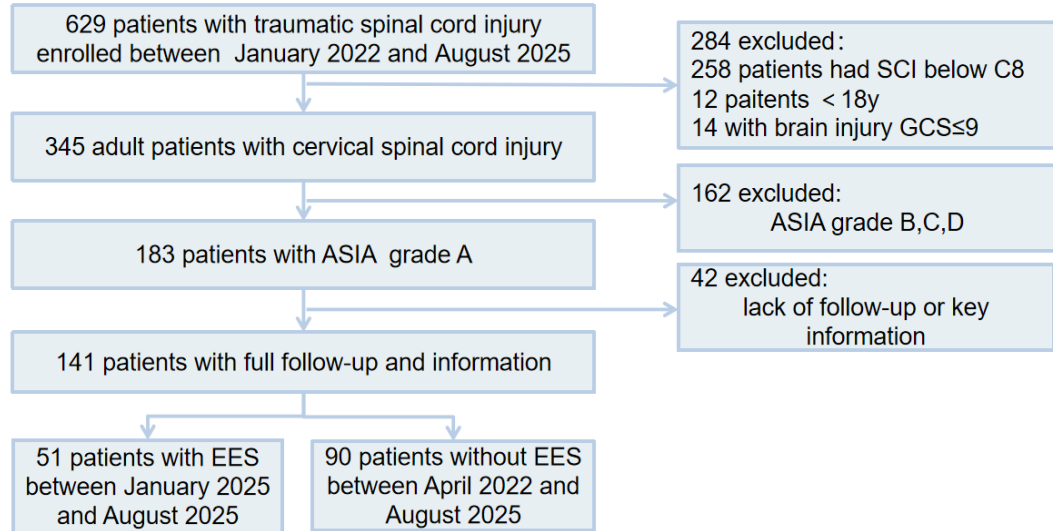
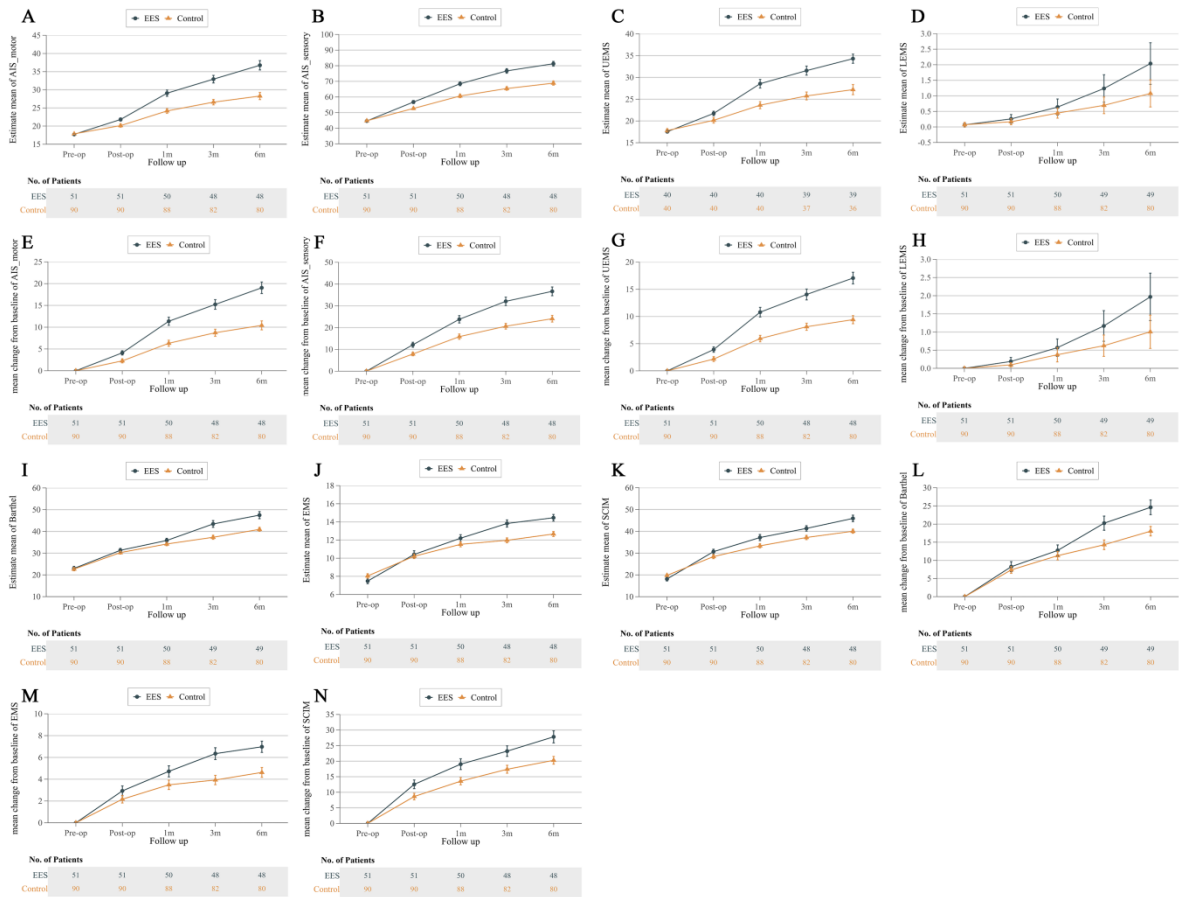


Table 1: Baseline factors by treatment group Articles

Variables	Total (N = 141)	EES (N = 51)	Control (N = 90)	P
Sex				0.989
Female	23 (16.3)	8 (15.7)	15 (16.7)	
Male	118 (83.7)	43 (84.3)	75 (83.3)	
Age	56.72±9.85	56.76±10.63	56.70±9.44	0.769
BMI	24.10±3.75	24.11±3.65	24.10±3.82	0.879
Basic Diseases				
Hypertension	48 (34)	15 (29)	33 (37)	0.339
Diabetes				
mellitus	19 (13)	5 (9.8)	14 (15)	0.370
Coronary				
disease	9 (6.4)	3 (5.2)	6 (7.1)	0.645
Ankylosing				
spondylitis	20 (14)	7 (13)	13 (15)	0.829
Chronic lung				
disease	3 (2.2)	1 (2.6)	2 (1.9)	0.793
Cerebral				
infarction	5 (3.4)	2 (3.2)	3 (3.5)	0.936
Injury level(%)				0.858
C0-3	62 (44)	21 (42)	40 (45)	

C3-5	73 (52)	28 (55)	45 (50)	
C5-7	6 (4.4)	2 (3.5)	4 (4.8)	
GCS score	13.00 (11.00, 14.00)	13.00 (11.00, 15.00)	13.00 (11.00, 14.00)	0.932
BASIC score				0.904
1	16 (11)	6 (13)	9 (10)	
2	32 (22)	13 (25)	19 (21)	
3	63 (45)	22 (42)	41 (46)	
4	31 (22)	10 (20)	20 (23)	
		230.00	222.00	
Operation time(min)	225.00 (195.00, 280.00)	(200.00, 280.00)	(194.00, 285.00)	0.406
		400.00	375.00	
Blood loss (ml)	380.00 (190.00, 560.00)	(200.00, 600.00)	(185.00, 550.00)	0.348
Combined injuries				
Craniocerebral injury	36 (25)	11 (22)	25 (27)	0.459
Rib fracture	47 (33)	14 (28)	32 (36)	0.320
Pleural effussion	25 (18)	8 (16)	17 (19)	0.639
Lung contusion	27 (19)	8 (16)	19 (22)	0.380
Aerothorax	12 (8.6)	4 (7.0)	9 (9.6)	0.608
Hyponatremia	30 (21)	10 (19)	20 (22)	0.714

Figure 2. Neurological Scores and Functional score



A-D:The estimate mean of AIS motor score, AIS sensory score, UEMS and LEMS; **E-H:** The mean change from baseline of AIS motor score, AIS sensory score, UEMS and LEMS; **I-K:**The estimate mean of Barthel index, EMS and SCIM; **L-N:** The mean change from baseline of Barthel index, EMS and SCIM.

Table 2. Safety Profile: Complications

Outcome	EES	Control	adj.OR	adj.p.value	adj.RR	adj.p.value	adj.RD	adj.p.value
Pulmonary infection	19/51 (37.3%)	25/90 (27.8%)	0.64 (0.30 to 1.34)	0.2315	0.74 (0.53 to 1.04)	0.0792	-9.99 (-27.21 to 7.23)	0.2555
Deep vein thrombosis	22/51 (43.1%)	23/90 (25.6%)	0.46 (0.22 to 0.97)	0.0406	0.60 (0.43 to 0.83)	0.0026	-17.26 (-34.79 to 0.27)	0.0537
Pulmonary embolism	2/51 (3.9%)	1/90 (1.1%)	0.32 (0.03 to 3.61)	0.3536	0.32 (0.03 to 3.02)	0.3216	-2.29 (-6.86 to 2.29)	0.3271
Failure of respiration	18/51 (35.3%)	20/90 (22.2%)	0.53 (0.25 to 1.16)	0.1131	0.64 (0.42 to 0.96)	0.0300	-12.57 (-29.12 to 3.98)	0.1365
Infection of incisional wound	4/51 (7.8%)	3/90 (3.3%)	0.33 (0.07 to 1.57)	0.1630	0.35 (0.09 to 1.32)	0.1215	-5.28 (-14.10 to 3.54)	0.2410
Central infection	5/51 (9.8%)	0/90 (0.0%)	0.00 (0.00 to 0.00)	< 0.0001	0.00 (0.00 to 0.00)	< 0.0001	-9.38 (-17.41 to -1.35)	0.0221
Leakage of cerebrospinal	15/51 (29.4%)	12/90 (13.3%)	0.38 (0.16 to 0.92)	0.0319	0.47 (0.26 to 0.84)	0.0104	-15.62 (-31.29 to 0.05)	0.0508
Hypoplasia	9/51 (17.6%)	6/90 (6.7%)	0.37 (0.12 to 1.16)	0.0895	0.42 (0.16 to 1.11)	0.0791	-9.89 (-23.60 to 3.83)	0.1577
Epidural hematoma	3/51 (5.9%)	2/90 (2.2%)	0.39 (0.06 to 2.52)	0.3225	0.40 (0.08 to 2.09)	0.2797	-3.07 (-9.38 to 3.25)	0.3415
Urinary infection	18/51 (35.3%)	20/90 (22.2%)	0.53 (0.24 to 1.15)	0.1094	0.64 (0.43 to 0.95)	0.0268	-12.91 (-30.11 to 4.29)	0.1414
Pathological muscle spasms	1/51 (2.0%)	18/90 (20.0%)	9.19 (1.18 to 71.74)	0.0344	7.55 (0.58 to 97.94)	0.1220	17.34 (6.40 to 28.28)	0.0019
Pathological pain	6/51 (11.8%)	16/90 (17.8%)	1.47 (0.55 to 3.96)	0.4450	1.39 (0.67 to 2.88)	0.3781	4.89 (-7.15 to 16.94)	0.4256
Ventilator weaning successfully	46/51 (90.2%)	59/90 (65.6%)	0.19 (0.07 to 0.54)	0.0018	0.72 (0.68 to 0.76)	< 0.0001	-25.70 (-38.46 to -12.95)	< 0.0001
dead	3/51 (5.9%)	10/90 (11.1%)	2.01 (0.51 to 7.92)	0.3183	1.90 (0.54 to 6.61)	0.3150	5.31 (-4.49 to 15.10)	0.2886
Electrodetachment shift	4/51 (7.8%)							
Infection at puncture site	1/51 (2.0%)							

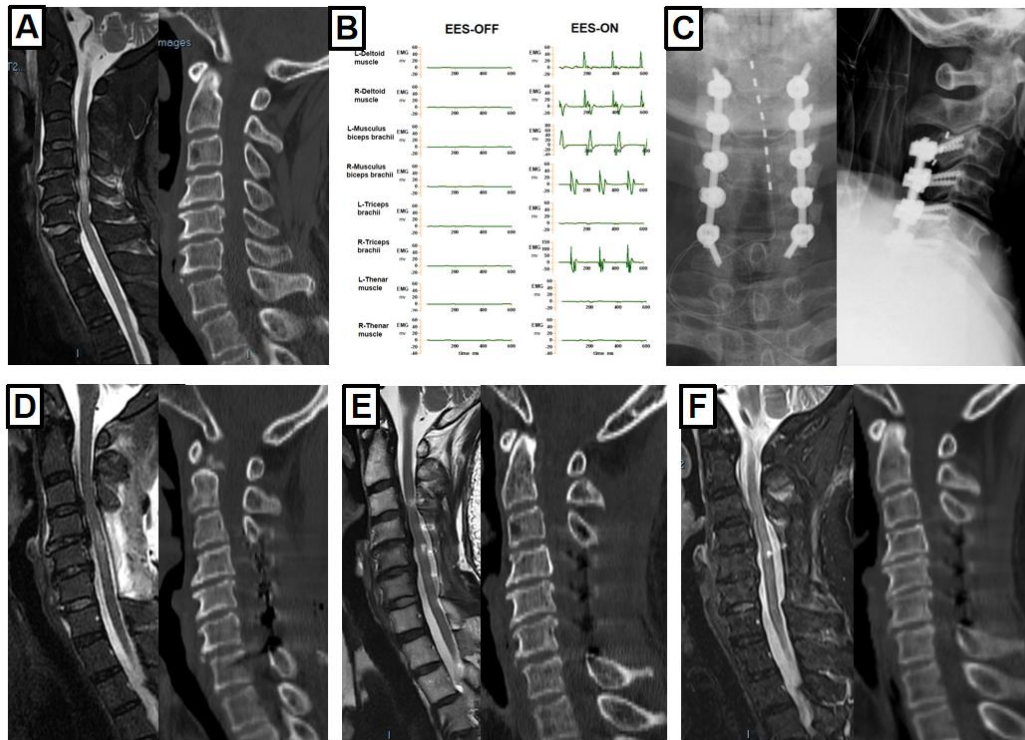


Figure 3. Demo case of the epidural stimulation.

A 60-year-old female was admitted to the hospital due to "limb motor impairment for more than one day after a fall from height." On October 31, 2024, at approximately 07:00, the patient accidentally fell from a height of 2 meters onto the ground, landing face first. She subsequently experienced neck pain accompanied by quadriparesis.

Preoperative physical examination revealed muscle strength graded at 2/5 in the biceps and triceps brachii, as well as forearm muscle groups, with grip strength assessed as 0/5. In the lower extremities, muscle strength was 0/5. A loss of superficial sensation was observed below the umbilical level. The patient presented to the emergency department on November 1, 2024. An emergency surgical procedure was performed that same noon, during which an epidural electrical stimulation (EES) device was implanted.

(A): Preoperative MRI of the patient demonstrated extensive spinal canal stenosis accompanied by spinal cord contusion. Preoperative CT imaging showed no significant ossification. The patient's Lower Extremity Motor Score (LEMS) was 12 prior to surgery.

(B): Intraoperative electrode configuration was set with contacts 3 and 4 as anodes, and contacts 5–8 as cathodes. Stimulation parameters were set at an amplitude of 6 V, a pulse width of 210 μ s, and a frequency of 5 Hz. Intraoperative electrophysiological monitoring showed significant signal changes upon activation of the stimulator in the bilateral deltoids, bilateral biceps brachii, and the right triceps brachii.

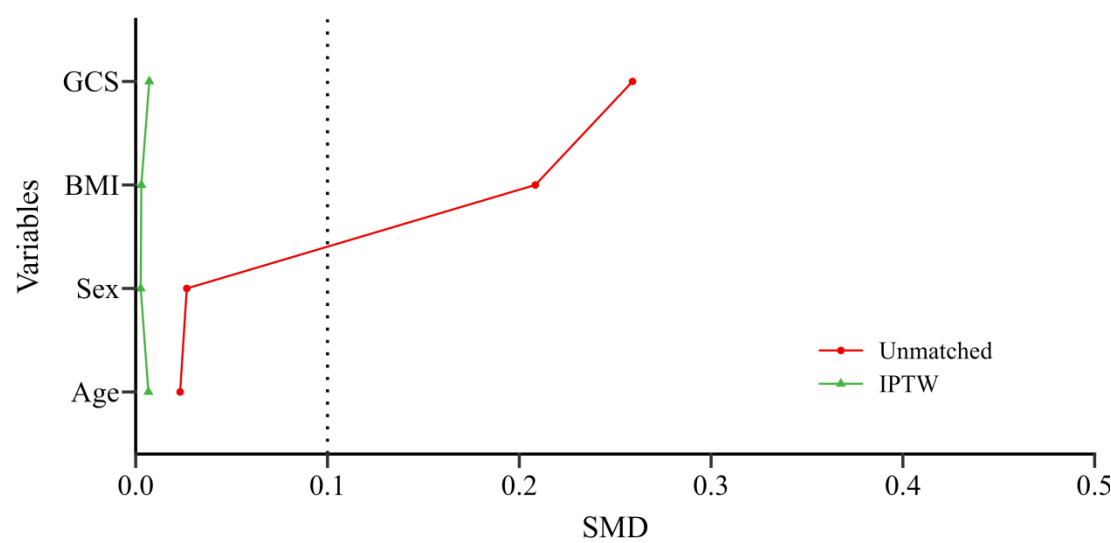
(C): Postoperative radiograph confirmed appropriate electrode positioning. The most rostral contact was designated as contact 1, and the most caudal as contact 8.

(D): Postoperative imaging indicated adequate decompression of the spinal canal and complete relief of spinal cord compression.

(E): A 3-month postoperative follow-up MRI revealed the formation of a syrinx cavity at the injury level. At this time, muscle strength in the upper limbs had improved to grade 4 (MRC scale) in the biceps brachii, triceps brachii, and forearm muscle groups, although grip strength remained at grade 0. The LEMS score improved to 24.

(F): A 6-month postoperative MRI showed no significant change in the size of the syrinx cavity. The patient's grip strength had recovered to grade 1 bilaterally, and the LEMS score further improved to 28.

eFigure 1. Evaluation of the effect of propensity score inverse probability weighted balanced baseline on confounding factors.

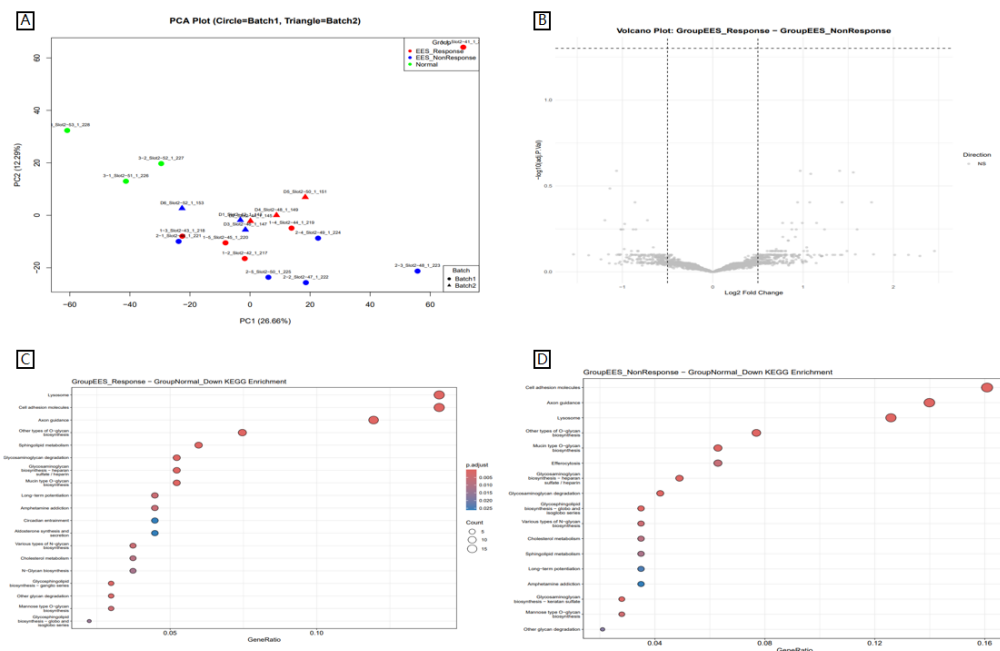


eTable 1.The imaging parameters of the patient.

Outcome	EES	Control	P
SCC			
Pre-op	49.83 (0.54)	47.69 (0.48)	0.002
Post-op	19.91 (0.77)	20.78 (0.58)	0.02
1m	18.13 (0.73)	20.01 (0.55)	0.001
3m	19.53 (0.66)	20.04 (0.52)	0.02
6m	19.60 (0.73)	19.95 (0.54)	0.06
SCCR			
Pre-op	35.00 (0.80)	36.13 (0.60)	0.25
Post-op	15.99 (0.49)	16.86 (0.53)	0.85
1m	15.41 (0.56)	16.44 (0.46)	0.94
3m	14.94 (0.63)	14.95 (0.46)	0.43
6m	14.47 (0.54)	14.30 (0.42)	0.36
T2HL			
Pre-op	18.76 (0.54)	19.89 (0.44)	0.18
Post-op	23.40 (0.72)	21.95 (0.62)	0.12
1m	21.13 (0.81)	21.88 (0.75)	0.78

SSD	3m	19.55 (1.15)	20.16 (0.86)	0.75
	6m	16.40 (1.13)	18.70 (0.95)	0.50
	1m	1.99 (0.14)	1.97 (0.12)	0.91
	3m	2.23 (0.11)	2.36 (0.10)	0.35
	6m	2.35 (0.11)	2.52 (0.10)	0.28
	SL			
SL	1m	2.94 (0.21)	2.76 (0.16)	0.50
	3m	3.30 (0.16)	3.31 (0.13)	0.98
	6m	3.46 (0.17)	3.53 (0.14)	0.77

Data are mean (SD) or number (%) or median (IQR). SCC: the spinal canal compromise (SCC) ratio ; SCCR: the spinal cord compression ratio; T2HL: the Length of T2 hyperintensity ; SSD: the maximum syrinx sagittal diameter; SL: the syrinx length.



eFigure 2. Proteomic landscape and pathway enrichment analysis of cerebrospinal fluid from spinal cord injury patients with differential response to epidural electrical stimulation (EES).

- (A) Principal component analysis (PCA) score plot of the first two principal components. The plot illustrates the overall separation between normal controls (Group Normal, green) and SCI patients (Groups EES Response and EES NonResponse), with considerable overlap between the two patient groups. (Circles = Batch 1, Triangles = Batch 2).
- (B) Volcano plot showing the lack of significantly differentially abundant proteins (FDR < 0.05) between EES responders and non-responders. The minimal adjusted p-value was 0.089. Log2FC = log2 fold change.
- (C) KEGG pathway enrichment analysis for proteins significantly downregulated in EES responders compared to normal controls. Key enriched pathways include Cell adhesion

molecules, Axon guidance, and Lysosome.

(D) KEGG pathway enrichment analysis for proteins significantly downregulated in EES non-responders compared to normal controls. Note the specific and significant enrichment of glycan metabolism-related pathways, including Glycosaminoglycan biosynthesis and N-Glycan biosynthesis (highlighted in red box), which are notably absent in the downregulated pathways of responders (Panel C). EES, epidural electrical stimulation; FDR, false discovery rate; KEGG, Kyoto Encyclopedia of Genes and Genomes; SCI, spinal cord injury.