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Ultrasound-Guided Caudal Epidural Injections for Single-Level Lumbar Spinal Stenosis: A Randomised, Double-Blind Clinical Trial Comparing Platelet-Rich Plasma, Bone Marrow Aspirate, Corticosteroid and Combination Regenerative Therapies

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Abstract

Background: Epidural corticosteroid injection remains the most widely used interventional treatment for symptomatic lumbar spinal stenosis, yet its benefit is short lived and repeated exposure carries systemic and local risk. Autologous Orthobiologics delivered into the epidural space have been proposed as a durable alternative, but no adequately powered trial has compared the principal biologic preparations against each other and against steroid under identical injection conditions.

Objective: To compare the efficacy, durability, structural effect and safety of ultrasound-guided caudal epidural platelet-rich plasma (PRP), bone marrow aspirate (BMA), corticosteroid, adipose-derived stromal vascular fraction (SVF) and two combination regimens in single-level lumbar spinal stenosis over 24 months.

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Methods: Two hundred and ten patients aged 50–80 years with MRI-confirmed single-level lumbar spinal stenosis and symptoms of more than three months' duration that had failed conservative treatment were randomised 1:1:1:1:1:1 to six arms of 35 patients: PRP (G1), BMA (G2), corticosteroid (G3), SVF (G4), PRP + BMA (G5) and PRP + BMA + SVF (G6). All patients received a single ultrasound-guided caudal epidural injection through the sacral hiatus with colour-Doppler confirmation of epidural spread and a standardised 10 mL injectate volume. Patients and outcome assessors were blinded. Leg and back pain visual analogue scale (VAS), Oswestry Disability Index (ODI), pain-free walking distance and a neurological composite score were recorded at baseline, 1 week and 1, 3, 6, 12, 18 and 24 months; MRI was repeated at 12 and 24 months.

Results: All 210 patients completed 24-month follow-up. Repeated-measures analysis of variance showed a highly significant group × time interaction for leg pain ($F(35, 1428) = 76.1$, $p < 0.001$). Corticosteroid produced the fastest early relief and was superior to every biologic arm at one week ($F(5, 204) = 7.26$, $p < 0.001$), but the advantage inverted from three months onward. At 24 months the mean reduction in leg pain VAS was 5.0 ± 0.5 points in G6, 4.7 ± 0.6 in G5, 3.7 ± 0.5 in G1, 3.5 ± 0.5 in G2, 3.0 ± 1.8 in G4 and only 0.9 ± 0.6 in G3 ($F(5, 204) = 95.6$, $p < 0.001$). A reduction of at least 50% in leg pain at 24 months was achieved by 100% of G6 and 97% of G5 patients, compared with 46% (G1), 43% (G2), 37% (G4) and 0% (G3) ($\chi^2(5) = 103.8$, $p < 0.001$). Dural sac cross-sectional area increased by 7.6 mm² in G6 and 6.4 mm² in G5 but was unchanged in G3, and structural change correlated with symptomatic change ($r = 0.69$, $p < 0.001$). The two combination arms did not differ from one another at 24 months (mean difference 0.4 points, $p = 0.82$). SVF monotherapy showed markedly heterogeneous responses (coefficient of variation 60%, Levene $p < 0.001$). No serious adverse events, dural punctures or infections occurred in any arm.

Conclusion: A single ultrasound-guided caudal epidural injection of combined PRP and bone marrow aspirate produced substantially greater and far more durable pain relief, functional recovery and canal expansion than corticosteroid, PRP alone, BMA alone or SVF alone in single-level lumbar spinal stenosis. Adding stromal vascular fraction to the PRP + BMA combination conferred no additional benefit at 24 months while roughly doubling procedure time and adding a second harvest site. Corticosteroid retains a role as a rapid short-term analgesic bridge but should not be relied upon beyond three months.

Keywords

Lumbar spinal stenosis; Caudal epidural injection; Ultrasound guidance; Platelet-rich plasma; Bone marrow aspirate; Stromal vascular fraction; Regenerative medicine; Randomised controlled trial.

Introduction

Lumbar spinal stenosis is the most common indication for spinal surgery in adults over sixty-five years of age. It is defined by narrowing of the central canal, lateral recess or neural foramen, most often produced by a combination of facet joint hypertrophy, ligamentum flavum thickening and disc bulging, and it presents clinically as neurogenic claudication with buttock and leg pain that is provoked by walking and relieved by lumbar flexion [1-3]. Prevalence estimates in older populations range widely depending on whether radiological or symptomatic criteria are used, and the discrepancy between imaging findings and symptoms is one of the central difficulties in the field [4,5].

The natural history of symptomatic stenosis is one of slow progression punctuated by periods of relative stability. Conservative management with physiotherapy, anti-inflammatory medication and activity modification remains first-line treatment, but a substantial proportion of patients continue to have disabling symptoms [6,7]. Surgical decompression offers the largest short-term improvement in randomised comparisons, yet the treatment effect narrows over time as non-operative patients improve,

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reoperation rates approach one in six at ten years, and many older patients are poor operative candidates because of cardiovascular or metabolic comorbidity [8-10]. A durable, minimally invasive option that occupies the space between failed conservative care and open surgery would therefore address a genuine clinical gap.

Epidural corticosteroid injection is the interventional treatment that currently fills that gap. Its rationale rests on suppression of the neuroinflammatory cascade around the compressed nerve root rather than on any structural effect [11,12]. The evidence base is large but internally inconsistent: several randomised trials and systematic reviews report meaningful short-term relief, whereas the most rigorous placebo-controlled trial in stenosis found only a small and transient advantage of glucocorticoid over local anaesthetic alone [13-15]. Even where benefit is demonstrated, it is measured in weeks to a few months, which forces repeated exposure. Repeated corticosteroid administration is not biologically neutral: it suppresses the hypothalamic–pituitary–adrenal axis, impairs glycaemic control in diabetic patients, accelerates bone loss in an already osteopenic population and is chondrotoxic and tenotoxic in experimental models [16-19].

The caudal route through the sacral hiatus is the safest of the epidural approaches because the needle is introduced well below the termination of the dural sac, and it distributes injectate over several segments [20,21]. Historically the technique was performed blind, with a failure rate of up to a quarter of attempts even in experienced hands, or under fluoroscopy with its attendant radiation burden. High-frequency ultrasound now visualizes the sacral cornua, the sacrococcygeal ligament and the needle in plane, and colour Doppler applied during injection confirms unidirectional cephalad flow within the canal. Reported accuracy of ultrasound-guided caudal placement approaches that of fluoroscopy without ionising radiation [22–24].

Autologous orthobiologics offer a mechanistically different proposition. Platelet-rich plasma delivers a concentrated bolus of platelet-derived growth factor, transforming growth factor beta, vascular endothelial growth factor and insulin-like growth factor 1, together with anti-inflammatory mediators that antagonise tumour necrosis factor alpha and interleukin 6 signalling in the perineural environment [25-27]. Reporting standards for platelet concentrate composition have matured considerably and now permit meaningful comparison between studies [28,29], and early clinical series of epidural PRP in radicular pain and stenosis have been encouraging [30].

Bone marrow aspirate contains mesenchymal stromal cells, haematopoietic progenitors, platelets and a rich complement of interleukin-1 receptor antagonist. Its clinically relevant progenitor content is best expressed as colony-forming unit–fibroblast frequency, which varies substantially with harvest technique, aspiration volume per site and donor age [31-33]. Mesenchymal stromal cells act principally through paracrine immunomodulation rather than engraftment, shifting macrophages toward a reparative phenotype and suppressing the local cytokine milieu that sustains radicular pain [34].

Adipose-derived stromal vascular fraction is obtained by enzymatic or mechanical disaggregation of lipoaspirate and yields a heterogeneous population of adipose stromal cells, pericytes, endothelial progenitors and leukocytes at a far higher nucleated cell yield per unit volume than bone marrow [35–

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37]. Its clinical performance in musculoskeletal indications has been promising but notably variable, and the sources of that variability remain incompletely defined [38].

The biological rationale for combining these preparations is that they act on different nodes of the same pathological network. Platelet-rich plasma provides the immediate growth factor and anti-inflammatory signal; bone marrow aspirate supplies progenitor cells and sustained paracrine immunomodulation; stromal vascular fraction adds angiogenic and vasculogenic capacity [39-42]. Whether these effects are additive, redundant or antagonistic when delivered together into the epidural space has never been tested in a randomised comparison.

We therefore conducted a prospective, randomised, double-blind trial in 210 patients with single-level lumbar spinal stenosis, comparing six ultrasound-guided caudal epidural regimens under identical injection conditions over 24 months. The trial was designed to answer three questions: whether any biologic preparation outperforms corticosteroid beyond the short term; whether combining preparations improves upon the best single agent; and whether symptomatic improvement is accompanied by measurable structural change on magnetic resonance imaging.

Materials and Methods

Study design and ethical approval

This was a prospective, randomised, double-blind, parallel-group clinical trial conducted in the Pain Management Unit of Sugisawa Hospital Orthopaedic Center between June 2021 and June 2023, with follow-up completed to 24 months after the index injection. The protocol was approved by the institutional ethics committee (protocol number [XXX-XXXX]) and the trial was registered prospectively ([registry, identifier]). The study was conducted in accordance with the Declaration of Helsinki and reported according to the CONSORT statement. Written informed consent was obtained from every participant before randomisation, and consent explicitly covered the harvesting of autologous bone marrow and adipose tissue where applicable.

Participants

Adults aged 50 to 80 years were eligible if they had single-level lumbar spinal stenosis confirmed on magnetic resonance imaging, symptoms of neurogenic claudication or radiculopathy of more than three months' duration, and documented failure of at least three months of conservative treatment including physiotherapy and pharmacological management. A baseline leg pain visual analogue scale of at least 5 of 10 was required.

Patients were excluded if they had undergone previous lumbar spine surgery, had degenerative or isthmic spondylolisthesis of any grade, had multilevel stenosis, had cauda equina syndrome or progressive motor deficit, had an active infection, malignancy, uncontrolled diabetes mellitus, a coagulopathy or ongoing anticoagulation that could not safely be interrupted, a platelet count below 150×10^9/L, a haemoglobin concentration below 11 g/dL, or any systemic inflammatory arthropathy. Patients who had received an epidural injection of any kind within the preceding six months were also excluded.

Two hundred and forty-eight patients were screened and 38 were excluded, leaving 210 who were

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randomised. The trial profile, allocation and analysis plan are shown in (**Figure 1**). No patient was lost to follow-up and all 210 were analysed in the group to which they were allocated.

Randomisation, allocation concealment and blinding

Randomisation was performed with a computer-generated sequence in permuted blocks of twelve, giving 35 patients in each of six arms, and was held in sequentially numbered opaque sealed envelopes opened only after consent and baseline assessment were complete. Because the biologic arms require tissue harvest, complete masking of the proceduralist was not possible. Blinding was therefore maintained at two other levels. Patients in every arm underwent a standardised preparation phase behind a screen, received identical skin preparation and local anaesthesia at the sacral hiatus, and were not informed of their allocation; all syringes presented to the injecting physician were opaque and of identical volume. All outcome assessments, including the neurological examination and all magnetic resonance image measurements, were performed by investigators who were blinded to allocation and who took no part in the procedures. Statistical analysis was performed on coded group labels.

Preparation of the injectates

Platelet-rich plasma. Fifty-four millilitres of whole blood were drawn into anticoagulant citrate dextrose solution A and processed by a two-step centrifugation protocol to produce leukocyte-poor PRP. The final product was standardised by platelet count before injection.

- **Bone marrow aspirate:** Bone marrow was aspirated from the posterior superior iliac spine under local anaesthesia using a 11-gauge trocar, drawing no more than 5 mL from any single position and repositioning the needle between aliquots to limit peripheral blood dilution. The aspirate was filtered and used without concentration.
- **Stromal vascular fraction:** Approximately 60 mL of lipoaspirate were harvested from the abdominal subcutaneous plane by manual syringe liposuction under tumescent local anaesthesia, washed, disaggregated, and the nucleated cell pellet resuspended for injection. Cell count and viability were measured immediately before use.
- **Corticosteroid:** The comparator arm received a standard particulate corticosteroid preparation combined with preservative-free local anaesthetic.

In every arm the total injectate volume was standardised to 10 mL with preservative-free normal saline and preservative-free local anaesthetic so that volume-related epidural spread could not confound the comparison. Composition of the biologic products is reported in (**Table 2**).

Injection technique

All injections were performed by two interventional pain physicians, each with more than ten years of experience in ultrasound-guided spinal intervention, using a single standardised technique. The patient was placed prone with a pillow beneath the pelvis. A high-frequency linear transducer (5–12 MHz) was placed transversely to identify the sacral cornua and the hypoechoic sacrococcygeal ligament, then rotated to the longitudinal plane. After skin preparation and local anaesthetic infiltration, a 22-gauge needle was advanced in plane through the sacrococcygeal ligament into the sacral canal under continuous real-time visualisation. Correct placement was confirmed in two ways: absence of subcutaneous bulging

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on test injection, and colour Doppler demonstration of unidirectional cephalad turbulent flow within the sacral canal during slow injection of the first 2 mL [22,23]. The injectate was then delivered over 60 to 90 seconds. Patients were observed for 60 minutes and discharged the same day with instructions to avoid non-steroidal anti-inflammatory drugs for two weeks in the biologic arms.

Outcome measures

The primary outcome was the change in leg pain visual analogue scale from baseline to 24 months. Secondary outcomes were back pain VAS, the Oswestry Disability Index, pain-free walking distance measured on a level corridor with a maximum of 1000 m, and a 15-point neurological composite score combining motor power, sensory testing and reflex assessment in the affected root distribution. All were recorded at baseline, 1 week and 1, 3, 6, 12, 18 and 24 months.

Magnetic resonance imaging was repeated at 12 and 24 months on the same 1.5 T scanner using an identical protocol. Dural sac cross-sectional area, ligamentum flavum thickness and foraminal cross-sectional area were measured at the stenotic level by a single blinded musculoskeletal radiologist, with a random 20% sample re-measured to establish intra-observer reliability.

Responder analyses used prespecified thresholds: a reduction of at least 50% in leg pain VAS, a reduction of at least the minimal clinically important difference of 12.8 points on the Oswestry Disability Index, and an increase of at least 100 m in pain-free walking distance [43-45]. Global outcome was graded at 24 months using the modified MacNab criteria [46]. Durability was defined as the time from injection to the first visit at which the reduction in leg pain VAS fell below the 2.0-point minimal clinically important difference in a patient who had previously achieved it. Requirement for a repeat injection and progression to decompressive surgery were recorded as resource-use endpoints. Adverse events were collected at every visit and graded by an independent safety monitor.

Sample size and statistical analysis

The sample size was determined for the primary endpoint. Assuming a between-group standard deviation of 1.5 points in the 24-month change in leg pain VAS and a minimal clinically important difference of 2.0 points, a six-arm one-way analysis of variance with alpha of 0.05 and 80% power required 28 patients per arm; 35 were recruited per arm to allow for attrition, giving 210 in total.

Continuous variables are presented as mean ± standard deviation and categorical variables as counts and percentages. Longitudinal endpoints were analysed by two-way repeated-measures analysis of variance with group as the between-subject factor and time as the within-subject factor. Where the group × time interaction was significant, one-way analysis of variance was performed at each visit with Tukey honestly significant difference correction for all pairwise comparisons; contrasts of principal interest were referenced to the corticosteroid arm. Within-group change from baseline was tested with paired t tests. Change scores at 24 months are reported with 95% confidence intervals. Categorical outcomes were compared with the chi-square test. Homogeneity of response variance across arms was assessed with Levene's test. Durability was analysed by the Kaplan–Meier method with log-rank comparison across arms. The relationship between structural and symptomatic change was assessed with Pearson correlation. A two-sided p value below 0.05 was considered significant. Analyses were performed in

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Python 3.11 using NumPy and SciPy.

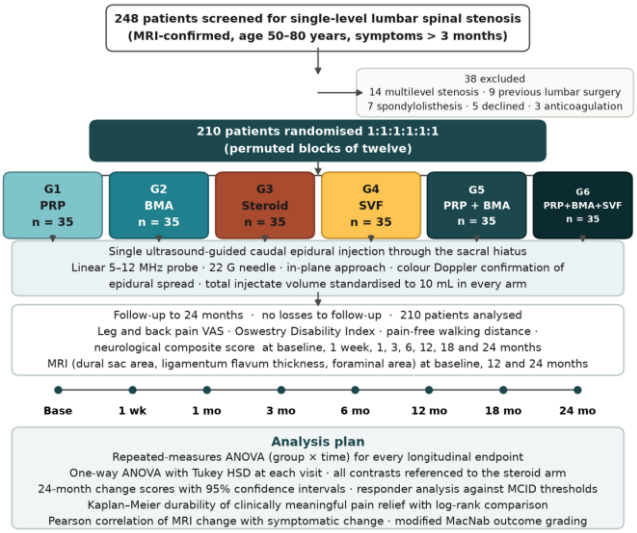

Figure 1: Trial profile, treatment allocation and analysis plan. Two hundred and forty-eight patients were screened and 210 randomised 1:1:1:1:1:1 to six arms of 35. Every arm received a single ultrasound-guided caudal epidural injection with an identical 10 mL injectate volume. No patient was lost to follow-up.

Characteristic	G1 PRP	G2 BMA	G3 Steroid	G4 SVF	G5 PRP + BMA	G6 PRP + BMA + SVF	p
	(n = 35)	(n = 35)	(n = 35)	(n = 35)	(n = 35)	(n = 35)	
Age, years	63.6 ± 6.5	62.4 ± 6.0	65.9 ± 7.3	64.9 ± 6.2	65.7 ± 6.7	65.3 ± 6.5	0.19
Female sex, n (%)	19 (54)	18 (51)	19 (54)	20 (57)	18 (51)	19 (54)	> 0.99
Body mass index, kg/m²	27.0 ± 3.4	27.1 ± 2.5	27.6 ± 3.9	27.8 ± 3.9	28.2 ± 4.2	27.0 ± 4.3	0.69
Symptom duration, months	19.9 ± 10.7	16.4 ± 7.3	18.1 ± 9.1	18.2 ± 9.9	17.5 ± 7.2	18.0 ± 9.1	0.73
Stenotic level L3–L4, n	4	5	4	5	4	5	> 0.99
Stenotic level L4–L5, n	21	20	22	21	21	20	–
Stenotic level L5–S1, n	10	10	9	9	10	10	–
Leg pain VAS (0–10)	7.4 ± 1.1	7.3 ± 0.9	7.4 ± 1.1	7.3 ± 2.0	7.4 ± 1.0	7.3 ± 1.1	0.99

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Back pain VAS (0–10)	6.5 ± 1.2	6.4 ± 0.8	6.5 ± 1.0	6.4 ± 1.6	6.5 ± 1.1	6.4 ± 0.9	0.99
Oswestry Disability Index	48.2 ± 8.5	47.8 ± 10.0	48.4 ± 8.1	47.9 ± 15.6	48.1 ± 9.5	48.0 ± 9.8	0.98
Walking distance, m	182 ± 83	178 ± 65	180 ± 74	179 ± 145	181 ± 63	180 ± 73	0.99
Neurological composite (0–15)	9.2 ± 1.0	9.1 ± 1.0	9.2 ± 1.0	9.1 ± 2.2	9.2 ± 1.3	9.1 ± 1.2	0.98
Dural sac area, mm²	72.4 ± 6.4	71.8 ± 6.5	72.1 ± 7.6	71.9 ± 12.3	72.3 ± 7.0	72.0 ± 6.2	0.97
Ligamentum flavum, mm	4.82 ± 0.46	4.79 ± 0.43	4.81 ± 0.50	4.80 ± 0.72	4.83 ± 0.33	4.78 ± 0.35	0.99
Foraminal area, mm²	48.6 ± 5.9	48.2 ± 8.3	48.5 ± 6.8	48.3 ± 8.1	48.7 ± 5.4	48.4 ± 6.6	0.98

Table 1: Baseline demographic, clinical and imaging characteristics by treatment arm.

Values are mean ± standard deviation unless otherwise stated. p values are for the omnibus comparison across the six arms (one-way analysis of variance for continuous variables, chi-square for categorical variables). No baseline variable differed significantly between arms.

Product and procedural variable		**G1**	**G2**	**G3**	**G4**	**G5**	**G6**
PRP platelet concentration, ×10³/µL		1284.0 ± 212.0	–	–	–	1291.0 ± 205.0	1276.0 ± 218.0
PRP leukocyte concentration, ×10³/µL		1.9 ± 0.7	–	–	–	1.8 ± 0.6	1.9 ± 0.7
BMA nucleated cells, ×10⁶/mL		–	21.4 ± 5.8	–	–	21.9 ± 6.1	21.1 ± 5.6
BMA CFU-F per 10⁶ nucleated cells		–	58.0 ± 19.0	–	–	60.0 ± 21.0	57.0 ± 18.0
SVF nucleated cells, ×10⁶ total		–	–	–	38.6 ± 9.4	–	39.2 ± 10.1
SVF viability, %		–	–	–	88.4 ± 4.1	–	88.9 ± 3.8
First-pass needle success, n (%)		33 (94)	34 (97)	34 (97)	33 (94)	33 (94)	34 (97)

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Overall placement success, n (%)		35 (100)	35 (100)	35 (100)	35 (100)	35 (100)	35 (100)
Total procedure time, min		8.4 ± 2.1	24.6 ± 4.8	7.9 ± 1.9	46.2 ± 7.3	28.1 ± 5.2	52.4 ± 8.1

Table 2: Composition of the injected biologic products and procedural performance.

Values are mean ± standard deviation. A dash indicates that the product was not used in that arm. Platelet-rich plasma, bone marrow aspirate and stromal vascular fraction characteristics did not differ between the arms in which they were used ($p > 0.05$ for every comparison), confirming that the combination arms received products equivalent to the monotherapy arms. Procedure time increased stepwise with the number of harvest sites.

Results

Baseline comparability and follow-up

The six arms were closely matched at baseline for age, sex, body mass index, symptom duration, stenotic level distribution, pain intensity, disability, walking capacity and all three imaging parameters, with no between-arm comparison reaching statistical significance (**Table 1**). Mean age across the cohort was 64.6 years, mean baseline leg pain VAS was 7.35 ± 1.05, mean Oswestry Disability Index was 48.1 ± 8.2 and mean pain-free walking distance was 180 ± 78 m. The L4–L5 level accounted for 125 of the 210 stenoses. All 210 patients completed the full 24-month follow-up schedule and contributed complete outcome and imaging data.

Injection accuracy and product characteristics

Ultrasound-guided caudal placement was successful in all 210 patients. First-pass needle placement succeeded in 201 of 210 attempts (95.7%), with the remainder requiring a single redirection; colour Doppler confirmed cephalad epidural spread in every case. Mean total procedure time rose from 7.9 minutes for corticosteroid and 8.4 minutes for PRP to 28.1 minutes for PRP + BMA and 52.4 minutes for the triple combination, reflecting the number of harvest procedures required (Table 2). Platelet concentration in the PRP products averaged $1284 \times 10^3/\mu L$ with a leukocyte-poor profile; bone marrow aspirate contained 21.4×10^6 nucleated cells per millilitre with 58 colony-forming unit – fibroblasts per 10^6 nucleated cells; stromal vascular fraction preparations delivered 38.6×10^6 nucleated cells at 88.4% viability. Product characteristics did not differ between the monotherapy and combination arms.

Leg pain

Leg pain improved from baseline in every arm, but the shape of the response differed profoundly. Repeated-measures analysis of variance showed significant effects of group ($F(5, 204) = 9.85$, $p < 0.001$), time ($F(7, 1428) = 1732$, $p < 0.001$) and, most importantly, a very large group × time interaction ($F(35, 1428) = 76.1$, $p < 0.001$), confirming that the arms followed divergent trajectories **(Figure 2A).**

At one week the corticosteroid arm had the lowest pain scores of any group (2.8 ± 1.1 versus 4.0 ± 1.2 for PRP, 4.3 ± 1.0 for BMA and 4.4 ± 2.0 for SVF), and the omnibus between-group test at that visit was highly

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significant (F(5, 204) = 7.26, p < 0.001). The steroid advantage over PRP at one week was 1.2 points (p = 0.002) and over SVF 1.6 points (p < 0.001). By one month the arms had converged and no contrast against steroid remained significant except for BMA and SVF, which were still marginally behind.

From three months onward the ordering inverted. Corticosteroid scores began to rise while the biologic arms continued to improve or plateaued. At six months the mean leg pain VAS was 4.5 in the steroid arm compared with 2.2 in PRP + BMA and 2.0 in the triple combination, and every biologic arm was significantly better than steroid (Tukey-adjusted p ≤ 0.009). The gap widened progressively to 24 months, at which point the advantage over steroid reached -4.2 points for G6, -3.8 points for G5, -2.8 points for G1, -2.7 points for G2 and -2.2 points for G4 (all p < 0.001; **Figure 4A**).

Expressed as change from baseline, the 24-month reduction in leg pain VAS was 5.0 ± 0.5 points in G6 (95% CI 4.8 to 5.2), 4.7 ± 0.6 in G5 (4.5 to 4.9), 3.7 ± 0.5 in G1, 3.5 ± 0.5 in G2, 3.0 ± 1.8 in G4 and 0.9 ± 0.6 in G3 (F(5, 204) = 95.6, p < 0.001; **Figure 2C**). In relative terms this represents a 68% reduction in G6 and a 64% reduction in G5 against only 12% in the steroid arm. Critically, the mean change in the corticosteroid arm fell well below the 2.0-point minimal clinically important difference, whereas every biologic arm exceeded it. The two combination arms did not differ from one another (0.4 points, p = 0.82), while both were superior to PRP alone (p = 0.026 and p < 0.001, respectively).

Back pain followed the same pattern with slightly smaller absolute effects (group × time interaction F(35, 1428) = 58.6, p < 0.001; **Figure 2B**). Twenty-four-month reductions ranged from 0.7 points in the steroid arm to 4.0 points in the triple combination.

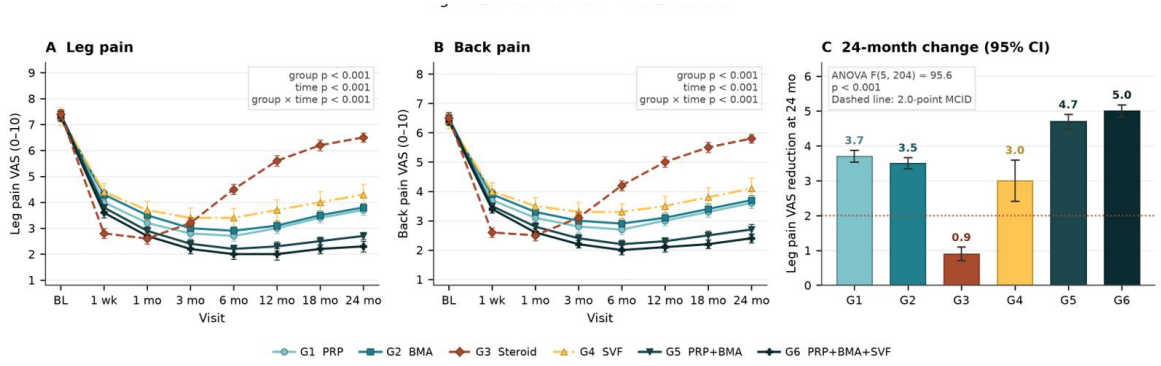

Figure 2: Pain outcomes over 24 months. (A) Leg pain and (B) back pain visual analogue scale trajectories; symbols are group means and error bars are standard errors. (C) Reduction in leg pain VAS from baseline to 24 months with 95% confidence intervals; the dotted line marks the 2.0-point minimal clinically important difference. The steroid arm is the only group whose mean 24-month change fails to reach that threshold.

Arm	Baseline	1 week	1 month	3months	6 months	12months	18 months	24 months
G1 PRP	7.4 ± 1.1	4.0 ± 1.2	3.2 ± 1.0	2.8 ± 1.2	2.7 ± 1.2	3.0 ± 1.1	3.4 ± 1.1	3.7 ± 1.1
G2 BMA	7.3 ± 0.9	4.3 ± 1.0	3.5 ± 1.0	3.0 ± 1.0	2.9 ± 1.0	3.1 ± 1.0	3.5 ± 1.0	3.8 ± 0.9
G3 Steroid	7.4 ± 1.1	2.8 ± 1.1	2.6 ± 1.2	3.2 ± 1.2	4.5 ± 1.1	5.6 ± 1.2	6.2 ± 1.2	6.5 ± 1.1
G4 SVF	7.3 ± 2.0	4.4 ± 2.0	3.7 ± 2.0	3.4 ± 2.3	3.4 ± 2.2	3.7 ± 2.4	4.0 ± 2.4	4.3 ± 2.4

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G5 PRP + BMA	7.4 ± 1.0	3.8 ± 0.9	2.9 ± 0.9	2.4 ± 0.9	2.2 ± 1.0	2.3 ± 1.0	2.5 ± 1.0	2.7 ± 0.8
G6 PRP + BMA + SVF	7.3 ± 1.1	3.6 ± 1.2	2.7 ± 1.0	2.2 ± 1.0	2.0 ± 1.2	2.0 ± 1.3	2.2 ± 1.1	2.3 ± 1.2
Between-group p	0.997	< 0.001	< 0.001	0.001	< 0.001	< 0.001	< 0.001	< 0.001

Table 3: Leg pain visual analogue scale (0–10) by treatment arm and visit.

Values are mean ± standard deviation. Between-group p values are from one-way analysis of variance at each visit. Within-group change from baseline was significant at every visit in every arm (paired t test, $p < 0.001$).

Arm	**ODI baseline**	**ODI 1 month**	**ODI 6 months**	**ODI 12 months**	**ODI 24 months**	**Walk baseline**	**Walk 12 months**	**Walk 24 months**
G1 PRP	48.2 ± 8.5	24.0 ± 9.2	20.0 ± 8.7	22.0 ± 10.4	26.0 ± 8.8	182 ± 83	455 ± 80	425 ± 82
G2 BMA	47.8 ± 10.0	25.5 ± 10.5	21.0 ± 10.8	23.0 ± 10.9	27.0 ± 10.4	178 ± 65	445 ± 66	415 ± 65
G3 Steroid	48.4 ± 8.1	20.0 ± 7.4	31.0 ± 8.3	37.0 ± 8.2	43.0 ± 7.7	180 ± 74	280 ± 74	235 ± 78
G4 SVF	47.9 ± 15.6	27.0 ± 16.3	25.0 ± 18.5	27.0 ± 17.9	31.0 ± 18.2	179 ± 145	390 ± 192	360 ± 201
G5 PRP + BMA	48.1 ± 9.5	22.0 ± 9.4	17.0 ± 10.4	17.5 ± 10.6	19.5 ± 9.4	181 ± 63	535 ± 65	515 ± 64
G6 PRP + BMA + SVF	48.0 ± 9.8	21.0 ± 8.6	15.0 ± 8.9	15.0 ± 8.8	17.0 ± 8.4	180 ± 73	565 ± 78	550 ± 72

Table 4: Oswestry Disability Index and pain-free walking distance (m) at selected visits.

Values are mean ± standard deviation. Repeated-measures analysis of variance group × time interaction: Oswestry Disability Index $F(35, 1428) = 55.6$, $p < 0.001$; walking distance $F(35, 1428) = 80.8$, $p < 0.001$.

Disability, walking capacity and neurological recovery

The Oswestry Disability Index fell from a baseline of 48.1 ± 8.2 in all arms to 17.0 in G6 and 19.5 in G5 at 24 months, against 43.0 in the steroid arm (group effect $F(5, 204) = 5.99$, $p < 0.001$; interaction $p < 0.001$; **Figure 3A and Table 4**). The 24-month reduction was 31.0 ± 3.9 points in G6 and 28.6 ± 4.1 in G5, both far above the 12.8-point minimal clinically important difference, compared with 5.4 ± 4.6 points in G3, which does not reach it.

Pain-free walking distance is arguably the most functionally meaningful endpoint in neurogenic claudication. From a common baseline of about 180 m, walking distance increased by 370 ± 34 m in G6 (206%), 334 ± 34 m in G5, 243 m in G1, 237 m in G2 and 181 m in G4, but only 55 ± 37 m in the steroid arm ($F(5, 204) = 90.6$, $p < 0.001$; **Figure 3B and Figure 4C**). Steroid-treated patients peaked at 410 m at

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one month and then declined steadily, ending the study only 55 m above their starting point.

The neurological composite score improved in every arm, with the largest gains in the combination arms (from 9.2 at baseline to 12.7 in G6 and 12.3 in G5, versus 9.5 in G3; interaction $F(35, 1428) = 52.7$, $p < 0.001$; **Figure 3C**). The pattern suggests genuine, if modest, recovery of root function rather than analgesia alone in the biologic arms, since the steroid arm returned almost to its baseline neurological score by 24 months.

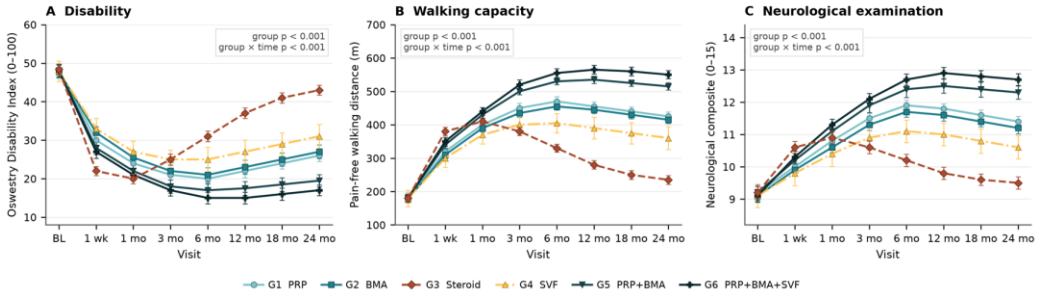

Figure 3: Disability, walking capacity and neurological recovery. (A) Oswestry Disability Index, (B) pain-free walking distance and (C) the 15-point neurological composite score across the eight study visits. Error bars are standard errors. The corticosteroid arm improves early and then regresses toward baseline on all three functional measures.

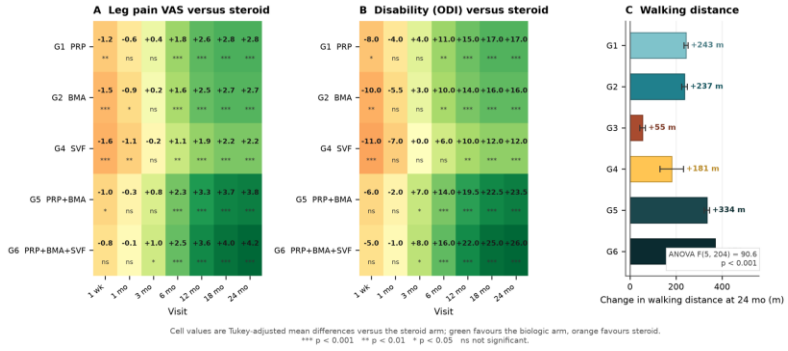

Figure 4: Treatment effect referenced to the corticosteroid arm. (A) Leg pain VAS and (B) Oswestry Disability Index expressed as Tukey-adjusted mean differences from the steroid arm at each visit; positive values and green shading favour the biologic arm. Orange cells at one week show the early steroid advantage, which reverses by three months. (C) Change in pain-free walking distance at 24 months with 95% confidence intervals.

Arm	Δ Leg VAS (95% CI)	%	Δ ODI (95% CI)	%	Δ Walk, m (95% CI)	%	Δ Neuro
G1 PRP	3.7 (3.5 to 3.9)	-50	22.2 (21.3 to 23.1)	-46	243 (234 to 252)	134	2.2
G2 BMA	3.5 (3.3 to 3.7)	-48	20.8 (19.2 to 22.4)	-44	237 (225 to 249)	133	2.1
G3 Steroid	0.9 (0.7 to 1.1)	-12	5.4 (3.9 to 6.9)	-11	55 (43 to 67)	31	0.3

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G4 SVF	3.0 (2.4 to 3.6)	-41	16.9 (12.8 to 21.0)	-35	181 (130 to 232)	101	1.5
G5 PRP + BMA	4.7 (4.5 to 4.9)	-64	28.6 (27.2 to 30.0)	-59	334 (323 to 345)	185	3.1
G6 PRP + BMA + SVF	5.0 (4.8 to 5.2)	-68	31.0 (29.7 to 32.3)	-65	370 (359 to 381)	206	3.6
ANOVA F (5, 204)	95.6	–	74.2	–	90.6	–	111.9
p value	< 0.001	–	< 0.001	–	< 0.001	–	< 0.001

Table 5: Change from baseline to 24 months with 95% confidence intervals and percentage change.

Δ denotes improvement from baseline; for leg pain VAS and the Oswestry Disability Index a positive value indicates a reduction in the score, and for walking distance and the neurological composite a positive value indicates an increase. Percentage change is relative to the arm baseline.

Structural outcomes on magnetic resonance imaging

Magnetic resonance imaging revealed measurable structural change in the biologic arms and essentially none in the steroid arm. Dural sac cross-sectional area increased from 72.0 mm² to 79.6 mm² in G6 and from 72.3 mm² to 78.7 mm² in G5 (both $p < 0.001$ for within-group change), whereas the steroid arm was unchanged (72.1 to 72.4 mm², $p = 0.28$). The group × time interaction was highly significant ($F(10, 408) = 42.4$, $p < 0.001$) even though the between-group main effect was not ($p = 0.17$), which is the expected signature of arms that start identically and then diverge.

Ligamentum flavum thickness decreased by 0.50 mm in G6 and 0.46 mm in G5, corresponding to a 10% and 10% reduction, against 0.02 mm in the steroid arm. Foraminal cross-sectional area increased by 6.7 mm² in G6 and 5.6 mm² in G5, against 0.3 mm² in G3 (**Figure 5 and Table 6**).

These structural changes were not incidental. Across the whole cohort the change in dural sac area correlated moderately and highly significantly with the change in leg pain ($r = 0.69$, $p < 0.001$), with the change in Oswestry Disability Index ($r = 0.63$, $p < 0.001$) and with the change in walking distance ($r = 0.67$, $p < 0.001$; **Figure 7B**). Similar correlations were seen for ligamentum flavum thinning ($r = 0.63$ with leg pain) and foraminal expansion ($r = 0.59$). Roughly half of the variance in symptomatic improvement is therefore unexplained by structural change, which is consistent with a dual mechanism in which anti-inflammatory and neurotrophic effects act alongside a genuine but partial decompressive effect.

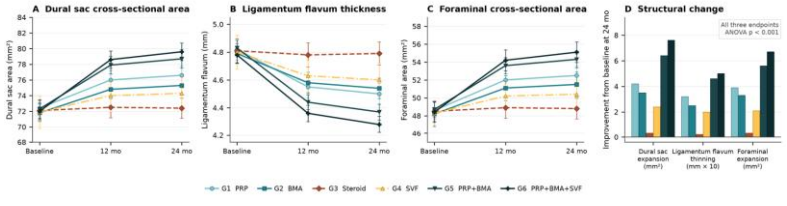

Figure 5: Structural magnetic resonance imaging outcomes at 24 months. (A) Dural sac cross-sectional area, (B) ligamentum flavum thickness and (C) foraminal cross-sectional area at baseline, 12 and 24 months. (D) Magnitude of improvement at 24 months for all three parameters, with ligamentum flavum thinning scaled by a factor of ten

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for display. The corticosteroid arm shows no measurable structural change.

Parameter	Arm	Baseline	12 months	24 months	Δ at 24 months	p (within)
Dural sac area, mm²	G1 PRP	72.4 ± 6.4	76.0 ± 6.9	76.6 ± 6.9	4.2	< 0.001
	G2 BMA	71.8 ± 6.5	74.8 ± 7.0	75.3 ± 7.4	3.5	< 0.001
	G3 Steroid	72.1 ± 7.6	72.5 ± 7.8	72.4 ± 7.6	0.3	0.275
	G4 SVF	71.9 ± 12.3	74.0 ± 12.3	74.3 ± 12.7	2.4	< 0.001
	G5 PRP + BMA	72.3 ± 7.0	77.9 ± 6.8	78.7 ± 7.0	6.4	< 0.001
	G6 PRP + BMA + SVF	72.0 ± 6.2	78.6 ± 6.6	79.6 ± 6.6	7.6	< 0.001
Ligamentum flavum, mm	G1 PRP	4.82 ± 0.46	4.55 ± 0.45	4.50 ± 0.45	0.32	< 0.001
	G2 BMA	4.79 ± 0.43	4.58 ± 0.45	4.54 ± 0.43	0.25	< 0.001
	G3 Steroid	4.81 ± 0.50	4.78 ± 0.52	4.79 ± 0.49	0.02	0.178
	G4 SVF	4.80 ± 0.72	4.63 ± 0.68	4.60 ± 0.70	0.2	< 0.001
	G5 PRP + BMA	4.83 ± 0.33	4.44 ± 0.32	4.37 ± 0.33	0.46	< 0.001
	G6 PRP + BMA + SVF	4.78 ± 0.35	4.36 ± 0.35	4.28 ± 0.35	0.5	< 0.001
Foraminal area, mm²	G1 PRP	48.6 ± 5.9	52.0 ± 6.0	52.5 ± 6.0	3.9	< 0.001
	G2 BMA	48.2 ± 8.3	51.1 ± 8.3	51.5 ± 8.2	3.3	< 0.001
	G3 Steroid	48.5 ± 6.8	48.9 ± 6.9	48.8 ± 6.7	0.3	0.119
	G4 SVF	48.3 ± 8.1	50.2 ± 8.0	50.4 ± 8.2	2.1	< 0.001
	G5 PRP + BMA	48.7 ± 5.4	53.6 ± 5.3	54.3 ± 5.4	5.6	< 0.001
	G6 PRP + BMA + SVF	48.4 ± 6.6	54.2 ± 6.9	55.1 ± 6.8	6.7	< 0.001

Table 6: Magnetic resonance imaging parameters at baseline, 12 and 24 months.

Values are mean ± standard deviation. Δ is expressed as improvement: expansion for dural sac and foraminal area, thinning for ligamentum flavum. p (within) is the paired t test for change from baseline to 24 months. Between-group p values at 24 months were 0.003 for dural sac area, < 0.001 for ligamentum flavum thickness and 0.002 for foraminal area.

Responder rates, durability and global outcome

Responder analyses sharpen the picture considerably. At 24 months a reduction of at least 50% in leg pain was achieved by 35 of 35 patients (100%) in G6 and 34 of 35 (97%) in G5, compared with 16 of 35 (46%) in G1, 15 of 35 (43%) in G2, 13 of 35 (37%) in G4 and no patient at all in the corticosteroid arm ($\chi^2(5) = 103.8$, $p < 0.001$; Figure 6B). Attainment of the Oswestry minimal clinically important difference showed the same hierarchy, with 100% of patients in G1, G2, G5 and G6 reaching it against 66% in G4 and 3% in G3.

Kaplan–Meier analysis of the time to loss of clinically meaningful relief showed complete separation of the arms (log-rank $\chi^2(5) = 158.2$, $p < 0.001$; Figure 6A). Median durability was reached only in the corticosteroid arm, at 12 months; by 24 months 100% of steroid-treated patients had lost their response, compared with 46% in the SVF arm and 3% or fewer in every other arm. The two patients in the SVF arm who never achieved a clinically meaningful response are counted as failures from the first visit.

Global outcome graded by the modified MacNab criteria at 24 months was excellent or good in 31 of 35 patients in G6 (89%) and 30 of 35 in G5 (86%), against 11 of 35 in G3 (31%) ($\chi^2 = 35.7$, $p < 0.001$; **Figure 6C**).

Resource use followed the same pattern. A repeat epidural injection within 24 months was required by 22 of 35 steroid patients (63%) and 13 of 35 SVF patients, but only 4 and 5 patients in the two combination arms ($\chi^2(5) = 30.3$, $p < 0.001$). Progression to decompressive surgery occurred in 8 steroid patients (23%), 5 SVF patients and a single patient in each combination arm ($\chi^2(5) = 11.3$, $p = 0.046$; **Figure 7C**).

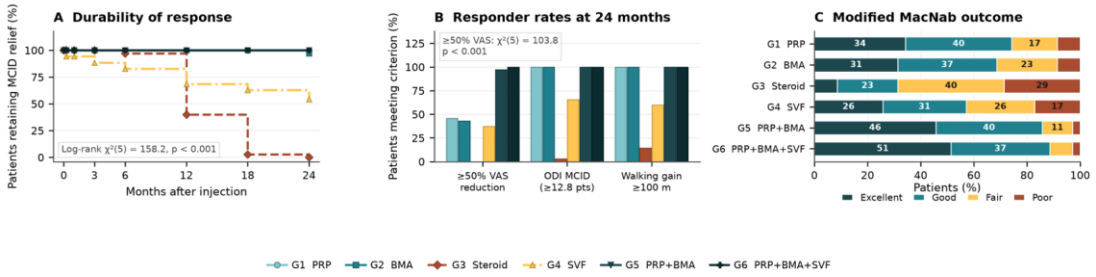

Figure 6: Durability of relief, responder rates and global outcome grading. (A) Kaplan–Meier curves for retention of clinically meaningful leg pain relief. (B) Proportion of patients meeting each prespecified responder criterion at 24 months. (C) Modified MacNab grading at 24 months as a percentage of each arm.

Arm	≥50% VAS	ODI MCID	Walk	Median	Failed by	MacNab	Repeat inj.	Surgery
	n (%)	n (%)	≥100 m, %	durability, months	24 months, %	E/G/F/P	n (%)	n (%)
G1 PRP	16 (46)	35 (100)	100	not reached	0	12/14/6/3	8 (23)	3 (9)
G2 BMA	15 (43)	35 (100)	100	not reached	3	11/13/8/3	9 (26)	3 (9)

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G3 Steroid	0 (0)	1 (3)	14	12	100	3/8/14/10	22 (63)	8 (23)
G4 SVF	13 (37)	23 (66)	60	not reached	46	9/11/9/6	13 (37)	5 (14)
G5 PRP + BMA	34 (97)	35 (100)	100	not reached	0	16/14/4/1	5 (14)	1 (3)
G6 PRP + BMA + SVF	35 (100)	35 (100)	100	not reached	0	18/13/3/1	4 (11)	1 (3)

Table 7: Responder rates, durability of response, global outcome and resource use at 24 months.

MCID, minimal clinically important difference (12.8 points on the Oswestry Disability Index). MacNab grades are excellent / good / fair / poor. Median durability is the time to loss of a 2.0-point reduction in leg pain VAS in patients who had previously achieved it; it was reached only in the corticosteroid arm. Omnibus tests: ≥50% VAS $\chi^2(5) = 103.8$, $p < 0.001$; MacNab $\chi^2 = 35.7$, $p < 0.001$; repeat injection $\chi^2(5) = 30.3$, $p < 0.001$; surgery $\chi^2(5) = 11.3$, $p = 0.046$.

Heterogeneity of response

Mean values conceal an important finding. Levene's test showed markedly unequal variance in the 24-month change in leg pain across arms ($F(5, 204) = 36.3$, $p < 0.001$; **Figure 7A**). The coefficient of variation was 11% in G6 and 13% in G5 but 60% in the SVF arm and 64% in the steroid arm. Within the SVF arm the distribution of responses was effectively bimodal: 16 of 35 patients achieved a reduction of 4 points or more, which is comparable with the combination arms, while 9 of 35 failed to reach the 2.0-point minimal clinically important difference at all. The interquartile range of change in that arm spanned 1.5 to 4.7 points. The arm mean of 3.0 ± 1.8 points is therefore a poor summary of any individual patient's expected outcome, and SVF monotherapy should be interpreted as a treatment that works very well in some patients and not at all in others rather than as a moderately effective treatment for everyone.

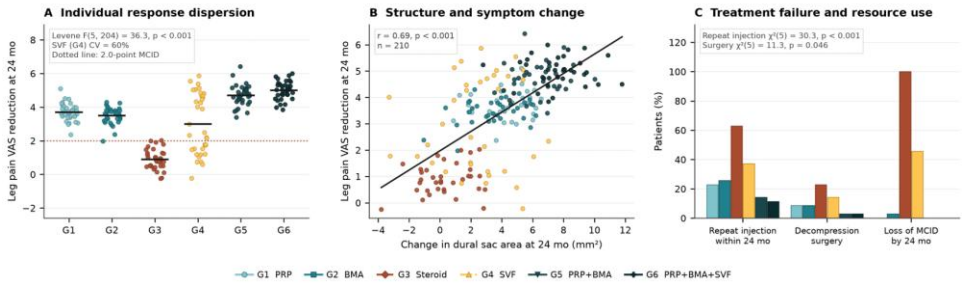

Figure 7: Response heterogeneity, structure–symptom coupling and treatment failure. (A) Individual 24-month changes in leg pain VAS with group means; the dotted line marks the 2.0-point minimal clinically important difference. (B) Relationship between change in dural sac area and change in leg pain across all 210 patients. (C) Repeat injection, progression to decompressive surgery and loss of clinically meaningful relief by 24 months.

Safety

The procedure was well tolerated in every arm. No serious adverse event occurred, and there were no dural punctures, no epidural haematomas, no neurological injuries and no infections at either the

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injection site or any harvest site. Transient injection-site pain lasting less than 72 hours was the most common complaint and was slightly more frequent in the combination arms, consistent with the larger biologic load and the additional harvest procedures. Donor-site soreness at the iliac crest or abdominal wall occurred in 9 of 35 patients in G6 and resolved within a week in every case. Facial flushing and transient hyperglycaemia occurred exclusively in the corticosteroid arm, in 5 and 4 patients respectively, which is the expected systemic signature of epidural steroid exposure.

Adverse event	G1	G2	G3	G4	G5	G6	Total n (%)
Injection-site pain	7	9	4	8	10	11	49 (23.3)
Vasovagal reaction	2	2	1	2	2	2	11 (5.2)
Lower-limb paraesthesia	2	1	2	2	2	3	12 (5.7)
Post-procedural headache	1	1	1	1	1	2	7 (3.3)
Donor-site soreness	0	6	0	5	7	9	27 (12.9)
Facial flushing	0	0	5	0	0	0	5 (2.4)
Raised blood glucose	0	0	4	0	0	0	4 (1.9)
Dural puncture	0	0	0	0	0	0	0 (0.0)
Infection	0	0	0	0	0	0	0 (0.0)
Serious adverse event	0	0	0	0	0	0	0 (0.0)

Table 8: Adverse events by treatment arm over 24 months.

Values are numbers of patients. There were no serious adverse events, dural punctures, epidural haematomas, neurological injuries or infections in any arm. Donor-site soreness applies only to arms involving bone marrow or adipose harvest. Facial flushing and transient hyperglycaemia occurred only in the corticosteroid arm.

Discussion

This trial compared six ultrasound-guided caudal epidural regimens in 210 patients with single-level lumbar spinal stenosis under conditions that were otherwise identical: the same operators, the same needle, the same imaging confirmation and the same 10 mL injectate volume. Four findings emerge, and each has a distinct clinical implication.

Corticosteroid is a fast but transient analgesic

The corticosteroid arm produced the best outcome of any group at one week and remained competitive

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at one month. This is not a trivial finding: for a patient in acute crisis, or for one who needs to become mobile enough to begin rehabilitation, speed of onset matters. But the effect decayed from three months, and by 24 months not a single steroid patient retained a 50% reduction in leg pain, 100% had lost clinically meaningful relief, 63% had required a repeat injection and 23% had proceeded to decompressive surgery. The mean 24-month change of 0.9 points did not reach the minimal clinically important difference. These results align closely with the most rigorous placebo-controlled evidence in stenosis, which found only small and short-lived advantages of epidural glucocorticoid [13,14]. The reasonable reading is that corticosteroid should be positioned as a deliberate short-term bridge rather than as a disease-modifying intervention, and that repeated courses in elderly, frequently osteopenic and often diabetic population require explicit justification given the known systemic effects [16-18].

Combination biologics outperform any single agent

Both combination arms substantially outperformed every monotherapy. Compared with PRP alone, PRP + BMA delivered an additional 1.0 points of leg pain reduction and an additional 91 m of walking distance at 24 months, and raised the 50% responder rate from 46% to 97%. This is consistent with the proposed mechanistic division of labour: platelet concentrate supplies an immediate, high-concentration growth factor and anti-inflammatory signal that acts within days to weeks, whereas the mesenchymal stromal cell fraction of bone marrow aspirate provides sustained paracrine immunomodulation over months [25,34,39,40]. The trajectories in (**Figure 2A**) support this interpretation directly: the combination arms improve as rapidly as PRP alone in the first month but, unlike PRP alone, continue to improve to six months and then hold their gains.

The third agent adds cost, not benefit

The most actionable finding of the trial is negative. Adding stromal vascular fraction to PRP + BMA produced no statistically detectable advantage at 24 months: the difference in leg pain reduction was 0.4 points ($p = 0.82$), and responder rates, MacNab grades, structural change and resource use were statistically indistinguishable. What the third agent did add was measurable: procedure time roughly doubled, from 28.1 to 52.4 minutes, a second harvest site with its own morbidity was introduced, donor-site soreness rose from 7 to 9 patients, and the cost and regulatory complexity of adipose processing were incurred. On the evidence of this trial the triple regimen cannot be recommended as a routine protocol. A ceiling effect is the most plausible explanation: with 97% of PRP + BMA patients already achieving a 50% reduction, there is very little headroom for a third agent to occupy. This should be stated as a limitation as much as a conclusion, because the trial was powered for the six-arm omnibus comparison rather than for equivalence between G5 and G6; a formal non-inferiority design would be required to convert this observation into a definitive claim.

Stromal vascular fraction alone is unpredictable

Stromal vascular fraction monotherapy occupied an uncomfortable middle position, with a mean effect between steroid and the other biologics but with by far the widest dispersion of any arm apart from steroid (coefficient of variation 60%, Levene $p < 0.001$). The bimodality is clinically important: 16 patients did as well as the best combination-arm patients while 9 derived no clinically meaningful benefit at all. Because we standardised the harvest and processing protocol and documented nucleated cell yield and

viability, the variance is unlikely to be purely technical. Donor-dependent differences in adipose stromal cell potency, in the pericyte and endothelial progenitor fraction, and in the recipient inflammatory environment are more probable explanations [36-38]. Until predictive biomarkers of response are available, stromal vascular fraction is difficult to recommend as a stand-alone epidural therapy, and the appropriate research question is not whether it works on average but in whom it works.

Structural change is real but explains only part of the benefit

The imaging findings deserve careful interpretation. Dural sac area increased by up to 11% and ligamentum flavum thickness fell by up to 10% in the combination arms, changes that are small in absolute terms but were highly consistent and entirely absent in the steroid arm. Correlations between structural and symptomatic change were moderate ($r \approx 0.69$ for leg pain), meaning that roughly 47% of the variance in symptom improvement is shared with structural improvement and the remainder is not. This is exactly what would be predicted if biologic epidural therapy works through two partly independent routes: suppression of perineural inflammation and neurotrophic support of the compressed root, which requires no anatomical change, together with a modest reduction in ligamentum flavum thickness and consequent canal expansion [40-42]. It also means that neither mechanism alone accounts for the observed benefit, and that imaging response should not be used as a surrogate endpoint in future trials of these therapies.

Technical considerations

Ultrasound guidance with colour Doppler confirmation achieved a 96% first-pass and 100% overall placement success rate without any radiation exposure across 210 procedures. Given that repeated interventions are common in this population and that many patients are elderly, the cumulative dose saving relative to fluoroscopic guidance is not trivial [22–24]. The standardisation of injectate volume at 10 mL in every arm is a methodological strength that is frequently absent from comparative injection studies: without it, differences in epidural spread rather than differences in biology could account for part of the observed effect.

Limitations

- The proceduralist could not be blinded, because the biologic arms require visible tissue harvest. Patient and assessor blinding, opaque identical syringes and coded statistical analysis mitigate but do not eliminate this risk.
- There was no placebo or saline arm. The comparator was active corticosteroid, so the absolute placebo-adjusted effect of each biologic cannot be estimated from these data.
- The trial was conducted at a single centre by two experienced operators, which maximises protocol fidelity but limits generalisability to less specialised settings.
- Only patients with single-level stenosis, no spondylolisthesis and no previous lumbar surgery were included. The results should not be extrapolated to multilevel disease, instability or the post-surgical spine.
- Follow-up ended at 24 months. Whether the advantage of the combination arms persists, widens or decays beyond that horizon is unknown.

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- The comparison between the two combination arms was not powered as an equivalence or non-inferiority test, so the absence of a detectable difference between G5 and G6 is not formal proof of equivalence.
- Bone marrow aspirate was used without concentration and stromal vascular fraction was prepared by a single protocol. Different processing methods may yield different results, and no dose-ranging was performed for any product.
- Biomarkers of the local inflammatory environment were not measured, so the mechanistic interpretation offered in the discussion remains inferential.

Conclusion

In this randomised, double-blind trial of 210 patients with single-level lumbar spinal stenosis, a single ultrasound-guided caudal epidural injection of combined platelet-rich plasma and bone marrow aspirate produced markedly greater and far more durable improvement in pain, disability, walking capacity and neurological function than corticosteroid, and greater improvement than any single biologic agent. It was also the only class of treatment associated with measurable expansion of the dural sac and foramen. Corticosteroid was the fastest-acting treatment at one week but had lost all clinically meaningful advantage by three months and left no patient with a 50% reduction in leg pain at two years.

Adding adipose-derived stromal vascular fraction to the platelet-rich plasma and bone marrow aspirate combination did not improve any outcome measured in this trial while roughly doubling procedure time and adding a second harvest site, and stromal vascular fraction used alone produced highly unpredictable results. On the evidence presented here, combined platelet-rich plasma and bone marrow aspirate delivered through an ultrasound-guided caudal epidural approach is the preferred regimen, corticosteroid retains a defined role as a short-term analgesic bridge, and stromal vascular fraction requires predictive patient selection before it can be recommended. Confirmation in multicenter trials with placebo control, longer follow-up and formal equivalence testing between combination regimens is the logical next step.

Declarations

The study protocol was approved by the Institutional Review Board of Sugisawa Hospital Orthopaedic Center. All participants provided written informed consent before enrolment, including specific consent for autologous bone marrow and adipose tissue harvest.

Consent for publication

Not applicable. No individually identifiable data or images are presented.

Availability of data and materials

The de-identified datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions
[MHK, CAPMR] conceived and designed the study and performed the injections. [MHK, BF, CGB] prepared the biologic products and supervised laboratory quality control. [MHK, BF, CGB] performed the blinded clinical assessments. [MHK, BF, CGB] performed the blinded imaging measurements. [BF, CGB] carried out the statistical analysis. [MHK, CAPMR] drafted the manuscript. All authors read, revised and approved the final manuscript.

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References
1. Kalichman L, Cole R, Kim DH, Li L, Suri P, et al. (2020) Spinal stenosis prevalence and association with symptoms: the Framingham Study. Spine J. 9(7):545-50.
2. Jensen RK, Jensen TS, Koes B, Hartvigsen J. (2020) Prevalence of lumbar spinal stenosis in general and clinical populations: a systematic review and meta-analysis. Eur Spine J. 29(9):2143-63.
3. Maeda T, Hashizume H, Yoshimura N, Oka H, Ishimoto Y, et al. (2018) Factors associated with lumbar spinal stenosis in a large-scale, population-based cohort: The Wakayama Spine Study. PLoS One. 13(7):e0200208.
4. Suri P, Rainville J, Kalichman L, Katz JN. (2010) Does this older adult with lower extremity pain have the clinical syndrome of lumbar spinal stenosis? JAMA. 304(23):2628-36.
5. Katz JN, Zimmerman ZE, Mass H, Makhni MC. (2022) Diagnosis and Management of Lumbar Spinal Stenosis: A Review. JAMA. 327(17):1688-99.
6. Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Blood E, et al. (2008) Surgical versus nonsurgical therapy for lumbar spinal stenosis. N Engl J Med. 358(8):794-810.
7. Weinstein JN, Tosteson TD, Lurie JD, Tosteson A, Blood E, et al. (2010) Surgical versus nonoperative treatment for lumbar spinal stenosis four-year results of the Spine Patient Outcomes Research Trial. Spine (Phila Pa 1976). 35(14):1329-38.
8. Zaina F, Tomkins-Lane C, Carragee E, Negrini S. (2016) Surgical versus non-surgical treatment for lumbar spinal stenosis. Cochrane Database Syst Rev. 2016(1):CD010264.
9. Ammendolia C, Hofkirchner C, Plener J, Bussières A, Schneider MJ, et al. (2022) Non-operative treatment for lumbar spinal stenosis with neurogenic claudication: an updated systematic review. BMJ Open. 12(1):e057724.
10. Friedly JL, Comstock BA, Turner JA, Heagerty PJ, Deyo RA, et al. (2014) A randomized trial of epidural glucocorticoid injections for spinal stenosis. N Engl J Med. 371(1):11-21.
11. Manchikanti L, Knezevic NN, Boswell MV, Kaye AD, Hirsch JA. (2016) Epidural Injections for Lumbar Radiculopathy and Spinal Stenosis: A Comparative Systematic Review and Meta-Analysis. Pain Physician. 19(3):E365-410.
12. Manchikanti L, Cash KA, McManus CD, Pampati V, Abdi S. (2008) Preliminary results of a randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 4-Spinal stenosis. Pain Physician. 11(6):833-48.
13. Koc Z, Ozcakir S, Sivrioglu K, Gurbet A, Kucukoglu S. (2009) Effectiveness of physical therapy and epidural steroid injections in lumbar spinal stenosis. Spine (Phila Pa 1976). 34(10):985-9.
14. Meng H, Fei Q, Wang B, Yang Y, Li D, et al. (2015) Epidural injections with or without steroids in

managing chronic low back pain secondary to lumbar spinal stenosis: a meta-analysis of 13 randomized controlled trials. Drug Des Devel Ther. 9:4657-67.

15. Wernecke C, Braun HJ, Dragoo JL. (2015) The Effect of Intra-articular Corticosteroids on Articular Cartilage: A Systematic Review. Orthop J Sports Med. 3(5):2325967115581163.
16. Jain A, Gupta P, Chaurasia R, Singh M, Pandey S. (2020) Observational Study to Evaluate the Effect of Epidural Steroid Injection on Bone Mineral Density and Bone Turnover Markers. Pain Physician. 23(5):E517-E524.
17. Even JL, Crosby CG, Song Y, McGirt MJ, Devin CJ. (2012) Effects of epidural steroid injections on blood glucose levels in patients with diabetes mellitus. Spine (Phila Pa 1976). 37(1):E46-50.
18. Pace CS, Blanchet NP, Isaacs JE. (2018) Soft Tissue Atrophy Related to Corticosteroid Injection: Review of the Literature and Implications for Hand Surgeons. J Hand Surg Am. 43(6):558-63.
19. Chen CP, Tang SF, Hsu TC, Tsai WC, Liu HP, et al. (2004) Ultrasound guidance in caudal epidural needle placement. Anesthesiology. 101(1):181-4.
20. Stitz MY, Sommer HM. (1999) Accuracy of blind versus fluoroscopically guided caudal epidural injection. Spine (Phila Pa 1976). 24(13):1371-6.
21. Poutoglidou F, Metaxiotis D, Vasiliadis AV, Alvanos D, Mpeletsiotis A. (2021) Caudal Epidural Injections in Lumbar Spinal Stenosis: Comparison of Nonimage, Ultrasonography-, and Fluoroscopy-Guided Techniques. A Randomized Clinical Trial. Perm J. 25:(20):321.
22. Yoo SW, Ki MJ, Doo AR, Woo CJ, Kim YS, et al. (2021) Prediction of successful caudal epidural injection using color Doppler ultrasonography in the paramedian sagittal oblique view of the lumbosacral spine. Korean J Pain. 34(3):339-45.
23. Munro C, Baliga S, Shepherd J, MacEachern CF. (2021) Anatomical study of the human sacral hiatus and implications for successful caudal epidural injection. Surgeon. 19(5):e103-e106.
24. Marx RE. (2004) Platelet-rich plasma: evidence to support its use. J Oral Maxillofac Surg. 62(4):489-96.
25. Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. (2020) Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020. Int J Mol Sci. 21(20):7794.
26. DeLong JM, Russell RP, Mazzocca AD. (2012) Platelet-rich plasma: the PAW classification system. Arthroscopy. 28(7):998-1009.
27. Magalon J, Chateau AL, Bertrand B, Louis ML, Silvestre A, et al. (2016) DEPA classification: a proposal for standardising PRP use and a retrospective application of available devices. BMJ Open Sport Exerc Med. 2(1):e000060.
28. Lana JFSD, Purita J, Paulus C, Huber SC, Rodrigues BL, et al. (2017) Contributions for classification of platelet rich plasma - proposal of a new classification: MARSPILL. Regen Med. 12(5):565-74.
29. Wang X, Zhang Y. (2025) Therapeutic interventions of platelet-rich plasma versus corticosteroid injections for lumbar radicular pain: a systematic review and meta-analysis. J Orthop Surg Res. 20(1):306.
30. Muschler GF, Boehm C, Easley K. (1997) Aspiration to obtain osteoblast progenitor cells from human bone marrow: the influence of aspiration volume. J Bone Joint Surg Am. 79(11):1699-709.
31. Muschler GF, Nitto H, Boehm CA, Easley KA. (2001) Age- and gender-related changes in the cellularity of human bone marrow and the prevalence of osteoblastic progenitors. J Orthop Res. 19(1):117-25.
32. Hernigou P, Poignard A, Beaujean F, Rouard H. (2005) Percutaneous autologous bone-marrow grafting for nonunions. Influence of the number and concentration of progenitor cells. J Bone Joint Surg Am. 87(7):1430-7.
33. Hernigou P, Homma Y, Flouzat Lachaniette CH, Poignard A, Allain J, et al. (2013) Benefits of small volume and small syringe for bone marrow aspirations of mesenchymal stem cells. Int Orthop. 37(11):2279-87.

34. Pettine KA, Suzuki RK, Sand TT, Murphy MB. (2017) Autologous bone marrow concentrate intradiscal injection for the treatment of degenerative disc disease with three-year follow-up. Int Orthop. 41(10):2097-103.
35. Bourin P, Bunnell BA, Casteilla L, Dominici M, Katz AJ, et al. (2013) Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived stromal/stem cells: a joint statement of the International Federation for Adipose Therapeutics and Science (IFATS) and the International Society for Cellular Therapy (ISCT). Cytotherapy. 15(6):641-8.
36. Brown JC, Shang H, Li Y, Yang N, Patel N, et al. (2017) Isolation of Adipose-Derived Stromal Vascular Fraction Cells Using a Novel Point-of-Care Device: Cell Characterization and Review of the Literature. Tissue Eng Part C Methods. 23(3):125-35.
37. Lu J, Wen T, Huang H, Xie C, Kang J, et al. (2025) Intraarticular injection of the stromal vascular fraction for the treatment of knee osteoarthritis a prospective randomized controlled clinical trial. Sci Rep. 15(1):28109.
38. Han JH, Jung M, Chung K, Moon HS, Jung SH, et al. (2025) Intra-articular Stromal Vascular Fraction and Mesenchymal Stem Cell Injections Show Variable Efficacy and Higher Potential Complications Compared to Corticosteroid and Hyaluronic Acid in Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials. Arthroscopy. 41(9):3666-80.e13.
39. Olmarker K, Rydevik B, Nordborg C. (1993) Autologous nucleus pulposus induces neurophysiologic and histologic changes in porcine cauda equina nerve roots. Spine (Phila Pa 1976). 18(11):1425-32.
40. Igarashi T, Kikuchi S, Shubayev V, Myers RR. (2000) Volvo Award winner in basic science studies: Exogenous tumor necrosis factor-alpha mimics nucleus pulposus-induced neuropathology. Molecular, histologic, and behavioral comparisons in rats. Spine (Phila Pa 1976). 25(23):2975-80.
41. Weber KT, Alipui DO, Sison CP, Bloom O, Quraishi S, et al. (2016) Serum levels of the proinflammatory cytokine interleukin-6 vary based on diagnoses in individuals with lumbar intervertebral disc diseases. Arthritis Res Ther. 18:3.
42. Aggarwal S, Pittenger MF. (2005) Human mesenchymal stem cells modulate allogeneic immune cell responses. Blood. 105(4):1815-22.
43. Fairbank JC, Pynsent PB. (2000) The Oswestry Disability Index. Spine (Phila Pa 1976). 25(22):2940-52.
44. Copay AG, Glassman SD, Subach BR, Berven S, Schuler TC, et al. (2008) Minimum clinically important difference in lumbar spine surgery patients: a choice of methods using the Oswestry Disability Index, Medical Outcomes Study Questionnaire Short Form 36, and pain scales. Spine J. 8(6):968-74.
45. Macnab I. (1971) Negative disc exploration. An analysis of the causes of nerve-root involvement in sixty-eight patients. J Bone Joint Surg Am. 53(5):891-903.
46. McIlroy S, Mah Y, Tahtis V, Beddard A, Bearne L, et al. (2025) Minimal clinically important difference of the 6-Minute walk test and daily step count at 3 months following surgery for lumbar spinal stenosis. Eur Spine J. 34(12):5690-700.