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Effectiveness and Factors Associated with Epidural Decompression and Adhesiolysis Using a Balloon-Inflatable Catheter in Chronic Lumbar Spinal Stenosis: 1-Year Follow-Up

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Abstract

Objectives. This study aimed to investigate the efficacy of the combined balloon decompression with a balloon-inflatable catheter (ZiNeu) in addition to conventional epidural adhesiolysis, and to identify factors that predict patient responses.

Study Design. An institutional single-armed prospective observational study.

Subjects. Chronic refractory lumbar spinal stenosis.

Methods. This study was performed in 61 patients with spinal stenosis who suffered from chronic (at least 3 months) lumbar radicular pain with or without lower back pain. Patients had failed to maintain improvement for more than 1 month with conventional epidural injection. The numeric rating scale (NRS) and Oswestry disability index (ODI) were each measured at 1, 3, 6, and 12 months after percutaneous epidural adhesiolysis and balloon decompression with a ZiNeu catheter.

Results. The percentage of successful responders was 72.1%, 60.7%, 57.4%, and 36.1% of patients at 1, 3, 6, and 12 months, respectively. A single combined treatment of percutaneous epidural adhesiolysis and balloon decompression with a ZiNeu catheter provided sufficient pain relief and functional improvement in patients with chronic refractory lumbar spinal stenosis, and the improvement was maintained for 12 months ($P < 0.001$). Multivariate logistic regression analysis showed that absence of diabetes independently predicted successful response at 12 months after percutaneous epidural decompression and adhesiolysis with the balloon catheter (Odds ratio = 0.080; 95% confidence interval = 0.009–0.676; $P = 0.020$).

Conclusions. The combined epidural adhesiolysis and balloon decompression with a ZiNeu catheter led to significant pain relief and functional improvement in a subset of patients with refractory spinal stenosis.

Key Words. Chronic Pain; Lumbar; Radiculopathy; Low Back Pain; Balloon Decompression

Introduction

One of the most common causes of chronic lower back and leg pain in the elderly is lumbar spinal stenosis, which also leads to impaired walking (neurogenic claudication) and various forms of functional disability [1,2]. Most lumbar spinal stenosis cases result from degenerative changes of the lumbar spine, although this condition can be congenital [2,3].

The initial management of lumbar spinal stenosis generally involves conservative modalities including simple epidural injections [4,5]. Recently, in patients who fail to respond to fluoroscopically directed epidural injections, percutaneous epidural adhesiolysis rather than surgery has been recommended [5–7]. This recommendation is based on epidural adhesions that can be observed in patients with spinal stenosis and disc herniation, although most cases commonly arise from epidural scarring after surgery [8–10]. Percutaneous epidural adhesiolysis is commonly performed with a Racz catheter or a more steerable navigation catheter [5,11,12]. However, the approach and correct placement of these catheters can be difficult in patients with severe adhesions or stenosis, which leads to incomplete resolution of the adhesions [13]. The long-term effects (i.e., greater than 6 months) of these treatments are uncertain and controversial [5]. Furthermore, these pre-existing techniques of percutaneous adhesiolysis cannot sufficiently relieve the stenotic area [13]. Importantly, no treatment has yet been developed to relieve stenosis itself using a nonsurgical method.

Previously, transforaminal balloon procedures have been shown to result in significant pain relief and functional improvement in patients with chronic refractory lumbar foraminal stenosis [14]. Based on this observation, a novel catheter (ZiNeu®, JUVENUI, Seoul, Korea; Figure 1A) with an inflatable balloon attached to the end of the catheter tip was developed and introduced for pain physicians [15,16]. It has been suggested that the ZiNeu catheter might be an effective alternative to percutaneous epidural adhesiolysis when conventional methods fail to remove adhesions or sufficiently relieve stenosis [16].

In our current study, we aimed to investigate the efficacy of the combined epidural adhesiolysis and balloon decompression with a ZiNeu catheter in patients with refractory lumbar spinal stenosis, and to identify factors that predict patient responses.

Methods

This prospective observational study was conducted at the pain management clinics of the Asan Medical Center in Seoul, Republic of Korea, and Hanyang University Guri Hospital in Guri-si, Republic of Korea. Permission to conduct this study was granted by the institutional review board of Asan Medical Center, and written informed consent was received from each study participant (approval number, 2012-0235).

Participants

Between September 2012 and October 2013, chronic lumbar spinal stenosis patients ≥ 20 years of age with leg pain intensity ≥ 6 (out of 10) on the numerical rating scale (NRS) for at least 3 months were examined to ascertain their eligibility. A thorough history and physical examination were performed for each patient to rule out a confounding diagnosis of vascular disease or other origins. Magnetic resonance imaging (MRI) was obtained in all patients to confirm the diagnosis of spinal stenosis. MRI grades of lumbar spinal stenosis were determined based on previous studies [17,18]. Inclusion criteria included chronic (at least 3 months) lumbar radicular pain with or without lower back pain, and a previous failure of conservative management, such as physiotherapy, exercise therapy, or analgesic medications. Epidural injections or percutaneous epidural adhesiolysis administered ≥ 12 weeks prior to recruitment were permitted because most of the patients visiting our clinic had a history of epidural injections. All eligible patients received a conventional diagnostic/therapeutic fluoroscopy-guided transforaminal or caudal epidural injection with local anesthetic and steroid administration before enrollment. Patients who showed no or a minimal pain reduction response ($< 50\%$) for a short duration less than one month following the epidural block were finally enrolled.

Exclusion criteria included the following: patient refusal to participate in the study, aged < 20 years, unbearable pain of 10 points on the NRS, acute pain < 3 months, signs of progressive neurological deficits or motor weakness, allergies to steroids or contrast dyes, coagulopathy, steroid injection within the previous 12 weeks, uncontrollable or unstable opioid use, pregnancy, lactation, systemic infection, injection site infection, malignancy, and unstable medical or psychiatric condition. Patients with lumbar spinal stenosis at ≥ 4 levels or a history of prior lumbar spine surgery were also excluded.

Intervention: Percutaneous Epidural Decompression and Adhesiolysis Using an Inflatable Balloon Catheter

All procedures in this study were performed on an outpatient basis, and no premedications or sedatives were used. Fluoroscopic guidance was implemented in all cases. A single fluoroscopy C-arm system (OEC 9800, General Electric Healthcare, Little Chalfont, United Kingdom) was used. Each patient was placed in a prone position with a pillow under the abdomen to minimize lumbar lordosis. After sterile preparation for the procedure, skin and soft tissue were infiltrated with 1% lidocaine. A 10 G guide needle, which was specially designed to prevent cutting or skiving of the catheter, was inserted into the epidural space through the sacral

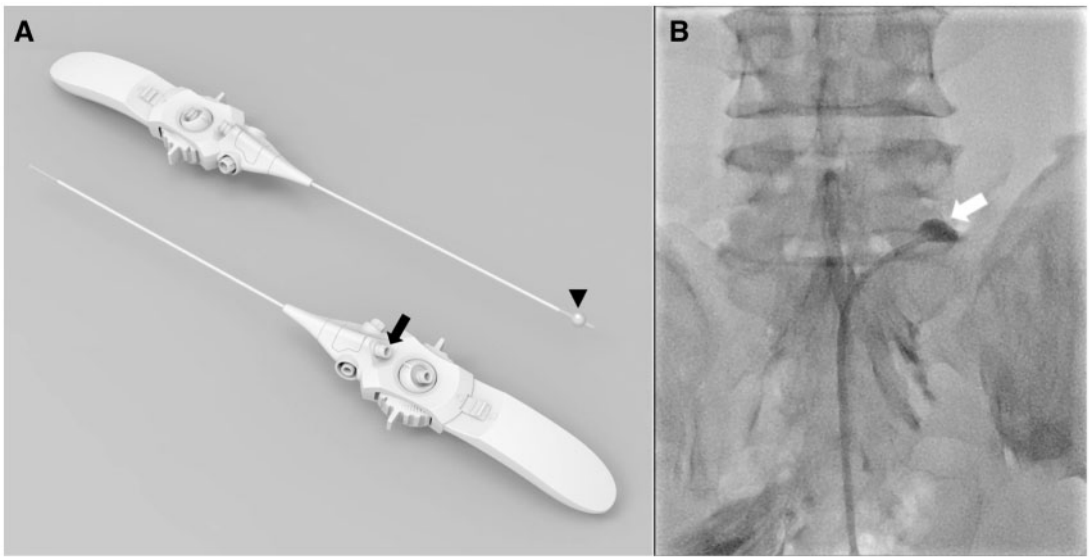

Figure 1 Inflatable balloon catheter (A) and a fluoroscopic image of an anteroposterior view of the lumbar spine during ballooning in percutaneous epidural decompressive adhesiolysis (B). This instrument can be adjusted from side-to-side and has an inflatable balloon (black arrow-head) attached to the end of the catheter tip. It also has a channel (black arrow) that allows drugs to be injected or another thin catheter to be kept at the target site for 2- or 3-day treatment regimens. Note that an epiduroscope can be inserted. Balloon filled with contrast dye (0.13 mL). Note the squeezed balloon shadow at the intervertebral foramen (white arrow), which suggests intervertebral foraminal stenosis.

hiatus under intermittent fluoroscopy. The epidural space was identified by injection of ~8 mL diluted contrast medium (Omnipaque, Nycomed Imaging AS, Oslo, Norway) under fluoroscopy. The diluted contrast mixture was composed of about 4 mL of pure contrast medium, 4 mL of 1% lidocaine and 1,500 IU hyaluronidase. Filling defects were identified by examining the contrast flow. If intravascular placement of the needle or contrast occurred, the needle was repositioned.

After appropriate determination of the epidurogram and target area, a ZiNeu catheter was advanced through the guide needle to the area of filling defect or the site of pathology, as determined by MRI or symptomatology (Table 1). Gentle mechanical adhesiolysis and decompression with the ZiNeu catheter was performed at appropriate target sites (i.e., the central ventral and dorsal epidural space, the lateral recess area, and/or each intervertebral foramen). Epidural decompression and adhesiolysis was conducted using gentle side-to-side movement of the catheter with intermittent ballooning. The balloon was filled with 0.13 mL contrast agent using a 1 mL Luer-Lock syringe (BD Medical, Franklin Lakes, NJ), and each ballooning process was limited to 5 sec (Figure 1B) [14]. The extent of balloon inflation was adjusted based on the degree of pain; if moderate to severe pain was noted during balloon inflation, no further attempt was made for safety reasons. The catheter moved only in the deflated state. After adhesiolysis and decompression, 1 mL of pure contrast was injected to detect subarachnoid or intravascular filling and to ensure satisfactory filling of the previous defects. Then, injections of 2 mL 1% lidocaine with steroid (5 mg dexamethasone or 20 mg triamcinolone) were performed at each target site. At the end of the procedure, a Perifix epidural catheter (B. Braun Melsungen AG, Melsungen, Germany) was kept at the main target site through the ZiNeu catheter lumen. At recovery room, a test injection of 2 mL lidocaine was administered through the Perifix catheter. After 10 to 15 min monitoring, another 4 mL of 10% hypertonic saline was injected through the Perifix catheter. The Perifix catheter was kept in place for a two-day drug injection. The catheter was then removed on the second day of the procedure after the same drugs (10% hypertonic saline and steroid) were injected again. Since the neuraxial (intrathecal or epidural) injection of triamcinolone acetonide was restricted by the Korean Ministry of Food and Drug Safety from March 15, 2013, particulate steroids, such as triamcinolone acetonide, were not used in epidural injections (caudal, interlaminar, or transforaminal) after January 2013. However, triamcinolone acetonide was administered to the study participants until December 2012 because this study was carried out between September 2012 and October 2013.

Outcome Assessments and Follow-Up

The baseline characteristics of all participants were collected. Outcome assessments were conducted at baseline, and at 1, 3, 6, and 12 months after the procedure.

Table 1 Baseline characteristics of the study subjects

Parameters	N = 61
Age (years)	67.4 ± 9.5
Gender (male/ female)	29 (47.5%) / 32 (52.5%)
Body mass index (kg/m^2)	24.6 ± 3.6
Concurrent disease	
Diabetes/hypertension/CV/ OA/osteoporosis	16 (26.2%)/30 (49.2%)/ 13 (21.3%)/8 (13.1%)/ 4 (6.6%)
Total duration of pain (months)	34.9 ± 32.7
Number of previous epidural injection	5.5 ± 3.8
Previous epidural adhesiolysis (no/yes)	45 (73.8%)/ 16 (26.2%)
Medication quantification scale	4.0 (0.0–7.4)
Opioid use (no/yes)	55 (90.2%)/ 6 (9.8%)
Spondylolisthesis (no/yes)	38 (62.3%)/ 23 (37.7%)
Stenosis grades	
Central (mild/moderate/ severe)	0 (0.0)/4 (6.6%)/ 10 (16.4%)
Foraminal (mild/moderate/ severe)	19 (31.1%)/20 (32.8%)/ 14 (23.0%)
Target level	
L4/ L5	2 (3.3%)/ 20 (32.8%)
L4-5/ L5-S1	23 (37.7%)/ 10 (16.4%)
L3-4-5/ L4-5-S1	1 (1.6%)/ 5 (8.2%)
Treatment location	
Left /Right	24 (39.3%)/ 11 (18.0%)
Both	14 (23.0%)
Central only	8 (13.1%)
Central with both foramina	2 (3.3%)
Central with unilateral foramen (Left/Right)	1 (1.6%)/ 1 (1.6%)
Pain intensity (numerical rating scale)	
Leg / Back	7.0 (6.0–8.0)/ 6.0 (4.0–8.0)
Oswestry Disability Index (%)	47.1 ± 16.1
Beck depression inventory	8.0 (2.0–21.8)

Data are expressed numbers (%), and means ± standard deviation, or medians (interquartile range).
CV = cardiovascular disease; OA = osteoarthritis of knee.

Prior to the procedure, all participants were instructed in the use of an 11-point NRS (0 = no pain, 10 = unbearable pain) to assess the intensity of both leg and lower back pain [19,20], the Korean version 10-item Oswestry disability index (ODI) questionnaire (range, 0–100; 0 = no disability) to assess physical function [21], and the Beck depression inventory to assess emotional status [20]. The medication quantification scale III (MQS) was also measured to quantify changes in analgesics [22]. The global perceived effect (GPE) according to the 7-point Likert scale was also used to assess patient satisfaction and improvement [23]. Adverse events during treatment and follow-up were individually recorded. A multidimensional approach was used to define the study outcomes. The primary outcome was the number of successful responders to treatment at each follow-up period. Successful response was determined based on previous studies with some modifications [20,24,25]. Successful response was defined as: 1) ≥ 50% (or ≥ 4-point) reduction from baseline leg NRS and no increase from baseline ODI and MQS, and ≥ 4 points on the GPE scale; or 2) ≥ 30% (or ≥ 2-point) reduction from baseline NRS with any one of the following criteria: simultaneous ≥ 30% (or ≥ 10-point) reduction in ODI from baseline, or ≥ 5 points on the GPE scale, or no increase from the baseline MQS.

Additionally, the NRS, ODI, MQS, and GPE scales of satisfaction were measured at 1, 3, 6, and 12 months post-procedure. The reductions in pain intensity, ODI, and MQS compared with baseline at each follow-up assessment were also determined. If present, complications during the procedure were reported, and any adverse events were further evaluated at follow-up visits.

Patients were advised to continue their previously prescribed analgesic medications. For the first month after the procedure, patients were instructed not to change any previously prescribed medications. All patients were aware of this guideline prior to participating in the study. The prescribed doses of each analgesic, except for opioids, were increased or decreased based on the remnant pain intensity of a patient at each follow-up visit. Patients who had alterations in analgesic medication or who wanted alternative treatments were considered as treatment failures after that follow-up visit and were dropped out of the study. Patients who were lost to follow-up, prescribed an increased dose of opioid, or treated surgically were also determined to be treatment failures at that point. Each case of treatment failure was defined as a non-responder at each subsequent follow-up visit.

Statistical Analysis

Categorical variables are presented as absolute numbers and percentages. Continuous variables are presented as means with standard deviation (SD), 95% confidence intervals (CI), or medians with the interquartile range (IQR) if skewed. All observed data were analyzed on an intent-to-treat basis, regardless of loss to follow-up or withdrawal from the study. As data loss resulting from drop-out, including treatment failure, were expected, a linear mixed effect model (LMEM) was used to analyze continuous variables (NRS, ODI, MQS, and GPE) at baseline and 1, 3, 6, and 12 months post-procedure. Changes from baseline at each time point were compared using the Mann–Whitney U-test.

To assess baseline differences between successful responders and non-responders at 12 months post-

procedure, continuous variables were compared using Student's *t*-test or the Mann–Whitney U test, as appropriate. Categorical data were compared using the chi-square test or Fisher's exact test to assess differences between two groups appropriately. The most relevant factors associated with a successful response at 12 months after the procedure were included in the univariate logistic regression analysis. The inclusion of variables into the final multivariate logistic regression analysis to evaluate independent factors associated with a successful response at 12 months post-procedure was based on biological plausibility, clinical importance, and statistical considerations ($P < 0.10$). Analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC). A two-tailed P value < 0.05 was considered to indicate a statistically significant difference.

Results

A series of 221 patients who had been diagnosed with lumbar spinal stenosis between September 2012 and October 2013 were screened for eligibility to participate in this study. These patients presented with chronic lumbar radicular pain with or without lower back pain. A total of 69 patients fulfilled both the inclusion and exclusion criteria. Among the 69 eligible patients, 4 declined to participate in the study or did not visit again, 2 received another procedure, and 2 patients failed the diagnostic/therapeutic epidural block. Ultimately, 61 patients agreed to participate (Figure 2). The baseline patient demographic characteristics are shown in Table 1.

The percentages of patients who exhibited successful treatment responses were 72.1%, 60.7%, 57.4%, and 36.1% of the study sample at 1, 3, 6, and 12 months, respectively (Table 2). The observed numbers of patients who satisfied the individual parameters of successful response at each follow-up visit are shown in Table 3.

The estimated mean changes from baseline in the NRS of pain and ODI functional status over the 12 months of follow-up are shown in Table 4 and Figure 3. The results of these intent-to-treat analyses showed that the pain intensities of both the lower back and leg were significantly improved and maintained following the combined percutaneous epidural decompression and adhesiolysis with a ZiNeu catheter during the 12 month follow-up period. Interestingly, functional capacity based on ODI continuously improved over the 12 months. However, quantificational changes in analgesics (MQS) did not alter significantly during follow-up period (data not shown). The patient satisfaction score (GPE) was ~5 or more during the 12 months follow-up period (Table 5).

Table 6 shows the comparison of baseline characteristics between the non-responders and successful responders at 12 months after the combined epidural decompression and adhesiolysis with a ZiNeu catheter. The absence of diabetes was higher in the successful responders than in the non-responders. The median NRS for lower back pain was greater in the non-responders than in the successful responders. No other baseline characteristics that we examined differed between the two groups. Univariate logistic regression analysis showed that diabetes and NRS for lower back pain were factors were significantly associated with a successful response at 12 months. Multivariate logistic regression analysis showed that an independent factor significantly associated with successful response over the 12 month follow-up period was diabetes (odds ratio = 0.080; $P = 0.020$; Table 7). In addition, lower back pain was also independently associated with successful response after 12 months of the combined treatment, although it showed a marginal significance (odds ratio = 0.799; $P = 0.051$; Table 7).

No serious adverse events were noted in any study participant, and all adverse events that presented throughout the entire study period were minor and temporary. No additional medications or treatments were required. Several patients reported temporary pain during needle insertion and paresthesia during balloon procedure, which was tolerable and did not require additional medications or discontinuation of the procedure. Several patients complained of 2–3 days of remaining pain in the post-procedural period; however, transient pain aggravation was mostly insignificant and relieved spontaneously without any neurological sequelae in any case. No other complications or adverse events, such as dural puncture, intravenous injection, persistent motor or sensory impairment, severe pain or paresthesia, or infection, were reported.

Discussion

Currently, percutaneous epidural adhesiolysis is frequently performed using a shearing-resistant catheter (the Racz-type catheter) or a more steerable navigation catheter (e.g., NaviCath, Myelotec, Roswell, GA) in refractory patients [5–7], although it remains unclear whether it actually relieves adhesions. Recently, experimental biomechanical evaluations of percutaneous epidural adhesiolysis showed that when performed with a Racz-type catheter, this procedure might be suitable for the targeted application of highly concentrated epidural medications and could have a lavage effect in reducing local inflammatory substances; however, it does not exert true mechanical lysis of adhesions [13]. A NaviCath-type catheter, which was developed in order to directly separate the adhered region around a nerve, has been reported to be clinically effective in treating chronic lower back pain that is unresponsive to transforaminal epidural injection [26,27]. However, this procedure has some limitations in patients with a severe degree of adhesion or spinal stenosis because of the difficulty in approaching and placing the catheter at the target area [27]. In addition, although epiduroscopic adhesiolysis also has shown effectiveness in treating post-lumbar surgery syndrome patients who failed to other modalities [6], it has not been widely accepted and has limited applicability as a treatment because of safety concerns, high cost, and technical issues related

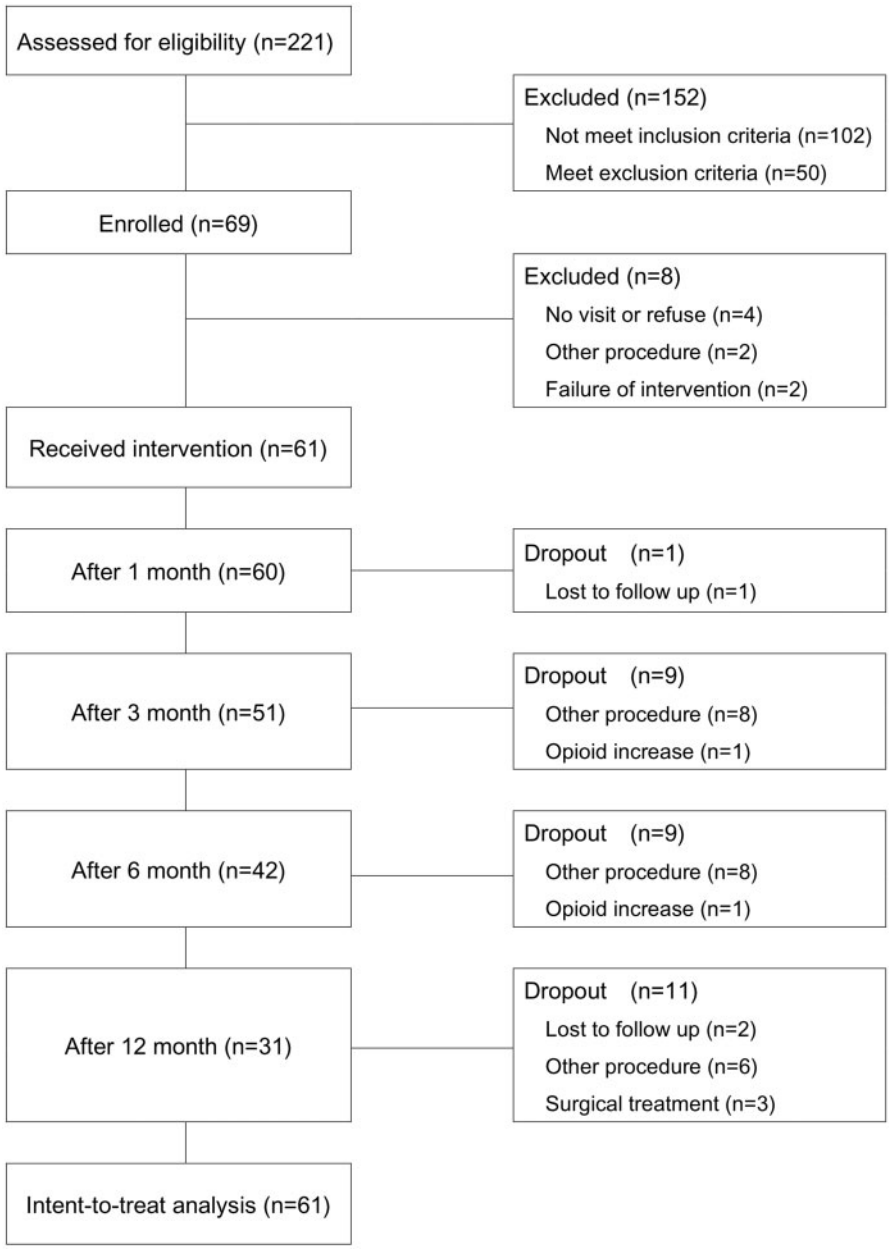

Figure 2 Study flow diagram.

to visualization equipment, focal length, and difficulty in identifying structures [6,28]. Specifically, epiduroscopic adhesiolysis cannot be applied to foraminal stenosis, nor can it directly relieve stenosis. The present prospective observational study showed the combined treatment with a ZiNeu catheter for epidural adhesiolysis and decompression provided sufficient pain relief in patients with chronic refractory lumbar spinal stenosis, and that pain improvement was maintained for 12 months. Interestingly, these patients also experienced significant functional improvements over the 12 months after balloon decompressive adhesiolysis, especially in ODI. Therefore, we suggest that this combined balloon decompression method with adhesiolysis can be a useful alternative to overcoming the limitations of the aforementioned pre-existing procedures.

Several potential explanations exist for the effective pain relief and functional improvement observed after the combined balloon decompression and adhesiolysis. First, distension of the epidural space by intermittent ballooning can lead to more effective mechanical detachment of a perineural adhesion, which could play a role in long-lasting symptom relief and functional improvement. At least partial restoration of nerve root mobility interfered by adhesion could contribute to long-term symptom relief, exceeding the intrinsic effective duration of epidural injections [14,16]. Second,

Table 2 Proportions of successful responders among patients who were treated using the combined decompression and adhesiolysis with an inflatable balloon catheter

Parameters	Follow-up (Months)	Number (%), N = 61
Successful responder	1	44 (72.1%)
	3	37 (60.7%)
	6	35 (57.4%)
	12	22 (36.1%)

Successful response was defined as: 1) ≥ 50% (or ≥ 4-point) reduction from baseline leg NRS; and no increase from baseline ODI and MQS; and ≥ 4 points on the GPE scale or 2) ≥ 30% (or ≥ 2-point) reduction from baseline NRS with any one of the following criteria; simultaneous ≥ 30% (or ≥ 10-point) reduction in ODI from baseline; or ≥ 5 points on the GPE scale; or no increase from the baseline MQS.
Data are expressed numbers (%).

Table 3 Observed number of patients who satisfied the individual parameters of successful response at each follow-up visit

Parameters	Follow-up (Months)	Number (%), N = 61
≥50% (or ≥ 4-point) reduction in NRS	1	29 (47.5%)
	3	23 (37.7%)
	6	24 (39.3%)
	12	19 (31.1%)
≥30% (or ≥ 2-point) reduction in NRS	1	43 (70.5%)
	3	37 (60.7%)
	6	34 (55.7%)
	12	23 (37.7%)
≥30% (or ≥ 10-point) reduction in ODI	1	31 (50.8%)
	3	33 (54.1%)
	6	29 (47.5%)
	12	21 (34.4%)
No change or reduction in MQS	1	43 (70.5%)
	3	39 (63.9%)
	6	32 (52.5%)
	12	20 (32.8%)
No change or reduction in opioid use	1	52 (85.2%)
	3	44 (72.1%)
	6	36 (59.0%)
	12	24 (39.3%)
≥5 points in GPES	1	40 (65.6%)
	3	37 (60.7%)
	6	33 (54.1%)
	12	22 (36.1%)

NRS, numerical rating scale; ODI, Oswestry disability index; MQS, medication quantification scale; and GPES, global perceived effect of satisfaction.
Data are expressed as numbers (%).

Table 4 Changes in the mean pain score and physical function in patients who were treated using the combined decompression and adhesiolysis with an inflatable balloon catheter

Variables*	Time (Month)	Values (95% CI)	*P* value compared with baseline†
Back pain	Baseline	5.23 (4.56–5.90)	
	1	3.47 (2.86–4.08)	< 0.0001
	3	3.52 (2.91–4.14)	< 0.0001
	6	3.47 (2.81–4.13)	< 0.0001
	12	3.57 (2.71–4.43)	0.0002
Leg pain	Baseline	6.82 (6.39–7.27)	
	1	4.01 (3.45–4.58)	< 0.0001
	3	4.26 (3.64–4.87)	< 0.0001
	6	3.98 (3.30–4.66)	< 0.0001
	12	4.03 (3.15–4.91)	< 0.0001
ODI	Baseline	47.10 (42.95–51.24)	
	1	30.34 (25.97–34.71)	< 0.0001
	3	30.73 (25.87–35.59)	< 0.0001
	6	27.98 (22.32–33.65)	< 0.0001
	12	21.60 (16.97–26.23)	< 0.0001

Numerical rating scale was used to assess the intensity of both lower back and leg pain. Oswestry disability index (ODI) was used to assess physical function. CI = confidence interval.
*Outcome variables measured after decompression and adhesiolysis with an inflatable balloon catheter in comparison with baseline values.
†A linear mixed model was used in the statistical analysis. Omnibus P of back pain, leg pain, and ODI were < 0.0001.

the combined balloon decompression in addition to conventional adhesiolysis may increase the marginal space of the stenotic area. The combined mechanical balloon decompression and adhesiolysis of the stenotic lesions can lead to reduced venous congestion or stasis, which has been suggested to be the essential factor that precipitates circulatory disturbance and induces neurogenic claudication [8,29]. Functional improvements over time after this combined treatment might contribute to maintenance of the reduced state of pain intensity. A previous randomized controlled study found that transforaminal balloon procedures showed better improvement in claudication distance, as well as ODI, compared with a sham procedure [14]. The ZiNeu catheter described herein can also be manipulated both vertically and side-to-side by physicians. This maneuverability allows physicians to more effectively perform mechanical adhesiolysis and to more easily place the catheter at the target lesion, including at the lateral recess, intervertebral foramen, and possibly the extraforaminal space. Third, more efficient delivery of epidural injections to target region(s) can be achieved by additional balloon dilatation during epidural adhesiolysis. Surprisingly, the thin epidural

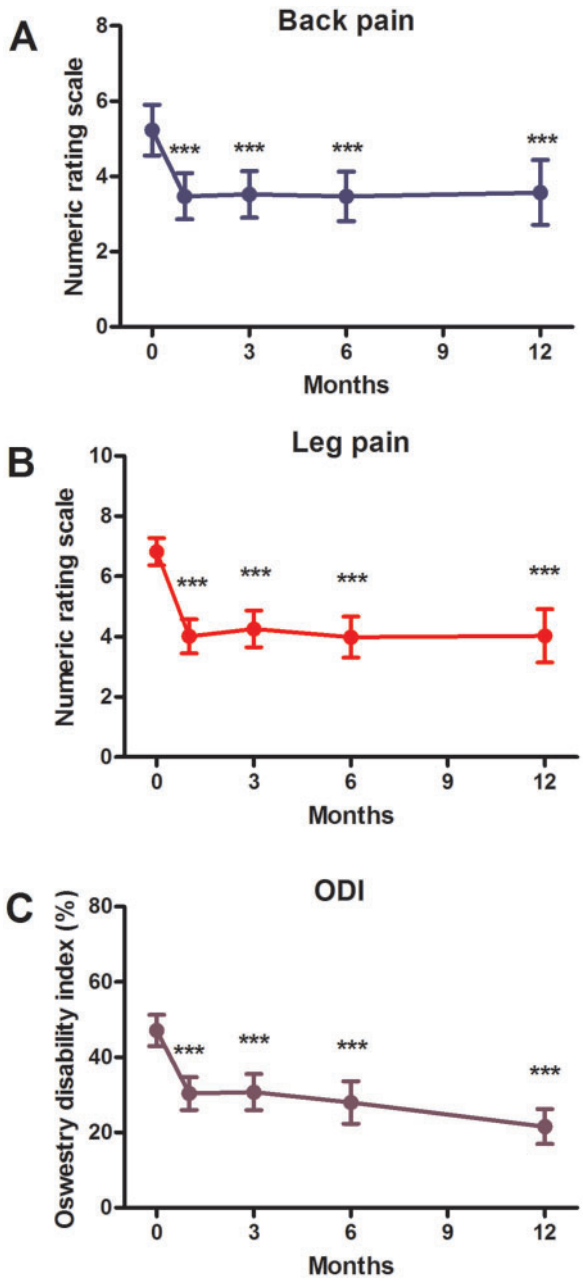

Figure 3 Numerical rating scale (NRS) of back (A) and leg (B) pain, and Oswestry disability index (ODI; C) at baseline (0), 1, 3, 6, and 12 months after the combined epidural decompression and adhesiolysis with a balloon-inflatable catheter. *** $P < 0.001$ vs. baseline. The data are presented as estimated mean ± 95% confidence interval.

catheter can be kept at the target site to enable drug injections over several days. Therefore, further improvements in the effects of the drug at the target lesion site might be possible and could more effectively remove or relieve severe degrees of adhesion [7,16,30].

Table 5 Changes in the global perceived effect of satisfaction in patients who were treated using the combined decompression and adhesiolysis with an inflatable balloon catheter

Time (Month)	GPES (95% CI)*
1	5.10 (4.68–5.52)
3	4.94 (4.49–5.38)
6	5.17 (4.69–5.64)
12	5.18 (4.67–5.68)

GPES was measured after decompression and adhesiolysis with an inflatable balloon catheter.
*Mean values were calculated using a linear mixed model. GPES = global perceived effect of satisfaction; CI = confidence interval.

Additionally, an epiduroscope could be applied to this catheter using two side ports, although this was not used in the present study. Lastly, to further demonstrate changes in the intervertebral foramen after balloon treatment, three-dimensional reconstructed images of the epidural space, identified by retained contrast medium within the tissue, were obtained using volume rendering (Figure 4). After the complete foraminal balloon treatment session, the epidural space that was filled with contrast medium had visually increased. This finding suggested the therapeutic mechanism of the balloon procedure, and provided evidence of successful epidural decompression. Indeed, similar findings were observed in a previous report that the transforaminal balloon treatment increased the epidural space in the region of the intervertebral foramen by 28.0%, and the average of the lumbar foraminal canal volume by ~98% [14]. Taken together, it can be postulated that the combined balloon decompression in addition to conventional epidural adhesiolysis can induce expansion of the marginal space around the nerve and may resolve venous congestion, to improve claudication and functional capacity, yielding long-term pain relief to patients with chronic refractory lumbar spinal stenosis. However, we cannot rule out the possibility of other components (e.g., saline flushing, or administration of drugs) of this combined treatment providing therapeutic effect due to the observational nature of our study.

Previously, the prognostic factors associated with the effectiveness of percutaneous epidural adhesiolysis were spondylolisthesis, prior lumbar spinal surgery, and foraminal stenosis [27,31]. Multivariate logistic regression analysis in the present study showed that an independent factor that was significantly associated with successful response over 12 months in patients with chronic lumbar spinal stenosis was diabetes. It is known that the prevalence of spinal stenosis is higher in patients with diabetic neuropathy than in the general population (between 1.7% and 8%) [32]. Moreover, the

Table 6 Characteristics of the non-responders and the successful responders at 12 months after the combined decompression and adhesiolysis with an inflatable balloon catheter

	Non-responder (n = 39)	Successful responder (n = 22)	*P* value
Age (years)	70.0 (64.0–74.0)	65.0 (57.8–73.0)	0.062
Gender (male/female)	17 (43.6%)/ 22 (56.4%)	12 (54.5%)/ 10 (45.5%)	0.289
BMI (kg/m^2)	24.8 ± 3.8	24.2 ± 3.5	0.552
Diabetes (no/yes)	24 (61.5%)/ 15 (38.5%)	21 (95.5%)/ 1 (4.5%)	0.005
Duration of pain (months)	36.0 (13.0–56.0)	17.0 (7.8–36.0)	0.119
Previous epidural injections (no)	5.0 (3.0–9.0)	4.0 (2.0–6.5)	0.085
Previous adhesiolysis (no/yes)	28 (71.8%)/ 11 (28.2%)	17 (77.3%)/ 5 (22.7%)	0.766
MQS	4.0 (0.0–7.4)	5.9 (0.0–7.5)	0.622
Opioid use (no/yes)	34 (87.2%)/ 5 (12.8%)	21 (95.5%)/ 1 (4.5%)	0.287
Spondylolisthesis (no/yes)	21 (53.8%)/ 18 (46.2%)	17 (77.3%)/ 5 (22.7%)	0.060
Stenosis grades			
Central (mild/moderate/severe)	0 (0%)/ 2 (5.1%)/ 6 (15.4%)	0 (0%)/ 2 (9.1%)/ 4 (18.2%)	0.628
Foraminal (mild/moderate/severe)	9 (27.3%)/ 13 (39.4%)/ 11 (33.3%)	10 (45.5%)/ 7 (31.8%)/ 3 (13.6%)	0.262
Target level (1/2 or more)	16 (41.0%)/ 23 (59.0%)	6 (27.3%)/ 16 (72.7%)	0.214
Pain intensity (NRS)			
Leg pain	7.0 (6.0–8.0)	6.5 (6.0–8.0)	0.769
Back pain	6.0 (4.0–8.0)	4.5 (2.0–6.0)	0.023
ODI (%)	45.5 ± 16.8	49.9 ± 14.7	0.306
BDI	15.2 ± 13.8	7.7 ± 9.4	0.257

Data are expressed as numbers (%), means ± standard deviation, or medians (interquartile range).
BMI = body mass index; MQS = medication quantification scale; NRS = numerical rating scale; ODI = Oswestry disability index; BDI = Beck depression inventory.

Table 7 Logistic regression analysis of factors that are associated with successful respondse at 12 months after the combined decompression and adhesiolysis with an inflatable balloon catheter

	Univariate analysis				Multivariate analysis			
Variables	Coefficient	OR	95% CI	*P* value	Coefficient	OR	95% CI	*P* value
Age (years)	−0.054	0.948	0.895–1.004	0.068				
Diabetes								
No (ref.)		1.000						
Yes	−2.575	0.076	0.009–0.627	0.017	−2.529	0.080	0.009–0.676	0.020
Number of previous epidural injections	−0.142	0.868	0.736–1.023	0.092				
Spondylolisthesis								
No (ref.)		1.000						
Yes	−1.070	0.343	0.106–1.116	0.075				
NRS of back	−0.236	0.790	0.639–0.976	0.029	−0.225	0.799	0.637–1.001	0.051

NRS = numerical rating scale; OR = odds ratio; CI = confidence interval.

prevalence of spinal stenosis is much higher in diabetic patients with moderate to severe pain than in diabetic patients with little or no pain [33]. Therefore, the diabetic patients in this study might have had neuropathic components, although this was not examined. Additionally, co-existing lower back pain might be also independently associated with successful response after 12 months of the combined treatment. It showed a marginal significance ($P = 0.051$) probably due to the small sample size of the present study.

This study has several potential limitations. First, the definition of successful response can be criticized, as different results might have been obtained if the definition had

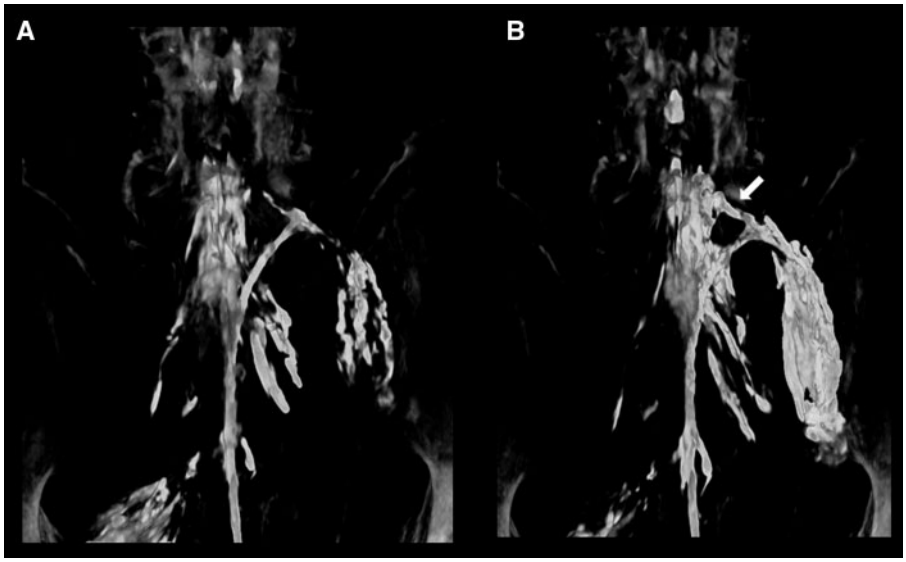

Figure 4 Three-dimensional reconstructed images of the epidural space, identified by retained contrast medium within the tissue, were obtained using the volume-rendering technique. Rotational angiography was used to visualize the target before (A) and after (B) balloon inflation, and images then transferred to the syngo InSpace 3D high-contrast imaging Workplace (Siemens AG) for post-processing. As shown for this representative patient, the diameter of the epidural space had increased in the region of the intervertebral foramen (arrow).

been changed. Therefore, the definition of successful response was established according to previous studies and recommendations [20,24,34]. We carefully selected response criteria to reflect treatment success as either substantial or clinically meaningful pain relief (minimal important changes) combined with patient-reported outcomes, including ODI, treatment satisfaction, and use of analgesic medications [19,35]. Second, follow-up loss or withdrawal from the study was considered as treatment failure and ~50% of the study sample had dropped out of the study by the 12 month follow-up visit. Therefore, we used the LMEM for analysis. Compared with analysis of variance, LMEM is known to be more flexible for accommodating longitudinal data features, and can more efficiently achieve greater power in datasets with missing data [36,37]. Third, stenotic lesions (i.e., foraminal or central stenosis) were not discriminated because of the small study sample, relatively preliminary nature of the study design, and the absence of a control group. Randomized controlled trials with larger sample sizes to assess the effects of this treatment modality will be needed in which careful and proper selection criteria are applied. Finally, the present combined intervention was complex treatment consisted of several components, such as ballooning, administrations of various drugs, and flushing with saline. Therefore, we did not rule out the possibility of other components of this combined treatment providing essential therapeutic effect.

Conclusions

In conclusion, the combined treatment with balloon decompression and conventional epidural adhesiolysis with a ZiNeu catheter can lead to significant pain relief and functional improvement up to at least 12 months in patients with chronic refractory spinal stenosis, and could be a useful alternative to overcoming the limitations of a pre-existing adhesiolysis procedure. Diabetes and co-existing lower back pain might be independently associated with a successful response 12 months after this procedure.

References

1 Kim HJ, Lee HM, Kim HS, et al. Life expectancy after lumbar spine surgery: One- to eleven-year follow-up of 1015 patients. Spine 2008;33:2116–21.

2 Benoist M. The natural history of lumbar degenerative spinal stenosis. Joint Bone Spine 2002; 69:450–7.

3 Katz JN, Harris MB. Clinical practice. Lumbar spinal stenosis. N Engl J Med 2008;358:818–25.

4 Tran DQ, Duong S, Finlayson RJ. Lumbar spinal stenosis: A brief review of the nonsurgical management. Can J Anaesth 2010;57:694–703.

5 Manchikanti L, Abdi S, Atluri S, et al. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: Guidance and recommendations. Pain Physician 2013;16:S49–283.

6 Jamison DE, Hsu E, Cohen SP. Epidural adhesiolysis: An evidence-based review. J Neurosurg Sci 2014;58:65–76.

7 Lee F, Jamison DE, Hurley RW, Cohen SP. Epidural lysis of adhesions. Korean J Pain 2014; 27:3–15.

8 Berthelot JM, Le Goff B, Maugars Y. The role for radicular veins in nerve root pain is underestimated: limitations of imaging studies. Joint Bone Spine 2011;78:115–7.

9 Cooper RG, Freemont AJ, Hoyland JA, et al. Herniated intervertebral disc-associated periradicular fibrosis and vascular abnormalities occur without inflammatory cell infiltration. Spine 1995;20:591–8.

10 Kobayashi S, Baba H, Uchida K, et al. Effect of mechanical compression on the lumbar nerve root: Localization and changes of intraradicular inflammatory cytokines, nitric oxide, and cyclooxygenase. Spine 2005;30:1699–705.

11 Manchikanti L, Bakhit CE. Percutaneous lysis of epidural adhesions. Pain Physician 2000;3:46–64.

12 Lee JH, Lee SH. Clinical effectiveness of percutaneous adhesiolysis versus transforaminal epidural steroid injection in patients with postlumbar surgery syndrome. Reg Anesth Pain Med 2014;39:214–8.

13 Birkenmaier C, Baumert S, Schroeder C, Jansson V, Wegener B. A biomechanical evaluation of the epidural neurolysis procedure. Pain Physician 2012; 15:E89–97.

14 Kim SH, Choi WJ, Suh JH, et al. Effects of transforaminal balloon treatment in patients with lumbar foraminal stenosis: A randomized, controlled, double-blind trial. Pain Physician 2013;16:213–24.

15 Shin JW. A new approach to neuroplasty. Korean J Pain 2013;26:323–6.

16 Choi SS, Joo EY, Hwang BS, et al. A novel balloon-inflatable catheter for percutaneous epidural adhesiolysis and decompression. Korean J Pain 2014; 27:178–85.

17 Schizas C, Theumann N, Burn A, et al. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. Spine 2010;35:1919–24.

18 Lee S, Lee JW, Yeom JS, et al. A practical MRI grading system for lumbar foraminal stenosis. AJR Am J Roentgenol 2010;194:1095–8.

19 Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain 2001;94:149–58.

20 Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005;113:9–19.

21 Kim DY, Lee SH, Lee HY, et al. Validation of the Korean version of the oswestry disability index. Spine 2005;30:E123–7.

22 Gallizzi M, Gagnon C, Harden RN, Stanos S, Khan A. Medication Quantification Scale Version III: internal validation of detriment weights using a chronic pain population. Pain Pract 2008;8:1–4.

23 Van Zundert J, Patijn J, Kessels A, et al. Pulsed radiofrequency adjacent to the cervical dorsal root ganglion in chronic cervical radicular pain: A double blind sham controlled randomized clinical trial. Pain 2007;127:173–82.

24 Geurts JW, van Wijk RM, Wynne HJ, et al. Radiofrequency lesioning of dorsal root ganglia for chronic lumbosacral radicular pain: A randomised, double-blind, controlled trial. Lancet 2003;361:21–6.

25 Koh W, Choi SS, Karm MH, et al. Treatment of chronic lumbosacral radicular pain using adjuvant pulsed radiofrequency: A randomized controlled study. Pain Med 2015;16:432–41.

26 Lee JH, Lee SH. Clinical effectiveness of percutaneous adhesiolysis using Navicath for the management of chronic pain due to lumbosacral disc herniation. Pain Physician 2012;15:213–21.

27 Lee JH, Lee SH. Clinical effectiveness of percutaneous adhesiolysis and predictive factors of treatment efficacy in patients with lumbosacral spinal stenosis. Pain Med 2013;14:1497–504.

28 Helm S, Hayek SM, Colson J, et al. Spinal endoscopic adhesiolysis in post lumbar surgery syndrome: An update of assessment of the evidence. Pain Physician 2013;16:SE125–50.

29 Kobayashi S, Takeno K, Miyazaki T, et al. Effects of arterial ischemia and venous congestion on the lumbar nerve root in dogs. J Orthop Res 2008; 26:1533–40.

30 Manchikanti L, Cash KA, McManus CD, Pampati V. Assessment of effectiveness of percutaneous adhesiolysis in managing chronic low back pain secondary to lumbar central spinal canal stenosis. Int J Med Sci 2013;10:50–9.

31 Choi E, Nahm FS, Lee PB. Evaluation of prognostic predictors of percutaneous adhesiolysis using a Racz catheter for post lumbar surgery syndrome or spinal stenosis. Pain Physician 2013;16:E531–6.

32 Hilibrand AS, Rand N. Degenerative lumbar stenosis: Diagnosis and management. J Am Acad Orthop Surg 1999;7:239–49.

33 Goldman SM. Diabetic peripheral neuropathy and spinal stenosis: Prevalence of overlap and misdiagnosis. An introductory report. Diabet Med 2004; 21:394–6.

34 Koh W, Choi S, Karm MH, et al. Treatment of chronic lumbosacral radicular pain using adjuvant pulsed radiofrequency: A randomized controlled study. Pain Med 2015;16:432–41.

35 Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: Towards international consensus regarding minimal important change. Spine (Phila Pa 1976) 2008;33:90–4.

36 Ma Y, Mazumdar M, Memtsoudis SG. Beyond repeated-measures analysis of variance: Advanced statistical methods for the analysis of longitudinal data in anesthesia research. Reg Anesth Pain Med 2012;37:99–105.

37 Fielding S, Fayers P, Ramsay CR. Analysing randomised controlled trials with missing data: Choice of approach affects conclusions. Contemp Clin Trials 2012;33:461–9.