Retrospective Study

Predictors of a Favorable Response to Transforaminal Epidural Steroid Injections for Lumbar Radiculopathy in the Elderly

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Background: The efficacy and its associated predictors of transforaminal epidural steroid injection (TFESI) in elderly patients with lumbar radiculopathy are unknown.

Objective: The purpose of this retrospective study was to identify the efficacy of TFESI in elderly patients with lumbar radiculopathy and its associated predictors of long-term outcomes.

Study Design: Retrospective study.

Setting: Interventional pain clinics in West China Hospital of Sichuan University.

Methods: In total, 294 elderly patients who were diagnosed with lumbar radiculopathy and underwent transforaminal epidural steroid injections from January 2019 through January 2022 were retrospectively analyzed. Demographic, clinical, magnetic resonance imaging, and TFESI-related information was collected to assess the predictive factors of long-term outcomes of the TFESI. Pain scores were assessed using the Numeric Rating Scale. Treatment success was defined as a ≥ 50% reduction in pain scores at 6 months.

Results: Multivariate logistic regression analysis revealed that the duration of symptoms, immediate postoperative response, and neutrophilic granulocyte percentage were independently associated with a favorable response to TFESI. In addition, the level of pain at the initial visit and the number of TFESI performed were also associated with a good response in the multivariate regression analysis, even though the association was not statistically significant.

Limitations: Approximately 6% of the patients were lost to follow-up; therefore, selection bias may have slightly influenced our findings. In addition, our patients were not compared with a control population, and consequently, a placebo effect could not be assessed.

Conclusion: This study revealed that a short duration of symptoms, good immediate postoperative response and high neutrophilic granulocyte percentage were long-term predictors of a good response to TFESI in elderly patients with lumbar radiculopathy.

Key words: Elderly, radiculopathy, epidural injection, predictors, neutrophil

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Low back pain and radiating pain are common and costly problems. The lifetime prevalence has been estimated to be approximately 40% to 60% (1) and increases with age, peaking at the ages of 80 to 89 years (2). Pain can have major adverse effects on mood, activities, social function, and

overall quality of life in older adults, even leading to depression (3).

Lumbar radiculopathy is a syndrome commonly caused by disc herniation or foraminal stenosis. According to previous reports (4), elderly patients with pain for more than 24 months who undergo lumbar disc herniation surgery have a dissatisfaction rate as high as 20%. Increased sensitivity to adverse drug reactions (5) and increased surgical complications (6) pose numerous risks for elderly patients compared to younger patients, especially older patients with comorbidities.

Increasing evidence has indicated the efficacy of transforaminal epidural steroid injections (TFESI) in the treatment of lumbar radicular pain (7). Several studies have been carried out to investigate the predictive factors that can affect TFESI outcomes (8-22). The factors associated with outcomes might differ in different age categories. Previous studies have shown that the duration of preoperative leg pain is associated with outcomes in adults (23) but not adolescents (24). However, most clinical trials of predictors of TFESI have not focused on the special population of elderly patients.

Considering the global aging of the population (25), the high prevalence of pain in older adults (26), and the high use of TFESI, we must try to identify those older patients who will actually benefit from TFESI since the procedure has risks (27).

To the best of our knowledge, studies investigating factors that may influence treatment outcomes in elderly patients are absent from the literature. The purpose of this study was to determine whether certain factors in older patients could predict the effect of injections for lumbar radiculopathy.

Methods

Patients

Under the approval of the ethics committee of West China Hospital of Sichuan University, the clinical data of patients receiving TFESI were reviewed in our hospital from January 2019 through January 2022. The inclusion criteria were as follows: 1) age ≥ 65 years; 2) history, physical examination, and pain pattern consistent with lumbar radiculopathy; 3) clear identification of the affected nerve root by imaging studies of the lumbar spine; and 4) TFESI treatment.

The exclusion criteria were as follows: 1) inadequate history, physical examination, or imaging data; 2) local or systemic infections; 3) a spinal injection of any type within the last 12 months; 4) abnormal blood test results; 5) previous neurological disease, cancer, or autoimmune disease; and 6) any known allergy to treatment agents. Because the patients had signed informed consent prior to the procedure, the ethics committee waived the requirement for patient informed consent because patient recontact was not established for this study.

Overall, 312 patients who met the abovementioned criteria were recruited for this study. In the 6-month follow-up period, 5 patients died and 13 patients could not be reached because of a change in phone number. Consequently, 294 of the 312 patients were included in the 6-month follow-up (Fig. 1). We used the Numeric Rating Scale (NRS-11) ranging from 0 to 10 to assess the severity of pain (≥ 1 and < 4 denoting mild pain; ≥ 4 and < 7 denoting moderate pain; and ≥ 7 and ≤ 10 denoting severe pain). The severity of pain and the pain score were evaluated before and at 24 hours and 6 months after the injection. Favorable responses were defined as a ≥ 50% decrease in pain scores at 6 months; the others were defined as poor responders (28,29).

Review of Clinical Data and Outcomes

Retrospective reviews of patient charts were performed by 2 physicians who were not involved in image analysis. Data included the following: demographic variables, such as age, gender, and body mass index (BMI); and clinical characteristics, such as current symptoms and past medical history. The duration of symptoms was classified as < 6 months, ≥ 6 months and < one year, and ≥ one year. Test measures, such as the percentage of neutrophils, were also included in the analysis. Magnetic resonance imaging (MRI) data were reviewed by a specialist radiologist at our hospital. Additional data reviewed were the presence of nerve root compression, the diagnosis (stenosis versus disc herniation versus lumbar spondylolisthesis) and TFESI-related information, such as the number of TFESI performed and immediate postoperative effect (a good response was defined as a ≥ 50% decrease in pain scores at 24 hours postinjection).

TFESI

All TFESIs were performed under computed tomography (CT) fluoroscopic guidance (Wittelsbacherplatz 2, DE-80333, Siemens AG) at the level that best matched the patient's clinical presentation. The patients were placed prone on a radiologic table and vital signs (blood pressure, pulse oximetry, electrocardiogram) were monitored. CT fluoroscopy was used to guide needle placement precisely and rapidly, finding visualization of the optimal needle path. A small area

beginning at the undersurface of the posterior lumbar spinous process was scanned to find a suitable approach for the needle, and the area was sterilized and anesthetized. A 22G disposable nerve block needle (Henan Tuoren Medical Equipment Co., Ltd.) was then partially inserted into the patient, and a CT fluoroscopic image was obtained to measure the depth and angle.

The needle was then advanced to the lateral side of the ligamentum flavum under the guidance of intermittent CT fluoroscopy. The needle was slowly advanced into the epidural space using the loss of resistance technique, followed by injecting a small amount of dilute contrast medium. Once the contrast medium was sufficiently spread into the epidural space and externally along the spinal nerve root, an injectate of a mixture of 3.5 mg of betamethasone, 1.5 mL of lidocaine 2% and 3 mL of physiological saline was slowly injected at each level. The patients were monitored in the recovery room for any signs of complications for 30 minutes postinjection (Fig. 2).

Statistical Analysis

Data analysis was performed with IBM SPSS Statistics 25.0 (IBM Corporation). The mean, standard deviation, median, interquartile range and percentages were used to describe the data. Differences between favorable and poor response groups were tested using independent samples t tests, χ^2 tests, or rank-sum tests. The relationship between demographics, clinical characteristics, MRI, operation-related information and favorable response was first validated by univariate logistic regression analysis. According to the number of independent variables and the number of patients with a favorable response, we included those with values of $P \leq 0.2$ in the univariate analysis in the multivariate logistic regression analysis. Odds ratios and 95% CIs were calculated to evaluate the effect of factors on a favorable response. The statistical significance was set at a level of $P < 0.05$.

Results

A total of 294 elderly patients out of 312 completed the 6 months of follow-up. Of these, 103 were men, and 191 were women, with a mean age of 73.78 ± 7.11 years. The mean duration of symptoms before injection was 2.0 (interquartile range 9.5) years. The mean preinjection pain score was 6.35 ± 1.41; 2.41 ± 1.34 at 24 hours postinjection; and 2.96 ± 2.02 at 6 months postinjection. The radiculopathy level was L2 in 4 patients, L3 in 17 patients, L4 in 53 patients, L5 in 271 patients, and S1 in 209 patients (Table 1).

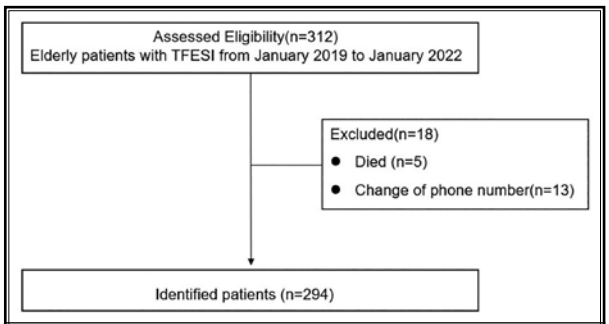

Fig. 1. *Flow diagram of patients included in this study.* TFESI, transforaminal epidural steroid injection.

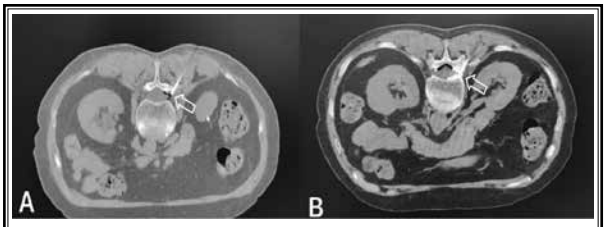

Fig. 2. *TFESI technique as demonstrated in a 73-year-old woman with low back pain. A) Computed tomography fluoroscopy image demonstrates the needle advanced into the epidural space. The white arrow shows the needle path. B) One mL of contrast medium was injected into the epidural space. The white arrow shows the contrast medium.*

Table 1. *Demographic and procedural characteristics.*

Variable	Value (n = 294)
Age, mean ± SD (years)	73.78 ± 7.11
Gender	
Men	103 (35.0%)
Women	191(64.9%)
BMI, mean ± SD (kg/m²)	24.17 ± 3.40
Duration of symptoms, median (inter-quartile range) (years)	2.0 (9.5)
Radiculopathy level	
L2	4 (1.4%)
L3	17 (5.8%)
L4	53 (18.0%)
L5	271 (92.2%)
S1	209 (71.1%)
Numeric Rating Scale, mean ± SD	
Preinjection	6.35 ± 1.41
Postinjection 24 h	2.41 ± 1.34
Postinjection 6 mo	2.96 ± 2.02

Note: Values expressed as mean ± SD, median (inter-quartile range), number and frequency, or as otherwise indicated.

The number of patients presenting with a favorable response 6 months post-TFESI was 152 (51.7%), and the number of poor responders was 142 (48.2%). There was a statistically significant difference in the duration of symptoms, the number of TFESI performed, and the immediate postoperative response between elderly patients with and without treatment success. Significant differences were not observed between the 2 groups in terms of their age, gender, BMI, comorbidities, or MRI indicators (Table 2).

Table 2. *The general data of patients in the good response group and the poor response group.*

Variables	Values		
	Good Responders (n = 152)	Poor Responders (n = 142)	*P* Value
Demographic			
Age (years)	73.91 ± 6.90	73.65 ± 7.35	0.755
Gender			
Men	52 (34.2%)	51 (35.9%)	0.759
Women	100 (65.8%)	91 (64.1%)	
BMI (kg/m²)			
<18.5 (Underweight)	6 (4.0%)	8 (5.6%)	
18.5-23.9 (Normal weight)	61 (40.1%)	72 (50.7%)	0.215
24.0-27.9 (Overweight)	61 (40.1%)	45 (31.7%)	
≥ 28.0 (Obesity)	24 (15.8%)	17 (12.0%)	
Clinical			
Hypertension			
Yes	88 (57.9%)	83 (58.5%)	0.923
No	64 (42.1%)	59 (41.5%)	
Diabetes			
Yes	31 (20.4%)	28 (19.7%)	0.885
No	121 (79.6%)	114 (80.3%)	
Coronary artery disease			
Yes	16 (10.5%)	15 (10.6%)	0.992
No	136 (89.5%)	127 (89.4%)	
Osteoporosis			
Yes	88 (57.9%)	70 (49.3%)	0.139
No	64 (42.1%)	72 (50.7%)	
Duration of symptoms			
< 6months	47 (30.9%)	19 (13.4%)	
≥ 6months and < 1year	10 (6.6%)	12 (8.5%)	0.002*
≥ 1 year	95 (62.5%)	111 (78.2%)	
Previous spine surgery			
Yes	14 (9.2%)	20 (14.1%)	0.192
No	138 (90.8%)	122 (85.9%)	
Lumbar trauma or sprain			
Yes	16 (10.5%)	17 (12.0%)	0.695
No	136 (89.5)	125 (88.0%)	
Neurogenic claudication			
Yes	59 (38.8%)	55 (38.7%)	0.988
No	93 (61.2%)	87 (61.3%)	
SLRE			
Yes	62 (40.8%)	68 (47.9%)	0.221
No	90 (59.2%)	74 (52.1%)	
The level of pain at the initial visit			
Mild	2 (1.3%)	1 (0.7%)	0.142
Moderate	90 (59.2%)	93 (69.5%)	
Severe	60 (39.5%)	48 (33.8%)	
Neutrophilic granulocyte percentage	59.09 ± 9.07	56.80 ± 9.88	0.147
Magnetic Resonance Imaging			
Root compression or contact			
Yes	19 (12.5%)	20 (14.1%)	0.689
No	133 (87.5%)	122 (85.9%)	
Disc herniation			
Yes	137 (90.1%)	120 (84.5%)	0.146
No	15 (9.9%)	22 (15.5%)	
Stenosis			
Yes	41 (27.0%)	45 (31.7%)	0.374
No	111 (73.0%)	97 (68.3%)	
Spondylolisthesis			
Yes	34 (22.4%)	42 (29.6%)	0.158
No	118 (77.6%)	100 (70.4%)	
TFESI			
The number of TFESI performed			
1	49 (32.2%)	63 (44.4%)	0.032*
>1	103 (67.8%)	79 (55.6%)	
Immediate postoperative response			
Good response	124 (81.6%)	70 (49.3%)	<0.001*
Poor response	28 (18.4%)	72 (50.7%)	

Note: $P < 0.05$ indicated a statistically significant difference. TFESI, transforaminal epidural steroid injection; BMI, body mass index; SLRE, straight leg raise test.

In the univariate regression analysis, the duration of symptoms, the number of TFESI performed, and immediate postoperative response were associated with a good response. The multivariate logistic regression analysis revealed that the duration of symptoms, immediate postoperative response, and neutrophilic granulocyte percentage were independently associated with a favorable response to TFESI. Among them, immediate postoperative response had a significant effect on the success of treatment ($P < 0.001$). In addition, the level of pain at the initial visit and the number of TFESI performed were also associated with a good response in the multivariate regression analysis, even though the association was not statistically significant (Table 3).

Table 3. *Univariate and multivariate logistic regression analysis of variables.*

	Univariate			Multivariate		
	Odds Ratio	**95% CI**	***P* Value**	**Odds Ratio**	**95% CI**	***P* Value**
Demographic						
Age	1.004	0.973-1.036	0.799			
Gender						
Men	1					
Women	0.928	0.574-1.499	0.759			
BMI (kg/m²)						
18.5– 23.9 (Normal weight)	1			1		
< 18.5 (Underweight)	0.885	0.291-2.692	0.830	0.485	0.129-1.826	0.284
24.0– 27.9 (Overweight)	1.600	0.957-2.676	0.073	1.640	0.909-2.962	0.101
≥ 28.0 (Obesity)	1.666	0.820-3.385	0.158	1.316	0.591-2.928	0.501
Clinical						
Hypertension						
Yes	1					
No	0.977	0.615-1.554	0.923			
Diabetes						
Yes	1					
No	1.043	0.589-1.847	0.885			
Coronary artery disease						
Yes	1					
No	0.996	0.473-2.098	0.992			
Osteoporosis						
Yes	1			1		
No	1.414	0.893-2.241	0.140	1.547	0.911-2.625	0.106
Duration of symptoms						
< 6months	1					
≥ 6months and < 1year	0.337	0.125-0.910	0.032	0.371	0.120-1.146	0.085
≥ one year	0.346	0.190-0.630	0.001	0.303	0.154-0.597	0.001*
Previous spine surgery						
Yes	1			1		
No	0.619	0.300-1.278	0.195	0.872	0.378-2.012	0.748
Lumbar trauma or sprain						
Yes	1					
No	0.865	0.419-1.785	0.695			
Neurogenic claudication						
Yes	1					
No	1.004	0.628-1.605	0.988			

Table 3 cont. *Univariate and multivariate logistic regression analysis of variables.*

	Univariate			Multivariate		
	Odds Ratio	**95% CI**	***P* Value**	**Odds Ratio**	**95% CI**	***P* Value**
SLRE						
Yes	1					
No	0.750	0.473-1.189	0.221			
The level of pain at the initial visit						
Mild	1			1		
Moderate	0.161	0.019-1.366	0.094	0.113	0.011-1.116	0.067
Severe	0.194	0.023-1.672	0.136	0.117	0.011-1.238	0.075
Neutrophilic granulocyte percentage	1.015	0.990-1.040	0.188	1.030	1.001-1.059	0.042*
Magnetic Resonance Imaging						
Root compression or contact						
Yes	1					
No	0.871	0.444-1.710	0.689			
Disc herniation						
Yes	1			1		
No	1.674	0.831-3.375	0.149	1.046	0.445-2.457	0.918
Stenosis						
Yes	1					
No	0.796	0.481-1.317	0.375			
Spondylolisthesis						
Yes	1			1		
No	0.686	0.406-1.159	0.159	0.756	0.399-1.429	0.389
TFESI						
The number of TFESI performed						
1	1			1		
> 1	1.676	1.043-2.695	0.033	1.599	0.929-2.751	0.090
Immediate postoperative response						
Good response	1			1		
Poor response	4.555	2.693-7.706	< 0.001	5.334	2.942-9.669	< 0.001*

Note: $P < 0.05$ indicated a statistically significant difference. TFESI, transforaminal epidural steroid injection; BMI, body mass index; SLRE, straight leg raise test.

Discussion

The main strength of our study is the inclusion of a special group of elderly patients with lumbar radiculopathy and the analysis of several clinical and radiological parameters. We found that a short duration of symptoms, good immediate postoperative response, and high neutrophilic granulocyte percentage were predictors of a favorable 6-month response to TFESI.

With economic development and the extension of the human lifespan, the aging of the population is accelerating worldwide (25), and the incidence of pain is increasing year by year (2).

Pain in the elderly is usually multifactorial and multifocal, with the common influence of multiple pathologies, thus limiting its treatment options (30). Pain relief is more difficult in older patients than in younger patients (31). Elderly patients tend to have a low basal metabolic rate and decreased liver and kidney function. Compared with young patients, elderly patients cannot tolerate drugs well and are more likely to have analgesic-related adverse reactions. Therefore, elderly patients tend to have poor compliance with analgesic drugs, resulting in poor analgesic effects (32). Furthermore, aging is also associated with an increased risk of a person having more than one disorder at the same

time (multimorbidity) (25), which also increases the complications of lumbar surgery in older patients (33). Therefore, TFESI has been recommended as a viable alternative to surgical intervention and is increasingly used in elderly patients who cannot benefit from conservative or surgical treatment (7).

In summary, it is of utmost importance for clinicians to identify which elderly patients will truly benefit from TFESI. To our knowledge, this is the first paper to investigate the efficacy of TFESI in elderly patients. The treatment success rate of TFESI has been reported to be between 35–75%, with the highest rates for patients with acute symptoms (34); however, there has been a lack of consistent findings on the long-term effectiveness of lumbar TFESI in patients with radicular low back pain (35). In our study, we measured long-term outcomes 6 months post-TFESI (36) in elderly patients, and 152 (51.7%) achieved treatment success.

In this study, a symptom duration ≥ one year was associated with a decreased odds of improvement with a TFESI. The results indicated a better response to TFESI for those with acute rather than chronic radicular pain, which is consistent with the results of numerous previous studies (8-10,14,16,35,37). A possible explanation is that chronic neural compression and inflammation become refractory to TFESI after a period of time (9), causing a failure to respond to steroid treatment. In our study, 70.0% of elderly patients had symptoms lasting longer than one year, indicating a possible poor reaction. It is crucial to identify these patients and implement treatment earlier in the course of their illness.

An immediate postoperative good response was the strongest factor associated with a decrease in pain scores at 6 months, indicating that decreased pain scores at 24 hours may increase the chance of treatment success. Şencan et al (14) reported that a decreased pain score at one hour is a predictor of a favorable 3-month response to a TFESI. A previous study also revealed that patients reporting < 50% of their baseline Visual Analog Score for leg pain at the end of the first week (day 6) post-TFESI were almost 7 times more likely to be responders at one month (38). There is ongoing debate about how long after surgery a decline in pain scores best predicts a good long-term response. There also have not been reports in older patients. However, our study suggests that, for elderly patients with poor pain relief in the short period post-TFESI, alternative treatment modalities can be discussed to avoid prolonged symptom duration, since the chances of success seem to be lower after several months.

We found that an increase in the percentage of neutrophils predicted a good response, which is an interesting finding. Neutrophils are one of several inflammatory parameters that are inexpensive and readily available. It shows phagocytosis and apoptosis by secreting various inflammatory mediators (39). A previous study (40) have shown that transient neutrophil-driven upregulation of inflammatory responses is protective against the transition to chronic pain and may lead to a favorable response at the 6-month follow-up after TFESI. In addition, Bozkurt et al (41) reported that patients with a high neutrophil/lymphocyte ratio have higher pain scores before and after lumbar surgery. Greater baseline pain on the Visual Analog Scale score predicted a greater likelihood of pain reduction during the follow-up period after TFESI (9,15,17), which is consistent with our finding, even though the association was not statistically significant in our study. To the best of our knowledge, few studies have investigated the relationship between peripheral inflammatory markers and the efficacy of TFESI. Future studies are needed to further confirm and clarify the present results.

Multiple TFESIs could be associated with a favorable response at the 6-month follow-up, even though the association was only present in the univariate analysis. Data in the literature concerning whether multiple TFESIs increase treatment efficacy have been inconsistent; however, in daily practice, it is generally accepted that if the first injection is not effective, a second or third injection should be given to improve the treatment effect. Consistent with most previous studies, we also found that gender, BMI, and the straight leg raise test were not predictors of treatment success in elderly patients. Similarly, no MRI-based outcome prediction was found in our research. TFESI is minimally invasive compared to surgery, and we feel that patients willing to try nonsurgical treatment should not be denied TFESI solely on the basis of MRI findings. In our study, 58.1% of the elderly patients had hypertension, 57.3% had osteoporosis, 20.0% had diabetes, and 10.5% had coronary artery disease; these comorbidities were not associated with poor responders. More prospective studies are needed to explore these questions.

As with every study, our work has some limitations. First, it was difficult to ask the patients to revisit the hospital only for the study if they had no pain or discomfort at the 6-month follow-up. Therefore, we selected telephone follow-up for these patients. In order to obtain accurate results, honest responses from

the patients were necessary. In addition, approximately 6% of the patients were lost to follow-up; therefore, selection bias may have slightly influenced our findings. Second, our patients were not compared with a control population, and consequently, a placebo effect could not be assessed. The degree of pain may vary with the natural course of the disease, and prospective randomized controlled studies are needed. Last, it is necessary to conduct a prospective study design with a larger sample size in the future to provide more reliable research evidence for the study of pain in patients of different age groups in terms of the same predictors.

Conclusion

This study reveals that a short duration of symptoms, good immediate postoperative response and high neutrophilic granulocyte percentage are predictors of a favorable 6-month response to TFESI in elderly patients with lumbar radiculopathy. Clinicians should pay more attention to pain in elderly patients, and TFESI should be administered as soon as possible in elderly patients with lumbar radiculopathy.

Ethics Approval

This study was approved by the ethics committee at West China Hospital (approval number: 343/2022)

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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