



# Treatments of Peyronie's disease with *Scutellaria baicalensis* and surgery according to the disease course: a single-center retrospective study of 261 patients

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**Background:** Oral medication therapies are more conventional than other non-surgical therapies in the acute phase of Peyronie's disease (PD). Although the commonly used oral drugs for PD have shown poor or indeterminate outcomes, most patients prefer oral medications. The aim of this study was to evaluate the efficacy and safety of *Scutellaria baicalensis* extract for treating acute-phase PD patients and examine the practicality of treatment strategies for PD according to the disease course.

**Methods:** This retrospective study was performed at our institution from 2005 to 2015 and analyzed the data of 261 patients with PD. The acute-phase PD patients received *Scutellaria baicalensis* extract for 6 months. After oral treatment, the patients with persistent curvature underwent surgical correction during the stable phase.

**Results:** During this study period, 183 patients received oral treatment with *Scutellaria baicalensis*, and 78 patients did not. Compared to the untreated patients, treatment with *Scutellaria baicalensis* had a significant effect in improving the symptoms of acute-phase PD. The mean time required for stabilization also showed a significant statistical difference. Treatment with *Scutellaria baicalensis* was safe and well-tolerated. After the disease stabilized, 70 and 31 patients with significant penile curvature underwent surgical correction by 16-dot plication and great saphenous vein grafting procedures, respectively. At the one-year follow-up, complete penile straightening and penile length shortening were observed in 92.86% and 41.43% of the patients after 16-dot plication and in 87.10% and 25.81% of the patients after grafting procedures, respectively. The postoperative Erectile Function domain of the International Index of Erectile Function scales were maintained in all patients after the 16-dot plication procedure and decreased in 54.84% of the patients after the grafting procedure. Overall, 92.86% and 83.87% of the patients who received 16-dot plication and grafting procedures, respectively, were satisfied with the final surgical results.

**Conclusions:** Treatment with extract of *Scutellaria baicalensis* seems to be beneficial for improvements in symptoms of acute phase PD and acceleration of the disease stabilization. The 16-dot plication and great saphenous vein grafting procedure seem effective options in the surgical management of the stable phase after *Scutellaria baicalensis* administration in the acute phase of PD.

**Keywords:** Grafting procedure; penile curvature; Peyronie's disease (PD); plication; *Scutellaria baicalensis*

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## Introduction

Peyronie's disease (PD) is recognized as a two-phase pathological condition of the penis, characterized by inelastic fibrous plaque formation in the tunica albuginea (1). Usually, the natural history of PD is progressive, and spontaneous regression is rare (2).

Many treatment approaches and their clinical outcomes have been described in the literature, including oral, intralesional, mechanical, topical, and surgical therapies (3,4). Several oral medications have been used for the treatment of PD based on their antioxidant and anti-fibrotic effects (3,4). However, the routine clinical use of oral agents for PD such as vitamin E, tamoxifen, or omega-3 fatty acids has shown poor or indeterminate outcomes. Therefore, these treatments are not supported by the American Urological Association guidelines or the 2010 International Consultation on Sexual Medicine (5). Even so, oral therapies are used more than other non-surgical therapies during the acute phase of PD, and most patients prefer oral medications in clinical practice. Therefore, it is necessary to explore a new oral pharmacotherapy for treating the acute phase of PD.

Previously, we found that monocyte chemoattractant protein 1 (MCP-1), a profibrotic factor, was expressed at higher levels in cells from plaques (P cells) in the tunica albuginea of PD patients (6,7). In another study, we found that wogonin, a flavonoid extracted from the root of *Scutellaria baicalensis*, significantly inhibited cell proliferation and downregulated MCP-1 expression in P cells, indicating that wogonin may be a worthy candidate for preclinical trials in men with PD (8). In clinical practice, we administered extract of *Scutellaria baicalensis* to treating acute phase of PD patients. After treatment with *Scutellaria baicalensis*, if the patients still had persistent penile curvature severely precluded intercourse, the patients underwent surgical correction during the stable phase. The aim of this study was to evaluate the therapeutic effect of different treatment strategies in PD according to the course of the disease, including evaluation of the efficacy and safety of *Scutellaria baicalensis* extract in treating acute-phase PD patients and the outcomes of surgical correction of persistent penile curvature during the stable-phase PD patients.

We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/apm-20-2389>).

## Methods

This retrospective study was approved by the institutional research ethics committee of the Ninth People's Hospital, School of Medicine, Shanghai Jiaotong University (No. SH9H-2019-T52-2). Since only a medical record review was performed, this study was exempt from informed consent. This study was conducted in accordance with the declaration of Helsinki (as revised in 2013). Following approval from the Institutional Ethics Review Board, we retrospectively reviewed the charts of patients with PD at a single center from 2005 to 2015. The inclusion criteria were (I) patients with acute-phase PD which defined as have any of the symptoms of penile plaques, erectile pain, or penile curvature in the previous 6 months; (II) acute-phase PD patients who received oral treatment with *Scutellaria baicalensis* extract and were followed until 6 months after the disease stabilized; (III) acute-phase PD patients who consented to be followed until 6 months after the disease stabilized although they refused oral treatment with *Scutellaria baicalensis*; (IV) patients who still had significant penile curvature (greater than 30 degrees) severely precluded intercourse after treatment with *Scutellaria baicalensis* were underwent surgical correction after the disease stabled for at least 6 months; (V) Among the patients who did not receive *Scutellaria baicalensis* treatment, the patients who had significant penile curvature (greater than 30 degrees) severely precluded intercourse were underwent surgical correction after the disease stabled for at least 6 months; and (VI) patients followed for at least one year after surgical correction, whether they were treated with *Scutellaria baicalensis* or not. The exclusion criteria were (I) among the patients treated with *Scutellaria baicalensis*, who received any treatment for PD before baseline assessment or received other treatments for PD concurrently during the follow-up period; (II) among the patients did not receive *Scutellaria baicalensis* treatment, who received any treatment for PD before the baseline assessment or received any treatment for PD during the follow-up period; and (III) patients who had

erectile dysfunction (ED) prior to the onset of PD.

The variables analyzed included patient demographics and disease characteristics. The duration of disease was determined by differences between the date at the examination and the date of onset of the first symptom. Penile pain during erection was assessed using a numerical rating scale (NRS). The angle and degree of penile curvature during maximum erection were documented by auto-photography using the Kelami technique (9). If a photograph could not be obtained, an artificial erection was induced by intra-cavernosal injection of papaverine (30 mg). The International Index of Erectile Function (IIEF) erectile function domain (EF) score was used to evaluate erectile function, and a score below 26 identified ED (10). Color Doppler ultrasound was used to measure the three dimensions of the plaque (length, width, and thickness) by an experienced sonographer, and the plaque volume was determined ( $\text{cm}^3$ ) using the prolate ellipsoid formula (11). The time required for stabilization was determined by the difference between the dates the patients had no painful erections and further progressive deformity or curvature for at least 3 months and the date of onset of the first symptom.

The acute-phase PD patients received *Scutellaria baicalensis* extract, which was prepared by boiling 12 g of the dried root of the plant in 600 mL water until only 300 mL of the solution remained. An oral administration of 150 mL of this solution was given each morning and evening for 6 months. To evaluate the safety of *Scutellaria baicalensis*, regular monitoring of adverse events was performed 1 and 3 months after treatment and at the end of treatment. The adverse events were classified as no or mild, moderate, or severe based on clinical scores. If the patient still had persistent significant curvature (greater than 30 degrees) after oral treatment, surgical management including the 16-dot technique and great saphenous vein grafting procedure were performed in patients who had stable disease for at least 6 months. Patients with persistent significant curvature among patients who refused *Scutellaria baicalensis* treatment also underwent the same surgical management. Before surgery, all patients underwent measurement of flaccid stretched penile length (SPL) dorsally from pubis to meatus under maximal extension of the phallus and compressing suprapubic fat pad to the pubic bone. The degree of penile curvature was also documented by using the Kelami technique (9). Although penile prosthesis (PP) implantation was recommended for those patients with ED who did not respond to phosphodiesterase type 5 inhibitors (PED5is), the patients refused PP implantation because they were

older and had a low sexual desire or because of economic reasons.

The indications for the 16-dot plication procedure in the present study were patients who had adequate erectile rigidity for intercourse with or without pharmacotherapy, an angle of penile curvature of less than  $60^\circ$  and without an indentation or hourglass deformity, a stretched length of more than 10 cm, and an anticipated loss of length less than 20% of the erect or stretched length (12). The surgical procedure was performed according to the technique described by Lue (13). The indications for the great saphenous vein grafting procedure in the present study were patients who had adequate erectile rigidity for intercourse with or without pharmacotherapy, more severe curves greater than  $60^\circ$ , a complex deformity, an indentation or hourglass deformity, a stretched length less than 10 cm, and an anticipated loss of length of more than 20% (12). The surgical procedure was performed according to the technique described by Lue (14).

After surgery, the patients were recommended to abstain from all forms of sexual intercourse for 2 months. Although penile traction therapy or vacuum devices were not used, the patients were recommended to take daily low dose PED5is two weeks after surgery and continue for 2 months to promote nocturnal erections and prevent graft contracture. At follow-up, erectile function was assessed using the IIEF-EF questionnaire at 3 and 6 months and one year postoperatively. The SPL and residual curvature were also measured in the same way as before operation at 3 and 6 months and 1 year postoperatively. To assess overall satisfaction, the patients were asked whether they were (I) very satisfied, (II) somewhat satisfied, or (III) not at all satisfied with the surgery and the subsequent results at 3 and 6 months and one year postoperatively.

### Statistical analysis

All statistical analyses were performed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). The baseline and follow-up continuous variables are presented as mean  $\pm$  standard deviation (SD) for normal distributions and as median (interquartile range, IQR) for non-normal distributions. To compare the demographic characteristics and therapeutic outcomes, we used Student's *t*-test for normally distributed data. Otherwise, the Mann-Whitney U-test was performed. The baseline and follow-up categorical variables are presented as n (%) and tested using the chi-squared ( $\chi^2$ ) test. A P value of  $<0.05$  was considered

statistically significant.

## Results

### *Evaluation of the therapeutic efficacy and safety of Scutellaria baicalensis extract*

During this study period, 261 acute-phase PD patients met the inclusion criteria and the age varied between 26 and 69 years. Among them, 210 (80.46%) and 226 (86.59%) patients presented with penile pain on erection and palpable penile plaques, respectively. Penile curvature was presented in 161 (61.69%) cases and ED was observed in 92 (35.25%) patients. Among them, 183 patients received oral treatment with *Scutellaria baicalensis* extract and 78 patients did not. Statistical comparison of the baseline demographics and disease characteristics in the two groups did not reveal any significant differences (Tables 1,2).

In the patients treated with *Scutellaria baicalensis* extract, disease stabilized at an average of 12.7 months, whereas further progression was stopped at an average of 18.01 months in the untreated patients (Table 1). Statistical analysis showed that treatment with *Scutellaria baicalensis* extract had some benefits for improving erectile pain, plaque volume, penile curvature, and erectile function (Tables 3-6).

After 6 months of *Scutellaria baicalensis* treatment, penile pain resolved or decreased in 16.89% and 69.59% of the patients, respectively. New onset of penile pain presented in only 11.43% of the *Scutellaria baicalensis*-treated patients. In the same period, none of the untreated patients had penile pain resolution. In contrast, 88.71% of the patients had increased erectile pain. Furthermore, the new onset of penile pain presented in 56.25% of the untreated patients (Table 3).

After 6 months of *Scutellaria baicalensis* treatment, the proportion of patients with reduced plaque volume and curvature was significantly higher than that of the untreated patients (43.4% and 40.0% vs. 26.87% and 13.04%). In addition, the proportion of new-onset of penile curvature in patients without prior curvature and the curvature degree was significantly higher in untreated patients than in *Scutellaria baicalensis*-treated patients (Tables 4,5). At the stable stage of the disease, the proportion of patients requiring surgical correction in the untreated group was significantly higher than that in the *Scutellaria baicalensis*-treated patients (57.69% vs. 32.79%) (Tables 4,5).

After 6 months of treatment, regular erections were recovered in 29.23% of the patients, whereas no recovery

occurred in the untreated patients. In addition, no onset of ED occurred in patients treated with *Scutellaria baicalensis* who had no problems of rigidity at the first visit, whereas 35.29% of the untreated patients had ED in the stable phase who did not present with it initially (Table 6).

After the administration of *Scutellaria baicalensis*, 146 adverse events occurred, and no serious adverse events were observed. All adverse events were rated as mild and resolved without further treatment. None of the patients discontinued treatment because of an adverse event (Table 7).

### *Evaluation of the therapeutic efficacy of surgery after Scutellaria baicalensis treatment*

At least 6 months after the disease stabilized, 60 (32.79%) and 45 (57.69%) patients treated with or not treated with *Scutellaria baicalensis* extracts, respectively, required surgical correction of penile curvatures. Among them, 70 and 31 patients underwent surgical correction by 16-dot plication and grafting procedures, respectively (Table 8). The remaining four patients with severe ED who did not respond to PED5is refused the recommended PP implantation.

At the 1-year follow-up, complete penile straightening was observed in 92.86% and 87.1% of the patients after 16-dot plication and grafting procedures, respectively. Although slight residual curvature (less than 20 degrees) was observed in the remaining cases, the patients did not receive further treatment because it did not affect sexual intercourse (Table 8).

Shortening of penile length occurred in 41.43% and 25.81% of the patients, and the range of loss was 0.5–2.6 cm and 0.2–1.2 cm after 16-dot plication and grafting procedures, respectively. Among these patients, five complained of a shortened penile length although sexual intercourse was not affected (Table 8).

Postoperative IIEF-EF scores were maintained in all patients who received the 16-dot plication procedure and slightly improved in 48.57% patients. Moreover, patients who had difficulty with intercourse because of penile curvature seemed to attain benefit in sexual activity after curvature correction while 54.84% of the patients who received the venous grafting procedure reported varying degrees of decreased erectile rigidity. However, all these patients achieved adequate erectile capacity after receiving PED5is and were able to have successful sexual intercourse (Table 8).

There was no postoperative curvature recurrence in any

**Table 1** Clinical and demographic features of PD patients

Clinical and demographic features	Not treated with <i>Scutellaria baicalensis</i> (78 cases)	Treated with <i>Scutellaria baicalensis</i> (183 cases)	Statistical analysis (P value)
Mean age $\pm$ SD (years)	47.27 $\pm$ 9.96	46.90 $\pm$ 10.06	0.784 ( <i>t</i> -test)
BMI $\pm$ SD (kg/m <sup>2</sup> )	23.21 $\pm$ 2.25	23.50 $\pm$ 2.69	0.402 ( <i>t</i> -test)
Mean disease duration $\pm$ SD (months)	3.76 $\pm$ 1.59	3.84 $\pm$ 1.36	0.681 ( <i>t</i> -test)
Mean time required for stabilization $\pm$ SD (months)	18.01 $\pm$ 2.22	12.70 $\pm$ 1.62	0.000 ( <i>t</i> -test)
Presence of penile pain at first visit, n (%)	62 (79.49)	148 (80.87)	0.796 ( $\chi^2$ test)
Mean NRS score, only in patients with penile pain at first visit $\pm$ SD	4.29 $\pm$ 1.38	4.33 $\pm$ 1.66	0.865 ( <i>t</i> -test)
Presence of penile plaque at first visit, n (%)	67 (85.90)	159 (86.89)	0.830 ( $\chi^2$ test)
Mean plaque volume at first visit $\pm$ SD (cm <sup>3</sup> )	0.66 $\pm$ 0.38	0.70 $\pm$ 0.45	0.501 ( <i>t</i> -test)
Cases with penile curvature at first visit, n (%)	46 (58.97)	115 (62.84)	0.556 ( $\chi^2$ test)
Dorsal	20 (43.48)	49 (42.61)	
Ventral	2 (4.35)	7 (6.09)	
Lateral	8 (17.39)	20 (17.39)	
Ventrolateral	2 (4.35)	6 (5.22)	
Dorsolateral	12 (26.09)	28 (24.35)	
Hourglass deformity with curvature	2 (4.35)	5 (4.35)	
Mean angle of penile curvature at first visit $\pm$ SD (°)	35.48 $\pm$ 5.92	34.05 $\pm$ 7.53	0.252 ( <i>t</i> -test)
Cases with ED at first visit, n (%)	27 (34.62)	65 (35.52)	0.889 ( $\chi^2$ test)
Mean IIEF-EF score in patients with ED at first visit $\pm$ SD	18.59 $\pm$ 3.84	18.28 $\pm$ 3.39	0.697 ( <i>t</i> -test)

ED, erectile dysfunction; IIEF-EF, International Index of Erectile Function (IIEF) erectile function domain (EF); SD, standard deviation.

patients treated with *Scutellaria baicalensis*. In patients not treated with *Scutellaria baicalensis*, curvature recurrence did not occur in the original area. However, the new onset of palpable plaques and curvature occurred in two (16.67%) patients at 12-month follow-up at sites distal or proximal to the location of the original penile curvature (Table 8).

Complications such as diminished postoperative penile sensation, palpable suture knots, and painful erection were noticed in 11.43%, 22.86%, and 5.71% of the patients who received 16-dot plication, and in 22.58%, 12.9%, and 6.45% of the patients who received grafting procedures, respectively. However, these complications did not affect sexual intercourse. Other surgery-related complications including penile hematoma, glandular ischemia, and wound infection were not observed in any patient (Table 9). Overall, 92.86% and 83.87% of the patients who received 16-dot

plication and grafting procedures were satisfied with the final surgical results (Table 8).

## Discussion

*Scutellaria baicalensis* is a widely used traditional Chinese herbal medicine and the roots of *Scutellaria baicalensis* contain more than 40 kinds of flavonoids. Among them, baicalin, baicalein, wogonin, and oroxylin A are the main active components (15). Several *in vitro* and *in vivo* studies have demonstrated that a wide range of *Scutellaria baicalensis* extract concentrations had excellent anti-fibrotic activity in kidney fibroblasts (16), renal fibrosis (17,18), myocardial fibrosis (19), hepatic fibrosis (20), and fibrotic lung disease (21). PD is a well-established fibrotic disease, and several anti-fibrotic therapies have been described for

**Table 2** Concurrent risk factors

Concurrent risk factors	Not treated with <i>Scutellaria baicalensis</i> (78 cases)	Treated with <i>Scutellaria baicalensis</i> (183 cases)	Statistical analysis (P value)
Coronary artery disease, n (%)	6 (7.69)	14 (7.65)	0.991 ( $\chi^2$ test)
Diabetes mellitus, n (%)	7 (8.97)	16 (8.74)	0.952 ( $\chi^2$ test)
Hypertension, n (%)	18 (23.08)	42 (22.95)	0.982 ( $\chi^2$ test)
Hyperlipidemia, n (%)	12 (15.38)	29 (15.85)	0.925 ( $\chi^2$ test)
Low testosterone, n (%)	7 (8.97)	16 (8.74)	0.952 ( $\chi^2$ test)
Penile trauma, n (%)	5 (6.41)	11 (6.01)	0.902 ( $\chi^2$ test)
Dupuytren's contracture, n (%)	1 (1.28)	2 (1.09)	0.896 ( $\chi^2$ test)
Cigarette smoking, n (%)	20 (25.64)	46 (25.14)	0.932 ( $\chi^2$ test)

**Table 3** Changes of erectile pain after treatment with *Scutellaria baicalensis*

Outcomes	Not treated with <i>Scutellaria baicalensis</i> (78 cases)	Treated with <i>Scutellaria baicalensis</i> (183 cases)	Statistical analysis (P value)
Mean pain resolution, n/N (%)	0	25/148 (16.89)	0.001 ( $\chi^2$ test)
Mean pain decrease, n/N (%)	4/62 (6.45)	103/148 (69.59)	0.000 ( $\chi^2$ test)
Mean pain decrease $\pm$ SD	-2.25 $\pm$ 0.50	-2.00 $\pm$ 0.94	0.599 ( <i>t</i> -test)
Mean pain increase, n/N (%)	55/62 (88.71)	14/148 (9.46)	0.000 ( $\chi^2$ test)
Mean pain increase $\pm$ SD	2.95 $\pm$ 1.25	1.93 $\pm$ 0.73	0.005 ( <i>t</i> -test)
Mean onset of penile pain in patients with no pain, n/N (%)	9/16 (56.25)	4/35 (11.43)	0.001 ( $\chi^2$ test)
Mean onset of penile pain $\pm$ SD	5.33 $\pm$ 1.23	1.50 $\pm$ 0.58	0.000 ( <i>t</i> -test)

SD, standard deviation.

**Table 4** Changes of plaque after treatment with *Scutellaria baicalensis*

Outcomes	Not treated with <i>Scutellaria baicalensis</i> (78 cases)	Treated with <i>Scutellaria baicalensis</i> (183 cases)	Statistical analysis (P value)
Mean plaque decrease, n/N (%)	18/67 (26.87)	69/159 (43.40)	0.020 ( $\chi^2$ test)
Mean plaque decrease $\pm$ SD (cm <sup>3</sup> )	-0.44 $\pm$ 0.31	-0.52 $\pm$ 0.33	0.384 ( <i>t</i> -test)
Mean plaque increase $\pm$ SD (cm <sup>3</sup> )	0.70 $\pm$ 0.72	0.50 $\pm$ 0.60	0.090 ( <i>t</i> -test)
Mean onset of plaque in patients with no plaque, n/N (%)	11/11 (100.0)	24/24 (100.0)	1.000 ( $\chi^2$ test)
Mean onset of plaque $\pm$ SD (cm <sup>3</sup> )	0.54 $\pm$ 0.43	0.37 $\pm$ 0.22	0.141 ( <i>t</i> -test)

SD, standard deviation.

PD, including potassium para-aminobenzoate (POTABA), tamoxifen, carnitine, pentoxifylline, and interferon  $\alpha$ -2b by oral or intralesional injection, with various outcomes reported (22).

In the present study, a raw extract of *Scutellaria baicalensis* was used for treating acute-phase PD because of its anti-fibrotic effect, which was demonstrated in our previous study (8). As a result, a significantly increased proportion

**Table 5** Changes of penile curvature after treatment with *Scutellaria baicalensis*

Outcomes	Not treated with <i>Scutellaria baicalensis</i> (78 cases)	Treated with <i>Scutellaria baicalensis</i> (183 cases)	Statistical analysis (P value)
Mean penile curvature resolution, n/N (%)	0	2/115 (1.74)	0.368 ( $\chi^2$ test)
Mean penile curvature resolution $\pm$ SD ( $^\circ$ )	0	24.00 $\pm$ 5.66	0.027 (t-test)
Mean penile curvature increase, n/N (%)	31/46 (67.39)	56/115 (48.70)	0.032 ( $\chi^2$ test)
Mean penile curvature increase $\pm$ SD ( $^\circ$ )	19.26 $\pm$ 11.30	13.71 $\pm$ 12.95	0.049 (t-test)
Mean penile curvature reduction, n/N (%)	6/46 (13.04)	46/115 (40.0)	0.001 ( $\chi^2$ test)
Mean penile curvature reduction $\pm$ SD ( $^\circ$ )	15.50 $\pm$ 5.13	16.52 $\pm$ 4.67	0.62 (t-test)
Mean onset of penile curvature in patients with no curvature, n/N (%)	27/32 (84.38)	36/68 (52.94)	0.002 ( $\chi^2$ test)
Mean onset of penile curvature $\pm$ SD	33.52 $\pm$ 14.48	24.14 $\pm$ 7.79	0.002 (t-test)
Requiring surgical correction at stable phase, n/N (%)	45/78 (57.69)	60/183 (32.79)	0.000 ( $\chi^2$ test)

SD, standard deviation.

**Table 6** Mean change in erectile function at stable phase

Outcomes	Not treated with <i>Scutellaria baicalensis</i> (78 cases)	Treated with <i>Scutellaria baicalensis</i> (183 cases)	Statistical analysis (P value)
Mean improvement in penile rigidity in patients with ED, n/N (%)	0/27 (0)	46/65 (70.77)	0.000 ( $\chi^2$ test)
Mean recovery of penile rigidity in patients with ED, n/N (%)	0/27 (0)	19/65 (29.23)	0.002 ( $\chi^2$ test)
Mean changes in IIEF-EF score in patients with ED $\pm$ SD	-1.63 $\pm$ 0.49	2.48 $\pm$ 3.33	0.002 (t-test)
Onset of ED in patients with previously normal penile rigidity, n/N (%)	18/51 (35.29)	0/118 (0)	0.000 ( $\chi^2$ test)

ED, erectile dysfunction; IIEF-EF, International Index of Erectile Function (IIEF) erectile function domain (EF).

of patients with reduced plaque volume and decreased penile pain during erection and penile curvature was observed in patients treated with *Scutellaria baicalensis* compared to the untreated patients. After treatment with *Scutellaria baicalensis*, IIEF scores also significantly increased and no onset of ED occurred. Furthermore, the disease stabilized 12.7 months after the onset of symptoms in the patients treated with *Scutellaria baicalensis*, whereas the disease progression did not stop until 18.01 months in the untreated patients. These results indicate that *Scutellaria baicalensis* extract had a benefit in the treatment of acute-phase PD. Although some studies demonstrated that *Scutellaria baicalensis* had potential toxicity, it has been widely regarded as a safe and nontoxic traditional Chinese

medicine in China for thousands of years (15). Preclinical safety data from laboratory assessments also showed that *Scutellaria baicalensis* was safe and well-tolerated by healthy subjects and showed no signs of liver or kidney toxicity (23). In our study, except for transient and mild adverse events, no serious adverse events were observed and none of the patients discontinued treatment because of an adverse event. The favorable safety profile warrants further clinical studies of *Scutellaria baicalensis* for PD treatment.

However, oral treatments appear to be moderately efficacious for symptomatic men in the acute phase of PD or in men in the chronic phase of PD who are not ready to consider surgical therapy. If conservative therapies have failed and the patient is significantly bothered by penile

**Table 7** Summary of *Scutellaria baicalensis* treatment-related adverse events

Adverse events	No. (%) of subjects (183 cases)	Grade
Abdominal pain	15 (8.20)	Mild
Abdominal distention	14 (7.65)	Mild
Constipation	11 (6.01)	Mild
Diarrhea	16 (8.74)	Mild
Nausea	24 (13.11)	Mild
Dry mouth	22 (12.02)	Mild
Erythema	11 (6.01)	Mild
Itchy skin	13 (7.10)	Mild
Blood pressure increase or decrease	0 (0.00)	Mild
Anemia	2 (1.09)	Mild
Blood leukocyte decrease	2 (1.09)	Mild
Proteinuria	5 (2.73)	Mild
Alanine transaminase increase	5 (2.73)	Mild
Aspartate aminotransferase increase	6 (3.28)	Mild

deformity, surgical correction can be considered (4). In the present study, 32.79% of the patients treated with *Scutellaria baicalensis* and 57.69% of the untreated patients still had persistent penile curvature at least 6 months after the disease stabilized. Intralesional injection therapy with collagenase *Clostridium histolyticum* (CCH) was shown to be efficacious and less invasive than surgery (24,25). However, surgical correction remains the gold standard treatment option for patients in the stable phase of PD (26). In addition, CCH was not commercially available in our country during the treatment of those patients. Therefore, surgical correction was recommended for those patients in our clinical practice.

Beginning with the Nesbit procedure, several techniques of plication have been offered to PD patients with various outcomes. The 16-dot plication technique is a minimally invasive procedure, which exhibited excellent results in the surgical management of patients with stable PD (13). Incision or partial plaque excision and grafting techniques are recommended for patients with adequate rigidity, more severe curves of greater than 60–70°, a complex deformity, or narrowing with an hourglass or hinge effect (12). Many different types of autograft, allograft, xenograft, or synthetic materials have been used in grafting surgical

**Table 8** Surgical outcomes at the one-year follow-up

Surgical outcomes	16-dot plication procedure	Grafting procedure
Cases treated with <i>Scutellaria baicalensis</i> (n)	37	19
Cases not treated with <i>Scutellaria baicalensis</i> (n)	33	12
Complete straightening, n/N (%)	65/70 (92.86)	27/31 (87.10)
Slight residual curvature (less than 20 degrees), n/N (%)	5/70 (7.14)	4/31 (12.90)
No onset of shortening, n/N (%)	41/70 (58.57)	23/31 (74.19)
Onset of shortening, <1.0 cm, n/N (%)	9/70 (12.86)	7/31 (22.58)
Onset of shortening, 1.0–2.0 cm, n/N (%)	15/70 (21.43)	1/31 (3.23)
Onset of shortening, >2.0 cm, n/N (%)	5/70 (7.14)	0
Mean shortening, cm ± SD	1.37±0.55	0.53±0.30
Improvement in IIEF-EF score, n/N (%)	34/70 (48.57)	0 (0)
Decrease in IIEF-EF score, n/N (%)	0 (0)	17/31 (54.84)
Mean changes in IIEF-EF score in patients with ED at first visit ± SD	1.18±0.39	–2.06±0.66
Onset of new palpable plaque and curvature	0 (0)	2/12 (16.67)
Satisfaction with surgical outcomes [somewhat or very satisfied, n/N (%)]	65/70 (92.86)	26/31 (83.87)

ED, erectile dysfunction; IIEF-EF, International Index of Erectile Function (IIEF) erectile function domain (EF); SD, standard deviation.

**Table 9** Surgical complications

Complications	16-dot plication procedure	Grafting procedure
Diminished penile sensation, n/N (%)	8/70 (11.43)	7/31 (22.58)
Palpable suture knots, n/N (%)	16/70 (22.86)	4/31 (12.9)
Painful erection, n/N (%)	4/70 (5.71)	2/31 (6.45)
Penile hematoma (%)	0	0
Glandular ischemia (%)	0	0
Wound infection (%)	0	0

procedures with various outcomes (27,28). Venous patch grafts for PD have gained wide popularity because of their physiological characteristics with no risk of rejection or shrinkage. In addition, the endothelial coating of the vein can easily contact cavernosal tissue and regain blood supply (29,30). The most frequently reported complications of surgical corrections are incomplete straightening, curvature recurrence, penile shortening, and ED either using plication procedures or grafting techniques (12). In the present study, at the one-year follow-up, complete penile straightening was observed in 92.86% and 87.10% of the patients after 16-dot plication and grafting procedures, respectively. However, the remaining patients complained of slight residual curvature but without an effect on sexual intercourse. Interestingly, the present study showed that neither postoperative palpable penile plaques nor curvature recurred in any patient treated with *Scutellaria baicalensis* extract or in the original area of the untreated patients, whereas palpable plaques and curvatures recurred at sites distal or proximal to the original penile curvature site in the untreated patients. These results showed that even though one lesion site is stable, new lesions may occur in other areas in PD. Therefore, prior to any treatment for PD, patients should be counseled on the possibility of palpable penile plaques and curvature occurrence in new areas. These results also indicated that the use of *Scutellaria baicalensis* extract had a benefit for preventing penile plaques and curvature occurrence.

One of the consequences of PD is penile shortening that can cause significant personal distress. An additional loss of penile length may occur after surgical management and that is a great concern for the patient. Previous studies have demonstrated that penile shortening occurred in 41–100% and 0–40% of the patients following various plication procedures and grafting techniques, respectively (22,28,31,32). In our study, SPL loss occurred in 41.43%

and 25.81% of the patients following 16-dot plication and grafting techniques with a mean loss of 1.37 and 0.53 cm, respectively. Although five patients complained of shortened penile length following 16-dot plication, none of the patients stated that sexual intercourse was adversely affected by the loss of penile length. Even though penile shortening rarely results in intercourse difficulty (33), patients often perceive that the loss of length is greater than the actual loss (34). Therefore, this side effect must be clearly explained to the patients prior to the surgery, and measuring and documenting the penile length preoperatively is recommended, regardless of what technique is used (31,34).

According to the literature, the plication procedure usually does not affect erectile function (13,35), whereas the postoperative ED rate after surgery with a venous patch graft ranged between 0 and 50% (27). In the present study, postoperative sexual function was maintained in patients who underwent the 16-dot plication procedure. Moreover, patients who had difficulty with intercourse because of penile curvature seemed to attain a benefit in sexual activity after curvature correction, whereas 54.84% of the patients who received a venous grafting surgical procedure reported varying degrees of decreased erectile rigidity. Therefore, the preoperative evaluation of erectile capacity is critical for choosing the surgical technique.

This study had several important limitations, such as the retrospective design, which includes inherent bias. In addition, a raw extract of *Scutellaria baicalensis* was used for treating acute-phase PD in the present study. Since the components of herbal extracts are complex, multiple constituents may have different effects, which may confound the exact role of *Scutellaria baicalensis* in treating acute-phase PD. This is one of the important limitations of this study. Further studies are needed to clarify the exact role of *Scutellaria baicalensis* by isolating an active fraction from *Scutellaria baicalensis*. Finally, only

the IIEF-EF questionnaire, a subjective tool, was used to evaluate erectile function in the present study. The IIEF-EF questionnaire is an applicable and amenable tool for the evaluation of erectile function, which may be influenced by some pre-and postoperative factors such as depression after clinical diagnosis, the surgical decision, stress, pain at the surgical site, and the resulting compromise of libido. Therefore, objective assessments such as the nocturnal penile tumescence test, video-provoked erectile response measurements, or penile Doppler ultrasound may provide more data on erectile function.

## Conclusions

The present study showed that treatment with *Scutellaria baicalensis* extract seemed to be beneficial in improving penile plaque volume, erectile pain, penile curvature, and erectile function in patients with acute-phase PD. Early treatment with *Scutellaria baicalensis* extract also accelerated the stabilization of the disease and reduced the possibility of recurrence. The 16-dot plication and great saphenous vein grafting procedures seem effective options in the surgical management of the stable phase after *Scutellaria baicalensis* administration in the acute phase of PD. Although our study achieved significant results, further randomized controlled trials are necessary to clarify the exact role of *Scutellaria baicalensis* extract in the treatment of PD.

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## Footnote

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[org/10.21037/apm-20-2389](http://dx.doi.org/10.21037/apm-20-2389)). The authors have no conflicts of interest to declare.

**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective study was approved by the institutional research ethics committee of the Ninth People's Hospital, School of Medicine, Shanghai Jiaotong University (No. SH9H-2019-T52-2). Since only a medical record review was performed, this study was exempt from informed consent. This study was conducted in accordance with the declaration of Helsinki (as revised in 2013).

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