

Comparison of the Effectiveness of Platelet-Rich Plasma, Corticosteroid, and Physical Therapy in Subacromial Impingement Syndrome

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ABSTRACT

Objectives: This study aims to investigate and compare the efficacy of platelet-rich plasma (PRP) injection, corticosteroid injection, and physical therapy in addition to exercise treatment on pain, shoulder functions, and quality of life in patients with subacromial impingement syndrome (SAIS).

Patients and methods: Ninety patients (37 males, 53 females; mean age 48.99 years; range, 33 to 60 years) who were diagnosed as Stage 2 SAIS were included in the study. Patients were randomized into three groups. PRP injection was administered into the subacromial space of the affected shoulder in group 1, corticosteroid injection was administered in the subacromial joint space in group 2, and 10 sessions of physical therapy were given in group 3 five times weekly including transcutaneous electrical nerve stimulation, ultrasound, and hot packs. Moreover, an exercise program was administered in all groups. visual analog scale (VAS) was used to determine the resting and moving shoulder pain; while the Shoulder Disability Questionnaire, Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) questionnaire, and the University of California, Los Angeles Shoulder Rating Scale (UCLA SRS) were used to evaluate the functionality of patients. Quality of life was analyzed using a generic Short Form 36 (SF-36).

Results: All scores improved in all three groups compared with the period before treatment. Comparison of the groups showed higher scores in group 1 compared to groups 2 and 3 at week eight on QuickDASH, UCLA SRS, VAS at rest and during activity, and SF-36 pain subgroup scores.

Conclusion: All three treatment modalities were effective in the treatment of SAIS. However, we suggest that the inexpensive and noninvasive methods of physical therapy and exercise should be the first preferred treatment in SAIS owing to causing no adverse events.

Keywords: Corticosteroid; exercise; physical therapy; platelet-rich plasma.

The prevalence of shoulder pain is 7-28% in the general population. Shoulder pain is the third most common disorder among the musculoskeletal disorders after diseases of the lumbar spine and neck. The most common cause of shoulder pain is subacromial impingement syndrome (SAIS). According to pathological changes, Neer¹ grouped SAIS in three stages. Edema and hemorrhage are detected in the

first stage of the disease and symptoms may be corrected with conservative treatment. The second stage of the disease is characterized by fibrosis and tendinitis; however, partial rotator cuff tears have recently been identified in Stage 2. The primary treatment in this stage is conservative treatment. The third stage is identified by bone changes affecting the rotator cuff and long head biceps tears.¹⁻⁵

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The purpose of treatment in SAIS is to stop the inflammatory process, reduce pain, prevent progressive degenerative changes, provide improved joint range of motion, increase muscle strength, and organize the daily life activities. In the literature, the limits of conservative and surgical treatments are indefinite, while primary treatment is conservative.^{6,7}

Platelet-rich plasma (PRP) contains many growth factors such as transforming growth factor, fibroblast growth factor, vascular endothelial growth factor, insulin-like growth factor, thrombocyte-derived angiogenic factor, epithelial growth factor, platelet-derived growth factor, and platelet activating factor-4.⁸ The interest in PRP has increased due to its inclusion of growth factors.⁹⁻¹¹

Local corticosteroid injections have frequently been used particularly in the first and second stages of disease, and found to have no long-term effect while half of the patients reported repeated symptoms.¹² In addition, corticosteroids have adverse effects such as atrophy, systemic absorption, infection, subcutaneous tendon rupture, and tendon rupture on the skin.¹³

Physical therapy has an effective role in the treatment of SAIS. The single or combined use of physical therapy agents and exercise are effective in treatment. Studies have shown that physical therapy and exercise have therapeutic effects for patients diagnosed with SAIS.¹⁴⁻¹⁶ Therefore, in this study, we aimed to investigate and compare the efficacy of PRP injection, corticosteroid injection, and physical therapy in addition to exercise treatment on pain, shoulder functions, and quality of life in patients with SAIS.

PATIENTS AND METHODS

The study was conducted at Düzce University Medical Faculty between September 2015 and September 2016 and included patients who presented with symptoms of shoulder pain at least for three months without major trauma. Patients with other types of shoulder pain due to cervical radiculopathy, thoracic outlet syndrome, dermatologic disease involving the shoulder, neuromuscular disease with muscle weakness, inflammatory joint disease, infection, metallic

implants in the shoulder, cardiovascular disease, history of malignancy, diabetes mellitus or other endocrine system diseases, pregnancy, shoulder, back or neck operations, or those who were cardiac pacemaker carriers using nonsteroidal antiinflammatory drugs in the last week were excluded. Detailed physical examinations were performed. Manual muscle strength and speed test, Hawkins test, Neer compression test, Jobe test, painful arch test, and Yergason's test results were evaluated, and the shoulder joint range of motion was also evaluated using a standardized goniometer. Routine blood tests including erythrocyte sedimentation rate, complete blood count, C-reactive protein, and rheumatoid factor were studied after detailed anamnesis and physical examination. Posteroanterior chest radiography, four-way cervical radiography, shoulder radiography for both shoulders, and magnetic resonance imaging (MRI) for the affected shoulder were performed. The study protocol was approved by the Düzce University Medical Faculty Ethics Committee. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Diagnosis of SAIS was established in accordance with the clinical and MRI information of the patients. Patients with Stage 1 and 3 SAIS were excluded. Ninety patients (37 males, 53 females; mean age 48.99 years; range, 33 to 60 years) diagnosed with fibrosis, tendinitis, and Stage 2 SAIS were included in the study. Visual analog scale (VAS) scores were measured at rest and during activity to detect the severity of pain, while shoulder functions were assessed using the Shoulder Disability Questionnaire (SDQ), Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH) questionnaire, and the University of California, Los Angeles Shoulder Rating Scale (UCLA SRS). Short Form 36 (SF-36) was used to evaluate the quality of life. Measurements were performed at weeks three and eight after treatment. The same blinded investigator performed all evaluations.

Approximately 100 patients were expected to visit the polyclinic with SAIS during the six month data collection period. The minimum required sampling size was calculated. Based on statistical calculations, it was decided to include at least 30 patients in each group. These patients were

divided into groups homogeneously based on their demographic characteristics with a balanced distribution.

Subacromial PRP injection and exercise were administered in group 1 (n=30), subacromial corticosteroid injection and exercise were administered in group 2 (n=30), and physical therapy including hot packs, transcutaneous electrical nerve stimulation (TENS), and ultrasound as well as exercise were administered in group 3 (n=30).

Shoulder rotation movements and overhead and back activities which might cause pain were avoided for the first two days before the initiation of the treatment. Patients were allowed to use paracetamol and cold application if needed. Nonsteroidal anti-inflammatory drugs were not used due to risk of reducing the effect of PRP. Two days later, patients were taken to a three-week exercise program.

The exercise program started with joint range of motion, Codman's exercises, posterior joint capsule, and stretching exercises including the pectoral muscles. Isometric strengthening exercises were included at the end of week two. Exercise protocol was performed for eight weeks by teaching the standard stretching and isotonic strengthening exercises.

Neotec Biotechnology PRP kit (Neotec Biotechnology Ltd., Istanbul, Turkey) and Elektromag device model 415P (Elektro-Mag AŞ.,

Istanbul, Turkey) were used for the PRP injection. Totally 8.5 mL cubital blood was drawn for the PRP method and 1.5 mL citrate was included to prevent clotting.

A total of 10 mL anticoagulated blood was centrifuged at 1200 G for five minutes by placing in a specially designed tube. After the first centrifugation, the poor plasma was withdrawn by an injector from the tube and was discarded. The tube was centrifuged a second time for 10 minutes at 1200 G to obtain 4 mL of PRP. No buffering or activating agent was used for PRP. The resulting 4 mL PRP was injected into the subacromial space.

A single dose of 40 mg/mL triamcinolone acetonide and 3 mL lidocaine 2% were administered to the subacromial area with steroid injection.

Physical therapy and superficial heating agents, namely hot packs, were applied for 10 sessions to the painful shoulder for 20 minutes. For Transcutaneous Electrical Nerve Stimulation (TENS), BTL-4000 combined therapy device (BTL India Pvt. Ltd., New Delhi, India) was used in conventional method for 20 minutes with four electrodes and in transarticular method for 10 sessions five times weekly. Ultrasonic deep heating was applied at a dose of 1.5 watts/cm², at 1 MHz frequency for eight to 10 sessions per week in continuous and circular mode.

Table 1. Periodic changes in VAS scores during activity

Group	Mean±SD	p
Differences before treatment and at week 3 after treatment		
Platelet-rich plasma injection	3.5±1.1	0.112
Corticosteroid injection	3.7±1.6	
Physical therapy	4.1±1.1	
Differences at week 3 and week 8 after treatment		
Platelet-rich plasma injection	*2.5±1.0	<0.001
Corticosteroid injection	1.4±0.8	
Physical therapy	†1.1±0.4	
Differences before treatment and at week 8 after treatment		
Platelet-rich plasma injection	*6.0±0.9	0.018
Corticosteroid injection	5.1±1.5	
Physical therapy	†5.2±1.1	

VAS: Visual analog scale; * p<0.05 and platelet-rich plasma injection versus corticosteroid injection; † p<0.05 and platelet-rich plasma injection versus physical therapy.

VAS: Visual analog scale; * p<0.05 and platelet-rich plasma injection versus corticosteroid injection; † p<0.05 and platelet-rich plasma injection versus physical therapy.

Table 2. Comparison of VAS at rest and VAS during activity with SDQ before and after treatment

	Group 1 PRP injection	Group 2 Corticosteroid injection	Group 3 Physical therapy	Group comparisons
	Mean±SD	Mean±SD	Mean±SD	p
VAS at rest				
Before treatment	4.9±0.87	4.8±0.6	4.9±0.5	0.673
Week 3 after treatment	1.3±0.5	1.2±0.4	1.1±0.5	0.182
Week 8 after treatment	0.8±0.6	0.9±0.6	0.8±0.6	0.744
Repeated measures comparisons (p)	0.001	0.001	0.001	
VAS during activity				
Before treatment	8.0±0.8	7.9±0.8	8.0±0.8	0.907
Week 3 after treatment	4.5±1.2	4.2±1.4	3.9±1.0	0.100
Week 8 after treatment	2.0±0.9	2.8±1.2	2.7±0.9	0.013
Repeated measures comparisons (p)	0.001	0.001	0.001	
SDQ				
Before treatment	82.1±17.1	79.5±17.7	78.1±19.5	0.692
Week 3 after treatment	29.5±13.5	27.3±12.0	28.9±15.9	0.802
Week 8 after treatment	10.0±5.3	13.2±12.3	12.8±9.2	0.344
Repeated measures comparisons (p)	<0.001	<0.001	<0.001	

VAS: Visual analog scale; SDQ: Shoulder Disability Questionnaire; PRP: Platelet-rich plasma.

Statistical analysis

Statistical analyses were performed using the IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for the continuous and categorical variables. Shapiro-Wilk test was used in variables with normal distribution. One-way analysis of variance (ANOVA) was used in the comparison

between the means of the group. The Pearson's chi-square and Fisher-Freeman-Halton tests were used in the evaluation of the association between the categorical variables. Repeated measures of ANOVA were conducted to test whether there was a significant change in the periods for variables with normal distribution, while Friedman's test was used in testing the

Table 3. Periodic changes in VAS scores at rest

Group	The mean differences	Differences in standard deviation	p
Differences before treatment and at week 3 after treatment			
Platelet-rich plasma injection	3.63	0.999	0.591
Corticosteroid injection	3.66	0.758	
Physical therapy	3.86	0.776	
Differences at week 3 and week 8 after treatment			
Platelet-rich plasma injection	0.46	0.507	0.081
Corticosteroid injection	0.23	0.430	
Physical therapy	0.23	0.430	
Differences before treatment and at week 8 after treatment			
Platelet-rich plasma injection	4.1	1.093	0.505
Corticosteroid injection	3.9	0.758	
Physical therapy	4.1	0.803	

VAS: Visual analog scale.

Table 4. Comparison of SDQ during activity before and after treatment

	Group 1 PRP injection	Group 2 Corticosteroid injection	Group 3 Physical therapy	Group comparisons
	Mean±SD	Mean±SD	Mean±SD	p
Before treatment	82.1±17.1	79.5±17.7	78.1±19.5	0.692
Week 3 after treatment	29.5±13.5	27.3±12.0	28.9±15.9	0.802
Week 8 after treatment	10.0±5.3	13.2±12.3	12.8±9.2	0.344
Repeated measures comparisons (p)	<0.001	<0.001	<0.001	

SDQ: Shoulder Disability Questionnaire; PRP: Platelet-rich plasma.

difference of periods for non-normal distribution. Kruskal-Wallis test was used for differences between groups in terms of periodic changes. A 5% type I error level was used to infer statistical significance.

RESULTS

The mean ages in groups 1, 2, and 3 were 49.4±9.1 years, 47.73±9.552 years, and 49.86±9.012 years, respectively. The durations of symptoms in groups 1, 2, and 3 were 0.77±0.664 months, 0.92±1.121 months, and 1.01±1.227 months, respectively. The durations of symptoms and mean ages were similar between the groups ($p>0.05$).

There was no significant difference in resting VAS values between the groups before treatment

($p=0.6$). After treatment, the mean VAS score significantly decreased in all groups from week three to week eight ($p<0.01$ for each periodic change); however, no change was detected in the amount of reduction ($p=0.2$ for week three and $p=0.7$ for week eight). The difference in VAS scores during activity between periods was statistically significant for each group ($p<0.01$ for all) (Table 1). The difference between periods was statistically significant for each group in terms of SDQ ($p<0.01$). However, there was no significant difference between the groups for each period ($p=0.7$, $p=0.8$, and $p=0.3$, respectively) (Table 2). Improvement in VAS scores at rest was similar in all groups after treatment ($p=0.6$, $p=0.1$, and $p=0.5$, respectively) (Table 3).

The mean SDQ scores in all groups were similar before treatment ($p=0.7$). After

Table 5. Comparison for UCLA SRS and QuickDASH during activity before and after treatment

	Group 1 PRP injection	Group 2 Corticosteroid injection	Group 3 Physical therapy	Group comparisons
	Mean±SD	Mean±SD	Mean±SD	p
UCLA SRS				
Before treatment	14.6±4.5	16.4±4.0	15.6±3.8	0.344
Week 3 after treatment	31.4±2.5	33.3±4.0	32.7±2.2	0.581
Week 8 after treatment	*38.3±3.3	†35±3.5	†34.5±2.5	0.001
Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
QuickDASH				
Before treatment	78.5±6.8	78.5±7.7	77.6±7.6	0.775
Week 3 after treatment	*62.3±8.7	†58.0±6.7	†56.8±9.5	0.032
Week 8 after treatment	24.5±5.2*	†28.9±7.2	†29.5±6.4	0.013
Repeated measures comparisons (p)	<0.001	<0.001	<0.001	

UCLA SRS: University of California, Los Angeles Shoulder Rating Scale; PRP: Platelet-rich plasma; QuickDASH: Quick Disabilities of Arm, Shoulder and Hand Score; * $p<0.05$ and platelet-rich plasma injection versus corticosteroid injection; † $p<0.05$ and platelet-rich plasma injection versus physical therapy.

Table 6. Comparison for SF-36 during activity before and after treatment

SF-36 Sub-dimensions	Period	Group 1 PRP injection	Group 2 Corticosteroid injection	Group 3 Physical therapy	Group comparisons
		Mean±SD	Mean±SD	Mean±SD	p
Physical function	Before treatment	58.2±20.1	62.2±27.0	59.2±25.2	0.628
	Week 3 after treatment	72.3±15.2	75.2±21.2	74.3±15.9	0.464
	Week 8 after treatment	84.5±12.8	80.7±17.8	78.5±16.2	0.442
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
Physical role	Before treatment	14.2±14.2	16.7±19.0	15.8±18.0	0.960
	Week 3 after treatment	74.5±6.7	76.0±7.5	75.2±6.6	0.594
	Week 8 after treatment	95.2±6.1	93.7±6.6	93.2±6.2	0.354
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
Pain	Before treatment	29.3±12.3	27.6±9.5	30.9±14.4	0.388
	Week 3 after treatment	72.8±6.0	75.2±9.4	72.4±6.0	0.087
	Week 8 after treatment	81.3±9.0	*77.5±7.6	†76.3±5.5	0.050
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
Social function	Before treatment	36.6±12.3	*34.2±11.8	†55.8±20.2	<0.001
	Week 3 after treatment	74.1±11.8	77.5±20.6	73.8±12.0	0.919
	Week 8 after treatment	86.3±11.1	85.6±15.4	81.8±11.7	0.869
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
Mental health	Before treatment	54.9±14.7	57.2±9.3	55.9±10.4	0.852
	Week 3 after treatment	72.9±8.7	71.9±7.3	70.9±4.5	0.632
	Week 8 after treatment	77.3±7.3	76.4±6.1	74.9±8.3	0.687
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
Emotional	Before treatment	40.0±33.2	37.8±36.9	40.0±36.5	0.931
	Week 3 after treatment	63.3±32.0	60.0±32.0	57.8±38.1	0.858
	Week 8 after treatment	71.1±21.0	67.7±22.3	66.6±26.3	0.761
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
Vitality	Before treatment	43.2±15.7	45.8±17.3	42.7±14.8	0.805
	Week 3 after treatment	54.2±15.3	54±17.7	52.3±14.1	0.857
	Week 8 after treatment	67.3±11.3	68.2±14.2	65.7±9.7	0.534
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	
General health	Before treatment	22.7±9.3	20.8±10.8	20.2±6.2	0.641
	Week 3 after treatment	62.5±11.9	63.3±14.3	62.3±11.2	0.775
	Week 8 after treatment	81.3±6.7	79.3±6.4	78.8±7.8	0.112
	Repeated measures comparisons (p)	<0.001	<0.001	<0.001	

SF-36: Short Form 36; PRP: Platelet-rich plasma; * p<0.05 and platelet-rich plasma injection versus corticosteroid injection; † p<0.05 and corticosteroid injection versus physical therapy.

treatment, the mean SDQ scores in all groups significantly decreased until the eighth week ($p<0.01$). The mean SDQ scores after treatment at weeks three and eight were statistically similar between the groups ($p=0.8$ and $p=0.3$, respectively) (Table 4).

There was no significant difference in the mean UCLA SRS values between the groups ($p=0.3$) before treatment. The mean UCLA SRS values in all groups significantly increased after treatment until week eight ($p<0.01$). The increased mean UCLA SRS values until week three were similar

between the groups ($p=0.6$). However, the mean UCLA SRS value was significantly higher in group 1 at week eight compared to groups 2 and 3 ($p<0.01$) (Table 5).

No statistically significant differences were detected between groups in the QuickDASH scores ($p=0.8$). The QuickDASH scores in all groups showed a significant decrease at weeks three and eight after treatment ($p<0.01$ for each). The mean QuickDASH score in week three in group 1 was lower compared to groups 2 and 3 ($p=0.03$). The decrease in week eight was significantly higher in group 1 compared to groups 2 and 3 ($p=0.01$). The improvement in QuickDASH scores in groups 2 and 3 was similar after treatment at weeks three and eight ($p>0.05$) (Table 5).

In terms of SF-36 results, the mean social function sub-dimension for group 3 was significantly higher than groups 1 and 2 ($p<0.01$); however, the means of social function scores were similar between groups 1 and 2 before treatment ($p>0.05$). The mean scores of the other seven subscales were similar in all groups before treatment. After treatment, improvement was detected in all subscales of the SF-36 until week eight ($p<0.01$ for each). Group 1 had more improvement at week eight compared to groups 2 and 3 only regarding pain and the improvement was statistically significant ($p=0.05$) (Table 6).

DISCUSSION

The initial treatment of SAIS is conservative and the most important part of this treatment involves exercise treatment.^{17,18} Michener et al.⁴ 19 have detected in 12 studies which investigated SAIS between 1966 and 2003 that patients benefitted from exercises; therefore, studies included exercise treatment.

Studies comparing exercise treatment with surgical treatment have found no long-term differences between exercise and surgical treatment.¹⁸⁻²⁰ Thus, we performed exercise treatment as a non-invasive and effective treatment in addition to all other treatments.

Although exercises are known to be effective in treatment, no consensus has yet been reached on the treatment program to be implemented.²⁰⁻²²

Levendoğlu et al.²³ have randomized 52 SAIS patients into two groups and administered exercises for both groups. In addition to exercises, they have performed 15 sessions of physical therapy including hot packs, ultrasound, and TENS and injected triamcinolone in subacromial space. The comparison of the efficacy of both treatments at day 15 and at months one and three showed a statistically significant improvement in the VAS pain scores at rest and in movement. However, corticosteroid injection was significantly superior to physical therapy. Significant differences were also shown in favor of the maximal muscle strength of the internal rotator in the injection group.²³

Moreover, Rha et al.²⁴ have investigated 39 patients diagnosed with supraspinatus tendon lesion (tendinosis or a partial tear less than 1.0 cm, but not a complete tear). PRP injection was administered twice every four weeks in 20 patients, while dry needling was administered every four weeks in 19 patients. In first injections, patients were instructed exercises of joint range of motion, stretching, and strengthening for two weeks. Evaluation results have shown that PRP injection provided more improvement in terms of pain, function, and joint range of motion than dry needling.²⁴

Additionally, Randelli et al.²⁵ have studied patients with a full-thickness rotator cuff tear who were performed PRP injection during arthroscopic repair. No additional treatment was administered. In PRP patients, the pain level decreased in the postoperative early period and at the end of third month, with a significant improvement in shoulder function tests and shoulder external rotation muscle strength. At the end of the second year, a significant improvement was detected in pain, functioning, and MRI in tendinopathy and tear scores in both groups; however, there was no difference between the groups. The subgroup analysis showed that muscle strength was higher in the PRP group in Stage 1 and 2 tears.²⁵

We have detected in our study that PRP injection, corticosteroid injection, and physical therapy had effective roles in terms of pain, quality of life, and shoulder functions. However, PRP injection was more effective compared to corticosteroid injection and physical therapy at week eight in terms of UCLA SRS, VAS during

activity, QuickDASH, and pain sub-dimension of SF-36. Shams, Randelli, Rha et al.²⁴ have also found that PRP treatment was similarly effective as in our study results. Rha et al.²⁴ have applied PRP twice and demonstrated that the activity continued even at month six; however, their sample size was smaller. On the other hand, Shams et al.²⁶ have administered a single dose of PRP; however, in month six, they detected that PRP activity did not continue. Furthermore, Randelli et al.²⁵ have shown that PRP treatment was effective during arthroscopic repair in patients with full-thickness tears, while no long-term efficacy was detected. Their patients had tendon tears. In our study, patients had no tendon tears. Therefore, the early disease stage of our patients may be one of the reasons for us to detect effective healing in all treatments. Unfortunately, we do not have information on the long term results since we did not continue follow-up after month two.^{25,26}

One of the limitations of our study was the lack of a study group that did not receive exercise treatment. Thus, we could not demonstrate the effect of exercise treatment. In addition, the inclusion of exercise treatment in all treatment groups may have increased the effectiveness of treatment. However, if we had not administered exercises, it may have led to ethical issues due to depriving patients of an effective treatment method. Another limitation of our study was the lack of long-term comparisons between treatments as well as the lack of MRI comparisons for demonstrating tendon healing.

In conclusion, the comparison of the study groups showed higher scores with PRP injection compared to corticosteroid injection and physical therapy at week eight on QuickDASH, UCLA SRS, VAS at rest and during activity, and SF-36 pain subgroup scores. Thus, PRP injection was more effective than corticostreoid injection and physical therapy for SAIS in the long period. We advise application of physical therapy and exercises, which are non-invasive and inexpensive methods without side effects, before invasive treatments such as PRP or corticosteroid injections, particularly in the early stage of SAIS. However, long-term follow-up studies are required with larger and more comprehensive patient groups.

Declaration of conflicting interests

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