Original Article

The use of platelet-rich fibrin in lumbar interbody fusion in lytic spondylolisthesis

ABSTRACT

Study Design: This was a retrospective observational study.

Aim: The aim of this study was to evaluate the effectiveness of applying the platelet-rich fibrin (PRF) with bone graft in accelerating the rate of lumbar interbody fusion.

Settings and Design: This was a retrospective study measuring the outcome of posterior lumbar interbody fusion (PLIF) combined with PRF versus PLIF alone in the management of lytic spondylolisthesis.

Subjects and Methods: Forty patients were treated with instrumented PLIF for low-grade lytic spondylolisthesis and divided into two equal groups: one with addition of PRF to the bone graft and the other without. The minimum follow-up was 2 years. Clinical outcome was measured by the Oswestry Disability Index (ODI) and Visual Analogue Pain Scale (VAS) at 3, 6, and 12 months postoperatively. Radiological outcome was measured by standing X-ray at 3, 6, 12, and 24 months and computed tomography at 6 and 12 months postoperatively.

Results: ODI for the PRF group improved by 60% and 79% at 6 and 12 months, respectively, whereas for the non-PRF group, it improved by 55% and 70%. Radiological outcome showed fusion in 15 of 20 cases in the PRF group (75%) by the 6th month and in 19 of 20 cases (95%) by 1 year and 100% at 2 years. In the control group, fusion was present in 12 of 20 cases (60%) by the 6th month and in 13 of 20 cases in the PRF group (65%) by 1 year and 90% at 2 years ($P < 0.05$).

Conclusions: These preliminary results show that PRF accelerates the rate of fusion in low-grade lytic spondylolisthesis in short-term follow-up.

Keywords: Autologous growth factors, lumbar interbody fusion, lytic spondylolisthesis, platelet-rich fibrin

INTRODUCTION

Lytic spondylolisthesis is a common condition, which occurs most frequently in the lower lumbar spine. The extent of the slip is usually graded using the Meyerding classification in which the displacement of one vertebral body on another is divided into four equal parts. Grades I and II, which represent 25% and 50% displacement, respectively, and cover the majority of cases, are referred to as low-grade slips.[1,2] The initial management is conservative. Surgery is indicated in persistent pain more than 6–12 months after failed conservative measures.[3,4] Posterolateral fusion (PLF) has long been considered the "gold standard" for surgical treatment of adult spondylolisthesis. Superior results have subsequently been reported with interbody fusion with cages and posterior instrumentation.[5] Posterior lumbar interbody fusion (PLIF) is an alternative technique which avoids the ventral approach; it has become a widely accepted surgical procedure to achieve a solid and stable arthrodesis.[6] Platelet-rich fibrin (PRF) is a platelet concentrate that has been used widely to accelerate soft-tissue and hard-tissue healing. It was first described by Choukroun *et al*.[7] It has been referred to as a second-generation platelet concentrate, which showed several advantages over traditionally prepared platelet-rich plasma (PRP).

Joseph Gamal Boktor[1,2], Ahmed Maher Sultan, Awf AlShahwani[1], Ahmed Samir Barakat, Wael Koptan, Yasser Elmiligui

Department of Orthopaedics, Cairo University, Cairo, [1]Department of Orthopaedic Surgery, Al Haram Hospital, Giza, Egypt, [2]Department of Orthopaedic Surgery, Royal Gwent Hospital, Newport, United Kingdom

Address for correspondence: Dr. Joseph Gamal Boktor, 10 Duke Road, Corby NN175FX, Giza, Egypt.
E-mail: jostawro@hotmail.com

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Its chief advantages include ease of preparation and lack of biochemical handling of blood. PRF is in the form of a platelet gel. The combination of bone grafts and autologous growth factors (AGFs) contained in PRF may be suitable to enhance bone density.[8,9]

This study aimed to evaluate the clinical and radiological outcomes of using PRF with bone graft in lumbar interbody fusion in low-grade lytic spondylolisthesis.

SUBJECTS AND METHODS

Patient population

A total of forty consecutive patients with lytic spondylolisthesis were selected for instrumented PLIF technique between December 2014 and January 2016 by the same spinal team of surgeons in two spinal centers. Twenty patients (Group A) using PRF and locally morselized autogenous bone graft and the other twenty patients (Group B) using locally morcellized autogenous bone graft alone. The patient demographics are summarized in Table 1. All the cases tried conservative measures for at least 6 months before going to surgical treatment. All the patients signed an informed and detailed consent describing the procedure, alternative treatment methods, and possible complications. Inclusion criteria were as follows: Grade I and Grade II spondylolisthesis, radiological instability, and back pain or leg pain with failed conservative treatment. We excluded patients older than 60 years, previous back surgery, and generalized osteoporosis. All the patients had a one-level interbody fusion, most commonly affecting level L4/5 (21 patients), followed by L5/S1 (15 patients); preoperatively, plain X-rays of the lumbar spine included anteroposterior, lateral, and dynamic flexion and extension views and a lumbosacral magnetic resonance imaging.

Surgical technique

Patients received general hypotensive anesthesia and were placed in the prone position, maintaining the lumbar lordosis by position on a padded spinal frame. The PLIF procedure begins with a posterior, midline exposure. The paraspinal muscles were elevated, exposing from the spinous processes to the tips of the transverse processes. Fixation of unstable level was done after detecting of entry point for each pedicle. The position of pedicle screws was checked by image intensifier [Figure 1a]; then, longitudinal rods were connected.

The complete exposure for the exiting root was achieved by removing the laminae and the facet joint over the affected level and release of compression. At this stage, the medial thecal sac, exiting nerve root, and disc space were visible. Disc space was prepared for fusion, and a nerve root retractor was often placed medially to protect the thecal sac [Figure 1b].

The disc space was incised between the thecal sac and the traversing nerve root, and a generous window was removed from the posterolateral annulus to allow proper discectomy and the placement autogenous bone graft with PRF. All disc material and cartilaginous endplate were thoroughly removed, leaving the bony endplate intact. Autogenous bone graft was prepared from removed laminae and facet for interbody fusion (PLIF). The weight was measured for bone graft to make sure of equality between all the patients (mean weight was kept to 5 g).

PRF preparation was done by collection of 60-ml whole blood in a sterile syringe. The content of syringe was divided into six 10-ml test tubes without an anticoagulant; then, tubes were put inside the centrifuge. Centrifugation designed at speed of 2700 RPM for 12 min. The resultant product consists of the following three layers: topmost layer consisting of acellular platelet-poor plasma, PRF clot in the middle, and red blood cells at the bottom [Figure 2a]. PRF can be obtained in the form of a gel or membrane by squeezing out the fluids in the fibrin [Figure 2b]. PRF was packed into the disc space followed by bone graft [Figure 2c and d]. PRF was weighted to make sure equality among patients (mean weight was 2 g).

Postoperatively, patients were allowed to mobilize full weightbearing without brace but avoid sitting for

Table 1: Patients' demographics (*n*=20)

Demographics		
	PRF group	Non-PRF group
Mean age±SD, range	40.75±7.8	43.9±9.01
Gender, *n*		
Male	4	7
Female	16	13
Level of slip, *n* (%)		
L3/4	1 (5)	3 (15)
L4/5	9 (45)	12 (60)
L5/S1	10 (50)	5 (25)
Grade of slip, *n* (%)		
G1	9 (45)	8 (40)
G2	11 (55)	12 (60)

SD - Standard deviation; PRF - Platelet-rich fibrin

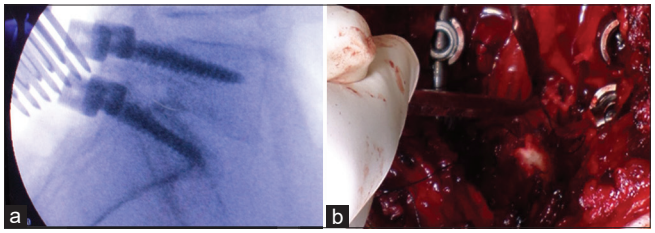

Figure 1: (a) Fixation checking by image intensifier. (b) Exposure of disc with nerve root

long duration for 3 weeks and lifting heavy objects for 6 months.

Outcome measures

Clinical outcome: Patients were asked to complete pre- and postoperative questionnaires Oswestry Disability Index (ODI) score and Visual Analog Pain Scale (VAS) for leg pain and back pain at 3-, 6-, and 12-month follow-up. Radiological outcome: The fusion results were evaluated at 3, 6, and 12 months using standing X-rays. Computed tomography (CT) lumbosacral spine was only used to assess the fusion when it was not clear in X-rays at 6 and/or 12 months. Fusion was evaluated according to the criteria of Brantigan and Steffee [Table 2].[10] The assessment of fusion was done blinded by two of the authors.

Table 2: Description of fusion by Brantigan and Steffee[10]

Fusion grade	Description
Obvious radiographic pseudoarthrosis	Collapse of construct, loss of disc height, vertebral slip, broken screws, or resorption of bone graft
Probable radiographic pseudoarthrosis	Visible gap or lucency >2 mm in the fusion area
Radiographic status uncertain	A small visible gap with at least half of the graft area showing no lucency between the graft bone and the vertebral bone
Probable radiographic fusion	Bone bridges the entire fusion area with at least the density originally achieved at surgery. There should be no lucency between the graft bone and the vertebral bone
Radiographic fusion	The bone in the fusion area is more dense and more mature than originally achieved in surgery; there is no interface between the donor bone and the vertebral bone; a sclerotic line between the graft and the vertebral bone indicates solid fusion. Other indicators of solid fusion are fusion of the facet joints and anterior progression of the graft in the disc

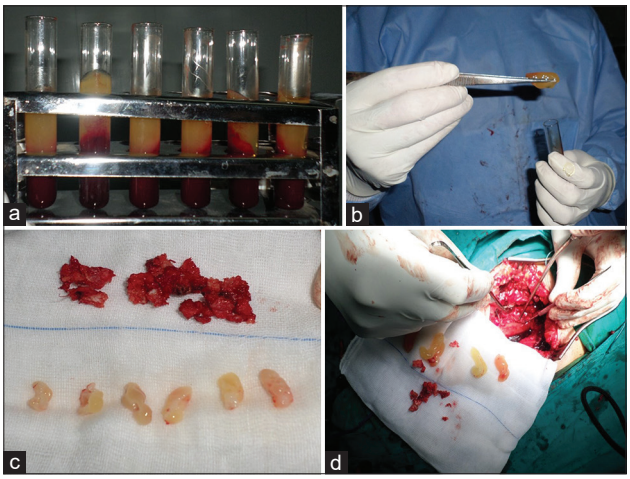

Figure 2: (a) Centrifuge products topmost layer consisting of acellular platelet-poor plasma, platelet-rich fibrin clot in the middle, and red blood cells at the bottom. (b) Platelet-rich fibrin in the form of gel. (c) Platelet-rich fibrin in the form of gel or membrane with bone graft. (d) Platelet-rich fibrin and graft packing into disc space

Statistical analysis

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, Student's *t*-test, paired *t*-test, and Chi-square test by Computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 17 for Microsoft Windows.

RESULTS

The average operative time for the PRF group was 110 ± 16 min, whereas for the non-PRF group, it was 103 ± 10 min. The mean blood loss was 535 ± 175 cc for the PRF group versus 480 ± 90 cc for the control group. Hospital stay per day: It was the same for both the groups ranging 2–4 days.

Clinical outcome

All the forty patients were evaluated postoperatively at 3, 6, and 12 months. ODI score for the PRF group improved from 60.9 ± 7.1 preoperatively to 36.4 ± 13.2, 22.4 ± 13.2, and 12.6 ± 11.1 at 3, 6, and 12 months postoperatively. The second group showed less improvement with ODI which improved from 61.4 ± 4.8 preoperatively to 41.7 ± 9.4, 27.6 ± 12.2, and 18 ± 11.2 at 3, 6, and 12 months postoperatively [Figure 3].

The mean back pain VAS decreased in the PRF group from 6.8 ± 0.8 preoperatively to 4.2 ± 1.2, 2.6 ± 1.9, and 1.7 ± 1.5 postoperatively at 3, 6, and 12 months, respectively. The second group VAS decreased less significantly from 6.5 ± 0.7 preoperatively to 4.5 ± 1, 3.6 ± 1.7, and 2.4 ± 1.3 postoperatively at 3, 6, and 12 months, respectively [Figure 4].

The mean leg pain VAS showed less difference. The PRF group improved from 6.4 ± 1.1 preoperatively to 2.5 ± 0.99, 0.85 ± 1.1, and 0.5 ± 1 postoperatively at 3, 6, and 12 months, respectively. The second group VAS was 5.9 ± 1.2 preoperatively to 2.4 ± 1, 1 ± 1, and 0.45 ± 0.7 postoperatively at 3, 6, and 12 months, respectively [Figure 5].

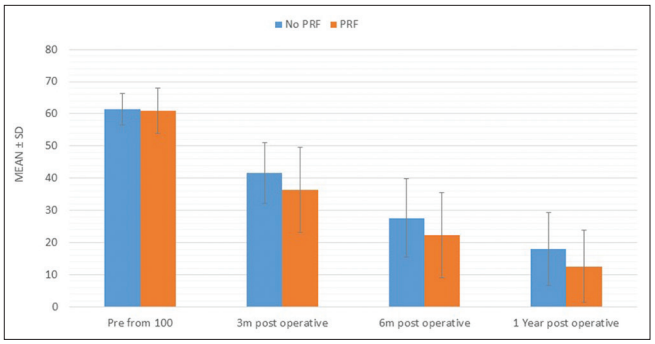

Figure 3: Oswestry Disability Index score over 12-month period

Radiological outcome

Fusion was present in 15 of 20 cases in the PRF group (75%) by the 6th month and in 19 of 20 cases (95%) by 1 year reaching 100% at 2 years. In the control group, fusion was present in 12 of 20 cases (60%) by the 6th month and in 13 of 20 cases in the PRF group (65%) by 1 year reaching 18 by 2 years 90% ($P < 0.05$) [Figure 6].

Complications

The complications and postoperative blood transfusion are shown in Table 3. There was no significant difference regarding need for postoperative blood transfusion or superficial infection.

Case presentation

A 45-year-old female patient, housewife, had L4 radiculopathy at the left side, Grade II L4/5 spondylolisthesis. The operation was done with the use of PRF after obtaining patient consent. Preoperative ODI was 60, improved postoperatively to 6 at 6 months and at one year was 2. Preoperative back pain VAS was 6, at 6 months postoperative was 0 and at 1 year was 0. CT done at 1 year showed Grade V union [Figure 7].

DISCUSSION

PRF is a fibrin clot with high concentration of platelets used as osteoinductive with AGFs. Over the last few years, some hemocomponents have been widely used in clinical spine surgery practice. This has diverted the attention to the role of platelets in healing process.[11] The majority of clinical studies have focused on platelet gel, and important results have already been obtained in terms of osteoinduction.[12]

In spinal surgery, the use of platelet gel has been employed in spinal fusion procedures. In 1999, Lowery *et al.* described a series of 19 patients in a retrospective review of AGFs combined with autograft and hydroxyapatite as an extender in posterior and anterior lumbar fusion. The authors reported a 100% fusion rate based on surgical

Table 3: Postoperative complications ($n=20$)

	PRF group, *n* (%)	NonPRF group, *n* (%)
Postoperative blood transfusion	4 (20)	3 (15)
Superficial infection	2 (10)	3 (15)
Failed screw (misplaced)	1 (5)	1 (5)
Dural tear	0	0
Deep infection	0	0
Need for revision surgery	0	0

PRF - Platelet-rich fibrin

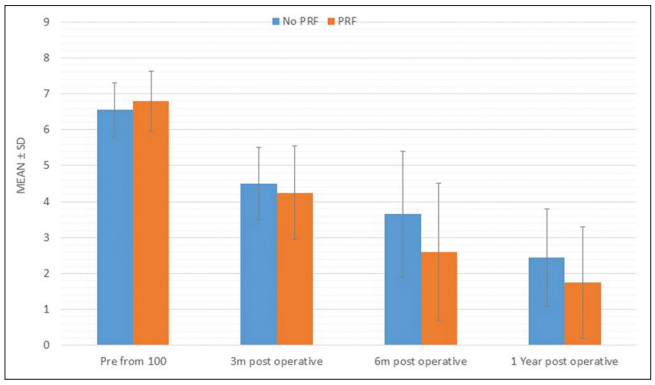

Figure 4: Back pain VAS over 12-month follow-up

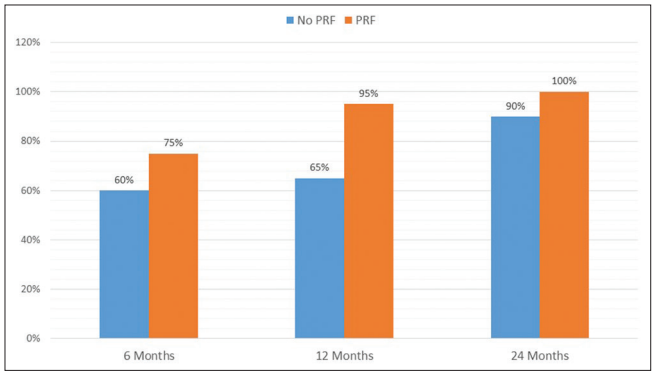

Figure 6: Radiological outcome in 2-year follow-up

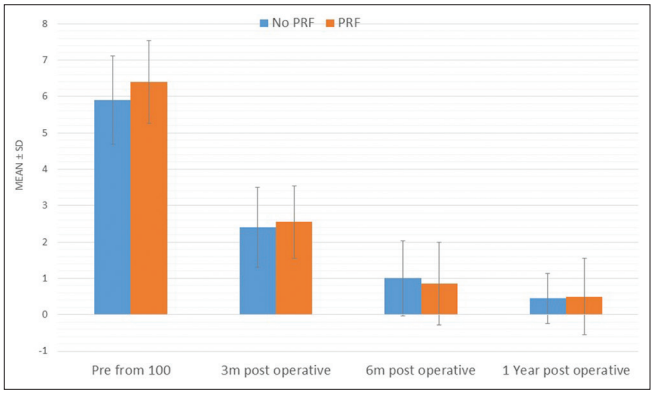

Figure 5: Leg pain VAS over 12-month follow-up

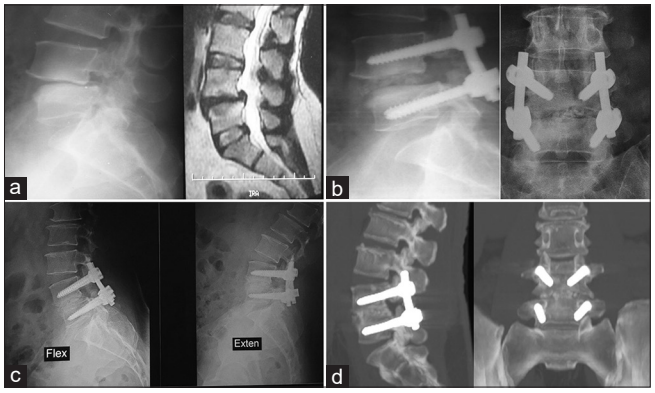

Figure 7: (a) Preoperative X-ray and magnetic resonance imaging. (b) Postoperative X-ray. (c) Follow-up X-ray 1-year lumbosacral spine lateral flexion and extension. (d) Follow-up computed tomography 1 year: Fusion Grade V

exploration in 5 patients and on plain X-ray films in 14 patients.[13]

In 2002, Bose and Balzarini described 60 cases of spinal fusion using AGF with autograft and reported a 96% fusion rate based on plain radiographic evidence.[14]

In 2003, Weiner and Walker reported on a retrospective study comprising the two groups of patients who had undergone single-level intertransverse fusion. A 62% fusion rate was observed in 32 patients in whom autogenous iliac crest graft augmented with AGF was used, compared to a 91% fusion rate in a group with bone graft alone. Their evaluation was based on flexion/extension radiographs.[15]

In 2003, Hee *et al*. evaluated the effects of AGF combined with autograft in transforaminal lumbar interbody fusion performed in 23 patients: they compared these results with those obtained in a group of 111 patients treated by autograft alone, with a minimum follow-up of 2 years. Radiographic evaluation was performed at 4, 6, and 24 months, with more rapid incorporation of fusion at 4 and 6 months in AGF patients. At 24-month evaluation, no significant differences in fusion rate were detected. The authors concluded that AGF was capable of promoting graft incorporation, thus stimulating faster fusion.[16]

In 2005, Jenis *et al*. described a study in which 37 consecutive patients were submitted to anterior lumbar interbody–PLIF with bone graft harvested from the iliac crest (22 patients) or allograft combined with AGF (15 patients). Patients were evaluated at 6 and 12 months by CT scan and at 24 months by plain X-rays. The results at 12 and 24 months demonstrated an 85% fusion rate in patients with autograft in comparison to an 89% rate with allograft and AGF. The authors concluded that allograft with AGF could represent a valid alternative to homologous fusion.[17]

In 2006, Carreon *et al*. reported that a series of 76 patients were treated with noninstrumental posterolateral arthrodesis using autologous bone with AGF, and the results were compared to those obtained in a group of patients treated with noninstrumental posterolateral arthrodesis using autologous bone alone. A 25% nonfusion rate was observed in the AGF group compared to 17% in the control group. The authors concluded by recommending the use of autologous bone graft because it guarantees a higher rate of fusion.[18]

In 2011, Landi *et al*. reported that a case series of 14 patients treated with a traditional PLF was performed in the left half of the operative field and a PLF with autograft and platelet gel in the right half. This technique made it possible to directly compare the two systems in each single patient, eliminating variability due to individual clinical conditions favoring nonfusion, such as smoking and diabetes. Evaluation of fusion was in the base of CT images. CT scan at 3 and 6 months after surgery documented a modest increase of bone density in fusion stimulated by platelet gel compared to that stimulated by autologous/heterologous bone alone, demonstrating a faster bone deposition during the first 3 months after surgery.[11]

In 2015, Elder *et al*. systematically reviewed all studies regarding PRP and PRF in spinal fusion from January 1990 to September 2014. The systematic review included both human and animal studies. They concluded that platelet gel may be a promising strategy in the future, particularly to its low cost, low-risk profile, and low complication rate. At this time, there is insufficient evidence to recommend its widespread use in spinal fusion surgery.[19]

In our study, the technique of using PRF was simple and cost-effective. The union rate was higher in the PRF group as well as better clinical outcome with no difference in postoperative complications.

CONCLUSIONS

The use of PRF in lumbar interbody fusion is still controversial, but it is proved in general for promoting bony union. Our study reports that PRF increases the rate of fusion in low-grade lytic spondylolisthesis and improves the clinical outcome in short-term follow-up. Moreover, its wide availability and low cost make it easy and cheap to use. Enhanced bone deposition means that patients recover faster and have less need of orthosis protection, less incidence of pseudoarthrosis, and rapid return to daily life activities. The ideal candidate for this procedure is low-grade lytic spondylolisthesis with long-standing low back pain.

Limitations of the study

This is a retrospective study. Our reported sample size is also relatively small with short-term follow-up, and as such, caution should be exercised when interpreting the results of the regression analysis, since the incorporation of multiple variables from a small number of patients may hide significant relationships between variables and pain improvement. This study did not compare of other biomechanical factors, i.e., disc height, foraminal height, and lordotic angle, which are important to measure long-term outcomes and adjacent segment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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