

1 **Abstract:**

2 Lateral Ankle sprain (LAS) is a common sports injury associated with recurrent ankle sprain,  
3 chronic ankle instability (CAI) and post-traumatic ankle osteoarthritis (PTOA). Platelet Rich  
4 Plasma (PRP) has been increasingly used for therapeutic applications in sports-related injuries,  
5 and is thought to stimulate tissue healing. We reported a case of LAS with complete tear of  
6 anterior talofibular ligament, which showed complete healing of ligament and early ankle  
7 stabilization after PRP. The healing is supported by dynamic ultrasound images and magnetic  
8 resonance imaging. We therefore proposed that PRP may serve as an alternative non-surgical  
9 treatment option in LAS in future research, with the potential to prevent the development of CAS  
10 and PTAO.

11 **Key words:**

12 Platelet Rich Plasma, Lateral Ankle Sprain, Anterior talofibular ligament tear, Ultrasound, Case  
13 reports.

14

15 **Introduction:**

16 Lateral ankle sprain (LAS) is the most common musculoskeletal injury in the physically active  
17 population; it is also a common condition in the general population (1). Apart from the pain and  
18 temporary period of reduced functioning and disability, it is also associated with increased risk of  
19 recurrent ankle sprain, the development of chronic ankle stability (CAI) and post-traumatic ankle  
20 osteoarthritis (PTOA). While the direct costs for treatment of an isolated LAS are relatively low,  
21 compounding these are indirect costs from follow up care, loss of productivity, time loss of  
22 activity and care of its long-term consequences. Therefore, it becomes apparent that the

23 healthcare burden that emerges from so called “simple” LAS is substantial.

24

25 Conservative management and early functional rehabilitation remain to be the standard of care  
26 for all grades of LAS. Platelet-rich plasma (PRP) is an autologous derivative of whole blood that  
27 stimulates a supra-physiological release of growth factors to jump start healing in chronic  
28 injuries. Growth factors are released from the alpha granules of platelets which induce  
29 chemotaxis, cell migration, angiogenesis, proliferation, differentiation and matrix production (2).  
30 PRP is progressively emerging at the forefront of sports and rehabilitation medicine, and its role  
31 in different soft injuries has become the focus of research in recent years.

32

33 Despite the popularity of PRP research, little was known about its role in the management of  
34 LAS. Therefore, we reported a case of high grade LAS with complete tear of the left anterior  
35 talofibular ligament (ATFL), its speedy healing and the early achievement of ankle stability after  
36 a single injection of PRP. The healing progress was supported by dynamic ultrasound and  
37 magnetic resonance imaging (MRI).

38

### 39 **Methods:**

#### 40 *Patient information:*

41 Consent for this publication has been obtained from the patient.

42 This is a case of a 39 years old enthusiastic runner who sprained his left ankle on 13<sup>th</sup> March  
43 2016. He first consulted his family doctor on 14<sup>th</sup> March with prescription of oral analgesics and  
44 a referral of physiotherapy. However, he was eager to recover soon for his running; therefore, he  
45 was referred to us on 22<sup>nd</sup> of March 2016 for the consideration of PRP injection. His pain

46 improved after a week of oral analgesic and rest. Physical examination found significant swelling  
47 over the left lateral ankle with moderate tenderness and ecchymosis. The talar tilt test was  
48 positive, which signified lateral ankle laxity.

49

50 *Diagnostic assessment:*

51 MRI was done on 15<sup>th</sup> March 2016 which confirmed the complete tear of ATFL with small to  
52 medium joint effusion; other ligaments and tendons were intact. [Figure 1a] Ultrasound was  
53 performed on 22<sup>nd</sup> March which showed significant discontinuation of compact fibrillar pattern  
54 of the ATFL compatible with complete tear. [Figure 1b] On dynamic scanning with left ankle  
55 inversion, there was gapping of the discontinuation of ligament and laxity was clearly  
56 demonstrated. [Video 1]

57

58 *Intervention:*

59 PRP injection was conducted on 24<sup>th</sup> March with Harvest SmartPrep System. 30ml venous blood  
60 was drawn and the blood product was then put into the centrifuge machine for centrifugation.  
61 Three ml of PRP was harvested and used for injection. Before the PRP injection, 0.5 ml of 10%  
62 Calcium Chloride was injected prior to the injection to activate the PRP; after that, three ml of  
63 the PRP was injected under ultrasound guidance to the tear site of the ATFL. A cast was used to  
64 immobilize the ankle for four weeks and patient was advised to have non-weight bearing  
65 walking.

66

67 *Follow up and outcomes:*

68 The patient was followed up four weeks after the PRP injection. No adverse side effect was

69 reported. Dynamic ultrasound scan showed no more gapping at the tear site. [Video 2] The cast  
70 was removed and he was advised to start active ankle mobilization exercise. At eight-week post  
71 PRP injection, dynamic ultrasound scan confirmed the absence of ATFL laxity and gapping, and  
72 the patient started on simple jogging activity. [Video 3] The patient was last seen on 19<sup>th</sup> August,  
73 around six months after the initial injury. There was no more ankle pain and he was running one  
74 hour every day without any sense of instability. Repeated USG showed healed ATFL. [Figure 1c]  
75 MRI was repeated on 25<sup>th</sup> August which showed that the ATFL was thickened to about twice the  
76 normal thickness because of healing, and the overall continuity was well maintained. [Figure 1d]

77

#### 78 **Discussion:**

79 Lateral ligament insufficiency secondary to LAS is one of the most frequently encountered  
80 musculoskeletal injuries. Despite the high prevalence and severity of lifestyle-limiting symptoms  
81 that follow the acute episode, LAS is often considered as an innocuous injury that will heal  
82 expediently and many patients received neither supervised nor professional administered care  
83 (3,4). It has been reported that up to 70% of individuals with history of ankle sprain have some  
84 type of residual and chronic symptoms, recurrent ankle sprains and perceived instability (5,6). A  
85 recent large longitudinal prospective study has examined the onset of sensorimotor deficits  
86 following a LAS, and has demonstrated that CAI may begin shortly after the acute sprain injury,  
87 with postural control deficits and multiple aberrant movement patterns during a variety of  
88 functional tasks (7). The chronic joint instability together with the osteochondral lesions  
89 eventually may lead to the development of PTOA (8), along with decreases in physical activity  
90 levels and health-related quality of life (9,10).

91

92 Conservative management and early functional rehabilitation remain to be the standard of care  
93 for all grades of LAS (11). However, the negative consequences of LAS are concerning, and  
94 improved efforts to address these conditions is essential. In view of this, the International Ankle  
95 Consortium had presented the Consensus Statement in 2016 which established the burden of  
96 LAS and its mid-term and long-term consequences, and called for prevention and early  
97 management of LAS. It also encouraged research to determine the optimal treatment of LAS  
98 with ultimate goal to improve global musculoskeletal health. It is believed that timely  
99 intervention and early restoration of biomechanical deficits will be the optimal treatment of LAS  
100 and prevention of CAI and PTOA (12).

101

102 The clinical evidence of PRP on soft tissue healing and repair is so far convincing; randomized  
103 controlled trial has demonstrated positive beneficial effect of PRP on patella tendinopathy (13)  
104 and the strongest level one evidence of PRP is found in the management of refractory tennis  
105 elbow with long term pain reduction and functional improvement (14). A systematic review (SR)  
106 conducted in 2014 evaluated the role of PRP in different foot and ankle pathologies; however, all  
107 the seventeen included studies did not include LAS as the pathology for treatment (15).

108

109 The strength of the current case report is that the healing of ATFL was supported with ultrasound  
110 and MRI images, and early ankle stabilization was supported with dynamic ultrasound images.  
111 Our results add to the growing evidence of PRP on soft tissue healing; we also suggest the  
112 possible beneficial effect of PRP in regaining ligamentous strength, reducing ligament laxity and  
113 achieving early ankle stability, which are essential elements in the management of LAS. Future  
114 randomized controlled trials may consider evaluating the long-term ankle stability in LAS after

115 PRP, its use in different severity of ankle sprain, and the role of it versus surgical reconstruction  
116 in complete ATFL tear refractory to conservative management.

117

118 **Conclusions:**

119 Our report suggested that PRP not only allows healing of the torn ligament, but also hastens its  
120 strength recovery. We believed that together with appropriate rehabilitation training, PRP may  
121 enhance early ankle stabilization in LAS, prevent the development of CAI and PTOA; it may  
122 also serve as an alternative non-surgical treatment option in the management of high grade LAS  
123 not responding to conservative therapy.

124

125 **Patient consent:**

126 An inform written consent was obtained from the study participant.

127

128 **Disclosure:**

129 The authors report no conflict of interest concerning the materials or methods used in this study  
130 or the findings specified in this paper.

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138 **References:**

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- 140 1. Doherty C, Delahunt E, Caulfield B, Hertel J, Ryan J, Bleakley C. The incidence and  
141 prevalence of ankle sprain injury: a systematic review and meta-analysis of prospective  
142 epidemiological studies. *Sports Med.* 2014;44(1):123-140.
- 143 2. Boswell SG, Cole BJ, Sundman EA, Karas V, Fortier LA. Platelet-Rich Plasma: A Milieu  
144 of Bioactive Factors. *Arthroscopy.* 2012;28(3):429-439.
- 145 3. Kaminski TW, Hertel J, Amendola N, Docherty CL, Dolan MG, Hopkins JT, Nussbaum  
146 E, Poppy W, Richie D. National Athletic Trainers' Association position statement:  
147 conservative management and prevention of ankle sprains in athletes. *J Athl Train.*  
148 2013;48(4):528-545.
- 149 4. McKay GD, Goldie P, Payne WR, Oakes B. Ankle injuries in basketball: injury rate and  
150 risk factors. *Br J Sports Med.* 2001;35(2):103-108.
- 151 5. Anandacoomarasamy A, Barnsley L. Long term outcomes of inversion ankle injuries. *Br*  
152 *J Sports Med.* 2005;39(3):e14-e14.
- 153 6. Konradsen L, Bech L, Ehrenbjerg M, Nickelsen T. Seven years follow-up after ankle  
154 inversion trauma. *Scand J Med Sci Sports.* 2002;12(3):129-135.
- 155 7. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Recovery from a first-  
156 time lateral ankle sprain and the predictors of chronic ankle instability: a prospective  
157 cohort analysis. *Am J Sports Med.* 2016;44(4):995-1003.
- 158 8. Golditz T, Steib S, Pfeifer K, Uder M, Gelse K, Janka R, Hennig FF, Welsch GH.  
159 Functional ankle instability as a risk factor for osteoarthritis: using T2-mapping to  
160 analyze early cartilage degeneration in the ankle joint of young athletes. *Osteoarthr.*

- 161            *Cartil.* 2014;22(10):1377-1385.
- 162    9.        Hubbard-Turner T, Wikstrom EA, Guderian S, Turner MJ. An acute lateral ankle sprain  
163            significantly decreases physical activity across the lifespan. *J Sports Sci Med.*  
164            2015;14(3):556.
- 165    10.        Arnold BL, Wright CJ, Ross SE. Functional ankle instability and health-related quality of  
166            life. *J Athl Train.*2011: 46(6):634-641.
- 167    11.        Doherty C, Bleakley C, Delahunt E, Holden S. Treatment and prevention of acute and  
168            recurrent ankle sprain: an overview of systematic reviews with meta-analysis. *Br J Sports*  
169            *Med.* 2016;51(2):113-125.
- 170    12.        Gribble PA, Bleakley CM, Caulfield BM, Docherty CL, Fourchet F, Fong DT, Hertel J,  
171            Hiller CE, Kaminski TW, McKeon PO, Refshauge KM, Verhagen EA, Vicenzino BT,  
172            Wikstrom EA, Delahunt E. 2016 consensus statement of the International Ankle  
173            Consortium: prevalence, impact and long-term consequences of lateral ankle sprains. *Br J*  
174            *Sports Med.* 2016;50(24):1493-1495.
- 175    13.        Dragoo JL, Wasterlain AS, Braun HJ, Nead KT. Platelet-Rich Plasma as a Treatment for  
176            Patellar Tendinopathy A Double-Blind, Randomized Controlled Trial. *Am J Sports Med.*  
177            2014;42(3):610-618.
- 178    14.        Mishra AK, Skrepnik NV, Edwards SG, Jones GL, Sampson S, Vermillion DA, Ramsey  
179            ML, Karli DC, Rettig AC. Efficacy of platelet-rich plasma for chronic tennis elbow: a  
180            double-blind, prospective, multicenter, randomized controlled trial of 230 patients. *Am J*  
181            *Sports Med.* 2014;42(2):463-471.
- 182    15.        Vannini F, Di Matteo B, Filardo G, Kon E, Marcacci M, Giannini S. Platelet-rich plasma  
183            for foot and ankle pathologies: A systematic review. *Foot and Ankle Sur.* 2014;20(1):2-9.



184 **Figure captions:**

185 Figure 1a: Baseline MRI of ATFL before PRP injection

186 Figure 1b: Baseline USG of the ATFL before PRP injection

187 Figure 1c: USG of ATFL 6-month post PRP injection

188 Figure 1d: MRI of ATFL 6-month post PRP injection

189

190 MRI: Magnetic Resonance Imaging

191 ATFL: Anterior Talofibular Ligament

192 PRP: Platelet Rich Plasma

193 USG: Ultrasound