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Review article

# Current concepts on posterior meniscal root lesion: A treatment algorithm based on the currently available evidence

Guan-Yang Song, Jin Zhang, Xu Li, Yue Li, Hua Feng\*

Sports Medicine Service, Beijing Jishuitan Hospital, Number 31, Xin Jie Kou East Street, Xi Cheng District, Beijing, China

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#### Abstract

Meniscal root lesion is defined as an avulsion of the tibial insertion of the meniscus or a radial tear close to the meniscal insertion, which is commonly observed at the posterior region in the clinical practice. Although a number of biomechanical and clinical studies have shown the importance of the integrity of the posterior meniscal roots, the appropriate treatment is still controversial. The purposes of this review are to develop a current understanding of how the posterior meniscal root functions and to review the available treatment options for posterior meniscal root lesion.

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Keywords: current understanding; meniscal root; posterior meniscal root lesion; treatment options

#### Introduction

The meniscus roots describe the insertions of the anterior and posterior meniscal horns on the tibial plateau.<sup>1-4</sup> These structures are important for maintaining the functional integrity of the meniscus because they prevent meniscus extrusion under axial load, thereby converting the axial load to a radially directed force.<sup>5,6</sup> Meniscus root lesions are defined as an avulsion of the tibial insertion of the meniscus or a radial tear occurring within 1 cm from the meniscal insertion site,<sup>7</sup> which typically involves the posterior meniscus roots. Previous biomechanical and clinical studies have shown that the posterior meniscus root lesion (PMRL) resulted in a loss of hoop stresses and exposed joint cartilage to abnormal contact forces similar to those after total meniscectomy.<sup>8–10</sup> Increasing attentions have been paid towards the PMRL during the past decades.

\* Corresponding author. Sports Medicine Service, Beijing Jishuitan Hospital, Number 31, Xin Jie Kou East Street, Xi Cheng District, Beijing, China.

E-mail address: fenghua20080617@126.com (H. Feng).

According to the literature, the posterior medial meniscus root lesions (PMMRLs) are typically degenerative lesions and frequently found in isolation in middle-aged patients.<sup>11</sup> On the contrary, the posterior lateral meniscus root lesions (PLMRLs) are usually traumatic in nature and commonly found in combination with anterior cruciate ligament (ACL) injury in younger patients.<sup>12</sup>

Clinical diagnosis of the PMRL is both sensitive and specific because of the advancing technology in magnetic resonance imaging (MRI) and arthroscopy. However, treatment is somewhat still controversial. Some authors preferred the partial meniscectomy, because it considerably improved symptoms immediately after the surgery.<sup>13</sup> By contrast, because the meniscal roots are well vascularized, several newly developed treatment strategies including the arthroscopic-assisted repair techniques and even the nonoperative approaches have recently been reported.<sup>14–16</sup>

The purposes of this review are to (1) develop a current understanding of how the posterior meniscal root functions and (2) to review the available treatment options for posterior meniscal root lesion. A treatment algorithm will also be recommended based on the currently available evidence.

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#### Anatomy and biomechanics

There are four meniscal root anchors that firmly attach the medial and lateral menisci to the anterior and posterior tibial intercondylar region.<sup>1</sup> The anterior root of the medial meniscus inserts along the anterior intercondylar crest on the anterior slope of the tibia. The posterior root of the medial meniscus inserts just anterior and medial to the posterior cruciate ligament (PCL) on the posterior medial intercondylar eminence of the tibia. As for the lateral meniscus, the anterior root inserts just lateral to the ACL tibial insertion site. The posterior root inserts on the horizontal portion of the posterior intercondylar area on the posterior slope of the lateral tubercle (Fig. 1).<sup>7</sup> It should be noted that the insertion pattern of the posterior lateral root was described as more diverse and complex depending on the presence of the meniscofemoral ligament.<sup>17</sup>

The roots of both menisci play an important role for pressure distribution and absorption.<sup>9</sup> The normal axial forces applying on the medial and lateral meniscus tend to extrude the menisci radially. However, it is the meniscal roots that hold the menisci in place without radial extrusion. The radial extrusion of the meniscus is considered to be one of the major causes of decreased tibiofemoral contact area and increased load pressure on the joint cartilage.<sup>9,10</sup>

The biomechanical consequences of a PMRL have been examined in human cadaver specimen by various studies. Allaire et al<sup>18</sup> have shown that a PMMRL caused a 25% increase in peak contact pressure compared with the intact condition within the medial compartment. Schillhammer et al<sup>19</sup> have reported that a PLMRL resulted in a significant increase in peak contact pressure (49%) by decreasing the tibiofemoral contact area (33%). Interestingly, both studies demonstrated that an arthroscopic-assisted surgical repair of the PMRL reduced the peak tibiofemoral contact pressure back to the normal level, emphasizing the importance of the structural integrity of the posterior meniscal roots in preventing the degenerative changes of the joint cartilage.



Fig. 1. Diagram of the anatomic positions of the four meniscal root anchors (axial view).

#### Epidemiology and aetiology

In terms of the duration from injury to surgery, the PMRL can be generally divided into either an acute or chronic case. The acute PMMRL is a rare injury pattern, which has been reported to be associated with multiligamentous injuries especially with the medial collateral ligament and ACL tears in younger patients.<sup>20</sup> Instead, the majority of patients with PMMRL are isolated chronic knee injury cases, with older age and higher body mass index reported to be the major risk factors. Ozkoc et al<sup>21</sup> reported in their study that about 80% of patients with chronic PMMRLs were older than 50 years and either obese or morbidly obese. In addition, some authors have also observed a correlation between the PMMRLs and the varus malalignment of the lower extremity, which will result in higher forces over the medial compartment, leading to the degenerative osteoarthrosis.<sup>7,22</sup>

By contrast, most PLMRL cases are acute injury cases and commonly associated with the ACL tears. Brody et al<sup>12</sup> reported an incidence rate of 9.8% for the PLMRLs in 264 patients suffering from an ACL deficiency. Other studies have found the PLMRLs in 7–12% of patients with ACL injuries.<sup>23,24</sup>

#### Diagnosis

Based on the previous studies, the clinical diagnosis of PMRL is generally difficult. Although patients may experience joint line tenderness and present a positive McMurray test over the affected compartment, the clinical symptoms are not specific enough to make a definitive diagnosis.<sup>25</sup> Therefore, MRI and arthroscopy are necessary to make further evaluations.

Overall, the MRI is considered to be a sensitive assessment tool to investigate the PMRL. In detail, three different direct MRI signs for the diagnosis of a PMRL have been described by previous studies,<sup>26–28</sup> including the radial linear defect in the axial plane; the vertical linear defect (truncation sign) in the coronal plane (Fig. 2A); and the so-called "ghost meniscus sign" in the sagittal plane (Fig. 2B), with acceptable sensitivity and specificity values.

In addition, meniscal extrusion is considered to be an indirect MRI sign indicating the PMRL. The meniscus is defined as "extruded" when it extends beyond the tibial margin (Fig. 3). Choi et al<sup>26</sup> have found an association between pathologic medial meniscal extrusion and the PMMRL. In the study conducted by Pagnani et al,<sup>20</sup> most patients with the PMMRL have shown a positive medial meniscal extrusion sign. However, the meniscus extrusion as an indirect MRI sign might be less common in patients with PLMRL. Petersen et al<sup>29</sup> have attributed this to the presence of the meniscofemoral ligament, which might not result in abnormal lateral meniscal extrusion even if the PLMRL existed.

The posterior medial meniscal root can be clearly visualized through a standard anterolateral portal. Thorough evaluation of the root using a probe is necessary. In case of a PMMRL, the root can be lifted up by the probe or displaced

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Fig. 2. (A) Coronal T2-weighted magnetic resonance image (MRI) showing a vertical linear defect in the posterior medial meniscus (white arrow). (B) Sagittal T2-weighted MRI demonstrating a posterior "ghost meniscus" of the medial meniscus following a root tear (white arrow).

anteriorly into the joint space. Moreover, the Gillquist manoeuvre has been well described as an additional technique for visualizing the posterior horn of the medial meniscus. This involved placing the arthroscope beneath the PCL in the notch of the knee and directing the visual field over the meniscal root.<sup>3</sup> The posterior lateral meniscal root can be visualized through the anterolateral portal while the knee is placed in the figure-of-four position. An associated ACL tear permits easier visualization of the PLMRL, in which the arthroscope can be advanced into the posterolateral compartment through the notch.<sup>9,29</sup>

#### Treatment

#### Partial meniscectomy

Traditional treatment of the PMRL was partial meniscectomy. The surgical target of this intervention is the torn meniscal tissue, with predictable improvement in meniscal based symptoms. However, studies evaluating the clinical success of partial meniscectomy for symptomatic PMRLs are contradictory. Bin et al<sup>13</sup> reported that subjective symptoms improved significantly after arthroscopic partial meniscectomy of the PMMRLs. Whereas Han et al<sup>30</sup> reported unfavourable clinical results following partial meniscectomy for the treatment of PMMRLs and recorded early osteoarthritis (OA) after a follow up of 5–8 years.

#### Nonoperative treatment

Because the posterior meniscal roots are well vascularized, some authors also reported the rationale of the nonoperative treatment in treating the PMRLs, especially for the treatment of the PLMRLs, when the posterior meniscofemoral ligament was still intact.<sup>29</sup> Shelbourne et al<sup>24</sup> reviewed 33 patients with

the PLMRLs left *in situ* during ACL reconstruction and reported similar subjective and objective scores compared with the patients with intact meniscus at the time of ACL reconstruction. In addition, Lim et al<sup>31</sup> also reported significant symptomatic relief and functional improvement provided by the nonoperative treatment in most patients with PMMRLs.

#### Meniscus root repair

Considering the biomechanical consequences of the PMRLs and the rich vascularization of the posterior meniscal roots, many authors have started considering a surgical repair



Fig. 3. Coronal T2-weighted magnetic resonance imaging showing the medial meniscus, which is considered "extruded" when the meniscus extends beyond the tibial margin (region between the two white lines).

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Fig. 4. Arthroscopic side-to-side repair of the lateral meniscus root. (A) Lateral meniscal root tear. (B) A PDS suture (Ethicon, Johnson & Johnson, Livingston, UK) is passed through the torn meniscus and the posterior horn of the lateral meniscus using a suture hook, respectively. (C) Both ends of the PDS sutures were tied with a sliding knot, creating a vertical side-to-side suture. (D) Second-look arthroscopy shows a completely healed meniscus at the 2-year follow-up.

of the PMRLs as the best treatment option to restore the meniscus function and to prevent degenerative OA.

The criteria for selecting the ideal patients for posterior meniscal root repair are still a matter of considerable debate. Based on the aetiology, some authors insisted that the acute PLMRLs combined with the ACL tears are suitable to be repaired.<sup>23,24</sup> With special focus on the good blood supply to the posterior lateral meniscal roots and the existence of the



Fig. 5. Arthroscopic transtibial pull-out suture repair of the lateral meniscus root. (A) Lateral meniscal root tear. (B) A tibial anterior cruciate ligament guide is positioned at the anatomical attachment site of the posterior lateral meniscal root and then a tibial tunnel is drilled. (C) A FiberWire suture (Arthrex, Naples, FL, USA) is passed through the posterior lateral meniscus root and then pulled out of the tibial tunnel using a PDS suture loop. (D) Both ends of the FiberWire sutures are secured with a knot over an ENDOBUTTON (Smith & Nephew, Mansfield, MA, USA) on the tibial cortex, and the meniscal root is reduced to the tibial insertion site.

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intact posterior lateral meniscofemoral ligaments, the meniscus root repair is highly recommended in acute meniscal root injuries.

More questions exist about patients with chronic meniscal root tears and predominating OA. Moon et al<sup>32</sup> pointed out that the Outerbridge Grade 3 or 4 chondral lesions and varus malalignment > 5° were independent predictors for unsatisfied clinical outcome following PMMRLs. It seems that chronic PMRL and significant meniscal extrusion may be the result of OA changes, and therefore such patients are not the ideal cases for meniscal root repairs.

#### Surgical techniques

The goals of performing the meniscal root repair should emphasize on restoring the biomechanical functions of the meniscus to a normal level. Techniques for meniscal root repair are transtibial pull-out suture (Fig. 4) and side-to-side repair (Fig. 5). For posterior meniscal root refixation, the use of suture anchors has also been described. To date, all of these techniques can be performed arthroscopically.

#### **Clinical outcomes**

Clinical data following an indexed surgical strategy in treating the PMRL are limited. Most studies are either Level III retrospective comparative or Level IV care series studies with relatively short-term follow-up time. We tried to summarize the currently available literature reporting on the clinical outcomes after treatments of the PMRLs based on the following information: (1) preoperative conditions of the patients; (2) indexed surgical option; (3) subjective clinical results; and (4) objective clinical findings (Tables 1-3).

Table 1 presents data of clinical outcomes collected after indexed treatments of PLMRLs. All of the included studies reported favourable objective and subjective clinical outcomes after either arthroscopic surgical repair technique or nonoperative management. The PLMRLs have been shown in previous literature to be more common in acute ACL injuries, when the meniscal tissue is still suitable for a surgical repair. In addition, some authors have pointed out that the bleeding from the bone marrow during ACL reconstruction may somewhat enhance the healing capability of the meniscus after the repair surgeries. Furthermore, because the posterior root of the lateral meniscus is well vascularized, it will promote the self-healing process even if the torn meniscal tissue was left in situ, and this self-healing process was evaluated by Shelbourne et al.<sup>24</sup> However, it should be noted that a significant worsening of the lateral joint space narrowing was still detected on the follow-up radiographic measurement in their study, which raised a question as to whether the quality and biomechanical strength of the self-healing PLMRLs would reduce the contact force of the lateral compartment back to the normal level. Therefore, further studies are still needed.

Table 2 summarizes the current clinical outcomes after the treatments of PMMRLs. Unlike the PLMRLs, the PMMRLs are more common in older patients with a chronic history of

Study	No. of knees	Time from injury to surgery (mo)	Diagnosis	Indexed treatments for PLMRTs	Follow up (mo)	Outcome measures	Results
Ahn et al <sup>33</sup>	29	35.8	PLMRL + ACL	All arthroscopic side-to-side repair	18.0	IKDC, Lysholm second-look arthrosconv	IKDC and Lysholm improved; complete healing on second-look arthroscony: 8/8
Lee et al <sup>34</sup>	G <sub>1</sub> : 27 G <sub>3</sub> : 27	G <sub>1</sub> : NA G <sub>2</sub> : NA	G <sub>1</sub> : PLMRL + ACL G <sub>2</sub> : ACL	G <sub>1</sub> : Left <i>in situ</i> G <sub>2</sub> : NA	G <sub>1</sub> : 36.5 G <sub>2</sub> : 37.3	IKDC, Lysholm, Tegner, MRI second-look arthroscopy	IKDC, Lysholm and Tegner improved with NS between groups: complete
	4	i i i	4		4		healing on MRI in G <sub>1</sub> : 12/15; complete healing on second-look arthroscopy in G <sub>1</sub> : 12/15
Shelbourne et al <sup>24</sup>	G <sub>1</sub> : 33 G <sub>2</sub> : 33	G <sub>1</sub> : NA G <sub>2</sub> : NA	$G_1$ : PLMRL + ACL $G_2$ : ACL	G <sub>1</sub> : Left <i>in situ</i> G <sub>2</sub> : NA	G <sub>1</sub> : 127.2 G <sub>2</sub> : 1260	IKDC, X-ray	IKDC improved, NS between groups I ateral ioint snace narrowino: G, > G,
Anderson et al <sup>35</sup>	24	22.4	PLMRL + ACL	All arthroscopic side-to-side repair: eight transtibial pull-out suture: 16	59.2	IKDC, Lysholm, Tegner	IKDC, Lysholm and Tegner all improved
Ahn et al <sup>23</sup>	25	40.8	PLMRL + ACL	All arthroscopic side-to-side repair	18.0	IKDC, Lysholm, MRI second-look arthroscopy	IKDC, Lysholm improved NS in reduction of coronal extrusion on MRI Complete healing on second-look arthroscopy: 9/9

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Table

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Table 2

Clinical outcomes after indexed treatments of posterior medial meniscal root lesions.

Study	No. of knees	Diagnosis	Indexed treatments for PMMRTs	Follow up (mo)	Outcome measures	Results
Ozkoc et al <sup>21</sup>	70	PMMRL + low-grade knee OA	Partial meniscectomy	56.7	Subjective satisfaction, Lysholm, X-ray, MRI	Subjectively satisfied; Lysholm improved; worsening JSN on X-ray; NS in reduction of meniscal extrusion on MRI
Lee et al <sup>36</sup>	21	PMMRL	Transtibial pull-out suture repair	31.8	HSS, Lysholm, X-ray, second-look arthroscopy	HSS, Lysholm improved; no worsening JSN on X-ray; complete healing on second-look arthroscopy: 10/10
Seo et al <sup>37</sup>	11	PMMRL	Transtibial pull-out suture repair	13.4	Subjective satisfaction, Lysholm, HSS, X-ray, second-look arthroscopy	Subjectively satisfied; Lysholm, HSS improved; no worsening JSN on X-ray; incomplete healing on second-look arthroscopy: 9/11
Kim et al <sup>38</sup>	G <sub>1</sub> : 30 G <sub>2</sub> : 28	G <sub>1</sub> : PMMRL G <sub>2</sub> : PMMRL	G <sub>1</sub> : Transtibial pull-out suture repair G <sub>2</sub> : Partial meniscectomy	G <sub>1</sub> : 48.5 G <sub>2</sub> : 46.0	IKDC, Lysholm, X-ray for both groups; MRI and second-look arthroscopy for $G_1$	IKDC, Lysholm improved, $G_1 > G_2$ worsening JSN on X-ray: $G_2 > G_1$ ; complete or partial healing on MRI (28/30) and on second-look arthroscopy (12/14) in $G_1$
Han et al <sup>30</sup>	46	PMMRL + low-grade knee OA	Partial meniscectomy	78	Subjective satisfaction, Lysholm, X-ray	Only 67% subjectively satisfied; Lysholm improved; 35% showed worsening JSN on X-ray
Lim et al <sup>31</sup>	30	PMMRL + low-grade knee OA	Nonoperative (NSAIDs) + muscle strengthening exercise	36	Subjective satisfaction, IKDC, Lysholm, VAS, X-ray	Subjectively satisfied; IKDC, Lysholm improved; VAS decreased; No worsening JSN on X-ray
Jung et al <sup>39</sup>	13	PMMRL	Arthroscopic suture anchor repair	30.8	Subjective satisfaction, Tegner, Lysholm, MRI	Subjectively satisfied; Tegner, Lysholm improved; complete or partial healing on MRI: 9/10
Moon et al <sup>32</sup>	51	PMMRL	Transtibial pull-out suture repair	33.0	AKS, Lysholm, VAS, MRI	AKS, Lysholm improved; VAS decreased; complete healing on MRI: 28/31
Neogi et al <sup>40</sup>	33	PMMRL + low-grade knee OA	Nonoperative (NSAIDs)+Muscle strengthening exercise	35.0	Lysholm, Tegner, VAS, X-ray	Lysholm, Tegner improved; VAS decreased; worsening JSN on X-ray
Kim et al <sup>41</sup>	G <sub>1</sub> : 22 G <sub>2</sub> : 23	G <sub>1</sub> : PMMRL G <sub>2</sub> : PMMRL	$G_1$ : Arthroscopic suture anchor repair $G_2$ : Transtibial pull-out suture repair	G <sub>1</sub> : 25.9 G <sub>2</sub> : 26.8	Subjective satisfaction; IKDC, Lysholm, HSS, X-ray, MRI	Subjectively satisfied; IKDC, Lysholm, HSS improve, NS between groups; no worsening JSN on X-ray and NS in healing rate of meniscus on MRI between groups

AKS = American Knee Society Knee and Function Scores;  $G_1 = \text{Group 1}$ ;  $G_2 = \text{Group 2}$ ; HSS = Hospital for Special Surgery Scores; IKDC = International Knee Documentation Committee; JSN = joint space narrowing; MRI = magnetic resonance imaging; NA = not available; NS = no significant difference; NSAIDs = nonsteroidal anti-inflammatory drugs; OA = osteoarthritis; PMMRL = posterior medial meniscus root lesion; PMMRT = posterior medial meniscus root tear; VAS = visual analogue scale.

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Table 3	
Clinical outcomes of the meniscal coronal extrusion on MRI	

Study	No. of knees	Diagnosis	Preop mean extrusion (mm)	Indexed treatment	Postop mean extrusion (mm)	Significant difference
Ahn et al <sup>23</sup>	25	PLMRL	0.73	Arthroscopic side-to-side repair	0.34	N
Pula et al <sup>42</sup>	22	PLMRL	0.80	NA	NA	NA
Brody et al <sup>12</sup>	26	PLMRL	2.60	NA	NA	NA
Kim et al <sup>38</sup>	30	PMMRL	3.13	Transtibial pull-out suture repair	2.94	Ν
Jung et al <sup>39</sup>	10	PMMRL	3.90	Arthroscopic suture anchor repair	3.50	Ν
Kim et al <sup>41</sup>	G <sub>1</sub> : 17	G <sub>1</sub> : PMMRL	G <sub>1</sub> : 4.30	G <sub>1</sub> : Arthroscopic suture anchor repair	G <sub>1</sub> : 2.10	$G_1$ : Y
	G <sub>2</sub> : 14	G <sub>2</sub> : PMMRL	G <sub>2</sub> : 4.10	G <sub>2</sub> : Transtibial pull-out suture repair	G <sub>2</sub> : 2.20	G <sub>2</sub> : Y
Moon et al <sup>32</sup>	31	PMMRL	3.60	Transtibial pull-out suture repair	5.00	Y

 $G_1 = Group 1$ ;  $G_2 = Group 2$ ; MRI = magnetic resonance imaging; N = no; NA = not available; PLMRL = posterior lateral meniscal root lesion; PMMRL = posterior medial meniscal root lesion; postop = postoperative; preop = preoperative; Y = yes.

symptoms, which is usually associated with knee OA. Partial meniscectomy was traditionally preferred in treating the PMMRLs because of its effectiveness in relieving the meniscal based symptoms. In Table 2, most of the patients reported significant improvement in the satisfactory outcomes and functional scores at the final follow up. However, significant

progressions of the medial joint narrowing were also frequently shown on the radiographic measurements after partial meniscectomy, which should be taken into consideration prior to making the surgical plans.

Recently, there is a growing interest in using arthroscopic surgical repair techniques in treating the PMMRLs. The



Fig. 6. Treatment algorithm. PLMRL = posterior lateral meniscal root lesion; PMFL = posterior meniscofemoral ligament; PMMRL = posterior medial meniscal root lesion.

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primary goal of meniscal repair is to restore the hoop tension of the meniscus and prevent the progression of the degenerative knee OA. Although some authors have pointed out that the posterior medial meniscal roots are almost impossible to be repaired because of the presence of degenerative meniscal tissue and low healing potential, most of the studies analysed in Table 2 still showed favourable subjective patients' satisfaction outcomes and the objective clinical results after the meniscal surgical repair procedures. However, as Moon et al<sup>32</sup> concluded, Outerbridge Grade 3 or 4 chondral lesions and varus alignment of > 5° were found to independently predict an inferior clinical outcome after the meniscal surgery, and one should also be cautious when choosing the appropriate candidate for the arthroscopic meniscal repair procedures.

Another important issue is whether the surgical repair of PMRLs would significantly reduce the postoperative meniscal extrusion on MRI assessments. Results shown in Table 3 demonstrated inconsistent clinical findings among studies. In general, most of the included studies reported that no significant reduction would be obtained in terms of the meniscal extrusion after the surgical repair of PMRLs postoperatively.<sup>23,38,39</sup> Surprisingly, Moon et al<sup>32</sup> even reported a significant increase of the medial meniscal extrusion after the transtibial pull-out suture repair surgery. The different outcomes might be attributed to the following reasons: (1) the reported rates of complete healing of the meniscus within studies were different among studies, which would influence the degree of meniscal extrusions; (2) some important risk factors of patients, such as obesity, varus malalignment, and preoperative high-grade chondral lesions, which might adversely impact the clinical outcomes of meniscal surgical repair should be excluded prior to evaluating the real clinical relevance of meniscal extrusion; and (3) the contributing role of the PMFLs in restraining the lateral meniscal extrusion is still a matter of considerable debate.

#### Conclusion

The PMRLs are injuries that cause devastating biomechanical consequences of the knee joints with respect to the mid-long-term progression of degenerative knee OA. Most cases of PMMRLs are due to a chronic and degenerative actiology, whereas the PLMRLs are always combined with the acute ACL injuries. Because of the good blood supply to the posterior meniscal root region, patients with acute PMRLs are considered to be the ideal candidates for surgical repair. Recently, several arthroscopic-assisted meniscal repair techniques for the treatment of PMRLs have been introduced. We tried to recommend a treatment algorithm of PMRLs based on the currently available evidence (Fig. 6). However, it should be noted that there is still a lack of clinical studies with a high level of evidence to prove the superiorities of the meniscal surgical repair compared with the nonoperative or partial meniscectomy procedures. Therefore, further studies are needed to clarify the real indications as well as the contraindications for meniscal root repair and to define an optimal treatment strategy.

#### **Conflicts of interest**

The authors declare that they have no financial or nonfinancial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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