Medial meniscus posterior root repair delays but not avoids histological progression of osteoarthritis: randomized in vivo experimental study

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Conflicting interest

L.D and II.LT declared no potential conflicts of interest.

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Compliance with ethical standards

The research complies with national legislation and was approved by the animal protection service and institutional review boards of the authors' affiliated institutions as well as the regional ethics committee (12216062369184208100087).

Authors´contribution

LD and II LT conceived the original idea, carried out the experiments, were in charge of overall direction and planning of the study, acquisition, analysis, interpretation of data, and drafting the manuscript.

EC contributed the original idea, helped carry out the experiment, provided critical feedback and helped shape the research. Helped with analysis, interpretation of the data, critical revision of the article for important intellectual content and final approval of the version to be submitted.

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Abstract

Objectives: The purpose of this study was twofold: (1) to describe and compare histopathological results of 3 different treatment options for medial meniscus posterior root tear: nonoperative management; partial meniscectomy, and meniscal root repair; and (2) to test the hypothesis that meniscal root tears treated conservatively predispose to a lower risk of osteoarthritic progression compared to partial meniscectomy.

Methods: Posteromedial meniscal root tears were carried out in 39 New Zealand White (NZW) rabbits. The animals were randomly assigned into three experimental groups: partial meniscectomy after root tear (PM, n=13); root tear left in situ (CT, n=13); and transtibial root repair (RR, n=13). Contralateral limbs were used as healthy controls. The animals were euthanized at 16 weeks postoperatively; tissue samples of femoral and tibial articular cartilage were collected and processed for macro and microscopic assessment to detect signs of early osteoarthritis (OA). Each sample was histopathologically assessed using the Osteoarthritis Research Society International (OARSI) grading and staging system.

Results: Osteoarthritic changes were the hallmark in all three experimental groups. The root repair group had the lowest scores for cartilage damage (2.5; 2-3) and the meniscectomy group exhibited higher and more severe sighs of OA (16; 9-16) compared to the conservative treatment group (5; 4-6). Between group comparison revealed significant differences as the PM group showed significantly higher rate macro and microscopic osteoarthritic changes compared to the RR ($p< 0.001$) and CT group (< 0.001). The weight-bearing area of the medial femoral condyle was the most severely affected and tidemark disruption was evident in all tissue samples.

Conclusion: Meniscus root repair could not completely arrest histopathological progression of knee OA but lead to significantly less severe degenerative changes than partial meniscectomy and nonoperative treatment. Partial meniscectomy leads to the most severe osteoarthritic progression while stable radial tears left in situ presented lower OA progression compared with partial meniscectomy.

Keywords: meniscal root tears, knee osteoarthritis, cartilage, animal model, experimental study

What are the new findings

- ✓ Meniscus root repair could not completely arrest histopathological progression of knee OA but lead to significantly less severe degenerative changes than partial meniscectomy and nonoperative management.
- ✓ Partial meniscectomy leads to the most severe osteoarthritic progression while stable radial tears left in situ presented lower OA progression compared with partial meniscectomy.
- ✓ The findings of the current study aid to set realistic expectations in medial meniscus posterior root injuries. This knowledge can help to develop and test the efficacy of future augmented techniques.

1. Introduction

It was estimated that approximately 14 million people in the USA have symptomatic knee OA, and this number is expected to reach 78 million by the year 2040 [1]. More than half of individuals with symptomatic knee OA are younger than 65 years [1-2]. Current practice demands a greater emphasis on OA prevention, early diagnosis, and treatment to arrest or delay disease progression.

Meniscal roots are critical structures for the knee stability, for load transmission, and shock absorption. The field of meniscal root preservation has undergone significant advancement over the past decades; however, the challenge remains to fully understand whether the meniscal root repair can ultimately arrest or delay osteoarthritic changes. There is a need to better understand the etiopathology of this type of injury in order to develop therapeutic approaches which not only relieve painful symptoms of OA but prevent disease progression.

Experimental research in humans involves different ethical concerns. In the face of such challenges, prospective, randomized, and experimental studies in animal model are now being pursued. Large animal models remain a cornerstone to validate, improve, and to aid early diagnosis of OA providing potential means to detect pathology at an earlier stage than is currently possible and to ascertain optimal future outcomes [3-7].

Since existing literature is limited to retrospective and small cohort studies, we conducted an in vivo randomized study in a rabbit model with the main goal to gather histopathological evidence on osteoarthritic progression after nonoperative management, partial meniscectomy, and root repair in medial meniscus posterior root injuries.

By setting this goal, the main hypothesis was that the meniscal root repair cannot completely avoid osteoarthritic changes and stable radial tears treated conservatively predispose to lower progression to knee OA than partial meniscectomy.

2. Material and Methods

2.1 Animals and OA model

A total of thirty-nine 4-weeks-old male New Zealand White (NZW) rabbits with no clinical or radiographic evidence of joint disease weighing 2.5 to 3.0 kg were randomly assigned into 3 experimental groups: root tear left in situ (CT group, N=13); partial meniscectomy after meniscal root tear (PM group, N=13); and meniscal root repair (RR group, N=13). Contralateral limbs were used as healthy controls. Surgical destabilization of meniscal root was conducted according to the previously described model [4]. The animals were euthanized at 16 weeks postoperatively; tissue samples of femoral and tibial articular cartilage were collected and processed for macro and microscopic assessment to detect signs of early OA.

The study complied and followed the National Research Council's Guide for the Care and Use of Laboratory Animals and was approved by the regional ethics committee (PROEX 297.8/21). The flow chart of the study is depicted in the supplementary information file (**Fig. S1**).

2.2 Statistical analysis

Required sample size was determined a priori using Statgraphics Centurion XV®. A total of 10 animals in each group were necessary to detect differences with power of a 90% for all statistical tests. Assuming an alpha level of .05 thirteen animals were included in each group to avoid unforeseeable future complications. Random number table method was used to prevent selection bias.

Normality of the data were assessed by the Shapiro-Wilk test. Due to the lack of normality, data were summarized by median and quartiles, graphically represented by box plot, and comparisons were performed using non-parametric tests. Comparisons between independent groups were performed using Kruskal-Wallis test when comparing three groups and Mann-Whitney U test when comparing two groups. Adjusted p-value was calculated considering the number of comparisons between the groups and using the Bonferroni correction. The Wilcoxon signed-rank test was applied for paired data. All statistical analysis was performed using R-3.6.0 (R Core Team 2020, Vienna, Austria).

2.3 Surgical technique

All surgeries were performed on the right knee and left knees were used as healthy controls. For the repair group a tibial tunnel was drilled. Briefly, a medial parapatellar skin incision was made and the knee was placed in full flexion. The medial meniscus posterior root was transected from its tibial insertion with a number 11 surgical blade. The meniscal remnant was then clearly visualized. The torn meniscal root was repositioned anatomically. A Kirschner wire (0.9mm) was used and anteromedial tibial tunnel was created through the root attachment. A 2-0 Ethicon suture (Johnson & Johnson, Nuevo Brunswick, Nueva Jersey, USA) was passed through the posterior horn of the medial meniscus and then pulled out through the transtibial tunnel and secured over cortical bone (**Fig. 1**). The collateral and cruciate ligaments were not damaged during the procedure.

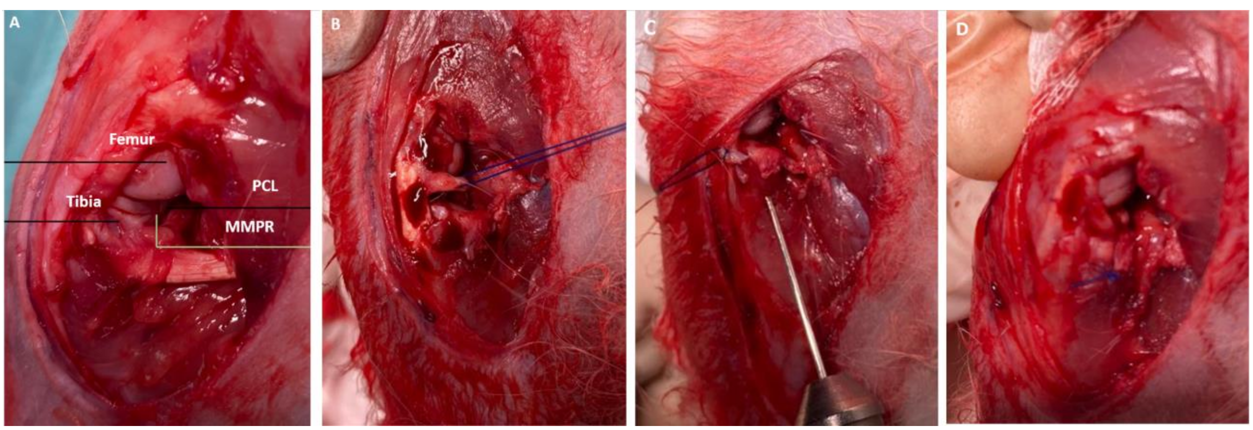

Fig. 1. Photographs depicting surgical destabilization and transosseous root repair. Medial meniscus posterior root was approached through medial parapatellar incision (A). Radial root tear was created then with a No. 11 blade and a 2-0 Ethicon suture was passed through the posterior horn (B). A Kirschner wire (0.9mm) is placed just medial to the tibial tubercule and tibial tunnel was drilled through the root attachment (C). Then the meniscal root was reduced to its anatomic position and the suture was pulled out through the transtibial tunnel and tied out over the cortical bone on the tibia (D).

Intramuscular metamizole injection was also applied for pain relief for 24 hours. Following surgery, animals were maintained in individual cages, with unrestricted activity.

2.4 Macroscopic examination

Tissue was harvested immediately after euthanasia and the right distal articular surfaces of the distal femur and proximal tibia were dissected. Blinded gross morphological assessments were made as follows: 0 (normal smooth surface), 1 (focal surface roughness), 2 (widespread surface irregularities), 3 (beginning surface fibrilation), 4 (severe surface fibrilation), 5 (beginning erosions), 6 (severe erosions), 7 (slight ulcerations), 8 (severe ulcerations) [8]. To minimize biased assessment, the final scores of macroscopic assessments were obtained by calculating the mean value of the results obtained of the two observers. The images were also documented digitally using a wireless digital magnifying glass (Yinama, Tokyo, Japan).

2.5 Microscopic examination

All harvested knees were fixed in 10% neutral buffered formalin and then decalcified using 20% formic acid. Each femoral condyle was sectioned sagittally at the midpoint and tibial plateaus were sectioned coronally at the midpoint in the anterior-posterior frame of reference. Bone samples of tibial plateaus and femoral condyles were embedded in paraffin and sectioned at 2 µm. Histological staining of all sections was performed with haematoxylin-eosin, alcian blue, and Periodic Acid–Schiff (PAS).

For a better understanding of the histological severity in each zone, medial femoral condyles were divided in three equal regions of interest (anterior, central, and posterior). Posterior and a part of the central region corresponding to the weight-bearing area as rabbits have a characteristic locomotion pattern, they walk on a flexed hind leg. For detailed information, please see the supplementary file (**Fig. S2**).

Histopathological assessment then performed and compared between the weight-bearing and non-weight bearing zones. Stained specimens were scanned and the articular cartilage was histologically graded using the OARSI grading and staging system [9]. A higher score indicates a more severe cartilage damage. The histologic sections were scored by 2 independent observers who were blinded to the treatment groups and gross pathology and samples were presented in random order. Matrix abnormalities, cellularity, and tidemark integrity were assessed and compared between bone tissue sections of the 3 different experimental groups.

3. Results

Two animals in the meniscectomy group and 1 in the conservative and root repair have died following surgery due to surgical site infection. Consequently, data from 35 rabbits were available.

3.1 Macroscopic features of cartilage

At sixteen weeks post-surgery all operated knees demonstrated some level of osteoarthritic changes including cartilage fibrillation, ulceration, and osteophyte formation.

Cartilage from the right femorotibial joints in the RR groups appeared eburnated with mild abnormalities such as slight yellowish discoloration, loss of brightness, and some areas of femoral pitting were also evident. Two specimens presented small superficial ulcers in the weight-bearing area and mild osteophytes at the medial rim of the femoral condyle and tibial plateau were observed (Fig.4).

Conversely, the PM group showed severe degenerative changes with cartilage erosions, periarticular joint osteophytes, as well as full thickness cartilage ulcers on the medial femoral condyle and tibial plateau. Osteophytes measured more than 1 mm with an osseous appearance.
In the CT group cartilage showed extensive irregularities with partial thickness ulcers predominantly located at the medial and posterior aspects of the femoral condyle. Osteophytes were small and whitish. No gross cartilage ulcerations were observed in any of the joint compartments in the contralateral unoperated knees. It is also interesting to note that in all 3 groups cartilage ulcerations in the femoral condyles mainly occurred in the weight-bearing area. Macroscopic findings of all 3 groups are illustrated in **Fig. 2**.

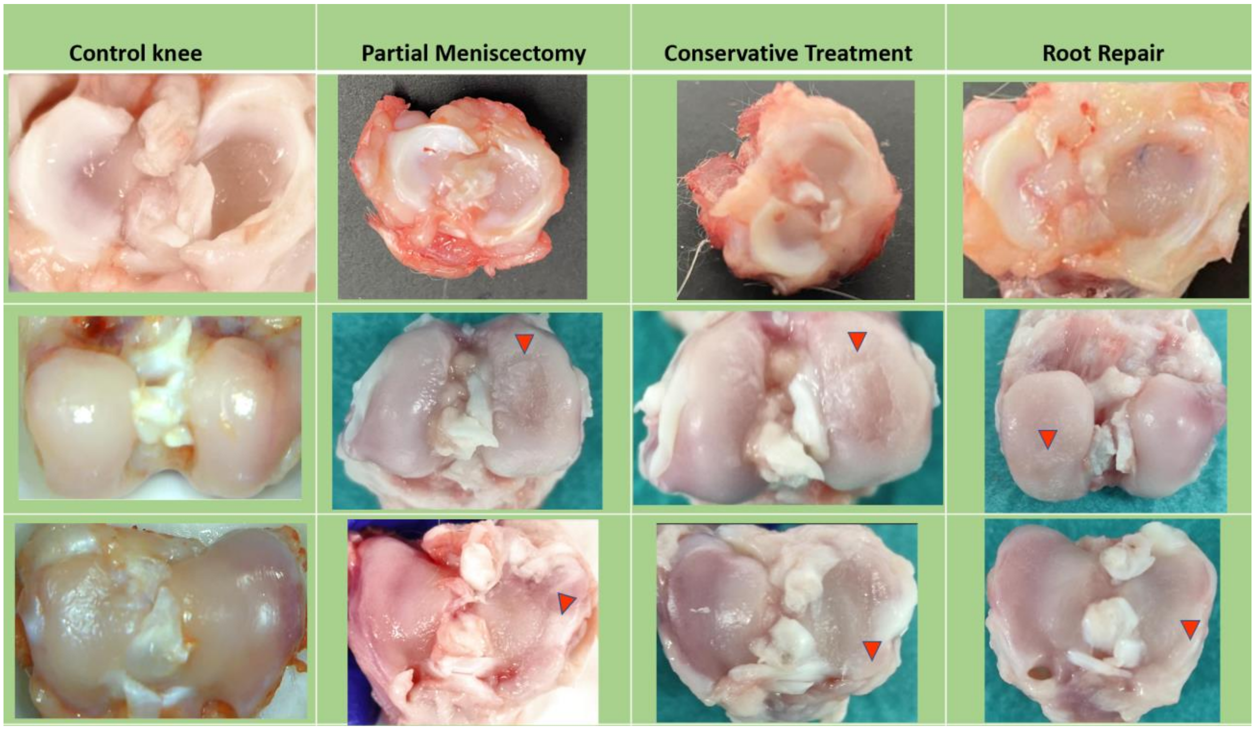

Fig. 2. Representative photographs showing the gross appearance of femoral and tibial cartilage in animals underwent meniscal root release and partial meniscectomy; root tear left in situ; and transosseous root repair. The arrowheads denote relevant macroscopic changes.

Interestingly, the root repair knees still demonstrated significant degenerative changes (2.5; 2-3) in all specimens, albeit to a lesser degree than the meniscectomy (7; 6-7.5) or conservative treatment group (4; 3-4.5). The root repair groups had the lowest scores for macroscopic cartilage damage whereas the meniscectomy group had the highest score, and the difference was statistically significant at comparison. Detailed comparisons of macroscopic assessments between the 3 study groups are described in **Table S1** (Supplementary material).

Macroscopic assessment of healing potential in the RR group demonstrated that the meniscus had fully healed in 7 knees (58.3%), had partially healed in 4 (33.3%) specimens, and had not healed in 1 (8,3 %) knee (**Fig. 3**).

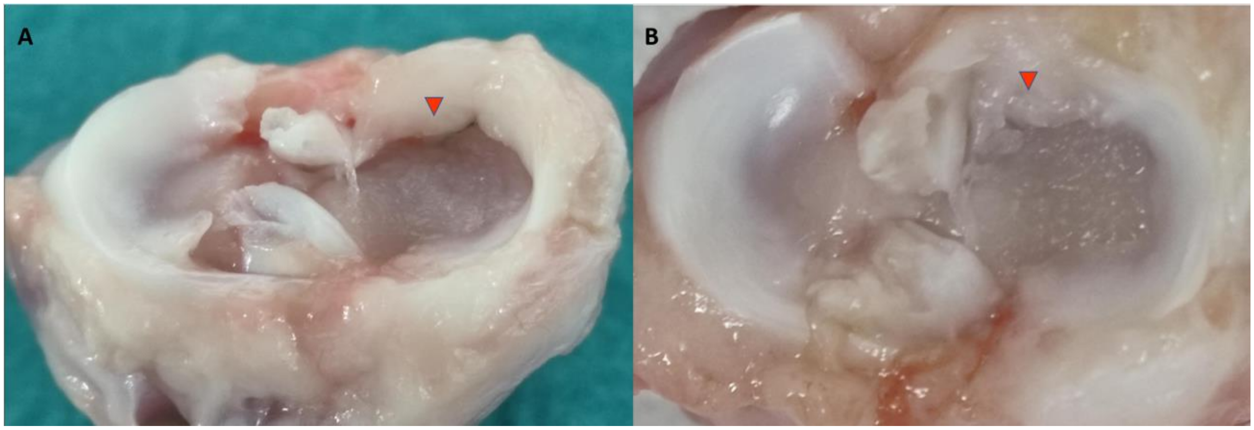

Fig. 3. Gross pathology after 16 weeks of healed (A) and not healed (B) root repair. A. The root repair suture is shown to run deeply below.

3.2 Microscopic analysis

In the RR group the surface of cartilage was evenly preserved; however, surface irregularities and some partial-thickness clefts were observed with mild reduction in matrix staining. Structural abnormalities consisted of focal loosening of the lamina splendens, mild fibrillation with superficial clefts, and loss of tidemark integrity.

In the vast majority of samples from conservative treatment knees had structural abnormalities and showed mild to moderate reduction in the matrix staining, fibrillation and clefts reached the radial zone. Damage was primarily characterized by loss of cellularity and tidemark disruption.

All the rabbits with partial meniscectomy revealed deep radial zone clefts and focal ulcers leaving ultimately the subchondral bone exposed. Cellular clones were localized in the superficial and deep zones of the cartilage and were demarcated by vertical and horizontal clefts together with loss of matrix staining that was predominantly observed on the weight-bearing area of the medial femoral condyle. Interestingly, the weight-bearing area of the medial femoral condyle was the most severely affected (**Fig. S3**) and the loss of tidemark integrity in the weight-bearing area of the medial femoral condyle was observed in all 3 treatment groups. Microscopic changes are demonstrated in **Fig. 4**.

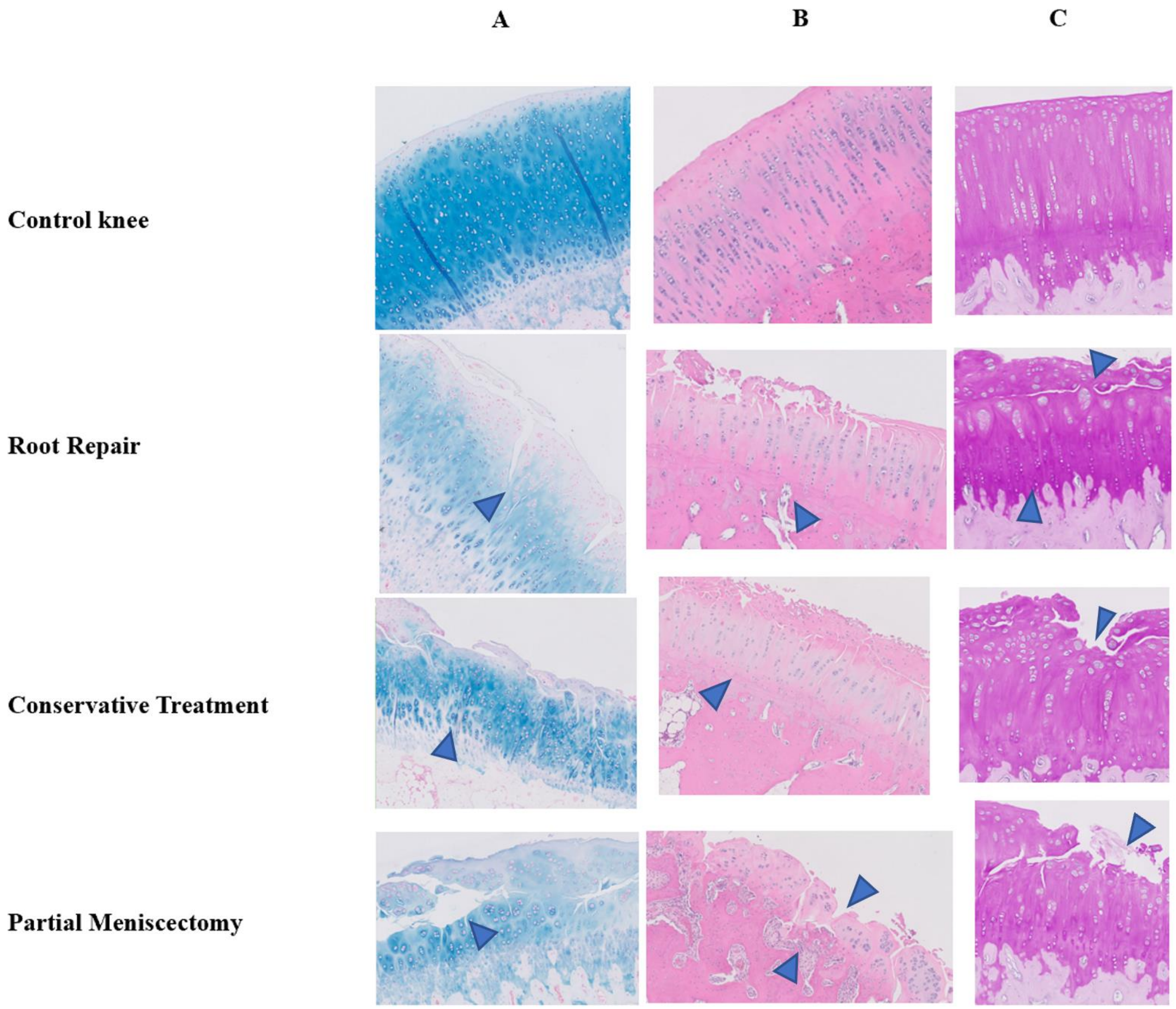

Fig. 4. Representative comparison of histopathological examples from each treatment group with a control group. Each group is represented by 3 examples stained with alcian blue (A), hematoxylin and eosin (B), and Periodic Acid-Schiff (C).

Overall assessment of articular cartilage using total scores of OARSI grading and staging system in the PM group was statistically higher when compared to the RR and CT groups (**Table S2**). The root repair group had the lowest average score for cartilage damage (2.5; 2-3) while the meniscectomy group exhibited higher and more severe sighs of OA (16; 9-16) compared to the conservative treatment group (5; 4-6). Macro and microscopic assessments of histopathological data and between-group comparisons after 16-weeks of follow-up are denoted in **Fig.5.**

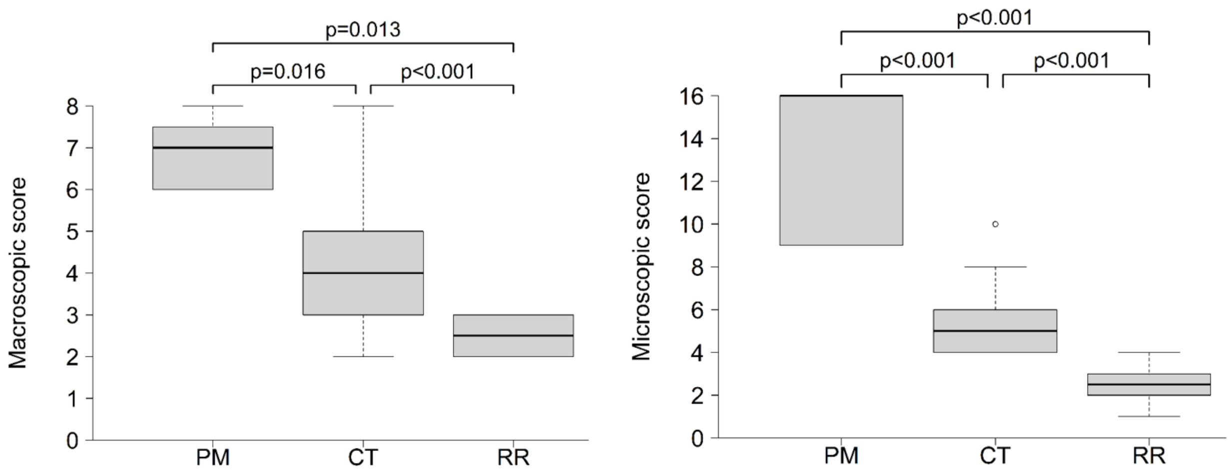

Fig. 5. Graphical representation of the comparisons in macro and microscopic assessments between the 3 study groups. PM: Partial Meniscectomy; CT: Conservative Treatment, RR: Root Repair.

Discussion

Based on the results of this experimental study, there is clear evidence that the meniscal root repair presents lesser and lower degree of osteoarthritic changes compared to the partial meniscectomy and conservative treatment groups. However, root repair did not prevent the progression of OA. Equally important to note is that the stable radial root tears left in situ revealed lower degree of OA compared to the partial meniscectomy group.

Histological assessment is an essential tool and metric for guiding and understanding osteoarthritic features, providing insight into the process of disease development and progression. It is widely reported that meniscal root repair improves postoperative patients´ reported clinical outcomes. Moreover, significantly better outcomes in terms of radiologic measures were reported in patients with meniscal root repair compared with partial meniscectomy [10,11]. Although the clinical outcomes improved, patients with meniscal repair showed Kellgren-Lawrence grade progression and medial joint space narrowing [10]. Chung et al. conducted a meta-analysis including studies that evaluated radiographic progression after meniscal root repair. The authors found that meniscus extrusion was not reduced and did not prevent the progression of arthrosis completely [12]. The hypothesis needed to be tested in a prospective, randomized experimental model. The histopathological findings described herein are in accordance with radiological progression of OA observed by Chung [12]. Moreover, our findings of spatial differences in cartilage wear are particularly interesting as we found that the cartilage is more severely affected within the weight-bearing area rather than across the condyle as a whole.

Interestingly, one of the most important histological finding was loss of tidemark integrity in the weight-bearing area in greater or lesser degree in all 3 study groups. Tidemark is an interface between calcified and non-calcified cartilage matrices and is considered an active or resting calcification front [13]. It is well known that tidemark undergoes structural changes in osteoarthritis [14]. In an anterior cruciate ligament transected (ACL) animal model [7,15] tidemark integrity is normally preserved and is only prominent at advanced stages of OA [3]. In our data tidemark was breached by blood vessels in the weight-bearing region of the medial femoral condyle and was evident in all specimens even in samples with intact cartilage surface where root repair was successfully healed (**Fig. S3**). This finding can be explained by the fact that the medial meniscal root injury induces advanced and severe degenerative changes than ACL injury and almost selectively affects the medial weight-bearing area. This viewpoint is based on the fact that the lack of stable anchorage of the posterior attachment results in functional and biomechanical meniscectomy and subsequently more severe histological changes can be expected. On the other hand, there is a need for improved peripheral-based augmentation techniques during root repair to better address knee kinematics and to arrest subsequent progression of knee OA.

There remains a lack of consensus regarding the preferred treatment option for stable radial tears. Krych et al. found that partial meniscectomy did not confer any advantage over conservative management as a palliative treatment option [16]. However, the authors found lower rate of progression to knee arthroplasty in nonoperative patients (34.6%) compared with partial meniscectomy group with 54% at a mean follow-up of 30.2 and 54.3 months, respectively. Additionally, Bernard et al. did not find significant differences among nonoperative, partial meniscectomy, and meniscal repair groups in subjective clinical knee scores [17].

Long term outcomes were reported comparing patients undergoing ACL reconstruction with untreated stable lateral meniscal posterior root (LMPR) tears to those with an intact meniscus [18]. They concluded that LMPR tears left in situ were of minimal clinically significant long-term detriment, with similar outcomes to having an intact meniscus. On the other hand, a biomechanical study conducted by Perez-Blanca et al. comparing outcomes of lateral meniscus root avulsion left in situ, after root repair, and after meniscectomy on contact pressure distribution in both tibiofemoral compartments at different flexion angles (from 0º to 90º) concluded that meniscectomy causes greater disorders than the avulsion left in situ [19].

Similarly, Shelbourne et. reported improved postoperative clinical outcomes after 10-years from a LMPR injury was left in situ with a matched control group without meniscal injury [20]. It also has been found that in 69% of patients the LMPR can heal completely during a second-look arthroscopy [21]. It is important to note that there is a lower incidence of LMPR tears in the setting of chronic ACL injury this can be a rationale for good healing potential over time. However, it is noteworthy that the biomechanical properties and etiology of posterior root injuries differ between the lateral and medial menisci. Macroscopic assessment of our data supports the observation as the large portion of tears have completely healed after 16 weeks of follow-up (**Fig. 6**).

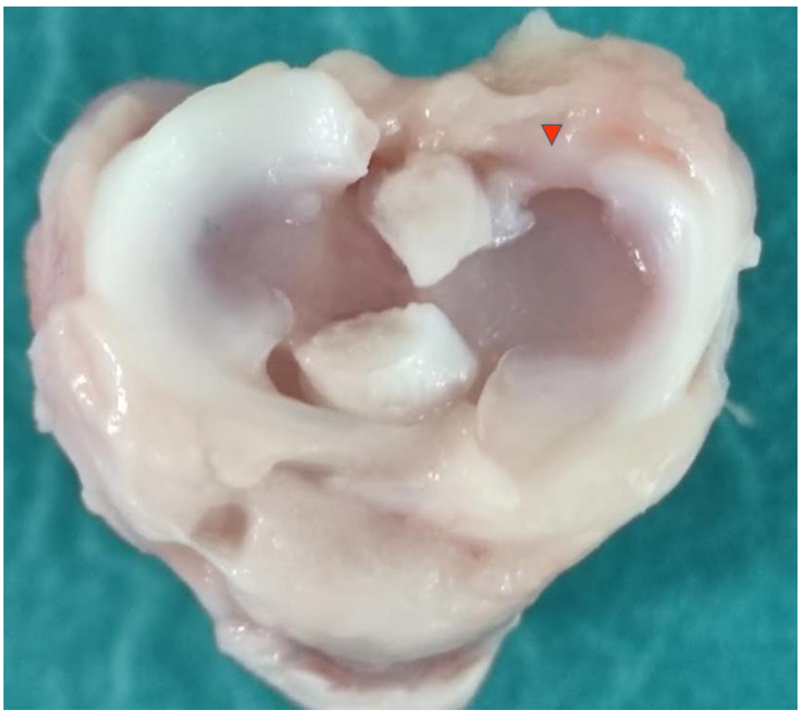

Fig. 6. Representative gross image after 16 weeks of in situ root radial tear. Arrowhead indicates gelatinous meniscoid regrowth that is spanning the previous defect.

Feutch et al. conducted a systematic review of healing potential of posterior medial meniscus transtibial root repair and reported that the healing status was complete in 48% of patients, partial in 42%, and failed in 10% [22]. This is in accordance with our macroscopic data obtained from harvested knees after 16-weeks of follow-up. Complete healing of the repaired root was observed in 7 knees in the repair group (58.3%; n=12). It should be stressed that the repair is not a guarantee of healing and the impact of incomplete or failed healing potential observed in macroscopic specimens can justify histological progression of cartilage degeneration.

The findings of the current study can aid to physician when counseling patients with the diagnosis of a stable radial root tear. Study´s findings could have a role to set realistic expectations in the setting of more advanced pre-existing degenerative changes of the articular cartilage and meniscal tissue where root repair cannot be feasible or in those patients who are poor surgical candidates conservative treatment can be an option. By saying so, now the challenge remains to identify appropriate patients and to disclose that failure is possible in the worst-case scenario. In cases in which conservative treatment fails after a reasonable amount of time a meniscectomy can be performed.

Recently, an increasing body of literature has sought to examine the importance of the meniscotibial (MT) ligament as a secondary restraint of meniscal extrusion [23,24]. Findings on magnetic resonance imaging (MRI) demonstrated that disruption of the MT ligament represents early and predisposing events contributing to medial meniscus posterior root tear (MMPRT) with meniscal extrusion and the subsequent development of osteoarthritis [24]. On the other hand, meniscal extrusion is considered as a major factor contributing to progression of osteoarthritis in patients undergoing meniscus allograft transplantation. A recent cadaveric model evaluating medial meniscus allograft transplantation with MT ligament reconstruction found improved biomechanical outcomes with decreased meniscal extrusion [23]. Clearly, the future of meniscal root repair should focus on the restoration of anatomy and biomechanical augmentation such as MT ligament reconstruction in an effort to avoid or delay osteoarthritic progression and consequently, to maximize clinical outcomes and joint survival.

There are several potential limitations of the study that should be considered when reviewing the presented outcomes. First, it should be kept in mind when extrapolating the results to human OA and include the difference in the speed of development of OA in this animal model (weeks) when compared with humans (years). Second, the controls used in this study were nonoperative controls; however, it was suggested that inflammatory responses of sham surgery are typically cleared away quickly [25], we have had an in-depth discussion about and have decided to eliminate any potential bias of inflammatory state that could affect normal cartilage homeostasis in control knees. Lastly, knees were harvested 4 months after surgery; hence, the progressive time-dependent changes during the first 16-weeks could not be assessed.

In an era of increasing methodological self-reflection, animal models are still a part of the 'Gold Standard' to assess the efficacy of current treatment options. The main strength of the present study lies in its prospective and experimental nature as study design is an important concept as the validity of any conclusion depends on the minimization of bias. In addition, large animal models have many advantages compared to small ones including ease of handling, allowing harvest of a greater amount of tissue samples, low cost, availability and rapidity of development of cartilage lesions. Moreover, it is well-described that the medial posterior meniscal root attachment of the NZW rabbit is very similar to the human knee [26]. Therefore, the findings of this study enhance the current literature which may allow meaningful comparisons to be made between studies and to contribute to the future therapeutic challenges.

To date, no experimental study has attempted to examine the histopathological evidence between nonoperative management, partial meniscectomy, and root repair. To the best of our knowledge, only 2 studies of anterior root destabilization in a rabbit model with or without ACL transection have been described [27,28] as it is more feasible technically to access anterior meniscal root within the rabbit knee. However, the model presented herein is clinically more relevant as injuries to the anterior horns of the menisci are way less common. In addition, animal models of meniscal root injury with concomitant ACL tear can largely bias final outcomes.

The findings of the current study aid to set realistic expectations in medial meniscus posterior root injuries. Proper patients' selection is a key step in ensuring a successful future outcome. Taken together and relying on the more robust evidence we can now conclude that meniscal root repair can delay osteoarthritic progression but not avoids histological progression of knee OA.

Conclusions:

Meniscus root repair could not completely arrest histopathological progression of knee OA but lead to significantly less severe degenerative changes than partial meniscectomy and nonoperative treatment. Partial meniscectomy leads to the most severe osteoarthritic progression while stable radial tears left in situ presented lower OA progression compared with partial meniscectomy.

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Figure legends

Fig. 1. Photographs depicting surgical destabilization and transosseous root repair. Medial meniscus posterior root was approached through medial parapatellar incision (A). Radial root tear was created then with a No. 11 blade and and a 2-0 Ethicon suture was passed through the posterior horn (B). A Kirschner wire (0.9mm) is placed just medial to the tibial tubercule and tibial tunnel

was drilled through the root attachment (C). Then the meniscal root was reduced to its anatomic position and the suture was pulled out through the transtibial tunnel and tied out over the cortical bone on the tibia (D).

Fig. 2. Representative photographs showing the gross appearance of femoral and tibial cartilage in animals underwent meniscal root release and partial meniscectomy; root tear left in situ; and transosseous root repair. The arrowheads denote relevant macroscopic changes.

Fig. 3. Gross pathology after 16 weeks of healed (A) and not healed (B) root repair. A. The root repair suture is shown to run deeply below.

Fig. 4. Representative comparison of histopathological examples from each treatment group with a control group. Each group is represented by 3 examples stained with alcian blue (A), hematoxylin and eosin (B), and Periodic Acid-Schiff (C).

Fig. 5. Graphical representation of the comparisons in macro and microscopic assessments between the 3 study groups. PM: Partial Meniscectomy; CT: Conservative Treatment, RR: Root Repair.

Fig. 6. Representative gross image after 16 weeks of in situ root radial tear. Arrowhead indicates gelatinous meniscoid regrowth that is spanning the previous defect.

Supplementary Information

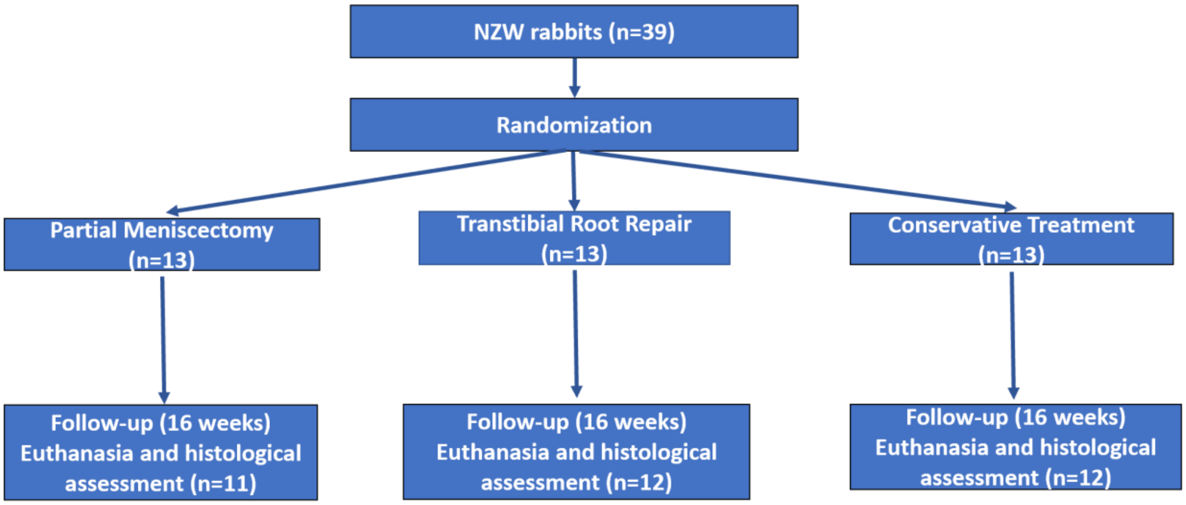

Fig. S1. Flow diagram outlining the steps from the randomization to the final follow-up and histologic assessment.

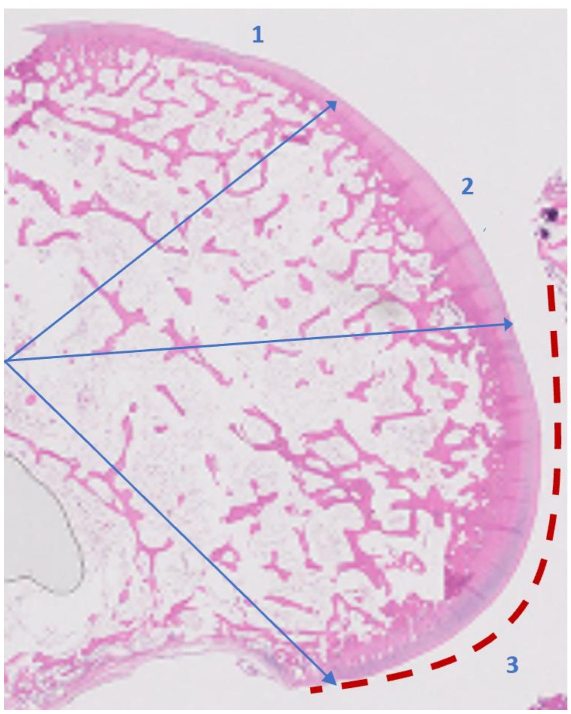

Fig. S2. Sagittal section of medial femoral condyles was divided in three equal zone of interest (1. anterior, 2. central, and 3. posterior). The red dotted line shows the weight-bearing area of the medial femoral condyle.

		Mean Difference	95% CI for Mean Difference		p-value
			Lower	Upper	
PM	CT	2.576	1.236	3.915	< .001
PM	RR	4.409	3.069	5.749	< .001
CT	RR	1.833	0.523	3.143	0.005
RR - PM, CT		-3.121	-4.069	-2.174	< .001

Table S1. Comparisons in macroscopic assessments between the 3 study groups. PM:Partial Meniscectomy; CT: Conservative Treatment, RR: Root Repair.

		Mean Difference	95% CI for Mean Difference		p-value
			Lower	Upper	
PM	CT	7.864	5.496	10.231	< .001
PM	RR	10.947	8.579	13.314	< .001
CT	RR	3.083	0.768	5.399	0.007
RR – PM- CT		-8.690	-5.340	0.822	< .001

Table S2. Comparison of microscopic assessments of the weight-bearing area of the medial femoral condyle between the 3 study groups using the OARSI grading and staging system. PM:Partial Meniscectomy; CT: Conservative Treatment, RR: Root Repair.

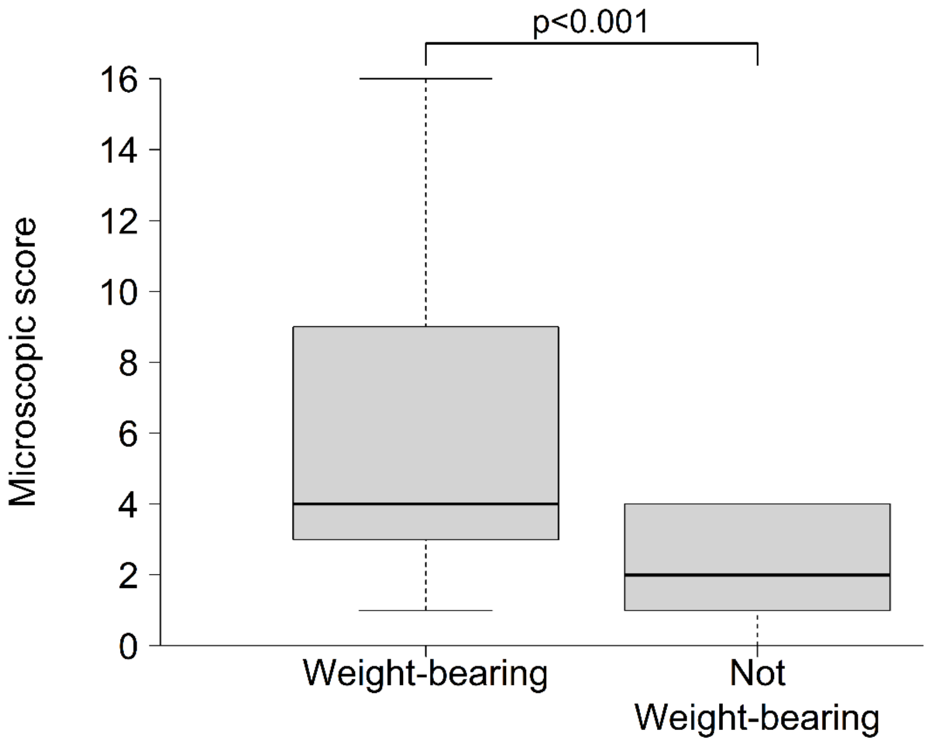

Fig. S3. The weight-bearing area of the medial femoral condyle was the most severely affected at comparison and in all 3 study groups.

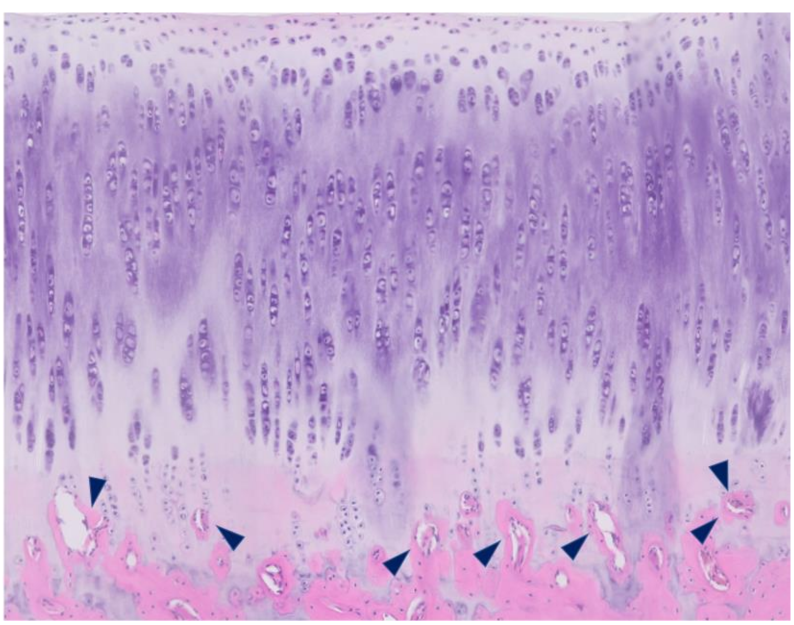

Fig. S4. tidemark breached by blood vessels (arrowheads) in the weight bearing region of the medial femoral condyle was evident in all specimens.