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Original Article

The influence of denervation therapy on knee joint function and the pain situation of patients with knee osteoarthritis complicated with cartilage injury

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Abstract: Objective: This study aimed to analyze the influence of denervation therapy on knee joint function and the pain situation of patients with knee osteoarthritis complicated with cartilage injury. Methods: 100 patients with knee osteoarthritis complicated with cartilage injury were selected for a retrospective analysis. According to the treatment method they received, the patients were divided into 2 groups, with 50 patients in the control group receiving arthroscopic knee debridement and 50 patients in the observation group receiving arthroscopic knee debridement combined with denervation therapy. We compared the therapeutic effects, their Lysholm Scoring Standards and Visual Analogue Scale (VAS) scores, and their complications. Results: The scores for knee joint function in the observation group were much higher than the scores in the control group at 6 months and 12 months after the operations (P<0.05). (2) The excellent rate of treatment in the observation group was higher than it was in the control group (X^2=10.714, P<0.05). The VAS scores of the observation group were much lower than those of the control group at 1 month, 3 months, 6 months, and 12 months after the operations (P<0.05). The two groups showed no significant differences in their rates of the occurrence of complications (X^2=0.344, P>0.05). Conclusion: Arthroscopic knee debridement combined with denervation therapy has an obvious therapeutic effect on knee osteoarthritis complicated with cartilage injury, which can improve knee joint function, relieve the degree of pain, reduce the rate of the occurrence of complications, and thus effectively promote patients' postoperative recovery.

Keywords: Denervation therapy, knee osteoarthritis, cartilage injury, knee joint function

Introduction

Osteoarthritis, a chronic joint disease, can be divided into traumatic arthritis, hypertrophic arthritis, osteoarthrosis, and degenerative arthritis, etc. based on the focus of its lesions [1]. Osteoarthritis occurs in all joints, but mainly in the knuckles, hip joints, and knee joints. The knee joints have the highest occurrence rate [2, 3]. Generally, knee osteoarthritis is mostly complicated with cartilage injury in clinical practice, primarily manifesting as a limb dysfunction. In the case of delayed treatment, it may directly lead to the loss of knee joint function and thus reduce the patients' quality of life [4].

There are a variety of treatment methods for knee osteoarthritis complicated with cartilage injury in clinical practice, and these are generally classified into drug therapy and operative therapy [5, 6]. Drug therapy often prevails in the early stage of onset, but this treatment method cannot achieve an ideal therapeutic effect in the case of deterioration of the disease. A common operative method for this disease in clinical practice, arthroscopic knee debridement can not only eliminate chemical and mechanical irritation, but it can also facilitate joint examinations directly conducted by physicians [7, 8]. This treatment method can achieve a certain therapeutic effect that will be further enhanced for patients with severe joint degen-

eration and resting pain. Denervation means removing the nerve surrounding the patella thus avoiding the patella pain during knee joint motion after the operation [5]. This study analyzed arthroscopic knee debridement combined with denervation therapy so as to improve the knee joint function of patients with knee osteoarthritis complicated with cartilage injury after an operation. Since no studies have focused on this combination therapy, this study will provide new directions for clinical applications.

This study aimed to analyze the clinical effect of arthroscopic knee debridement combined with denervation therapy and its influence on knee joint function and the pain situation of patients with knee osteoarthritis complicated with cartilage injury so as to provide more effective and safe methods for the treatment of knee osteoarthritis complicated with cartilage injury.

Materials and methods

Data

100 patients with knee osteoarthritis complicated with cartilage injury who were admitted to our hospital were selected as our study cohort and were divided into two groups according to the treatment method each patient received. There were 50 patients in the control group who received arthroscopic knee debridement, including 31 men and 19 women, ranging in age from 40-75. There were 50 patients in the observation group who received arthroscopic knee debridement combined with denervation therapy, including 33 men and 17 women, ranging in age from 41-78. (1) Inclusion criteria: Patients who were diagnosed with knee osteoarthritis complicated with cartilage injury by imaging [9].

The informed consents were obtained. There were no operative contraindications. The disease location was a single knee. This study was approved by our hospital's medical ethics committee. (2) Exclusion criteria: This study excluded patients with nervous system diseases or mental disorders, those with multiple osteophytes or severe joint space narrowing, those with a severe force line abnormality, those with severe systemic diseases, those suffering from infectious diseases, those with allergies, and those with operative contraindications.

Methods

The patients in the control group were only treated with arthroscopic knee debridement. The patients were guided to keep a supine position for the operative treatment, and epidural anesthesia was the anesthesia method used in this study. A pneumatic tourniquet was bound to the upper end of the affected limb and an operative incision was made for the arthroscopic portals. During the operation, the joint cavity and joint were washed continuously and the prepatellar fat pad was removed appropriately to examine and clean the knee joint cavity carefully. The diseased neoplastic tissues and the synovial hyperplasia were removed, the corpus liberum was excised completely, the osteophytes that affected the knee joint motion were removed, and the unstable bony spurs inside the joint cavity were ground and removed completely. The next step was to observe whether there was exfoliated articular cartilage or residual fragments of the meniscus inside the joint cavity. If any were found, they were completely removed. The osteophytes of the patella were cleaned to ensure a smooth state of the facies ossea. Arthroscopy was used to observe the degree of knee joint motion carefully. The osteophytes were removed from the anterior apophysis of the tibia and the malleolar fossa, which was followed by repairing the damaged cartilage, cleaning the bony spurs and hyperplastic tissues on the surface, debriding the diseased area, and removing the calcification. The unstable flaps were excised and the edge of the meniscus was carefully trimmed. Also, the original structure of the meniscus was retained to the maximum extent. The meniscus could be excised completely if the pain worsened or if the cartilage injury appeared loose. The retinaculum patellae laterale was released if it was under tension. Arthroscopy was used to observe the pressure on the patella carefully and thus determine the degree of release based on the observations. Then, the fibrous layers of the retinaculum patellae laterale were cut off layer by layer, and the patella was pushed 1 cm inward to move the joint and observe the degree of improvement. The affected limb was wrapped with an elastic bandage. And at the same time, the patients were taught to perform functional exercises according to their actual situations.

The patients in the observation group were treated with arthroscopic knee debridement

combined with denervation therapy. Microscopic radiofrequency ablation was conducted on the nerve surrounding the patella and hypercator cauterization was done on the medial and lateral malleoli of the femur and on the attachment site of the joint capsule so as to conduct the denervation treatment, with a therapeutic range within 5-10 cm. Then, the joint cavity was examined and cleaned carefully. Finally, the operative incision was sutured.

Observation targets

(1) The knee joint function was evaluated according to the Lysholm Scoring Standards before the operation and at 1 month, 3 months, 6 months, and 12 months after the operation, including claudication, support, blockage, instability, pain, swelling, climbing stairs, and squatting, etc. The total scores of this scale were 100, and the knee joint function was directly proportional to the scores [10, 11].

(2) The therapeutic effect was evaluated based on the Lysholm scores, with scores less than 60 scores indicating "poor," scores of 60-75 indicating "OK," scores of 76-85 indicating "good," and scores over 85 indicating "excellent."

(3) The VAS scoring system was used to evaluate the degree of pain in the two groups before the operations and at 1 month, 3 months, 6 months, and 12 months after operations. The degree of pain was represented by 11 figures from 1 to 10, with 0 and 10 representing painless and most painful. The patients selected a figure to represent the degree of pain based on their own pain feeling. A score of 0 meant that the patients felt no pain. Scores from 7-10 that the patients had a growing intense pain and could not tolerate it and therefore needed analgesia. Scores from 4-6 meant that the pain was significant and therefore affected the patients' sleep, but the patients could tolerate it and only needed simple treatment. Scores from 1-3 meant that the patients suffered from minor pain and could tolerate it completely [12, 13].

(4) The complications included joint swelling, deep vein thrombosis, and postoperative infection, etc.

Statistical methods

SPSS22.0 software was used for the statistical analysis. The measurement data were represented by the means ± standard deviations. An independent-samples t test was used for the data in conformity with a normal distribution and a Mann-Whitney U test was used for the data not in conformity with a normal distribution. A paired-samples t test was used for the comparisons before and after the operations in each group. The enumeration data were represented by [n (%)]. An X^2 test was used for the comparisons of the enumeration data between the groups. ANOVA with hoc post LSD tests was used for multiple comparisons. $P<0.05$ indicated statistical significance.

Results

Comparison of the general data between the observation and control groups

In the observation group, there were 33 male patients, accounting for 66.00%, and 17 female patients, accounting for 34.00%. In the control group, there were 31 male patients, accounting for 62.00%, and 19 female patients, accounting for 38.00%. The average age was (32.15± 1.18) in the observation group and (32.19±1.25) in the control group. In the observation group, there were 36 patients with the lesion located on the left knee, accounting for 72.00%, and 14 patients with the lesion located on the right knee, accounting for 28.00%. In the control group, there were 38 patients with the lesion located on the left knee, accounting for 76.00%, and 12 patients with the lesion located on the right knee, accounting for 24.00%. As for the clinical staging in the observation group, there were 29 patients in Phase II, accounting for 58.00%, and 21 patients in Phase III, accounting for 42.00%. And in the control group, there were 31 patients in Phase II, accounting for 62.00%, and 19 patients in Phase III, accounting for 38.00%. There was no statistical significance in the comparison of the general data in two groups, such as gender, average age, disease location (**Figure 1**) and clinical staging (**Figure 2**) ($P>0.05$) (**Table 1**).

Comparison of the knee joint function scores between the observation group and the control group

There were no significant differences in the scores for knee joint function before the operations in the two groups ($P>0.05$). The knee joint function scores clearly increased at 1 month, 3 months, 6 months, and 12 months after the operations in the two groups compared to the

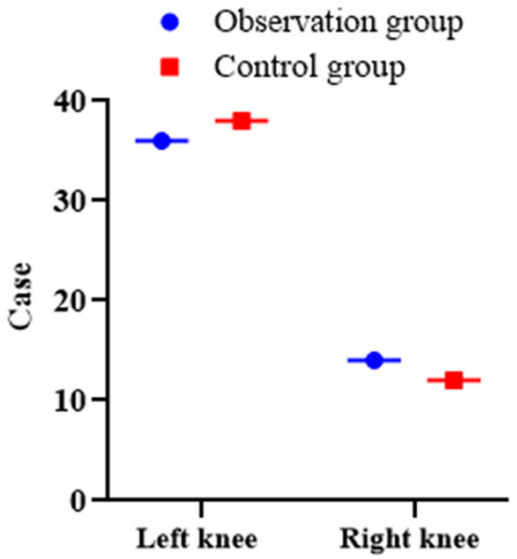

Figure 1. Distribution of the disease locations in two groups. The patients with the lesion located in the left knee accounted for 72.00% in the observation group and 76.00% in the control group (P>0.05), and the patients with the lesion located in right knee accounted for 28.00% in the observation group and 24.00% in the control group (P>0.05).

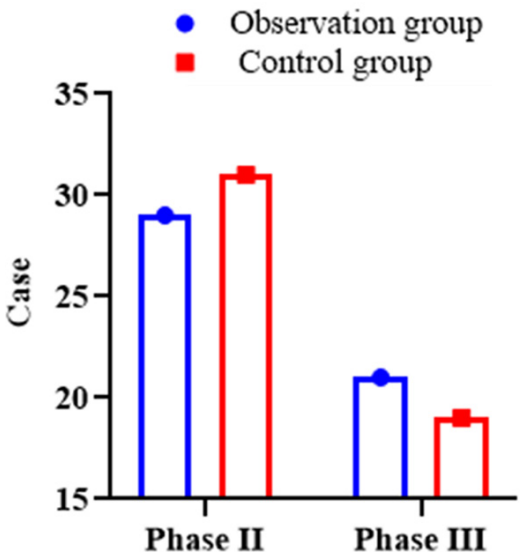

Figure 2. Comparison of the clinical staging between the observation group and the control group. The patients in Phase II accounted for 58.00% in the observation group and 62.00% in the control group (P>0.05), and the patients in Phase III accounted for 42.00% in the observation group and 62.00% in the control group (P>0.05).

scores before the operations (P<0.05). There were no statistically significant differences in the scores for knee joint function at 1 month and 3 months after the operations in the two groups (P>0.05). The knee joint function scores in the observation group were much higher than the scores in the control group at 6 months and 12 months after the operations, which showed a significant statistical difference (P< 0.05) (**Table 2**).

Comparisons of the clinical effects between the observation and control groups

In the observation group, there were 34 patients with an excellent therapeutic effect, accounting for 68.00%, 14 patients with a good therapeutic effect, accounting for 28.00%, 1 patient with an OK therapeutic effect, accounting for 2.00%, and 1 patient with a poor therapeutic effect, accounting for 2.00%. The excellent rate in the observation group was 96.00%. In the control group, there were 23 patients with an excellent therapeutic effect, accounting for 46.00%, 13 patients with a good therapeutic effect, accounting for 26.00%, 9 patients with an OK therapeutic effect, accounting for 18.00%, and 5 patients with a poor therapeutic effect, accounting for 10.00%. The excellent rate in the control group was 72.00%. Therefore, the difference in the excellent rates was statistically significant between the two groups (X^2=10.714, P<0.05) (**Table 3**).

Comparison of the VAS scores between the observation and control groups

There was no statistical difference in the VAS scores before the operations between the two groups (P>0.05). The VAS scores were clearly reduced at 1 month, 3 months, 6 months, and 12 months after the operations in the two groups in comparison with the scores before the operations, indicating a significant statistical difference (P<0.05). The VAS scores in the observation group were much lower than they were in the control group at 1 month, 3 months, 6 months, and 12 months after the operation, indicating a significant statistical difference (P<0.05) (**Table 4**).

Comparison of the occurrence of complications between the observation and control groups

No patient suffered from deep vein thrombosis, postoperative infection, or other severe compli-

Table 1. Comparison of the general data between the observation and control groups [n (%)]/($\bar{x}$ ± s)

Data	Observation group (n=50)	Control group (n=50)	t/X^2	P
Gender (case)				
Male	33 (66.00)	31 (62.00)	0.174	0.677
Female	17 (34.00)	19 (38.00)		
Age (years old)	32.15±1.18	32.19±1.25	0.165	0.870
Disease location (case)				
Left knee	36 (72.00)	38 (76.00)	0.208	0.648
Right knee	14 (28.00)	12 (24.00)		
Clinical staging (case)				
Phase II	29 (58.00)	31 (62.00)	0.167	0.683
Phase III	21 (42.00)	19 (38.00)		

cations after the operations in the two groups. 2 patients from the control group suffered from joint swelling after the operations, with the occurrence rate of complications being 4%, and 1 patient from the observation group suffered from joint swelling after the operation, with the occurrence rate of complications being 2%. Therefore, the difference in the occurrence rate of the complications had no statistical significance (X^2=0.344, P>0.05).

Discussion

In clinical practice, knee osteoarthritis complicated with cartilage injury is an orthopedic disease with a high incidence rate. The pathological changes include lesions on the articular cartilage, bone exposure, subchondral sclerosis, cartilage destruction, and other symptoms. In addition, there is a large number of compensatory osteophytes and a contracture of the tissues around the joint capsule [14, 15]. This disease progresses, so it has a serious impact on the patients' quality of life.

The clinical treatment methods for knee osteoarthritis complicated with cartilage injury are mainly divided into drug therapy and operative therapy [6]. If a patient's condition is mild, he/she shall be treated with oral medication, such as analgesics or non-steroidal anti-inflammatory drugs. But this treatment method can only alleviate the pain and other symptoms for a short time. And the long-term treatment with oral medication will cause a series of toxic and other side effects in the patients [16]. Arthroscopic knee debridement is a common clinical treatment method for knee osteoarthritis complicated with cartilage injury. The osteophytes located in the malleolar fossa of the femur are removed to correct the deformity of joint varus and eversion and repair the cartilage so as to avoid the formation of corpus liberum inside the joint, and therefore relieve the degree of mechanical pain. Eventually, limb function can be improved accordingly [17, 18]. Furthermore, the excision of the osteophytes surrounding the joint can improve the symptoms of knee joint disorder effectively. And the meniscus repair can clearly relieve the periosteal stimulus, avoid the entrapment of the injured parts, and therefore maintain the joint stability effectively [19, 20]. The abnormality in the mechanical property of the patellofemoral joint can be improved by releasing the retinaculum patellae laterale [21]. The continuous and thorough washing of the joint cavity can regulate the pH value inside the cavity, reducing the cavity pressure and removing the mediators and inflammatory proteins thoroughly. Finally, the appropriate excision of the inflammatory synoviums can mitigate the erosions in the knee joint, remove the inflammatory factors to prevent them from getting into the blood circulation, and thus relieve the degree of joint damage [22, 23].

In this study, the excellent rate in the observation group was 96.00%, which was higher than of the rate in the control group (P<0.05). This implied that the clinical effect was further enhanced by treating the patients with knee osteoarthritis complicated with cartilage injury through arthroscopic knee debridement combined with denervation therapy. Also, the scores for knee joint functions in the observation group were higher than the scores in the control group at 6 months and 12 months after the operations, and the VAS scores of observation group were lower than the scores in the control group (P<0.05), which further confirmed the efficiency of denervation therapy and proved that denervation therapy could obviously relieve the patients' pain and improve their knee joint function. When the microscopic radiofrequency ablation was conducted on the nerve surrounding the patella and the hypercator cauterization was conducted on the medial

Table 2. Comparison of the knee joint function scores in the two groups ($\bar{x}$ ± s, scores)

Group	Before the operation	1 month after the operation	3 months after the operation	6 months after the operation	12 months after the operation
Observation group (n=50)	51.24±4.15	80.15±4.29*	81.59±4.31*	87.89±4.98*	90.12±5.12*
Control group (n=50)	51.29±4.12	80.12±4.31#	81.62±4.28#	82.05±4.63#	83.15±4.62#
t	0.062	0.015	0.036	6.876	8.213
P	0.922	0.981	0.912	0.000	0.000

*P<0.05 compared with those before the operations. #P<0.05 compared with those before the operations.

Table 3. Comparison of the clinical effects in the two groups (case, %)

Group	Number of cases	Excellent	Good	OK	Poor	Excellent rate
Observation group	50	34 (68.00)	14 (28.00)	1 (2.00)	1 (2.00)	48 (96.00)
Control group	50	23 (46.00)	13 (26.00)	9 (18.00)	5 (10.00)	36 (72.00)
X^2						10.714
P						0.001

Table 4. Comparison of the VAS scores in the two groups ($\bar{x}$ ± s, scores)

Group	Before operation	1 month after operation	3 months after operation	6 months after operation	12 months after operation
Observation group (n=50)	7.12±1.05	4.42±0.76*	3.15±0.56*	2.82±0.26*	1.02±0.15*
Control group (n=50)	7.18±1.03	5.69±0.85#	4.52±0.48#	3.46±0.62#	1.95±0.36#
t	0.288	7.876	13.134	6.731	16.862
P	0.774	0.000	0.000	0.000	0.000

*P<0.05 compared with those before the operations. #P<0.05 compared with those before the operations.

and lateral malleoli of the femur and the attachment site of the joint capsule, the denervation decreased the number of visceral nociceptive neurons, reducing the amount of neuropeptide substances released and thus alleviating the pain. The nerves of the patella are always overlapped, so the surrounding innervation and cutaneous sensation will not be noticeably affected when these nerves are cut off. At the same time, this will not cause a patella fracture or other severe complications [24]. What's more, the denervation therapy can also block the nerve conduction caused by joint lesions and relieve the degree of pain. Meanwhile, due to its small effect on neurological function, this therapy can shorten the duration of the postoperative immobilization and promote the recovery of joint function. By comparing the occurrence rates of complications after the operations in two groups, it was determined that the complication occurrence rate was 4% in the control group and 2% in the observation group (*P*>0.05), which means that arthroscopic knee debridement combined with denervation therapy, performed in a highly safe manner, cannot increase or enhance the complication occurrence rate.

In conclusion, arthroscopic knee debridement combined with denervation therapy has a clear therapeutic effect on knee osteoarthritis complicated with cartilage injury, and can improve knee joint function, relieve pain, reduce the complication occurrence rate, and therefore promote patients' postoperative recovery effectively.

However, the cohort involved in this study was small, so the results were not representative enough. Much attention shall be paid to the size of the cohort in future studies through larger sample size, longer observation times, and a more comprehensive research and analysis. Additional future research on the clinical effects of arthroscopic knee debridement combined with denervation therapy on knee osteoarthritis complicated with cartilage injury is warranted.

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Disclosure of conflict of interest

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References

[1] McDougall JJ, Muley MM, Philpott HT, Reid A and Krustev E. Early blockade of joint inflammation with a fatty acid amide hydrolase inhibitor decreases end-stage osteoarthritis pain and peripheral neuropathy in mice. Arthritis Res Ther 2017; 19: 106.

[2] Flowers PPE, Cleveland RJ, Schwartz TA, Nelson AE, Kraus VB, Hillstrom HJ, Goode AP, Hannan MT, Renner JB, Jordan JM and Golightly YM. Association between general joint hypermobility and knee, hip, and lumbar spine osteoarthritis by race: a cross-sectional study. Arthritis Res Ther 2018; 20: 76.

[3] Thienpont E, Vanden Berghe A, Schwab PE, Forthomme JP and Cornu O. Joint awareness in osteoarthritis of the hip and knee evaluated with the 'Forgotten Joint' Score before and after joint replacement. Knee Surg Sports Traumatol Arthrosc 2016; 24: 3346-3351.

[4] Song YZ, Guan J, Wang HJ, Ma W, Li F, Xu F, Ding LB, Xie L, Liu B, Liu K and Lv Z. Possible involvement of serum and synovial fluid resistin in knee osteoarthritis: cartilage damage, clinical, and radiological links. J Clin Lab Anal 2016; 30: 437-443.

[5] Cong C, Ma Y, Geng B, Tan X, Bo Z, Kumar JC, Shahidur KM, Meng H, Ning D and Jin J. Intercondylar notch stenosis of knee osteoarthritis and relationship between stenosis and osteoarthritis complicated with anterior cruciate ligament injury: a study in MRI. Medicine 2016; 95: e3439.

[6] Martel-Pelletier J, Raynauld JP, Mineau F, Abram F, Paiement P, Delorme P and Pelletier JP. Levels of serum biomarkers from a two-year multicentre trial are associated with treatment response on knee osteoarthritis cartilage loss as assessed by magnetic resonance imaging: an exploratory study. Arthritis Res Ther 2017; 19: 169.

[7] Siebold R, Karidakis G, Feil S and Fernandez F. Second-look assessment after all-arthroscopic autologous chondrocyte implantation with spheroides at the knee joint. Knee Surg Sports Traumatol Arthrosc 2016; 24: 1678-1685.

[8] Yamasaki S, Hashimoto Y, Takigami J, Terai S, Takahashi S and Nakamura H. Risk factors associated with knee joint degeneration after arthroscopic reshaping for juvenile discoid lateral meniscus. Am J Sports Med 2017; 45: 570-577.

[9] Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS and Tugwell P. OARSI recommendations for the management of hip and knee osteoarthritis, part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008; 16: 137-162.

[10] Chung KS, Ha JK, Ra HJ, Nam GW and Jin GK. Pullout fixation of posterior medial meniscus root tears. Am J Sports Med 2017;45: 42-49.

[11] Eshuis R, Lentjes GW, Tegner Y, Wolterbeek N and Veen MR. Dutch translation and cross-cultural adaptation of the lysholm score and tegner activity scale for patients with anterior cruciate ligament injuries. J Orthop Sports Phys Ther 2016; 46: 976-983.

[12] Swart JF, van Dijkhuizen EHP, Wulffraat NM and de Roock S. Clinical Juvenile Arthritis Disease Activity Score proves to be a useful tool in treat-to-target therapy in juvenile idiopathic arthritis. Ann Rheum Dis 2018; 77: 336-342.

[13] Tarvasmäki T, Lassus J, Varpula M, Sionis A, Sund R, Køber L, Spinar J, Parissis J, Banaszewski M, Silva Cardoso J, Carubelli V, Di Somma S, Mebazaa A and Harjola VP; CardShock study investigators. Current real-life use of vasopressors and inotropes in cardiogenic shock - adrenaline use is associated with excess organ injury and mortality. Crit Care 2016; 20: 208.

[14] Guermazi A, Hayashi D, Roemer FW, Niu J, Quinn EK, Crema MD, Nevitt MC, Torner J, Lewis CE and Felson DT. Partial- and Full-thickness focal cartilage defects equally contribute to development of new cartilage damage in knee osteoarthritis-the Multicenter Osteoarthritis Study. Arthritis Rheumatol 2016; 69: 560-564.

[15] Lee P, Davis P and Prat A. The efficacy of diflunisal in osteoarthritis of the knee. A Canadian multicenter study. J Rheumatol 1985; 12: 544-8.

[16] Rohdewald PJ. Review on sustained relief of osteoarthritis symptoms with a proprietary extract from Pine Bark, Pycnogenol. J Med Food 2018; 21: 1-4.
[17] Filbay SR, Roos EM, Frobell RB, Roemer F, Ranstam J and Lohmander LS. Delaying ACL reconstruction and treating with exercise therapy alone may alter prognostic factors for 5-year outcome: an exploratory analysis of the KANON trial. Br J Sports Med 2017; 51: 1622-1629.
[18] Sihvonen R, Paavola M, Malmivaara A, Itälä A, Joukainen A, Nurmi H, Kalske J and Järvinen TL; Finnish Degenerative Meniscal Lesion Study (FIDELITY) Group. Arthroscopic partial meniscectomy versus sham surgery for a degenerative meniscal tear. N Engl J Med 2013; 369: 2515-24.
[19] Roczniak W, Brodziak-Dopierała B, Cipora E, Jakóbik-Kolon A, Kluczka J and Babuśka-Roczniak M. Factors that affect the content of cadmium, nickel, copper and zinc in tissues of the knee joint. Biol Trace Elem Res 2017; 178: 201-209.
[20] Schüttler KF, Pöttgen S, Getgood A, Rominger MB, Fuchs-Winkelmann S, Roessler PP, Ziring E and Efe T. Improvement in outcomes after implantation of a novel polyurethane meniscal scaffold for the treatment of medial meniscus deficiency. Knee Surg Sports Traumatol Arthrosc 2015; 23: 1929-35.
[21] Pajarinen J, Lin TH, Nabeshima A, Jämsen E, Lu L, Nathan K, Yao Z and Goodman SB. Mesenchymal stem cells in the aseptic loosening of total joint replacements. J Biomed Mater Res A 2017; 105: 1195-1207.
[22] Burks JD, Bonney PA, Conner AK, Glenn CA, Briggs RG, Battiste JD, Mccoy T, O'Donoghue DL, Wu DH and Sughrue ME. A method for safely resecting anterior butterfly gliomas: the surgical anatomy of the default mode network and the relevance of its preservation. J Neurosurg 2017; 126: 1795-1811.
[23] Klenovšek T, Kryštufek B, Amori G and Janžekovič F. Captured in 'continental archipelago': phylogenetic and environmental framework of cranial variation in the European snow vole. J Zool 2016; 297: 270-277.
[24] Arcourt A, Gorham L, Dhandapani R, Prato V, Taberner FJ, Wende H, Gangadharan V, Birchmeier C, Heppenstall PA and Lechner SG. Touch receptor-derived sensory information alleviates acute pain signaling and fine-tunes nociceptive reflex coordination. Neuron 2017; 93: 179-193