Intact Bone Vitality and Increased Accumulation of Nonmineralized Bone Matrix in Biopsy Specimens of Juvenile Osteochondritis Dissecans

A Histological Analysis

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Background: Although commonly proposed to be the starting point of juvenile osteochondritis dissecans (JOCD), avascular osteonecrosis (AVN) has been an inconsistent finding in histological studies. Analysis of early-stage lesions is required to elucidate the origins of OCD and justify proper treatment.

Purpose: To analyze histological sections of JOCD lesions with special emphasis on bone vitality.

Study Design: Cross-sectional study; Level of evidence, 3.

Methods: Of 64 patients with 74 JOCD lesions (20 females, mean age, 11.4 years; 44 males, mean age, 12.7 years), 34 required surgery because of lesion instability or failed nonoperative treatment. From 9 patients, 11 histological specimens were obtained. Lesions were classified according to the International Cartilage Repair Society (ICRS). Two additional histological control sections were harvested from children without JOCD manifestation. Undecalcified histological sections were histomorphometrically analyzed. To analyze the skeletal health of the patients, biochemical analyses with special emphasis on bone metabolism were performed.

Results: Histologically, no osteonecrosis was visible in any of the cases. Osteocyte distribution was similar among OCD lesions and controls. ICRS OCD I lesions (n = 6) showed no intralesional separation. In ICRS OCD II and III lesions (n = 5), there was a subchondral fracture concomitant with histological characteristics of active repair mechanism (increased bone formation: osteoid volume $P = .008$, osteoblast number $P = .046$; resorption: osteoclast number $P = .005$; and tissue fibrosis compared with controls). Instead, in ICRS OCD I lesions, subchondral osteoid volume ($P = .010$) and osteoblast number ($P = .046$) were significantly increased compared with controls; however, no active repair mechanisms (no increased bone resorption or fibrous tissue) were detected, suggesting a focal lack of mineralization. Fifty-seven of 64 patients (89.1%) showed a vitamin D deficiency. The median vitamin D serum level of the patients with ICRS OCD I lesions was 13.6 μg/L.

Conclusion: In the present study, osteonecrosis was not found in histological specimens of JOCD. As a secondary finding, focal accumulations of nonmineralized bone matrix indicating a lack of mineralization in ICRS OCD I lesions were revealed. This finding correlated with a low level of vitamin D in the affected children.

Keywords: osteochondritis dissecans; bone vitality; histology; vitamin D deficiency

Osteochondritis dissecans (OCD) of the knee is an encountered cause of pain and is a functional knee disorder among children, adolescents, and young adults. Currently, OCD is considered to constitute an acquired, focal, potentially reversible lesion of the subchondral bone. The lesion may result in osseous collapse and fragmentation. There is possible involvement of cartilage through tears and delamination. Eventually, lesion instability and dissection/sequestration of the lesion may be the final result. Based on physeal maturity, OCD is distinguished in a juvenile (JOCD) and an adult form, as JOCD lesions have been...
associated with a better prognosis than adult ones.\textsuperscript{29,56} However, healing rates up to 50\% for nonoperative treatment in stable JOCD lesions are still poor and unpredictable. Hence, a consensus on a general treatment algorithm for JOCD is still missing.\textsuperscript{12,17,31,57} As for every other disease, the optimal treatment is based on the knowledge of its origin. However, despite more than 125 years of mostly clinical research and discussion, a reasonable etiological concept is still debated.\textsuperscript{17} Many different theories have been discussed, including genetics, ossification abnormalities, mechanical overloading due to knee malalignment, repetitive or acute trauma, insufficiency fracture, chondronecrosis, or avascular osteonecrosis (AVN).\textsuperscript{9} Although commonly proposed, AVN has been an inconsistent finding in histological studies. In a recent meta-analysis regarding the histological evaluation of OCD lesions, 7 of 10 studies found necrotic subchondral bone stock; however, they failed to elucidate whether AVN was the primary lesion or a secondary phenomenon.\textsuperscript{51} Given the disparity of histological findings, the primary goal of the present study was to analyze histological sections of arthroscopically stable early stage JOCD lesions with special emphasis on bone vitality. We hypothesized that osteonecrosis is not the starting point of JOCD and may therefore not be the predominant finding in our analysis of early stage JOCD lesions. Furthermore, given the frequent appearance of JOCD in highly active patients, repetitive trauma has been considered to be a risk factor for JOCD. It is assumed that the subchondral bone structure may be affected, resulting in a stress fracture.\textsuperscript{10,28} Hence, our secondary goal was to histologically analyze subchondral bone architecture, turnover, and bone metabolism in the affected children.

MATERIALS AND METHODS

Study Group

Between 2009 and 2014, a total of 124 patients with an initial diagnosis of JOCD knee lesions were admitted to our clinic. At initial presentation, patient demographics and medical history, including age at surgery, sex, ethnicity, sports activity (none, 1-2× per week, ≥3× per week), interval between diagnosis and surgical treatment, and magnetic resonance imaging (MRI), were obtained. MRI images with T1-, PD-, and T2-weighted turbo spin echo (TSE) sequences in axial, coronal, and sagittal planes of the knee, which were performed by colleagues from outpatient clinics, were requested at the first visit in our clinic.

To exclude patients with a suspected ossification anomaly, the JOCD lesion had to present a perilesional high signal and be located in the anterior and middle third of the femoral condyle.\textsuperscript{25} Consequently, 27 patients had to be excluded because an ossification anomaly was finally diagnosed. The location of the JOCD was defined in the coronal view (medial or lateral condyles) using the Cahill and Berg\textsuperscript{11} classification and in the sagittal view (anterior, middle, and posterior third), as previously described.\textsuperscript{51} To analyze the skeletal health of the patients, biochemical analyses with a special emphasis on bone metabolism, including serum levels of 25(OH)D, calcium, phosphate, and parathyroid hormone, were performed. Out of the remaining 97 patients, another 33 patients had to be excluded due to missing biochemical analyses. None of the patients had other metabolic bone disorders such as primary hyperparathyroidism, hypocalcaemia, renal insufficiency, glucocorticoid therapy, or bone cancer. Hence, a total of 64 patients with 74 JOCD lesions (20 females, mean age, 11.4 ± 2.3 years; 44 males, mean age, 12.7 ± 1.9 years) were included in the study. Out of 64 patients, 9 had (14.1\%) bilateral JOCD lesions. One of the patients had 2 JOCD lesions in the same knee (medial and lateral femur condyle). The local ethics committee approved the study protocol of retrospective clinical data analysis and biopsy specimen retrieval from patients with OCD manifestation (PV3795).

Biochemical Analysis

Blood samples available for the cohort, with special emphasis on 25(OH)D levels, were analyzed using a radioimmunoassay (DiaSorin) with an interassay coefficient of variation between 8.2\% and 11\%. The sensitivity of this method was 1.5 mg/L. The 25(OH)D levels were categorized as follows\textsuperscript{29}: sufficient (≥30 μg/L), insufficient (20-29 μg/L), deficient (10-19 μg/L), and severely deficient (<10 μg/L).

Surgical Treatment

Surgical treatment was indicated in case of JOCD lesion instability or failure of nonoperative treatment. Lesion instability was defined as the detection of a cartilage break on MRI\textsuperscript{3} and/or secondary signs of instability (rim of fluid signal intensity, multiple breaks in the subchondral plate, and a second outer rim of low T2-weighted signal intensity).\textsuperscript{27} Out of 64 patients, 34 required surgical intervention because of failed nonoperative treatment. Failure of nonoperative treatment was defined as persistent pain and functional impairment of the injured knee.

\textsuperscript{9}References 8, 10, 18, 24, 36, 38, 41, 53, 60.

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(n = 17) or lesion size progression as assessed by MRI after at least 6 months restriction of repetitive impact sports (n = 17). Arthroscopic findings were evaluated according to International Cartilage Repair Society (ICRS) OCD classification. Twenty-nine patients had an ICRS OCD grades I and II lesion and required drilling, and 1 patient required fixation due to instability. Nine patients gave informed consent to obtain a histological specimen while requiring surgery. In 1 male (patient No. 2), a follow-up arthroscopic drilling intervention was necessary because of failed bony consolidation 6 months after the first arthroscopic intervention. In 1 female patient (patient No. 8), JOCD lesions of the medial and lateral femur of the same knee were diagnosed, and biopsy specimens were taken from each lesion in the same arthroscopic session. Arthroscopic retroarticular drilling was performed with a 1.4 mm–diameter Kirschner wire for marking the lesion under radiographic control followed by overdrilling with a 2.9 mm–diameter cannulated drill. Additionally, an osteochondral cylindrical tissue sample was gently obtained retrograde, preferably from the center of the lesion, using a 14-gauge bone-biopsy needle (Ostycut; Angiomed/Bard). A postoperative MRI revealed intralesional drilling and correct biopsy sampling in all of the cases.

**Histological Analysis**

The cylindrical tissue samples were subjected to an undecalcified infiltration process and embedded in methyl methacrylate for 2-dimensional histomorphometry. The sections were cut to a thickness of 4 μm with a heavy-duty microtome (Carl Zeiss) and stained with modified von Kossa stain, toluidine blue, and Goldner trichrome. The undecalcified histological specimens obtained were divided into 2 regions of interest (ROIs): a “juxta-articular,” directly subchondral ROI and a “peripheral” ROI, distant to the articular surface and juxta-articular ROI. These ROIs were evaluated with respect to viability, subchondral bone architecture, and bone turnover. Parameters of static histomorphometry were quantified, including osteocyte number (N.Oc/BPm; mm⁻²), number of empty osteocyte lacunae (N.Empty.Le/BPm; mm⁻²), osteoblast number (N.Ob/BPm; mm⁻²), osteoblast surface (ObS/BS; %), osteoid volume (OV/BV; %), osteoid surface (OS/BS; %), osteoid thickness (O.Th; mm), bone volume (BV/TV; %), trabecular thickness (Tb.Th; mm), trabecular number (Tb.N; mm⁻¹), and trabecular separation (Tb.Sp; mm), according to the American Society for Bone and Mineral Research standards using the OsteoMeasure histomorphometry system (Osteometrics) connected to a Zeiss microscope. Two additional, aged-related histological specimens were obtained during autopsy from 2 females (both 14 years old) without JOCD lesions or any bone disorder. Causes of death related histological specimens were obtained during autopsy from 2 females (both 14 years old) without JOCD lesions or any bone disorder. Causes of death were postoperative sepsis and pneumonia due to aplastic anemia. Written informed consent to participate in the study was obtained from each patient or legal guardian. The local ethics committee approved the study protocol.

**Statistics**

Statistical analysis was carried out using SPSS Statistics v21 (IBM Corp.). Data distribution is given as mean ± standard deviation and median (range) for continuous variables. The Mann-Whitney U test was used to report group differences concerning different regions of interest. All tests were 2-sided, and a P value of <.05 was considered significant.

**RESULTS**

**Characterization of the Complete Study Group**

Patient characteristics are reported in Table 1. Except for 5 patients (7.1%), all participated in repetitive sports activities. Fifty-one patients (72.9%) participated in organized competitive sport activities at high levels (≥3× per week) before the onset of symptoms. Soccer was the most common sport exercised, followed by athlete trampoline jumping. None of the patients reported an incidental memorable injury leading to functional decline and pain in the knee. Thirty-five of 64 patients (54.7%) showed a deficient vitamin D level. Seven patients (10.9%) had severe vitamin D deficiency. Overall, 89.1% of patients had a vitamin D level below the recommended 30 μg/L. There was no significant difference between males and females (P = .352).
Characterization of the Patient Group
With Histological Analysis

Eleven histological specimens were obtained from 6 males (mean age, 13.7 ± 1.0 years) and 3 females (mean age, 12.0 ± 1.0 years) with open epiphyses (Table 2). The median time between diagnosis and arthroscopy was 7 months. In 6 of 11 JOCD lesions, the cartilage surface appeared arthroscopically normal without suspicious color change, fissures, or softening in the center of the lesion (ICRS OCD I) (Figure 1). The median vitamin D serum level was 13.6 μg/L (range, 13.1-37.2 μg/L) in the patients with ICRS OCD I lesions (n = 4). In another 4 lesions in 4 patients, the cartilage was fissured either partially or completely at the edge of the lesion but was stable while arthroscopic probing (ICRS OCD II) (Figure 1).
No. 9, open reduction and internal fixation of the osteochondral lesion with resorbable PLLA pins was necessary (ICRS OCD III). The median vitamin D serum level in patients with ICRS OCD II and III lesions was 15.1 μg/L (range, 12.5–24.3 μg/L). Of these 9, only 1 patient, who had a vitamin D deficiency at his initial visit and was prescribed vitamin D supplementation, had a sufficient vitamin D level at his follow-up visit 6 months later. The most common location of the JOCD lesion was the classic site at the mid- to posterolateral aspect of the medial femoral condyle (Table 2).

Controls

In the 2 control patients, the overlying cartilage looked normal from surface to bottom with respect to viability and potential degeneration (Figure 2A). Bone marrow consisted of regular fat cells and regular vascularization. Trabecular bone stock was viable, as lacunae were filled with osteocytes throughout the complete histological section (Figure 2, B and C). Only sporadic accumulation of nonmineralized bone matrix (ostoid) was detected in the peripheral and the juxta-articular ROI (Figure 2D). At the cartilage-bone junction, remnants of partial ossification in the center of viable single trabeculae were visible (Figure 2E).

ICRS OCD I Lesions

In all ICRS OCD I lesions (n = 6), no subchondral bony disruption, cleft, or separation was found (Figure 2F).

Peripheral ROI. In the peripheral ROI, viable trabeculae were visible (Figure 2G). Osteocyte number was comparable with controls and ICRS OCD II and III lesions. The number of empty osteocyte lacunae even tended to be lower than in controls (Figure 3). Trabeculae showed a normal thickness of 120 μm and were regularly shaped but thinner compared with controls (Tb.Th P = .008) (see Appendix Figure A1, available online at http://ajsm.sagepub.com/supplemental). In addition, trabeculae were covered with significantly more nonmineralized bone matrix (OV/BV, OS/BS each P = .015, O.Th P = .039) (Figure 4) and osteoblasts (N.Ob/BPm P = .023) compared with controls. However, osteoclasts were only sporadically found (Figure 3).

Juxta-articular ROI. In the juxta-articular ROI, there was also no osteonecrosis visible in any of the cases (Figures 2G, 2H, and 2J). Osteocytes were evenly distributed, and the number of empty osteocyte lacunae was even lower than in controls (Figure 3). As an additional finding, we found an unexpectedly high content of osteoid accumulation (OV/BV > 2%) (Figure 4) without signs of active repair mechanisms (increased resorption or tissue fibrosis), indicating focal defects of mineralization (Figure 2J).15,59 Osteoid content increased significantly compared with the peripheral ROI (OV/BV P = .042) (Figures 2H and 2I). Concomitantly, osteoblast numbers and size were significantly increased compared with controls. The overlying hyaline cartilage revealed a regular appearance of the chondrocytes with respect to size and number.

ICRS OCD II and III Lesions

In 3 of 4 ICRS OCD II lesions and in the 1 ICRS OCD III lesion, a complete or partial disruption of an osseous...
fragment was detected (n = 5). Mean disruption depth was 3.75 ± 2.22 mm (Table 2).

**Peripheral ROI.** Similar to controls and ICRS OCD I lesions, the peripheral ROI consisted of viable trabeculae with numerous osteocytes and regular bone marrow (Figure 3; Figure 4, B and C). There was no evidence of increased cell death indicated by a low number of empty osteocyte lacunae (Figure 3). The cleft between the peripheral ROI and the juxta-articular ROI was filled with fibrocartilaginous tissue or fibrous tissue containing numerous blood vessels (Figure 4D). In 1 case, premature callus formation could be observed, representing the healing potential of the lesion (Figure 4E).

**Juxta-articular ROI.** In the juxta-articular ROI, again, no signs of AVN, such as a high number of empty osteocyte lacunae or low number of osteocytes, could be observed. Compared with controls, irregularly formed trabeculae were covered with more osteoblasts producing osteoid (N.Ob/BPm P = .046; Ob.S/BS P = .032) (Figure 3). However, in contrast to controls (N.Oc/BPm P = .005, Oc.S/BS P = .032) and, most importantly, ICRS OCD I lesions (N.Oc/BPm P < .001, Oc.S/BS P = .001), these were accompanied by a great number of bone resorbing osteoclasts (Figure 3F). The additional finding of a high vascularization, lymphocyte infiltration, and tissue fibrosis suggested an active repair mechanism. Although, in 1 ICRS OCD II lesion, no obvious cleft was detected, but there were comparable signs of increased bone turnover in the course of an active repair mechanism including increased bone resorption, bone marrow fibrosis, and elevated osteoid indices. We assume that the biopsy specimen was taken very close to an intralesional cleft.

**DISCUSSION**

Despite several attempts to elucidate the origin and pathophysiology of OCD, currently no universally accepted concept exists. Different theories are still equivalently proposed to be causative of OCD. Although OCD may most likely have a multifactorial origin, 3 of the most commonly discussed causes include genetics, repetitive...
In a recent review analyzing histological studies, 7 of 10 publications reported necrosis of the subchondral bone. Unfortunately, these studies varied in the sources of the specimens (detached vs partially detached vs stable OCD lesions), histological methods used, and patients included (JOCD vs adult OCD vs mixed cohort). It is commonly believed that the majority of adult OCD lesions represent persistent, uncured juvenile OCD lesions. Therefore, and in contrast to previous histological studies, our histological analysis of subchondral bone vitality included juvenile OCD biopsy specimens only. Our results demonstrate that the subchondral bone stock of juvenile OCD lesions is viable and shows no signs of AVN, neither in the peripheral ROI nor in the juxta-articular ROI in any of the cases. Despite inconsistent results, reduced blood supply is still under debate to cause focal AVN at the lateral aspect of the medial femoral condyle, the predilection site of an OCD lesion. In an analysis of 5 arthroscopically unstable adult OCD lesions with subchondral bone stock, Uozumi et al found necrotic trabeculae in 2 cases, necrotic next to viable trabeculae in 2 cases, and viable bone stock in 1 case. The authors concluded that AVN could be the initial incident or secondary to fracture of the subchondral bone. Subsequently, necrotic bone would be remodeled, and new bone would be generated, explaining the simultaneous occurrence of necrotic and viable bone in the same biopsy specimen. Our present results of stable juvenile OCD biopsy specimens, reflecting the early stage of OCD, do not support this consideration of Uozumi et al. The number of empty osteocyte lacunae in ICRS OCD I lesions, defining osteonecrosis, was even lower than in skeletally healthy controls. Also, even in more advanced stages of JOCD (ICRS OCD II and III lesions), there were evenly distributed osteocytes connected by canaliculi, representing viable bone (Figure 3). Our results are in accordance with previous findings by Yone-tani et al, who also demonstrated viable subchondral trabeculae in stable JOCD lesions (ICRS OCD I and II). On the contrary, in 7 histological studies previously reporting AVN, osteonecrosis was either found in loose bodies or partially detached OCD lesions. Hence, these lesions primarily represented arthroscopically unstable JOCD.
lesions, which were naturally either completely or partially separated from their subchondral blood supply. In addition, previous studies demonstrated that the blood supply of the distal femur, especially the lateral aspect of the medial femoral condyle, 1 of the common sites for OCD, was not impaired. Early findings by Chiroff and Cooke and Koch et al even showed viable subchondral bone stock in unstable or dissected JOCD lesions. Based on our present results, we agree with the assumption of Edmonds and Polousky that osteonecrosis associated with OCD rather seems secondary to lesion detachment than to be the initial event. In addition, the histological evaluation of OCD lesions by Chiroff and Cooke and Koch et al showed high bone formation, resorption, osteoid accumulation, and tissue fibrosis, representing classic characteristics of cancellous fracture repair. These findings were confirmed in the present study in ICRS OCD grade II and III lesions with an intralesional cleft. These data are also in line with previous findings of histological sections with intralesional separation or the margins of loose bodies. Most interestingly, in 1 case with an intralesional separation in the present study, immature callus formation could be observed between the 2 fragments. This supported the concept of an active fracture repair mechanism in ICRS II and III lesions and emphasized the healing and reunion potential of subchondral fractures identified on MRI. Regarding our secondary goal, surprisingly, in all 6 histological sections of ICRS OCD I lesions, no circumscribed healing processes were observed. Instead, regular fat cells were seen without fibrocartilage, phagocytes, increased vascularization, or increased bone resorption. In fact, osteoclasts were only sporadically seen. Postoperative

Figure 4. (A) Static histomorphometry and (B-F, patient No. 6) undecalcified histological section of an unstable ICRS OCD III lesion. (A) Osteoid indices with respect to the peripheral and juxta-articular regions of interest in controls, ICRS OCD grade I lesions, and ICRS OCD grade II and III lesions. Bars represent mean ± SD of osteoid volume (OV/BV), osteoid surface (OS/BS), and osteoid thickness (O.Th). (B) Overview of ICRS grade III lesion: 1, viable peripheral bone stock; 2, intralesional cleft; 3, dissected fragment adjacent to metaplastic cartilage; 4, regular articular cartilage (Goldner trichrome stain). (C) The viable host bone (white arrows) showed regular bone marrow proximal to the fragment site. Closer to the intralesional cleft, there was increased bone turnover (white dotted line, formation; red dotted line, resorption) in addition to tissue fibrosis (red stars; toluidine blue stain). (D) The intralesional cleft was filled with fibrous or fibrocartilage tissue (toluidine blue stain). (E) In another case, the intralesional cleft was filled with immature callus (red dotted lines; toluidine blue stain). (F) The fragmented OCD lesion was viable (white arrows). Increased bone turnover (dotted lines, formation; black arrows, resorption) was present (toluidine blue stain; inset = 400× magnification). *P < .05.
MRI follow-up assessments revealed intralesional drilling and correct biopsy sampling. However, we observed an unexpectedly higher accumulation of osteoid (osteoidosis) increasing from the peripheral to the juxta-articular ROI compared with controls (Figure 3A). Osteoidosis, representing a mineralization defect (definition: osteoid volume [OV/BV] >2%), can be observed in cases of malignancies such as bone forming tumors, osteoid osteoma, or onco-genic hypophosphatemic osteomalacia; systemic diseases like renal osteodystrophy, primary hyperparathyroidism, fibrous dysplasia, or Paget disease; in the course of fracture healing, chemical bone demineralization, and metabolic diseases like malabsorption, fluorosis, malnutrition, or vitamin D deficiency. There was no evidence for any of these diseases or conditions in our patients. However, we found low serum vitamin D levels in all but 1 patient and concluded that the focal lack of mineralization in ICRS OCD grade I lesions could, at least in part, be explained by vitamin D deficiency. This conclusion may be supported by a case study linking vitamin D deficiency with OCD manifestation in a patient with rickets and bilateral OCD of the knee. A vitamin D level >30 μg/L is considered a prerequisite for skeletal health and proper fracture healing. In the present study, the median vitamin D serum level in the patients who were biopsied was 14.9 μg/L. In our cohort of 64 patients with a JOCD lesion, 57 (89.1%) showed a vitamin D level below recommendations of 30 μg/L. Seven patients (10.9%) even showed a severe vitamin D deficiency to a nondetectable vitamin D level. Yet, vitamin D deficiency is not a unique feature in patients requiring orthopaedic treatment and is a common finding among European adolescents. The numbers range between 81% and 87%. Hence, vitamin D deficiency is not the sole explanation for OCD occurrence. However, given our present findings of a potential subchondral bone stock of early stage, stable ICRS OCD grade I and II lesions compared with ICRS OCD III lesions, and nonaffected controls. A higher number of controls would have been desirable, but the number was limited to autopsies due to ethical reasons. Unfortunately, the vitamin D level of the controls could not be evaluated. Second, only 1 biopsy specimen of each JOCD lesion was obtained. One biopsy specimen might not represent the complete histological spectrum of the entire JOCD lesion. Third, the gold standard to assess mineralization defects is the histological analysis of iliac crest biopsy specimens, which was not part of the present study. However, laboratory measurements revealed vitamin D deficiency in all but 1 patient with biopsy sampling. Fourth, in cases of osteoid accumulation, the method of choice to differentiate osteoidosis from either lack of mineralization or increased bone formation is labeling before taking a biopsy specimen. Unfortunately, because of limited approval from the ethics committee, labeling was not part of the study protocol. However, increased osteoid accumulation compared with controls, only sporadically seen osteoclasts, and vitamin D deficiency as a laboratory finding seen in our ICRS OCD I patients suggested a lack of mineralization as a reason for osteoidosis.

CONCLUSION

In the present study, we were able to confirm our hypothesis and demonstrated that the subchondral bone of ICRS OCD I, II, and III lesions was viable. We conclude that ischemia leading to avascular osteonecrosis is not a predominant pathological feature of OCD. As a secondary finding, histological analysis revealed osteoidosis in early stage JOCD lesions. We speculate that this lack of mineralization makes this bone segment more prone to mechanical stress, which may result in subchondral insufficiency fractures.
Summarizing, we hypothesize that JOCD of the knee is a multifactorial burden, and osteonecrosis only constitutes a secondary finding, for example, due to a subchondral fracture and consecutive detachment. We additionally hypothesize that vitamin D deficiency supports the development of OCD lesions. Vitamin D deficiency, a recognized risk factor for insufficiency fracture, was a common finding among our group of patients with JOCD. Vitamin D supplementation is proposed as a potential additional therapeutic approach to classic nonoperative treatment in patients with stable JOCD and vitamin D deficiency. Future prospective studies are needed to evaluate the efficiency of vitamin D supplementation on JOCD healing.

REFERENCES