A RETROSPECTIVE STUDY OF THE MECHANISM, DIAGNOSES, TREATMENTS AND PROGNOSES OF OSTEOCHONDRITIS DISSECANS AND AN ANALYSIS OF THE DIFFERENT TREATMENTS' EFFECTIVENESS IN THE HORSE

An Undergraduate Research Scholars Thesis

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ABSTRACT

A Retrospective Study of the Mechanism, Diagnoses, Treatments and Prognoses of Osteochondritis Dissecans and an Analysis of the Different Treatments' Effectiveness in the Horse

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Osteochondritis dissecans (OCD) is a joint disease in which the cartilage and/or bone dissociates from the articular bone, causing chondronecrosis and lameness. As such, OCD is a major issue in the equine sports industry and general equine industry. OCD can develop in virtually any joint, presenting bilaterally or unilaterally in multiple or single joints. The mechanisms that cause OCD are hypothesized to include developmental issues (anatomic and genetic) and possible positive correlations with over-training. This review was performed via gathering data from previous studies to inform the reader about OCD in horses including the various methods of identifying and treating OCD. The diagnostic methods discussed include the lameness exam, radiography, ultrasonography and arthroscopy. Regarding treatments, a primary goal of this is to ascertain whether surgical or regenerative treatments are more successful. The treatments discussed include conservative management (rest), arthroscopic debridement, polydioxanone (PDS) pinning and tissue grafts. To discern between the success of the surgical and regenerative treatments, several criteria were discussed including the success rates of the

treatments taking into account their population size, average age of the population, time for recovery, risk of fibrous cartilage replacement, limitations based on the lesion severity within the joint and treatment costs. While rest was successful in returning 33 ± 12% of horses to soundness, it was less effective than surgical and regenerative treatments, which were 73 ± 3% and 87 ± 4% effective, respectively. The results of regenerative treatments for OCD appear to be superior to those of the surgical debridement. Further research topics that would be beneficial include the further development of regenerative treatments and identifying which gene products support hyaline cartilage repair instead of fibrous cartilage replacement.

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NOMENCLATURE

Arthroscopy	A minimally invasive surgical technique involving visual examination of the interior of the joint
Arthrotomy	A surgical exploration of a joint
BMP	Bone morphogenic protein
COMP	Cartilage oligomeric matrix protein
Effusion	Swelling
EGF	Epidermal growth factor
FGF-2	Fibroblast growth factor two
GDF-5	Growth differentiation factor five
IGF-1	Insulin-like growth factor one
Loose body	A fragment of cartilage and/or bone seen in a radiograph
LTR	Lateral Trochlear Ridge of the femur
Necrosis	Cellular death/decay
OCD	Osteochondritis Dissecans
PDS	Absorbable poly-p-dioxanone
Synoviocentesis	Synovial fluid collection for diagnosis and analysis
Synovitis	Inflammation of the joint
TGF-β	Transforming growth factor beta

1. INTRODUCTION

Osteochondritis dissecans (OCD) is a rising issue in the equine sports medicine field, as well as other veterinary fields (like companion animal) and the human medicine field (Boorman et al, 2021). It has been reported that 20 to 25% of all newborn foals will have some type of OCD with 20,000 to 25,000 foals affected annually in Northwestern Europe, alone (Bourebaba et al., 2019). In horses, this degenerative joint disease occurs due to improper development of the cartilage canals or the biomechanical shearing of the cartilage canals causing chondronecrosis and potential osteochondral fragmentation primarily at an early age of one to three years old (Semevolos, 2017). OCD can also cause a secondary disease manifestation of osteoarthritis (Semevolos, 2017). This can have a lasting effect on the gross earnings of the horse's owner if the disease were to go untreated. The prospects of a horse in many facets of the equine sports industry are affected by this disease, including steeplechase, point-to-point, show jumping, reining, and so on. Generally, any sport in which the horse will have to maintain an elevated level of movement is affected by this disease. In further regard to the equine sports industry, Thoroughbreds, a major breed in the horse flat racing industry, seem to be more susceptible to the disease since they are exercised rigorously when they are young. This heightened level of exercise, along with irregular or inadequate exercise methods, can aggravate initial stages of osteochondritis lesions by focusing shearing forces along the endochondral junction of the cartilage with the bone, leading to the development of OCD flaps (Semevolos, 2017). This has led to the reduction of exercise as one of the preliminary therapeutic measures taken if a foal is found to have early clinical symptoms of osteochondrosis.

In horses, OCD can manifest itself in virtually any joint, including the femoropatellar joints, tarsocrural joints, fetlock joints, the medial and lateral aspects of the trochlear ridge of the talus, the shoulder joint, the metacarpal/metatarsal joints and the phalangeal joints (McIlwraith, 2013).[1] OCD can develop unilaterally or bilaterally for any given joint and can arise in different joints in the same animal. Further, the disease has the tendency to develop differently depending on the gait of the horse, with standardbred trotters having a higher chance of developing an OCD affected joint, compared with standardbred pacers, and standardbred pacers having a higher chance of developing multiple OCD affected joints, compared with standardbred trotters (Boorman et al., 2021). There have also been studies over OCD developing in the occipital condyles located on the caudal portion of the cranium. This disease is very detrimental to the equine sports industry because of its presentation as lameness in the horse, affecting their ability to race or their mobility, in general, and having the possibility to lead to the secondary disease of osteoarthritis.

A widely used diagnostic test for OCD is radiography, the current primary method to examine the extent of the disease before any invasive techniques are performed (Bourzac et al., 2009). It can allow the viewer to discern the size of the lesion and whether there is detached, mobile material within the joint. Recently, another diagnostic test, ultrasonography, has become more appreciated for its ability to assess this disease, specifically in difficult sites for radiography to assess such as the medial trochlear ridge of the distal femur, due to its increased sensitivity for detecting the lesions and its swift on-site diagnostic capabilities (Bourzac et al, 2009). Genetic studies have been performed to determine the specific loci in the genes responsible for increased susceptibility for OCD including matrilin 1 and laminin (Bates et al.,

[1] Humeroulnar joint OCD is quite rare in Equidae, so it will not be covered in this review.

2014). There have been many different procedures over the decades to treat this disease, from the conservative management and arthrotomy to the more modern arthroscopic surgeries and bone marrow-derived mesenchymal stem cell treatments (Bourebaba et al., 2019; McIlwraith, 2013). This study will discuss whether modern surgical techniques or regenerative medical treatments such as novel stem cell injections and resorbable polydioxanone pinning have a higher success rate in returning horses to soundness. I hypothesize that the regenerative medicine treatments will have a higher success rate since they are not removing the already limited tissue from the articulating site, allowing for more mechanical support in the articular joint.

2. METHODS

In order to analyze the efficacy of the different OCD treatments, as well as gather background data on the disease and learn of its diagnostic tests, twenty-four articles were collected, reviewed and analyzed. These articles were gathered from reliable data bases such as the Texas A&M Library Database, ScienceDirect and PubMed. Specific key words and phrases were used in the searches including: "osteochondritis dissecans history," "OCD pathology," "OCD surgical treatments" and "OCD regenerative medicine treatment." To further focus on the more relevant articles, the content was reviewed, and a decision was made as to how the article would add to this analysis. Studies were obtained from these sources and the mean success rates of returning horses to soundness were derived with standard errors for each class of treatment.

3. RESULTS

3.1 Background and Mechanisms Involved in Development of OCD

Although this study is focusing on the equine population, there have been clinical confirmations and studies of this disease in humans and other animals such as pigs and dogs. OCD is a developmental disease that is synonymous with osteochondrosis (technically OCD is the stage after osteochondrosis) that is primarily caused by an issue with the endochondral ossification development leading to bone and cartilage fragments or cysts in the joint (Semevolos, 2017). There have been many different hypotheses posed to explain how this disease develops including the lack of forming cartilage canals, increased mechanical stress on the joint and changes in the molecular signaling during early development. For instance, one study to support the increased mechanical stress hypothesis indicated that osteochondrosis lesions developed differently in horses depending on their type of gait, whether they were harness racing pacers or trotters (Boorman et al., 2020).

There are four main stages of OCD (Bourebaba et al., 2019). In the first stage, OCD lesions begin to form at the subchondral bone level where a large subchondral intraosseous osteopenia occurs. Next, the lesions are quickly accompanied by an intraosseous edema of the subchondral bone. Following the edema, the injured tissue will progress to form a sclerotic ring visible via radiology. Lastly, the disease's progression will lead to softening and alterations of the mechanical properties of the cartilage allowing for the presence of an osteochondral fragment (or multiple loose fragments) that are characteristic of OCD, which will be discussed more in the next section.

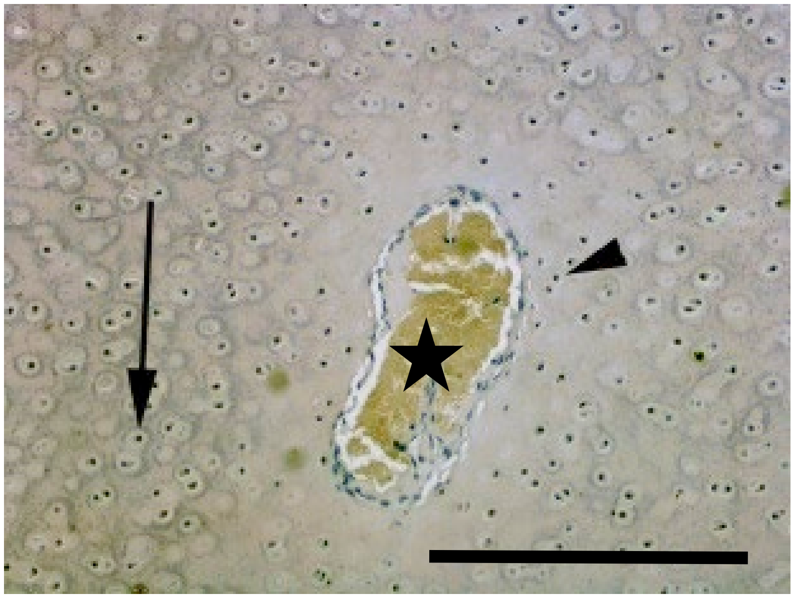


Figure 1 *Histological picture of a normal cartilage canal. In this image, the cartilage canal (blood vessel) is indicated by the black star. From this H&E stain at 100x magnification (The black line indicates 0.5 mm), the difference in size of the chondrocytes near the canal (smaller and rounder) and further away from the canal (hypertrophied) can be distinguished using the black arrowhead and black arrow, respectively. (Semevolos, 2017)*

The result of the failure to form the cartilage canals is a lack of nutrition sent to the chondrocytes during development (Semevolos, 2017; Laverty and Girard, 2013). Reference Figures 1 and 2 for comparison between normal and diseased cartilage canals. This leads to hypoxia and ischemia, since the arterioles and venules that are within each cartilage canal cannot fully supply the chondrocytes that are too distant from the synovial fluid. This can naturally occur during the postnatal period when primary ossification fails to anastomose the cartilage canals (Semevolos, 2017). The failed anastomoses can lead to chondronecrosis focal points, which can further lead to endochondral ossification delays and osteochondrosis. Also, the instability in the newly formed vascular anastomoses and the surrounding matrix's weakness can contribute to the risk of OCD by providing inadequate mechanical support (Laverty and Girard, 2013). In either case, the hypertrophic growth plate zone in OCD is undernourished because of the absence of penetrating capillaries, causing the retention of a thickened layer of cartilage (Bourebaba et al., 2019). The necrosis of the basal layers of the cartilage complex then leads to lesion manifestations such as subchondral fractures, subchondral cysts and fractures of the cartilage flaps (Figure 3).

Figure 2 *Histological view of necrotic chondrocytes surrounding a cartilage canal. This image is an HPS (Hematoxylin, Phloxin and Safranin) stain of a pig cartilage canal with OCD. The collapsing canal has been invaded by the matrix of the necrotic chondrocytes. The reference bar is 0.1 mm in length. (Laverty and Girard; 2013)*

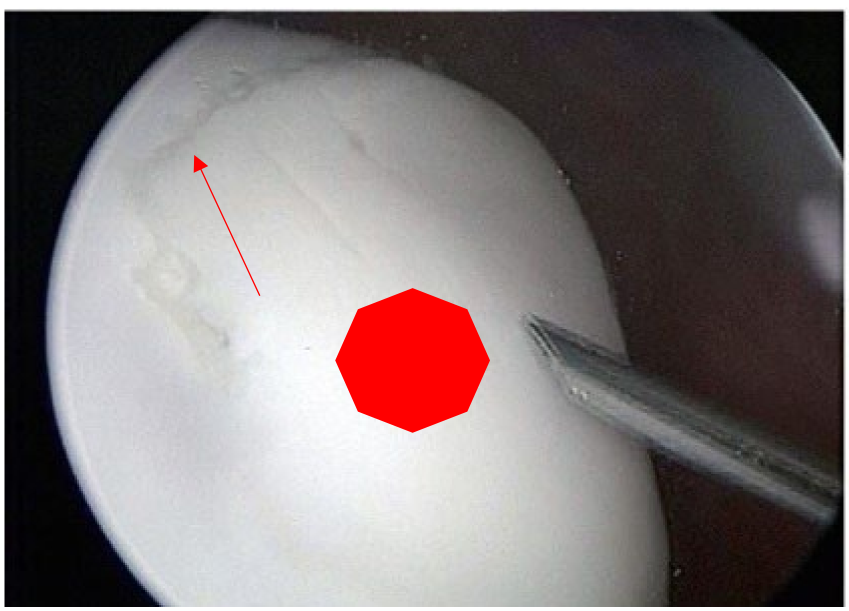


Figure 3 *Physical presentation of OCD of the lateral trochlear ridge of the femur. The lesion is marked via the red octagon. The contrast between the lesion and normal cartilage can be best appreciated looking toward the top of the lesion, indicated by the red arrow. (McIlwraith, 2013)*

Another proposed mechanism that causes the development of OCD is mechanical shearing (Semevolos, 2017; Laverty and Girard; 2013). The shearing movement of joints causes them to be particularly susceptible to developing osteochondrosis lesions. This is caused by the increased type II collagen proliferation developing a metabolic alteration at the joint (Laverty and Girard, 2013). This altered collagen type II network could leave the veins more susceptible to mechanical stresses because of the altered joint geometry. Although this upregulation of type II collagen proliferation is believed to be the cause of lesion repair in some cases, there is not a subsequent increase in the proteoglycan production that would be needed to support the increased cartilage matrix. It has also been noticed that, in some cases, the degradation of type II collagen precedes its reduced concentration. This may be secondary to the degenerative processes of chondronecrotic cartilage of lesions or a post-traumatic event upregulating collagenolytic activity.

Other than developmental and mechanical causes, a genetic connection has been identified with OCD in the horse and other species. Certain genes such as UDP-glucose dehydrogenase (UGDH), matrilin 1 (MATN1), laminin$_{\beta}$ 1 (LAMB1), solute carrier family 35D1 (SLC35D1) and parathyroid hormone 1 receptor (PTH1R), have mutations that have been associated with an increased risk of OCD development, along with others (Bates et al., 2014). Some of the identified genes contribute to producing extracellular matrix proteins, such as LAMB1 and MATN1 (Bates et al., 2014). Looking at MATN1 specifically, its mutations have been linked to osteochondrodysplasias. Mutations in other genetic components contributing to secreted proteins, secretory pathway proteins, cell signaling pathway and growth plate maturation have been associated with OCD. These genes have a variety of effects on the endoplasmic reticulum stress and calcium-dependent proteins within chondrocytes (as with other cells), along with joint tissue development and its resistance to mechanical stress. Genetics will be discussed further in the next section as it relates to the identification of the potential risks of a horse developing OCD before clinical disease onset.

3.2 Clinical Presentations and Diagnoses

In a clinical setting, OCD primarily manifests itself as joint effusion and lameness (McIlwraith, 2013; Boorman et al., 2020). The severity of lameness can range from prominent, where the horse will not flex that joint and may have difficulty moving, to mild cases where the horse appears stiff in its movement and a shortened stride is observed (McIlwraith, 2013). When looking at the history of the patient, a sudden increase in exercise is noteworthy as it increases the risk of developing OCD in young horses. Depending on the duration that the condition has been allowed to progress, the horse may develop secondary osteoarthritis, which will cause any movement of the joint to be painful. Also, depending on which joint the OCD develops in, this disease can be mistaken for a neurological disorder, as seen with stifle OCD lesions in horses which causes circumducting motion of the affected limb. Looking at the affected joint, OCD manifests itself as a dissecting lesion of the cartilage (and can include bone) that ultimately has reached the joint surface, causing the manifestation of the disease. This arises from either a defect in the subchondral bone or a separation of the cartilage from normal subchondral bone. The dissociation of the cartilage, and potentially bone, from the joint can manifest itself in two different ways: either it can remain loosely attached to the healthy articular cartilage and simply float about in the articular space or it can become entirely detached from the articular cartilage, becoming a loose body[2]. In either case, the disease causes the lameness and joint effusion seen through the OCD fragments causing synovitis.

[2] Loose body can be cartilage and/or bone depending on the lesion. Also, another term that may be used to describe a loose body is "joint mouse."

As for the diagnosis of OCD, the main exam for this disease is the lameness exam, which includes a preliminary gait analysis and flexion and blocking of joints to analyze the gait of the horse from the hoof upward on the leg (Boorman, 2020; Baxter and Stashak, 2011). After the preliminary testing, there are three primary methods of diagnosis which include radiography, ultrasonography and arthroscopy (McIlwraith, 2013; Bourzac et al., 2010).[3] There are also genetic tests that indicate high risk for the disease manifestation (Bates et al., 2014).

The lameness is the first step in diagnosing an equine patient with OCD. The lameness exam is given based on a horse's gait changing, or it can be given based on the horse refusing to do tasks such as galloping or turning in one direction. The purpose of the lameness exam is to determine whether (1) the horse is lame, (2) which limb is affected, (3) the site of the problem, (4) the specific cause of the problem, (5) the appropriate treatment and (6) the prognosis for recovery (Baxter and Stashak; 2011). The lameness exam includes in order, (1) analyzing the patient's history, (2) a visual exam when the horse is at rest, (3) palpations of the musculoskeletal system including testing the hooves with hoof testers, (4) observing the horse in motion, (5) manipulative tests like flexion tests, (6) diagnostic anesthesia for the nerve or joint (if necessary) and (7) diagnostic imaging.

Lameness exams begin with defining whether the horse has lameness (Baxter and Stashak, 2011). The history is significant since it can define if the issue was progressive and whether this has been a chronic issue. During the visual examination when the horse is at rest, the specific location of where the issue is located and swelling could be seen. In severe cases of lameness, the hoof may be smaller on the affected limb due to the difference in long-term weight distribution. When palpating the muscles and skeletal structures, a wide variety of presentations

[3] It should be noted that arthroscopy is a surgical technique that can be used to diagnose lesions that did not appear on a radiograph or ultrasound.

may appear such as a degenerative appearance being seen with the muscles or effusion at the site of the lesion during the visual examination and a response to pain from the horse during the palpations. Using the hoof testers, if pain is seen when evaluating the integrity of the foot structures then it could indicate that the foot is the source of the problem. During the movement portion of the exam, the movement of the horse will be visually assessed including: the arc and path of the foot in flight, how the foot lands, how the joints extend and the flexion angles, the symmetry and duration of the gluteal muscle use and the head and pelvic movements. In any of the previously stated cases, the issue can appear unilateral or bilateral.

Flexion diagnostic tests are performed to get a basis for where the lesion(s) are in preparation for the radiography or ultrasonography to be performed (Baxter and Stashak, 2011). It is diagnostic as far as which joint has pain, The use of local anesthetics in the joint can assess whether the lameness is removed or improved by the absence of pain, as seen with shoulder joint OCD (McIlwraith, 2013). It should be noted that there were some older horses that had OCD lesions when radiographed but showed no signs of lameness or pain. So, radiography should not be relied upon solely.

Radiography is a diagnostic test for equine OCD in the femoropatellar, tarsocrural, fetlock and shoulder joints. Beginning with the femoropatellar joint, the primary diagnostic signs include the presence of loose bodies, in some instances, and a flattening or variability with depth in the size of the trochlear ridge (Figure 4) (McIlwraith, 2013). Other signs of OCD in the femoropatellar joint include a partial mineralization of the cartilage tissue within the deformed or fragmented lesion. Lateral-to-medial radiographs are the most useful for identifying OCD at the femoropatellar joint. The regions of this joint where lesions can occur include the lateral and medial trochlear ridges of the femur.

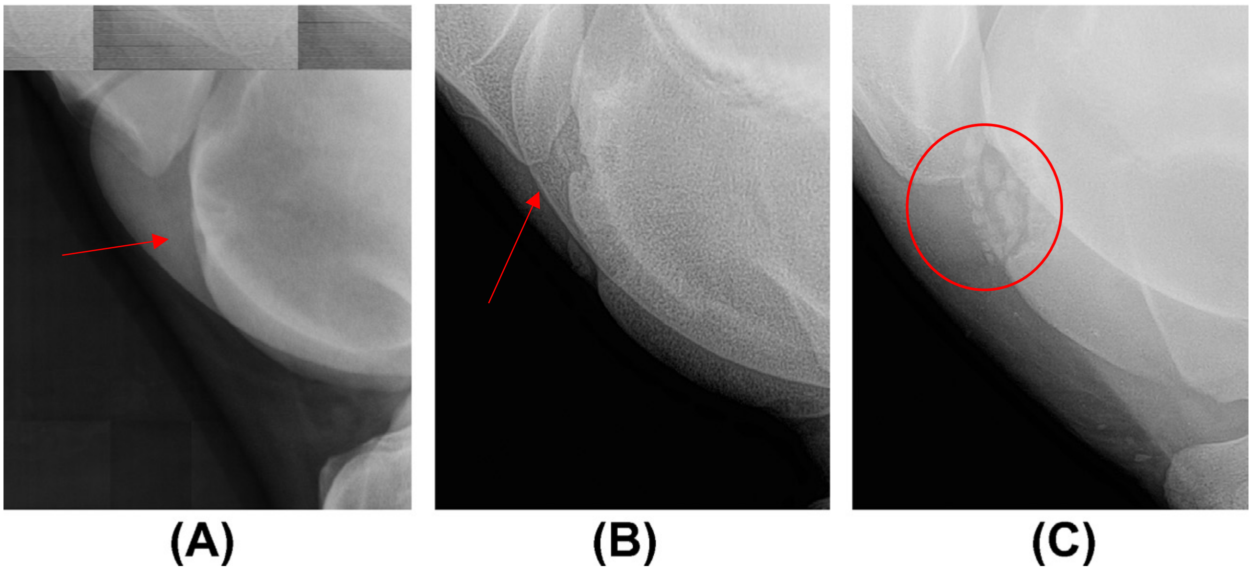
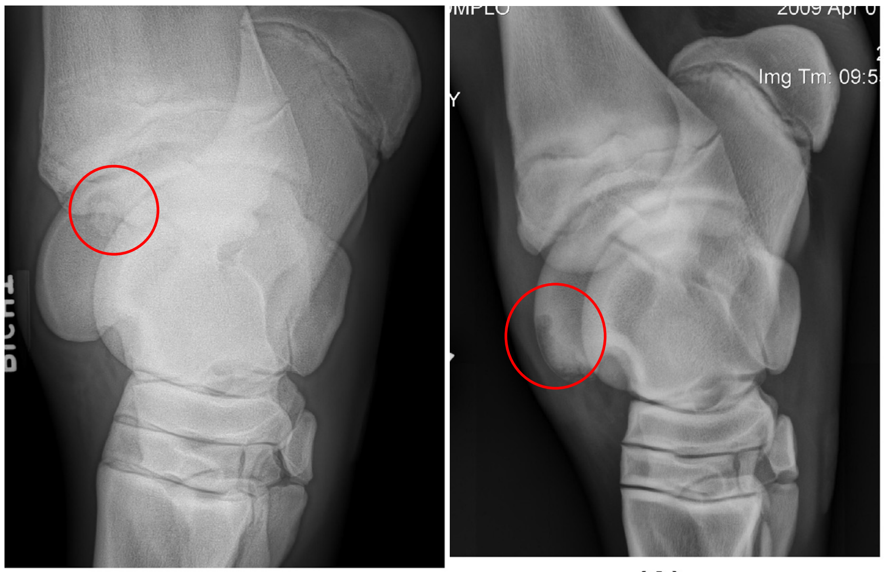


Figure 4 *Three different representations of OCD of the lateral trochlear ridge of the femoropatellar joint. Viewing from images A to C, the severity of OCD at the afflicted joint can be seen via the red arrow or circle. In image A, there is virtually no presence of OCD with a small defect in the lateral trochlear ridge. In image B, there is a more obvious presence of OCD with fragmentation occurring. In image C, there is a strong presence of OCD within the joint. This severity is, in general, directly related to the severity of symptoms seen in the animal. (McIlwraith, 2013).*

When considering the radiographs of the tarsocrural joint (hock joint), the sites in which OCD lesions can occur include the distal intermediate ridge of the tibia, the lateral trochlear ridge of the talus and medial trochlear ridge of the talus (Figure 5) (McIlwraith, 2013). Diagnostic features for this joint site are defects in the cartilage or contaminating (cartilaginous) fragmentation. At this specific site, the lesion severity tends to not be accurately depicted by radiography alone. It should be noted that this type of lesion appeared most often on racehorses at two years of age and non-racehorses as yearlings before their training. This kind of lesion was also the most common to be absent in the radiographs but present when arthroscopically viewed.



(A) **(B)**

Figure 5 *Radiograph of OCD lesions in tarsocrural joints in the distal intermediate ridge of the tibia (panel A) and lateral ridge of the talus (Panel B). Both lesions are indicated by the red circles highlighting the fragmented bone. It should be noted that these radiographs are taken at an angle in the medial-to-lateral direction. (McIlwraith, 2013)*

In radiographs of the fetlock joint, the OCD lesions can appear as either irregularities or fragmentations on the dorsal aspect of the sagittal ridge and the condyles of the metacarpus or metatarsus, referred to as cannon bones in Equidae (Figure 6) (McIlwraith, 2013). Further, there may be secondary manifestations occurring on the dorsal aspect of the proximal phalanx. Since there is a primary and secondary manifestation, this disease diagnosis will be discussed in two sections at the fetlock joint, each being discussed exclusively. Beginning with the dorsal aspect of the metacarpus or metatarsus, the radiographic presentations have many different manifestations at this particular site. Some joints show only flattening or defects of the sagittal ridge (type I), some joints present as fragments within the flattened space (type II) and some joints have loose bodies, either accompanied by fragments or not, within the joint (type III) (McIlwraith, 2013). As for the OCD fragments of the proximal dorsal aspect of the proximal phalanx, they are also variable in presentation. The fragments usually present rounded and are from the proximal medial eminence of the proximal phalanx.

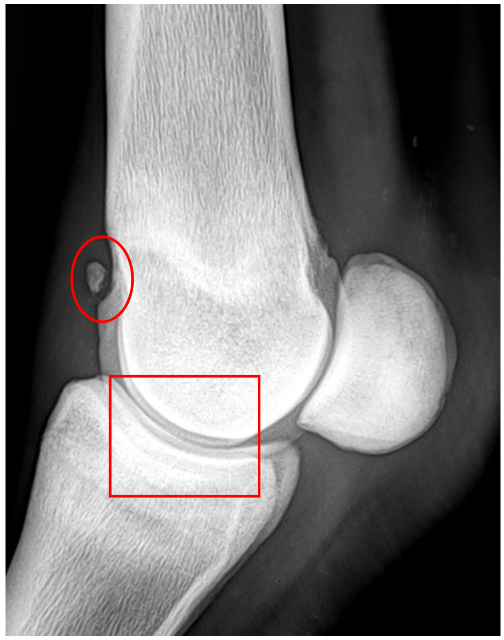


Figure 6 *Fetlock joint OCD development at the proximal aspect of the sagittal ridge. The red oval is indicative of a loose body found in the radiograph. Looking at the joint indicated by the red rectangle, some flattening may be seen. (McIlwraith et al., 2016)*

Looking at the radiography for shoulder OCD, it should be mentioned that this disease presents clinically as an atrophy of the supraspinous and infraspinous muscles and a variable lameness in the limb with a potential to develop a club-like or high appearance on the foot (Figure 7) (McIlwraith, 2013; Nixon et al., 1984). This form of disease also has the possibility of the foot of the specific limb being smaller. In the radiographs, the most common sign is flattening or indentations in the cartilage of the humoral head or a defect in the glenoid cavity. It is also usually accompanied by bony proliferation along the caudal border of the glenoid cavity.

***Figure** 7 OCD lesion of the humeroscapular (shoulder) joint. This radiograph depicts an osteochondrosis lesion which is indicative by the articular surface defect at the site of the joint (indicated by the red circle). (McIlwraith, 2013)*

One interesting diagnostic test that is being utilized more for this disease lately is ultrasonography. This diagnostic test is especially useful for OCD lesions that are difficult to get a clear radiograph of the lesion due to the absence of subchondral bone changes, such as some lesions in the femoropatellar joint (Bourzac et al., 2010). Comparing the accuracy of radiography to ultrasonography, their specificity was significantly different. The specificity of ultrasonography was 100% and unaffected by the site, excluding the distal third of the medial trochlear ridge where it was 94% specific. However, the specificity with radiography was less with it missing two lateral trochlear ridge lesions and three medial trochlear ridge lesions. In other words, from this study, ultrasonography proved to be more specific than radiography when detecting medial trochlear ridge lesions of the distal femur.

Arthroscopic diagnoses were found to be more accurate than radiographs when it comes to assessing the severity of the disease, as well as the location of the disease in certain joints and presentations of the disease (McIlwraith, 2013). However, this type of diagnostic test requires being performed as a part of a surgery where the scope has to be placed within the afflicted joint. Further, this type of diagnostic test is invasive and is only performed after a radiograph or ultrasound has been utilized and a lesion has been identified. Additionally, arthroscopy may identify additional lesions or loose bodies during the surgery that were not identified via radiography or ultrasonography.

The last test to be discussed is a newer method of analyzing the genetics of a horse and identifying potential risks genes before the disease develops. This type of diagnostic test is performed via genotyping using the Illumina Equine SNO50 BeadChip[4] with 54,602 SNPs (Bates et al., 2014). This test will look for mutations in genes such as UDP-glucose dehydrogenase, MATN1 and LAMB1 that are associated with the disease. Genetic testing could be used preventively if both parents are heterozygous for the OCD-associated gene mutations and can allow for preemptive care for a foal that is at higher risk for developing OCD.

3.3 Treatments[5]

3.3.1 Conservative Treatment

Conservative management is one of the oldest forms of treatment for this disease as it entails providing the horse an extended rest period to allow the lesion to heal on its own accord. Generally, this is done by confining the horse to a stall (McIlwraith, 2013). There has been varying results with this form of treatment (Table 1). Overall, the successful return to soundness was 33 $\pm$ 12%. Specifically looking at cases with OCD of the femoropatellar joint, some have

[4] It should be noted that there are other beads used for this type of genetic testing, as well.
[5] For the purposes of this review, surgical treatments will be considered as treatments that purely debride or remove the cartilage from the joint, while regenerative treatments may require a surgical incision to be administered and debridement or loose body removal (such as with PDS pins) but are meant to either nurture cartilage reattachment or stimulate cartilage regrowth.

indicated that the prolonged resting period allows for a natural resolution if the OCD fragments were not visible via radiography while others presented a worsened case when conservative therapy was applied (Foland et al., 1992). In one study following seven horses over two years using conservative management, only one horse was able to perform successfully. In another study where there were 76 horses suffering from OCD with 48 having femoropatellar osteochondrosis, under conservative management (management time not identified), 15 of the 48 still presented with fully realized OCD, with a 54% success rate of returning to soundness, overall. In a third case in thoroughbred horses, conservative management's success rate was correlated with the severity of the lesion with the highest rate of success using this treatment being when the lesion is < 2 cm long, < 5 cm deep and no fragmentation of the cartilage within the joint was seen (McIlwraith, 2013). This treatment is only attempted when the foal is under 11 months old since that is when the healing can be completed. If the horse is older than 11 months, arthrotomic or arthroscopic surgery takes precedence.

Table 1: *Summary of Conservative Management Studies Throughout the Results Section*

Treatment Type - *Subtype*	Time of Measure	Horse Number	Average Age of Horse Population	% Sound after treatment	Reference
Conservative Management - *Rest*	2 years	7	Not Provided	14%	(Foland et al., 1992)
Conservative Management - *Rest*	Not Provided	76		54%	
Conservative Management - *Rest*	Not Provided	48		31%	

3.3.2 *Surgical Treatments*

3.3.2.1 Arthrotomic Surgery

Arthrotomy was the original way of accessing the joint for dissociated cartilage and loose body removal (McIlwraith, 2013). During this procedure, the joint would be more exposed to the external environment and increase the risk for a bacterial infection to take hold. However, with some forms of OCD, such as OCD of the shoulder, this form of surgery persists since an alternative has not been well identified when considering the level of enhanced visualization of the anatomical structures that the arthrotomic approach provides (Nixon et al., 1984). Two different methods of this treatment have been identified in order to access the shoulder joint: transverse tenectomy and longitudinal tenectomy of the infraspinous ligament. It was determined that transverse tenectomy will allow for better exposure while still maintaining the stability of the joint through the infraspinous ligament. Further, when looking at arthrotomic surgery of the femoropatellar joint, it was indicated that a different approach could change the effectiveness of the treatment depending on where the lesion was located (Trotter et al., 1983). If the lesion was located in the distal portion of the lateral trochlear ridge, then a craniolateral approach provided better exposure then a lateral approach, which provided better access to the whole lateral trochlear ridge.

However, because of the increased exposure that this form of treatment causes to the affected joint, arthroscopy is preferred for other OCD lesions in the limb, such as femoropatellar OCD lesions, to reduce the risk of post-operative infection (McIlwraith, 2013; Trotter et al., 1983). For example, when a necropsy was performed on a horse recently euthanized following post-surgical complications, Streptococcus species were identified in the synovial fluid (Trotter et al., 1983). With that in mind, this form of treatment is easier to use compared to arthroscopy

(McIlwraith et al., 1991). On a separate note, this form of surgery is also a preparational procedure to the implantation of bone graphs, which will be discussed later due to it being a regenerative form of treatment (McIlwraith, 2013; Fortier and Nixon, 2005).

3.3.2.2 Arthroscopic Surgery

The primary treatment taken against OCD in horses is currently arthroscopic surgery. This form of surgery offers many advantages compared to the previous method of arthrotomy, including a reduction in exposure and post-operative pain at the joint, increased diagnostic accuracy and a decreased damage to the tissue along with better cosmetic results (McIlwraith et al., 1991). This surgery entails making two portals at the joint site and inserting an arthroscope into one portal while the other portal is used for the debridement instrument. The positioning of the portals depends on the joint location of OCD and the visibility in a certain orientation. In general, the portals for the arthroscope are shifted depending on whether the scope can accurately present the location and severity of the lesions (McIlwraith, 2013). When considering the tarsocrural joint, medial arthroscopic portals are used when the lesions are on the lateral trochlear ridge of the talus while dorsolateral arthroscopic portals were also used for this lesion location when the visibility was diminished and dorsomedial portals (through the dorsomedial pouch) were used for lesions associated with the medial malleolus of the tibia (McIlwraith et al., 1991).

Another aspect to consider is that the success of arthroscopic treatments based on the severity of the lesion has been somewhat disputed. According to one study, when the width of the lesion increases, the surgical success rate shifts insignificantly relative to the study population size, as seen with a 74.1% (86 out of 116) success rate for cartilage lesions that are ten to nineteen millimeters wide while there is an 87.2% (41 out of 47) success rate for cartilage lesions that are twenty millimeters or wider (McIlwraith, 2013; McIlwraith et al., 1991). This could be caused by the removal of the damaged and dissociated cartilage purely reducing the inflammation and lameness of the horse. It should be noted that there were no long-term results associated with the study. However, another case study indicated that there is a significant increase in the chance for recovery when performing on lesions that are less than two centimeters in length compared with performing a surgical debridement on lesions longer than two centimeters (Foland et al., 1992). Another important attribute that this surgical technique has is that the age of the horse receiving the treatment did not affect the success of the surgery (McIlwraith, 2013; Foland et al., 1992).

One of the primary issues seen with the use of surgical cartilage removal is the development of fibrocartilage replacing the removed hyaline cartilage (Nixon et al., 2010). With regard to this development, the fibrocartilage is less flexible and makes it more prone to the development of cartilage irregularities on the subchondral bone plate. The irregularities can lead to the development of osteoarthritis as a long-term prognosis.

3.3.3 Regenerative Treatments

As seen with surgical treatments, regenerative treatments follow the diagnostic tests that confirm the disease. Regenerative treatments of this disease include resorbable pinning, stem cell transplantation such as bone grafting and tissue grafting.

3.3.3.1 Resorbable Pinning

Resorbable pinning is the most well-known regenerative treatment for OCD. The pins used are composed of polydioxanone (PDS) so that they will resorb into the cartilage and bone after the healing has occurred (McIlwraith, 2013; Laverty and Girard, 2013; Nixon et al., 2010). This procedure is generally performed under the conditions that the cartilage lesion is extensive

(> 2 cm), attached to the surrounding cartilage in at least 180° of the lesion center as well as presenting with a lack of mineralization within the cartilage flap (Nixon et al., 2010; Fortier and Nixon, 2005). An additional requirement of this treatment is that the surface of the OCD cartilage be relatively smooth (Nixon et al., 2010). In order to perform this procedure, arthroscopic techniques will be used to access the cartilage and assess the viability of the treatment. After determining the viability of the treatment, a portal is made directly over the affected condyle or trochlea in which an arthroscopic guide cannula is inserted to create the insertion points for the pins.

K-wire perforations are drilled perpendicular to the articular surface with multiple degrees of flexion (Nixon et al., 2010). Two 20 cm pins are placed with approximately 2 cm protruding from the insertion to secure the cartilage flap. One case presented the treatment of 16 out of 18 OCD joints with PDS pinning of 12 horses with a mean age of 6.8 months. In this case, most of the pinning showed subchondral bone resolution within 9 months after surgery, with exceptions in three cases: (1) two bilateral stifle joint OCD lesions being incompletely resolved with two racing horses and (2) one fetlock lesion slowly healing around 18 months. In another instance where PDS pins were used in 40 of the 44 joints afflicted in a study population of 27 horses suffering from a myriad of OCD lesions, 32 of the joints were treated with simple pinning and 8 were treated with debridement and pinning. These 40 joints presented a significant improvement of their respective lesions within 6 months of the treatment (McIlwraith, 2013; Sparks et al., 2011). 20 of the horses were able to provide long-term data in which 19 were sound and were able to perform athletically. However, one of the biggest issues with PDS pinning is its inability to rehabilitate necrotic tissue, so there are occasions where debridement and PDS pinning must be used in unison in order to better treat the patient (Nixon et al., 2010).

3.3.3.2 Stem Cell Transplantation (Bone Grafts and Tissue Grafts)

Bone grafts are another viable, yet limited, option for treating OCD in specific cases. This type of treatment is generally reserved for deep lysis of the bone within the OCD flap region (Fortier and Nixon, 2005). This type of graft is especially beneficial in OCD flap treatment in the glenoid cavity and humeral head region of the shoulder joint. However, since OCD resolved via removing the loose bodies or necrotic cartilage, removing and replacing the bone is not necessary in most cases.

Compared with bone grafts, cartilage tissue grafts are a more suitable option in treating various cases of OCD lesions. This form of treatment uses autologous chondrocytes to heal the articular defects (Barnewitz et al., 2006). This type of treatment has been shown to improve the condition of the patient in 75% of the recorded cases. One such tissue graft is the matrix-induced autologous chondrocytes, which are embedded in a collagen sponge. This graft is generally secured in the lesion with sewing and an additional fixture with fibrin glue. However, depending on the type of lesion, fixation may not be necessary, as seen with smaller lesions, due to the sponge's adhesiveness. In some cases, the use of PDS pins may be indicated as an extra fixative. Hyaluronan-based scaffolding with autologous chondrocytes has also been implicated as an emerging treatment option for arthritic defects. In general, this form of treatment combines the tissue-growth promoting benefits of the matrices and mechanical properties of the scaffolds and regenerative properties with the autologous chondrocytes in order to promote the proper structuring of the cartilage and expedite the tissue graft establishment. More specifically, the type of tissue-proliferating matrices used include protein-rich plasma, with its TGF-β1 and platelet-derived growth factor, in tandem with other growth factors such as Bone Morphogenic

Protein 2 (for subchondral bone healing) and the cellular component will comprise of chondrocytes and mesenchymal stem cells (Tsuzuki et al., 2013).

In one study, a polymer-based cartilage tissue engineering graft treatment of eight horses with OCD was conducted (Barnewitz et al., 2006). There were no clinical differences in the horses with OCD after the treatment compared with a normal control. During histological examinations and MRI scans, the horses with the tissue grafts showed an established and integrated cartilage graft where the defect had been 12 months after the surgery with six of the patients being able to walk and trot with no lameness at 12 weeks, compared to the control subjects that developed fibrous cartilage to replace the removed hyaline cartilage cavity. Another study was performed in regard to bioengineered osteochondral precursor treatment for a 13-month-old filly with OCD on her medial tibial malleolus (Tsuzuki et al., 2013). The study indicated the successful treatment with the lesion disappearing radiographically in 12 weeks. However, this case indicated that the regrown cartilage was fibrous in nature rather than hyaline cartilage. Further, there was also a report of using a graft that had both type I and type II collagen to correct an OCD lesion in an Irish sport horse (Stack et al., 2016). The horse was presenting bilateral proximal and middle lateral trochlear ridge (LTR) lesions in its distal femur. In this case, 22 months after surgery, the lesions were radiographically reviewed and were determined to (1) show healing of the subchondral bone, (2) be smoother and flatter than normal and (3) there was no presence of free bodies or osteoarthritis. At the 5-month evaluation, the lesions' length and depth were measured to be 46 mm and 17 mm in the left LTR and 40 mm and 18 mm in the right LTR. Upon reviewing the 22-month evaluation, the lesions' length and depth was reduced to 33 mm and 17 mm in the left LTR and 35 mm and 17 mm in the right LTR.

Regardless, the lesions were covered with cartilage and the integrity of the joint surface was restored.

3.3.3.3 Gene Product Adjunct Therapy

Gene product adjunct therapy is one of the most desired treatments as the disease has underlying genetic causes. In regard to using gene product, the use of TGF-β, BMP-2, IGF-1 or BMP-7 have been shown to increase the healing ability of the cartilage (Nixon et al., 2007). Other growth factors, such as FGF-2, EGF and GDF-5, have been indicated in increasing the healing capabilities of the articular cartilage. This therapy is used in tandem with the stem cell transplantations in order to promote the repair rate, as seen with IGF-1 and its stimulatory effects on chondrocytes. There have also been studies using RNA interference to decrease the activity of catabolic, proinflammatory proteins, such as IL-1 and TNF-α, that limit growth via continually degrading the cartilaginous matrix, in order to promote tissue growth and articular homeostasis.

3.4 Success of Treatments[6]

Additional studies that have been performed on the efficacy of arthroscopic debridement of OCD should be noted.

3.4.1 Additional Surgical Treatment Cases

Several studies of treating OCD in horses with surgical techniques, specifically arthroscopic debridement, have been done. In one instance where 12 racehorses were afflicted with OCD in 16 joints (combined), 14 of the joints were radiographically confirmed to have their lesions resolved with the remaining two joints developing small, mineralized flaps of 3 to 5 mm (Fortier and Nixon, 2005). 10 of the horses were deemed sound and joint effusion had subsided in nine of the horses in 6 to 8 weeks. After the recovery period, they were able to successfully

[6] It should be noted that the conservative management is not discussed due to it being a separate type of treatment from surgical and regenerative treatments.

return to racing. In another study with 124 racehorses (various breeds including standardbred, thoroughbred and quarter horses) and 59 non-racehorses[7] with tarsocrural joint lesions that were followed-up after arthroscopic debridement surgery, it was reported that the success rate of returning to soundness was 73% and 83%, respectively (McIlwraith et al., 1991). In another study population of 134 horses, 79 racehorses and 55 non-racehorses, which underwent femoropatellar arthroscopic surgery, it was recorded that 86 horses of the 134 (64%) were successful at returning to soundness while 21 (16%) horses were unsuccessful due to reasons related to the surgery, 18 (13%) horses were unsuccessful due to reasons independent of the surgery and 9 (7%) horses remained in training (Foland et al., 1992). In the same study with regard to OCD in different joints being treated simultaneously with the femoropatellar joint OCD, 11 of the horses that were available for data collection presented a 55% success rate for the surgery with the other 5 (45%) horses being unsuccessful. One study focusing on treatment of the lateral femoral trochlear ridge osteochondrosis, specifically, determined that 27 (73%) of the 37 horses that received the arthroscopic debridement surgery were complication-free in the short-term, while only 19 (66%) of the 29 horses available for a long-term follow-up check being athletically sound with half (17%) of the 10 remaining horses performing less than expected and the other half (17%) being unable to perform (UpRichard et al., 2013). Lastly, a study that focused more on the effusion reduction after surgery was performed based on the cartilage oligomeric matrix protein (COMP) and fibromodulin concentrations in 115 horses before surgery compared to 73 horses in a follow-up examination using synoviocentesis (Brink et al., 2015). In the study, a statistical difference was identified as significant ($p = 0.01$) with the post-surgery COMP and fibromodulin concentration based on the age of the horse (age < 10 years). The

[7] Horses that did not compete in the sports industry as professional athletes.

severity of the joint effusion was also determined to be significant (p = 0.004) with concentrations of fibromodulin but not COMP. The last significant difference seen with the two measured protein concentrations was a significant (p = 0.001) drop in fibromodulin and a significant (p = 0.001) decrease in the fibromodulin-to-COMP ratio post-surgery. This would indicate a reduction in the swelling at the site of the joint post-surgery.

3.4.2 Analysis of Surgical and Regenerative Treatments

Looking at surgical treatments compared to regenerative treatments, there are positive and negative aspects for each and some potential problems with the regenerative treatments that need to be rectified. First, looking at the general success rates with the surgical and regenerative OCD joint treatments, based on the accessed studies, the surgical treatments have an average success rate of 73± 3% (Table 2) while the regenerative treatments have a higher average success rate of 87 ± 4% (Table 3). It should be noted that case studies with cartilaginous graphs were not included in the average regenerative success rates since they have one horse each (Table 4). This statement should be tempered by the difference in large sample population arthroscopic studies available compared with regenerative treatment studies as the arthroscopic studies are more plentiful and have more horses included.

Table 2: *Summary of Surgical Treatment Studies Throughout the Results Section*

Treatment Type - *Subtype*	Time of Measure	Horse Population	Average Age of Horse Population	% Sound after treatment	Reference
Surgical – *Arthroscopic Debridement*	Not Provided	116 (11 – 19 mm lesion)	Not Provided	74%	(McIlwraith, 2013; McIlwraith et al., 1991)
Surgical – *Arthroscopic debridement*		47 (20+ mm lesion)		87%	
Surgical – *Arthroscopic Debridement*	Not Provided	37 (Short-term)	Not Provided	73%	(UpRichard et al., 2013)
Surgical – *Arthroscopic Debridement*		29 (Long-term)		66%	
Surgical – *Arthroscopic Debridement*	Not Provided	12 (16 joints)	Not Provided	83%	(Fortier and Nixon, 2005)
Surgical – *Arthroscopic Debridement*	Variable (Timeframe Not Given)	124 (racing)	2.4 years	73%	(McIlwraith et al., 1991)
Surgical – *Arthroscopic Debridement*		59 (non-racing)		83%	
Surgical – *Arthroscopic Debridement*	Variable (Timeframe Not Given)	134	2 years	64%	(Foland et al., 1992)
Surgical – *Arthroscopic Debridement*	Not Provided	11 (OCD in different joints)	2 years (subpopulation of previous study)	55%	

Table 3: *Summary of Regenerative Treatment Studies Throughout the Results Section*

Treatment Type - *Subtype*	Time of Measure	Horse Population	Average Age of Horse Population	% Sound after treatment	Reference
Regenerative – *PDS Pinning*	18 months	12 (18 joints)	6.8 months	89%	(Nixon et al., 2010)
Regenerative – *PDS Pinning*	15.6 months (average)	27 (44 joints)	9.7 months	91%	(McIlwraith, 2013; Sparks et al., 2011)
Regenerative – *PDS Pinning*		20 (Long-term)		95%	
Regenerative – *Autologous Cartilage Graft*	12 months	8	2 years	75%	(Barnewitz et al., 2006)

Table 4: *Summary of Case Studies for Autologous Cartilage Grafts*

Treatment Type - *Subtype*	Time of Measure	Horse Population	Average Age of Horse Population	% Sound after treatment	Reference
Regenerative – *Autologous Cartilage Graft*	16 weeks	1	13-month-old	100%	(Tsuzuki et al., 2013)
Regenerative – *Autologous Cartilage Graft*	22 months	1	15-month-old	100%	Stack et al., 2016)

Surgical treatments are better at handling severe OCD lesions. It was noted that OCD lesion size did not significantly affect the prognosis of the outcome with success in both larger and smaller lesions, as indicated in a study with OCD in the distal intermediate ridge of the tibia (McIlwraith, 2013). This could be due to the surgical debridement relying solely on removing the damaged and necrotic cartilage rather than attempting to stimulate the cartilage to repair. However, due to the nature of articular joints replacing the removed hyaline cartilage with fibrous cartilage, long-term athletic performance duration may be decreased due to the relative inelasticity of fibrous cartilage (Boorman et al., 2020; Semevolos, 2017). This lack of elasticity can eventually lead to the development of arthritis. It is important to note that the surgical techniques have achieved similar success rates with horses that are over three years of age, not including other complications that can occur as horses age. However, the regenerative treatments for OCD are generally performed on younger horses, as indicated in some of the previous studies. It can be deduced that the regenerative treatments, such as using PDS pins for articular cartilage reattachment, would be more effective with younger patients with higher levels of growth factors if there are not IGF-1 and BMP-7 therapies included to the recovery period. The difference in age ranges with the treatments may also be indicative of certain severity conditions that the lesion cannot pass, as also seen with PDS pin treatments. However, there are some regenerative therapies that use debridement in conjunction with tissue grafting, so they would most likely not be affected by the severity. Also, regenerative treatments that utilize gene product adjunct therapy may negate the issue with age previously mentioned. Whatever the case, it seems that arthroscopic surgeries are favored in older horses.

In regard to the previously mentioned fibrous cartilage repair as it relates to regenerative treatments, there are diverging results. In some instances where IGF-1 and BMP-7 gene protein adjunct therapies are used along with allogenic chondrocyte placement, articulating cartilage has been repaired, while other cases such as where TGF-β was used along with a bioengineered tissue graft, the result was fibrous cartilage repair (Nixon et al., 2007; Tsuzuki et al., 2013). It should be noted that in cases where the original cartilage is pinned for reattachment, the fibrous cartilage repair is minimum. In this case, more research needs to be conducted to ensure that hyaline cartilage repair occurs so that the long-term success rate will be improved.

Comparing the relative times for recovery between surgical and regenerative treatments, the duration is similar with approximately 3 months of recuperation before training can resume.

For instance, it was reported that walking exercises in horses treated with PDS pinning could begin at the 14-day mark after surgery (Fortier and Nixon, 2005). Compared with the seven-day stall period for arthroscopy, followed by hand walking, the difference in a week seems to be minimal. It should be noted that arthroscopy could heal faster or slower than the regenerative medicines depending on the severity of the cartilage degeneration. Also, tissue grafts may take longer, on average, due to some of the complications that may arise from implementing foreign tissue into the joint site such as seen in one study with fluid secretion and dehiscence of the wound at the site of arthrotomy (Stack et al., 2016). Other plausible causes for discrepancies in the healing process duration include the presence of foreign material, as seen with the regenerative methods, or an increased tissue repair load as seen in the surgical treatments. One factor that may prove indispensable in reducing the recovery period for both methods would be the gene protein adjunct therapies that are already implemented along with most regenerative treatments. Lastly, it would seem that surgical methods are less costly, treatment-wise, than regenerative therapies as the extra materials needed to perform the later type of treatment are specially made and more costly than straight removal of the cartilage. For instance, the current estimate for each PDS pin is approximately $100, in addition to the surgical fees (Fortier and Nixon, 2005). However, it was found in one study that horses with OCD that was surgically treated had approximately four fewer winning races and raced for approximately one-third fewer years compared with non-OCD affected horses (Boorman et al., 2020). One potential reason for this discrepancy could be that the horses which were treated surgically developed more fibrous cartilage which could have reduced their ability to perform athletically. It should be noted that the conservative management was not discussed as a part of analyzing the treatment success for this review since it does not fall in either the surgical or regenerative category.

4. CONCLUSION

Overall, regenerative treatments are more effective based on the studies provided regarding hyaline cartilage retainment and in younger animals while surgical methods are more effective on older patients with more severe cases of OCD. As far as costs are concerned, regenerative therapies tend to be more expensive short-term but surgical techniques may reduce the career lifespan that an equine athlete has. In reference to the duration of recovery, the regenerative therapies and surgical methods have a similar recovery period with the surgical methods having the potential to be quicker or slower depending on the severity of the cartilage degradation. The gene product adjunct therapies that often accompany the regenerative treatments may also play a role in increasing the tissue replacement rate of regenerative treatments currently and both surgical and regenerative treatments in the future. In regard to the review, regenerative treatments tended to have a higher success rates compared with surgical treatments. However, surgical treatments tended to be more suitable to a wider variety of OCD lesion presentations. Additional improvements that need to be further researched includes the following: (1) the gene product adjunct therapy that will allow hyaline cartilage repair, (2) a PDS pinning technique that allows for a lesion to have less than half of its circumference still attached and (3) the use of gene product adjunct therapy combined with PDS pinning. The results of the research could increase the success rate of OCD lesion treatment in the future.

REFERENCES

Ahmadi, F., Mirshahi, A., Mohri, M., Sardari, K., Sharifi, K., 2021. Osteochondrosis dissecans (OCD) in horses: Hormonal and biochemical study (19 cases). Veterinary research forum: an international quarterly journal. URL https://pubmed.ncbi.nlm.nih.gov/34815844/.

Barnewitz, D., Endres, M., Krüger, I., Becker, A., Zimmermann, J., Wilke, I., Ringe, J., Sittinger, M., Kaps, C., 2006. Treatment of articular cartilage defects in horses with polymer-based cartilage tissue engineering grafts. Biomaterials 27, 2882–2889. doi:10.1016/j.biomaterials.2006.01.008

Bates, J.T., Jacobs, J.C., Shea, K.G., Oxford, J.T., 2014. Emerging genetic basis of osteochondritis dissecans. Clinics in Sports Medicine 33, 199–220. doi:10.1016/j.csm.2013.11.004

Baxter, G.M., Stashak, T.S., 2011. Examination for Lameness, in: Adams and Stashak's Lameness in Horses. Wiley-Blackwell, Hoboken, New Jersey, pp. 109–207.

Boorman, S., Hofmeister, E.H., Ross, M.W., Ralston, S., Bell, G., Mackie, S., Ortved, K., 2021. Influence of osteochondrosis on the longevity and racing performance of Standardbred Trotters and Pacers. Veterinary Surgery 50, 507–516. doi:10.1111/vsu.13568

Bourebaba, L., Röcken, M., Marycz, K., 2019. Osteochondritis dissecans (OCD) in horses – molecular background of its pathogenesis and perspectives for progenitor stem cell therapy. Stem Cell Reviews and Reports 15, 374–390. doi:10.1007/s12015-019-09875-6

Bourzac, C., Alexander, K., Rossier, Y., Laverty, S., 2009. Comparison of radiography and ultrasonography for the diagnosis of osteochondritis dissecans in the equine femoropatellar joint. Equine Veterinary Journal 41, 686–692. doi:10.2746/042516409x452134

Brink, P., Smith, R.K.W., Tverdal, A., Dolvik, N.I., 2015. Changes in synovial fluid biomarker concentrations following arthroscopic surgery in horses with osteochondritis dissecans of the distal intermediate ridge of the tibia. AVMA. URL https://avmajournals.avma.org/view/journals/ajvr/76/7/ajvr.76.7.599.xml#d1237361e492.

Foland, J.W., McIlwraith, C.W., Trotter, G.W., 1992. Arthroscopic surgery for osteochondritis dissecans of the femoropatellar joint of the horse. Equine Veterinary Journal 24, 419–423. doi:10.1111/j.2042-3306.1992.tb02870.x

Fortier, L.A., Nixon, A.J., 2005. New surgical treatments for osteochondritis dissecans and subchondral bone cysts. Veterinary Clinics of North America: Equine Practice 21, 673–690. doi:10.1016/j.cveq.2005.07.005

Laverty, S., Girard, C., 2013. Pathogenesis of epiphyseal osteochondrosis. The Veterinary Journal 197, 3–12. doi:10.1016/j.tvjl.2013.03.035

McIlwraith, C.W., 1990. Osteochondral fragmentation of the distal aspect of the patella in horses. Equine Veterinary Journal 22, 157–163. doi:10.1111/j.2042-3306.1990.tb04236.x

McIlwraith, C.W., 2013. Surgical versus conservative management of osteochondrosis. The Veterinary Journal 197, 19–28. doi:10.1016/j.tvjl.2013.03.037

McIlwraith, C.W., Foerner, J.J., Davis, D.M., 1991. Osteochondritis dissecans of the tarsocrural joint: Results of treatment with arthroscopic surgery. Equine Veterinary Journal 23, 155–162. doi:10.1111/j.2042-3306.1991.tb02746.x

McIlwraith, C.W., Frisbie, D.D., Kawcak, C.E., Weeren René van, Barrett, M.F., 2016. Fetlock, in: Joint Disease in the Horse. Elsevier, pp. 305–307.

Nixon, A.J., Fortier, L.A., Goodrich, L.R., Ducharme, N.G., 2010. Arthroscopic reattachment of osteochondritis dissecans lesions using resorbable polydioxanone pins. Equine Veterinary Journal 36, 376–383. doi:10.2746/0425164044868477

Nixon, A.J., Goodrich, L.R., Scimeca, M.S., Witte, T.H., Schnabel, L.V., Watts, A.E., Robbins, P.D., 2007. Gene Therapy in Musculoskeletal Repair. New York Academy of Sciences vol. 1117, 310-27. Doi:10.1196/annals.1402.065

Nixon, A.J., Stashak, T.S., McIlwraith, C.W., Aanes, W.A., Martin, G.S., 1984. A muscle separating approach to the equine shoulder joint for the treatment of osteochondritis dissecans. Veterinary Surgery 13, 247–256. doi:10.1111/j.1532-950x.1984.tb00803.x

Semevolos, S.A., 2017. Osteochondritis dissecans development. The Veterinary clinics of North America. Equine practice. URL https://pubmed.ncbi.nlm.nih.gov/28551287/.

Sparks, H.D., Nixon, A.J., Fortier, L.A., Mohammed, H.O., 2011. Arthroscopic reattachment of osteochondritis dissecans cartilage flaps of the femoropatellar joint: Long-term results. Equine Veterinary Journal 43, 650–659. doi:10.1111/j.2042-3306.2011.00362.x

Stack, J.D., Levingstone, T.J., Lalor, W., Sanders, R., Kearney, C., O'Brien, F.J., David, F., 2016. Repair of large osteochondritis dissecans lesions using a novel multilayered tissue engineered construct in an equine athlete. Journal of Tissue Engineering and Regenerative Medicine 11, 2785–2795. doi:10.1002/term.2173

Trotter, G.W., McIlwraith, C.W., Norrdin, R.W., 1983. A comparison of two surgical approaches to the equine femoropatellar joint for the treatment of osteochondritis dissecans. Veterinary Surgery 12, 33–40. doi:10.1111/j.1532-950x.1983.tb00700.x

Tsuzuki, N., Seo, J.P., Haneda, S., Yamada, K., Furuoka, H., Tabata, Y., Sasaki, N., 2013. Bioengineered osteochondral precursor for treatment of Osteochondritis dissecans in a thoroughbred filly. Australian Veterinary Journal 91, 411–415. doi:10.1111/avj.12104

UpRichard, K., Elce, Y.A., Piat, P., Beauchamp, G., Laverty, S., 2017. Outcome after arthroscopic treatment of lateral femoral trochlear ridge osteochondrosis in sport horses. Veterinary and Comparative Orthopaedics and Traumatology. URL https://www.thieme-connect.com/products/ejournals/abstract/10.3415/VCOT-11-12-0182.

Wright, I.M., Minshall, G.J., 2013. Identification and treatment of osteochondritis dissecans of the distal sagittal ridge of the third metacarpal bone. Equine Veterinary Journal 46, 585–588. doi:10.1111/evj.12187