EFFECTS OF THERAPUTIC SHOEING INVOLVING ENHANCEMENT OF THE DIGITAL CUSHION AND DE-ROTATION OF THE P3 (COFFIN BONE) ON VASODILATION OF THE PALMAR DIGITAL ARTERIES, PAIN RELIEF, AND ENDOCRINE VALUES IN LAMINITIC HORSES.

A Report of a Senior Study

by

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ABSTRACT

Laminitis is a painful disease that results in the loss of function of the equine hoof. Laminitic treatments vary widely, and this study sought to provide an improved shoeing method using rubber shoes and location specific gel. Four horses, 2 sound and 2 laminitic, were examined for 276 days. Sound horses followed standard trimming, whereas laminitic horses received Polyflex Morrison Open Roller glue on shoes and Equi-pak CS (copper sulfate) soft gel, which provided support for ½ to ¾ of the digital cushion. Progression was monitored using ultrasonography of the palmar digital arteries, radiographs of the coffin bone, BCS values, lameness scores, and endocrine values. A larger decrease occurred in digital artery area for the laminitic equids in comparison to the controls as the study progressed. Due to small sample size, the digital artery area was not found to be significant at the end but did progress toward lower values throughout days 63, 237, and 262 ($p= 0.50$, $p= 0.06$, and $p= 0.09$ respectively). Radiographic images of the coffin bone in the forelimbs did decrease as laminitic equids returned to standard values more similar to the sound equids through days 57.5, 162, and 261 ($p= 0.15$, $p= 0.77$, and $p= 0.35$ right fore, and $p= 0.11$, $p=0.42$, and $p= 0.45$ left fore). BCS values did not significantly decreased ($p= 0.19$), whereas lameness scores were significantly different at the beginning of the study ($p<0.001$) but not different at the end ($p= 0.15$). Cortisol values were significantly reduced in treated horses ($p=0.05$). In conclusion, therapeutic shoeing via stimulation of the digital cushion resulted in

decreased digital artery area leading to increasing blood profusion in the hoof, de-rotation of the coffin bone, normalization of lameness scores, and significant reduction of cortisol levels. The use of rubber shoes with supportive gel covering ½ to ¾ of the back of the hoof is an effective treatment method. Furthermore, ultrasonography was useful as a non-invasive prognostic and diagnostic tool for monitoring blood profusion in laminitic horses.

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CHAPTER I

INTRODUCTION

Laminitis is a disease that results in the loss of function in equine hooves due to laminar cell death. The effects of laminitis can range from minor to extreme lameness, and horses with chronic laminitis suffer from extreme pain and restricted mobility. Laminitis is not significantly more prevalent in any region of the United States but does increase during the spring and summer seasons (USDA, 2000). Laminitis is also seen to have a profound monetary effect on the equine industry. It is estimated that 15% of horses in the United States will develop laminitis during their life and 75% of these horses will have severe laminitis that will require euthanasia (Eades et al., 2002). Treatment and diagnostic costs of laminitis can reach $8 million annually with an additional $5 million due to the horse’s death (Eades et al., 2002). In summary, laminitis results in a large sum of monetary loss to the owner and extreme suffering to the horse with few recoveries.

Laminitis:

Laminitis is a painful debilitating disease of the equine hoof with multiple causes that all lead to the same physiological outcome. Toxic insult or dysfunction in perfusion to the laminae tissue results in an exaggerated response when compared to other species due to the hard-keratinized structure of the hoof wall. The hoof walls hard structure allows limited expansion of laminar capillary tissue. The main function of the laminar tissue is to attach and support the coffin bone to the hoof wall (see figure 1). Destruction of laminar tissue leads to hoof wall separation with rotation and sinking of the coffin bone. The horse's bodyweight and the pull from the deep digital flexor tendon mechanically cause laminar separation. Inflammation of the laminae tissues also results in edema, lower blood profusion in the hoof, vasoconstriction, hypoxia, and eventual laminar cell death. Any insult to vascular profusion causes laminar cell death resulting in the same debilitating laminitic disease in the equine. The severity of laminitis depends upon the degree of laminar damage (Adams, 1974; Belknap, 2019).

Causes of Laminitis:

The main predisposing factors of laminitis are grass founder, grain founder, endocrine dysfunction (PPID, EMS), road founder, stress founder, and foal founder. Grass founder is caused by over consumption of grass, which results in high levels of glucose (see Figure 2).

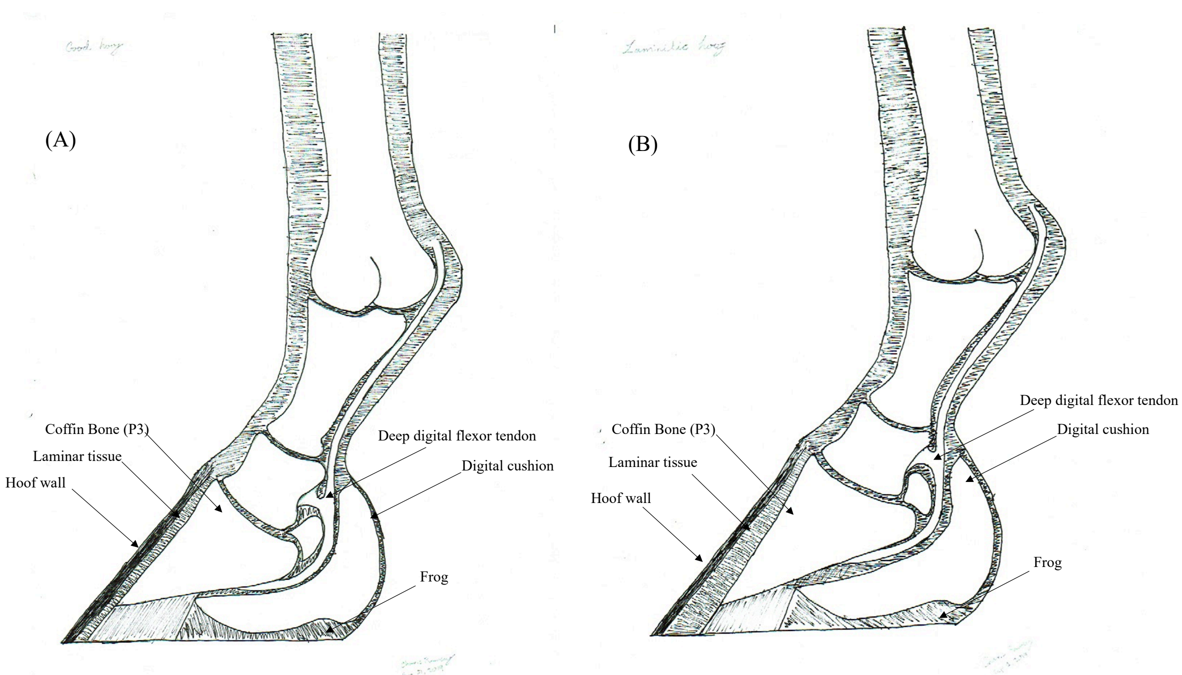

Figure 1: Hoof anatomy. (A) Healthy laminae of a horse's hoof attaching the P3 bone to the hoof wall. (B) Separation of laminae with rotation of coffin bone.

The high concentrations of circulating glucose stimulate the secretion of insulin. The effects caused by increased concentrations of glucose and insulin are seen mainly in the fore limbs of the horse due to the fore limbs bearing 60% of the body weight. High levels of glucose due to obesity can result in insulin resistance. Insulin resistance causes vasoconstriction in the endothelial layer of vessels causing vascular dysfunction (Morgan et al., 2016). It is also heavily correlated with laminitis (De Laat et al., 2019). However, only high concentrations of insulin infused with glucose can cause laminitis (Sillence et al., 2007).

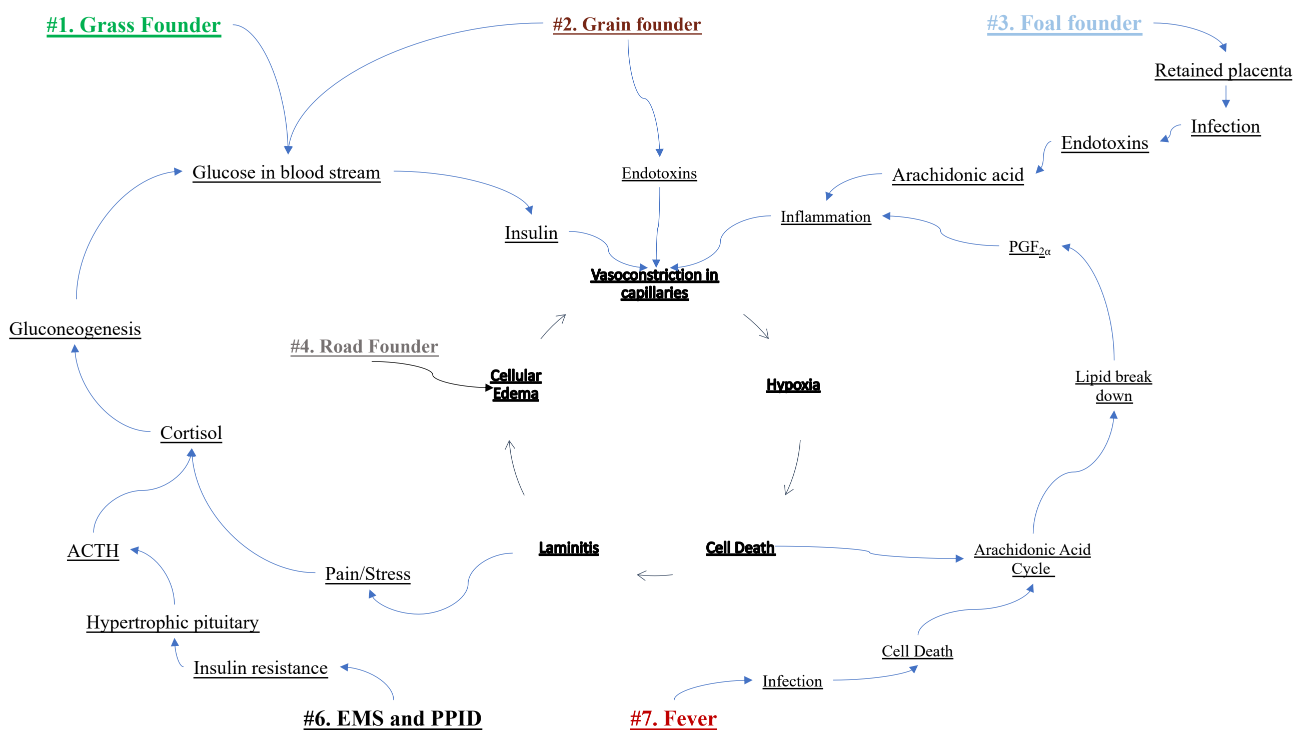

Figure 2: Laminitic cycle. A flowchart of the effects of grass founder, grain founder, foal founder, road founder, equine metabolic syndrome (EMS), Pars pituitary intermedius disorder (PPID), and stress/fever on laminitis.

The tissues in a horse's hoof require large amounts of glucose daily to maintain proper function (Huntington et al., 2009). Glucose uptake in laminar tissues is not affected by insulin concentrations, due to the presences of the glucose transporter GLUT1. However, the uptake of glucose in the endothelial cells of the vessels (i.e. the laminar capillaries) are dependent on insulin. The increased insulin and glucose concentrations in the blood stream cause the endothelial cells to increase the amount of intracellular glucose. This leads to vasoconstriction which results in decreased blood flow to the laminar tissue, causing deprivation of glucose. Decreased amounts of glucose consumption in the laminar tissue results in tissue separation. When glucose and oxygen decrease in the laminar tissue, cell death occurs. Laminar cell death is intensified by pressure from the horse's weight and pull of the deep digital tendon results in rotation of the coffin bone and further separation of the laminae resulting in severe lameness.

An additional cause of laminitis is over consumption of grain (Pollitt, 1999). This leads to an overgrowth of bacteria and a pH change in the hindgut due to fermentation causing pain and discomfort. The cause of laminitis by grain founder is poorly known. However, it is thought to be caused by the microorganism *Streptococcus bovis.* This microorganism is seen to activate the enzyme metalloproteinase-2 (MMP-2) which has caused laminitis *in vitro*. However, the absorption of *S. bovis* from the gut into the blood stream is yet to be determined.

Other causes of laminitis are associated with abnormalities in endocrine and hormonal values (see figure 3; see also Morgan et al., 2016). One endocrine abnormality is equine metabolic syndrome (EMS), which is characterized by obese horses expressing insulin resistance (IR) (Huntington et al., 2009). Obesity and IR lead to lipid abnormalities with increased triglyceride concentrations in the blood. This can result in vasoconstriction and tissue injury. Tissue injury can activate the arachidonic acid cycle which produces prostaglandin E_2 (PGE_2). This results in the stimulation of fever, pain, and $PGF_{2\alpha}$. $PGF_{2\alpha}$ causes inflammation which results in vasoconstriction, reduction of oxygen and glucose concentrations, and laminar cell death (Ricciotti & FitzGerald, 2011).

Another possible endocrine related cause is pituitary pars intermedia dysfunction (PPID) also known as Cushing's disease (Donaldson et al., 2004). This results in increased production of adrenocorticotropic hormone (ACTH) which leads to the enlargement of the pituitary gland. ACTH testing is used to diagnose PPID in horses, but there is not significant evidence showing that PPID is a stimulus for laminitis. The production of ACTH is thought to be stimulated by severe pain, such as is experienced in laminitic episodes.

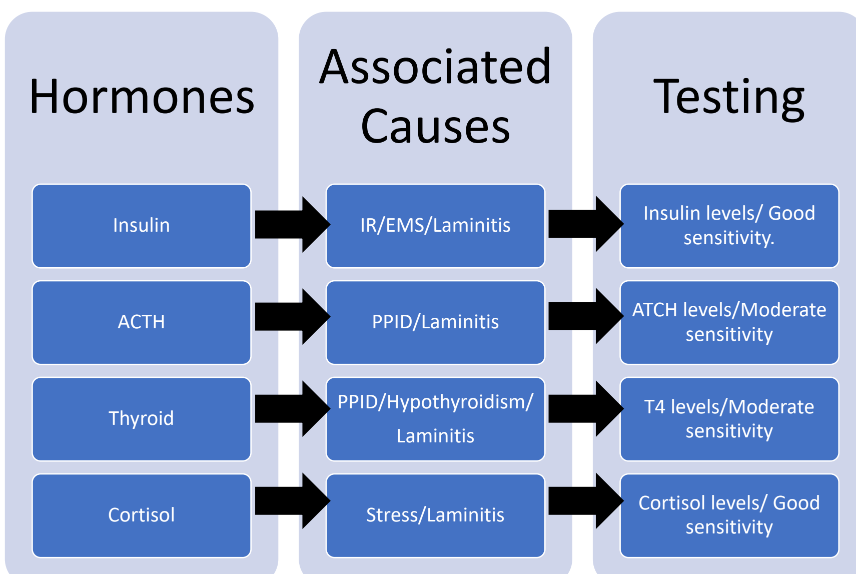

Figure 3: Hormonal productions during laminitis with associated causes and testing. All causes of laminitis result in vasoconstriction, hypoxia, and laminar cell death.

Using ACTH testing as an indicator for laminitis is challenging due to the effects of photoperiods on ACTH concentrations (Beech et al., 2009). ACTH levels were seen to increase from February to late August and to decline through late September to October. However, current reference values for ACTH do not fully represent normal ACTH values based on seasonal effects. This results in skewed interpretation of ACTH values determined during testing. Further research is needed for defining accurate ACTH reference values that reflect seasonal changes (Beech et al., 2009). PPID can also be diagnosed by monitoring the response of ACTH and cortisol levels to TRH (thyroid releasing hormone) or DST (dexamethasone suppression test). TRH and DST are useful tests for determining PPID because they directly affect the production of ACTH, cortisol, and thyroxine (T_4) (Beech et al., 2007).

Road founder is now a less common stimulus for laminitis. Laminitis results from excessive pounding of the hooves on hard surfaces. This leads to bruising and inflammation of the tissue in the equine hoof. Swelling in the laminar tissues results in decreased blood flow to the damaged area due to the restricted expansion caused by the hoof wall. Lack of blood flow leads to decreased concentrations of oxygen and glucose in the laminar tissue resulting in cell death. Death and separation of the laminar tissue results in rotation of the coffin bone causing laminitis (Lucas, 1963; see also Adams, 1974; Belknap, 2019).

A final cause for laminitis is foal/stress founder. This can result from a retained placenta causing stress, tissue injury, and productions of endotoxins (Rose et al., 1993). During high levels of chronic stress, cortisol is released from the adrenal gland. This results from the release of ACTH which in turn stimulates further production of cortisol (Singh, 2003). Laminitis is associated with increased cortisol levels especially in the hoof (Johnson et al., 2004). Increased cortisol levels do cause endothelial dysfunction and vasoconstriction (Morgan et al., 2016). However, hypercortisolemia is not associated with PPID or EMS, but there is strong evidence of peripheral cortisol dysfunction in horses with chronic laminitis (Morgan et al., 2016). High cortisol concentrations lead to gluconeogenesis, mainly in the liver, producing increased concentrations of glucose in the blood stream (Khani & Tayek, 2001). Increased glucose concentrations stimulate insulin production which results in vasoconstriction and eventually laminar cell death (Huntington, Pollitt, & McGowan, 2009). This results in pain which stimulates the production of cortisol and other hormones leading to further production of glucose. The cycle then repeats causing more laminar cell death.

Treatments for Laminitis:

The most effective way to combat laminitis is prevention. Since grass and grain overload results in 50% of all laminitic cases, regulating a horse's diet is wise (USDA, 2000). Healthy diets should consist of properly administered nutrient supplements with regulated consumption of grass and carbohydrates and an adequate exercise routine. Following a strict dietary and exercise routine will result in a horse that is less prone to laminitic episodes.

Treatment for laminitis depends on the stage of the disease. There are 3 progressive stages of laminitis that will affect horses (see figure 4 and 5). The first stage consists of a developmental phase where laminar separation occurs. The second phase is an acute phase, where lameness is noticeable and rotation of the coffin bone begins, and the third is a chronic phase that can last throughout the horse's life with mild to severe pain and rotation of the coffin bone (Pollitt, 1999).

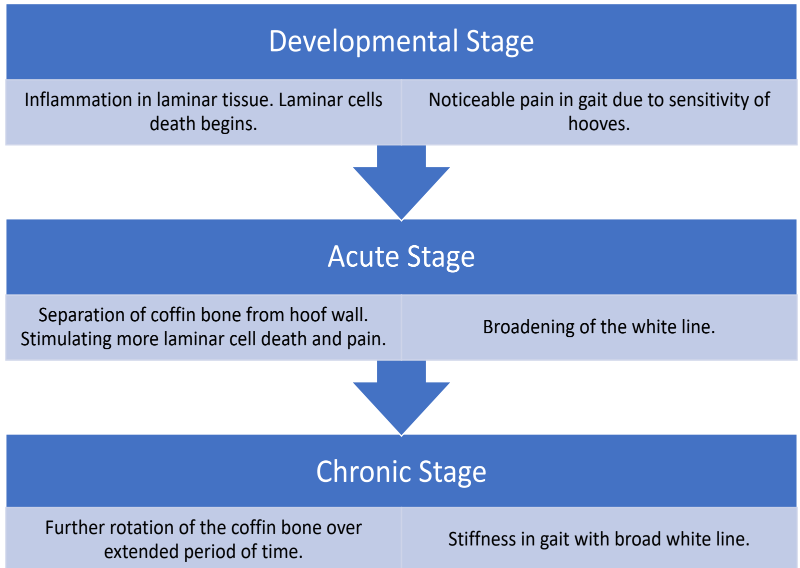

Figure 4. Disease stage progression during laminitis in equids.

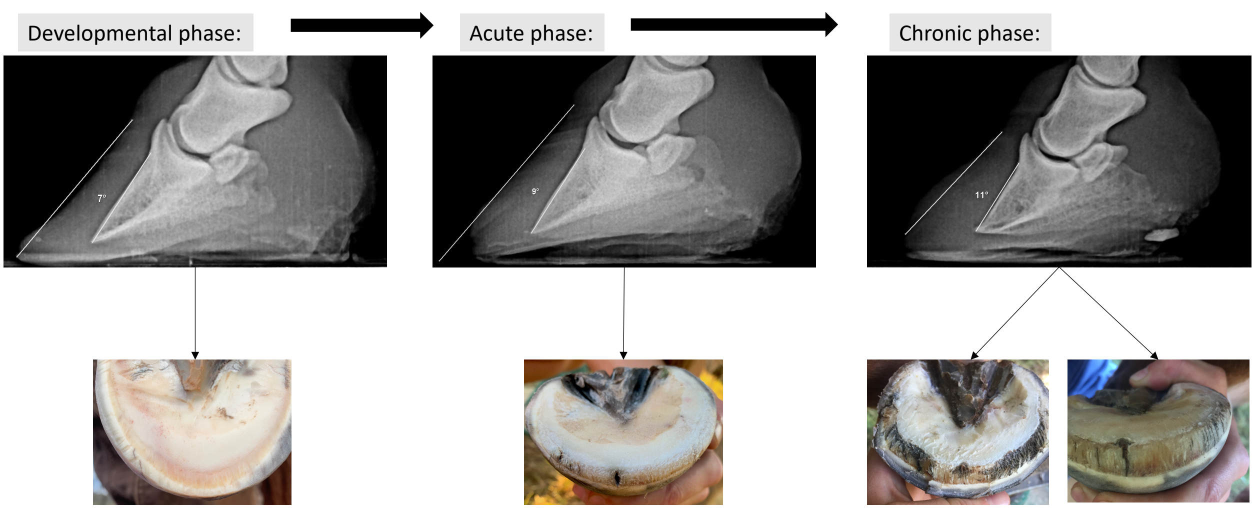

Figure 5. Radiographic images of rotation of the coffin bone with broadening of the white line, i.e. laminar tissue, during the 3 phases of laminitis.

Before treating laminitis, it is extremely important to determine the cause (Rose et al., 1993; see figure 2). Once the cause has been determined, the main course of action is to prevent further insult (Rose et al., 1993). During the developmental phase, if laminitis is caused by grain overload, then all access to grain should be strictly prohibited (Sillence et al., 2007). The same action should be taken for grass founder. That is, the horse should be removed from all lush pastures (Sillence et al., 2007). If laminitis is caused by mechanical trauma to the hoof, i.e. road founder, the horse should be placed in a soft padded stall and relieved of all work (Belknap, 2016). When caused by a retained placenta or fever, the source of infection should be removed and prompt treatment with antibiotics should be conducted (Lucas, 1963). To determine whether laminitis is caused by EMS or PPID, appropriate tests must first be conducted (Sillence et al., 2007; see also Rose et al., 1993). EMS treatment should consist of a no sugar diet and hay that has been soaked overnight to remove excess sugars (Sillence et al., 2007). A pergolide tablet is usually administered at the correct dosage to directly inhibit the par intermedius gland in treating PPID (Donaldson et al., 2002). Further treatments for all causes should consist of providing a soft bed, slipper shoes that will divert the forces applied to the horse's hoof, and support the frog (Belknap, 2016). Inhibiting inflammation and vasoconstriction is now the main focus of treatment which will hopefully prevent further laminar cell death. Drugs such as heparin, aspirin, and Polymyxin B could be used to prevent inflammation (Eades et al., 2002). Acepromazine or Nitroglycerin could be used for vasodilation (Belknap, 2001). Anything that can stimulate blood flow and prevent laminar cell death should be attempted. Another treatment to preform is distal limb cryotherapy (DLC). DLC is the application of cold water to the surrounding hoof, which significantly reduces inflammatory effects caused by laminitis (Van & Pollitt, 2009). These treatments can prevent or reduce the progression of laminitis hopefully allowing the horse to return to its normal activities.

If laminitis progresses into the acute phase, the same treatment progression should be followed as in the developmental phase. A more aggressive trimming and mechanical alleviation of pain should be taken to prevent further separation and rotation of the coffin bone. Hoof trimming that involves proper heel alignment and balance of the toes can reduce the rotation of the coffin bone (Rose et al., 1993). Permanent shoe support should also be applied to alleviate pain by redirecting the external forces on the hoof wall and for stimulation of the digital cushion (O'Grady & Parks, 2008). This should be followed by some form of weight reduction, such as a no sugar diet, water-soaked hay, and painless light exercise.

Once the horse progresses into the chronic phase, constant trimming and support shoes are recommended for treatment throughout the horse's life. The type and amount of trimming should be monitored by radiographs. If a more aggressive course of action is desired, a dorsal wall resection can be performed or the deep flexor tendon can be cut; however, effectiveness of these procedures is still unknown (Rose et al., 1993). Prevention of further incidents of laminitis is the main focus during the chronic phase, due to the horse being more prone to new laminitic attacks. A routine exercise plan that progresses as the level of foot pain decreases is an effective way to prevent further laminitic episodes (Brumbaugh et al., 1999).

Successful rehabilitation for chronic laminitis has been achieved using therapeutic trimming and shoeing (Curtis et al., 1999). Therapeutic shoeing provides reduction of pain, decreased lameness scores, and a return of normal stance and gait. It also prevents further rotation of the coffin bone and provides normal blood flow and laminar cell growth. The three main goals that therapeutic shoeing attempts to achieve are: (1) reduction of pain, (2) return of normal function of the hoof, and (3) return of normal conformation. These goals are achieved by increasing mechanical function, decreasing the forces applied to the laminar tissue, increasing the stability of the coffin bone, stimulating normal blood flow, and normalizing laminar cell growth. The majority of normal function lost in the hoof is caused by the rotation of the coffin bone, which causes abnormal forces on the hoof wall, coronary band, and subsolar soft tissue. The rotation of the coffin bone also causes disrupted blood flow and accelerated, incorrect laminar cell growth. A stepwise procedure for trimming and shoeing can be formulated by preforming a physical examination, that will determine major points of pain and the current physical stamina of the hoof. Radiographs should also be used for determining the amount and direction of trimming. Once the severity of the disease has been determined several trimming and shoeing options can be used. The most common procedures consist of trimming the distal regions to improve alignment and prevent capsular rotation. Returning the phalangeal axis and solar surface to their proper alinements and lowering the heels is also a favorable trimming procedure. Further trimming consists of removing any excess toe, which acts as a lever arm to further stimulate laminar separation and applying rolling or rocker shoes to prevent further separation due to external and internal forces. Shoes should be applied in a manner that support the frog and sole of the hoof and correctly replace the forces applied to the hoof. A more aggressive trimming procedure called coronary grooving, which allows normal cell growth and circulation, can be administered. Therapeutic shoeing consists of abnormal alterations of the hoof that will return the hoof to normal and provide stabilization. It also focuses on the importance of biomechanics over normal conformation until the hoof returns to soundness. Therapeutic shoeing is a treatment that should last for a minimum of 3-4 months and if the case is severe it should become part of the horse's monthly health routine.

One promising future treatment for laminitis is the Hyperbaric Oxygen Chamber (Slovis, 2008). The hyperbaric oxygen chamber affects a patient through mechanical pressure and increased supply of oxygen. During the pressurization, oxygen is mainly delivered through respiration and not through external absorption. The pressurized oxygen chamber does not significantly affect the rate of oxygen binding to hemoglobin but allows oxygen to be transported to the tissue in its physical solution by increasing capillary oxygen transport. This allows the poorly oxygenated tissues to be able to receive oxygen. The mechanical effects of increased pressure reduce pain and increase the removal of nitrogen. The hyperbaric oxygen chamber has many therapeutic effects. It can reverse hypoxia, alter blood supply to organs, reduce edema, regulate production of growth factors and cytokine and their receptors, and it can increase the production of vascular endothelial growth factors (VEGF) which stimulate capillary budding and granulation of a wound. These are very promising results that could be used to decrease the effects of laminitis.

Another relatively new treatment is stem cell therapy (Schnabel et al., 2013). This treatment process requires the practitioner to obtain either bone marrow- derived mesenchymal stem cells (MSC) or adipose tissue-derived MSC. The bone marrow- derived MSCs can be collected from two locations, either the sternum or the ilium. The samples can be cultured over a 2 to 3-week process, resulting in bone marrow-derived mesenchymal stem cells (BM-MSCs), or centrifuged at the location for bone marrow concentrate (BMC). The use of BMC is favored over BM-MSC, but the stem cell concentration is much lower. Stem cells obtained from adipose tissue is collected from the tail-head of the horses. These samples are digested in collagenase. One preparation process, which takes several weeks, results in adipose tissue-derived MSCs (AT-MSC). The sample can also be processed commercially within 4-24 hours resulting in adipose-derived stromal vascular fraction MSCs (AD-SVF). The use of AD-SVF is favored over AT-MSC due to the quicker process. However, AD-SVFs have a much lower concentration of stem cells. Once a stem cell derivative is obtained, it is given by regional IV limb profusion in the lateral digital vein at the sesamoid bone. However, aggressive treatment to the underlying cause must be dealt with first for stem cell therapy to have any affect. The regional IV limb profusion is normally administered twice during a laminitic episode. The first treatment should be administered as early as possible and the second 14 days later. However, there is limited data on the effectiveness and administration techniques. There is also limited research on which type of stem cell should be used and its correct dosage.

Present Study:

At present, there is no standardized shoeing procedure to treat laminitis. The purpose of this study is to first establish a standardized therapeutic shoeing procedure using a location specific gel application procedure, and second to determine blood perfusion through the small capillaries of laminar tissue using a field ultrasound. It is hypothesized that de-rotation of the coffin bone, through corrective trimming, will decrease mechanical stresses on the laminar hoof wall resulting in laminar cell growth, increase in vascular profusion and reduction of cortisol, insulin, ACTH, and thyroxine.

CHAPTER II

MATERIALS AND METHODS

Four horses were used in this study, two experimental and two controls. One was a miniature horse with chronic laminitis that had persisted over several years, and one was a small pony who had foundered in the spring a month before the study. The control horses consisted of a sound Tennessee Walker and a sound miniature horse who had experienced a light case of laminitis 5-6 years ago. All horse's feet were trimmed every 5 to 9 weeks and shoes were applied to the forefeet of the two horses with laminitis. Due to the extensive end point measurements, a larger sample size was not feasible. The experiment and procedures were approved by the Maryville College Institutional Animal Care and Use Committee (IACUC, see Appendix 1).

Trimming/Shoeing:

Trimming was conducted on days 57, 106, 154, 261. Initial preparation of the hoof required trimming that results in medial to lateral balance and cranial to caudal balance. The amount of trimming is determined using anterior to posterior radiographs and lateral to medial radiographs. Radiographs were also used to determine the intensity of the trim. Furthermore, trimming intensity was lessoned as the horses improved during treatment (see figure 6). The appropriate amount of heel was removed to give caudal balance and the appropriate amount of toe was removed to give cranial balance. The walls of the hoof were removed as needed to give lateral to medial balance. The frog was trimmed so that it remained in contact with the ground to stimulate the digital cushion.

The horse's hooves were prepared for shoeing by thoroughly cleaning the trimmed hoof. The hoof was smoothed using a random orbital sander with 60/8 course sandpaper. This was then brushed with a wire brush and all lose hoof filings were removed using a micro-torch. The hoof was then brushed and covered to prevent contact with dirt and other contaminants.

Polyflex Morrison Open Roller glue on shoes from No Anvil LLC, (Royal Palm Beach, FL) were used in this study. Each horse's hoof was individually measured for correct shoe sizing. The shoes were applied to properly trimmed and cleaned hooves using the Polyflex Bond slow set glue mixed with Glue and Sole Pack Additive (Copper Sulfate). The shoes were allowed to set for 5-7min before the horse could bare weight. All excess glue was removed. Any glue that could not be removed until the shoe had set was removed using a Dremel 3000 (see figure 7).

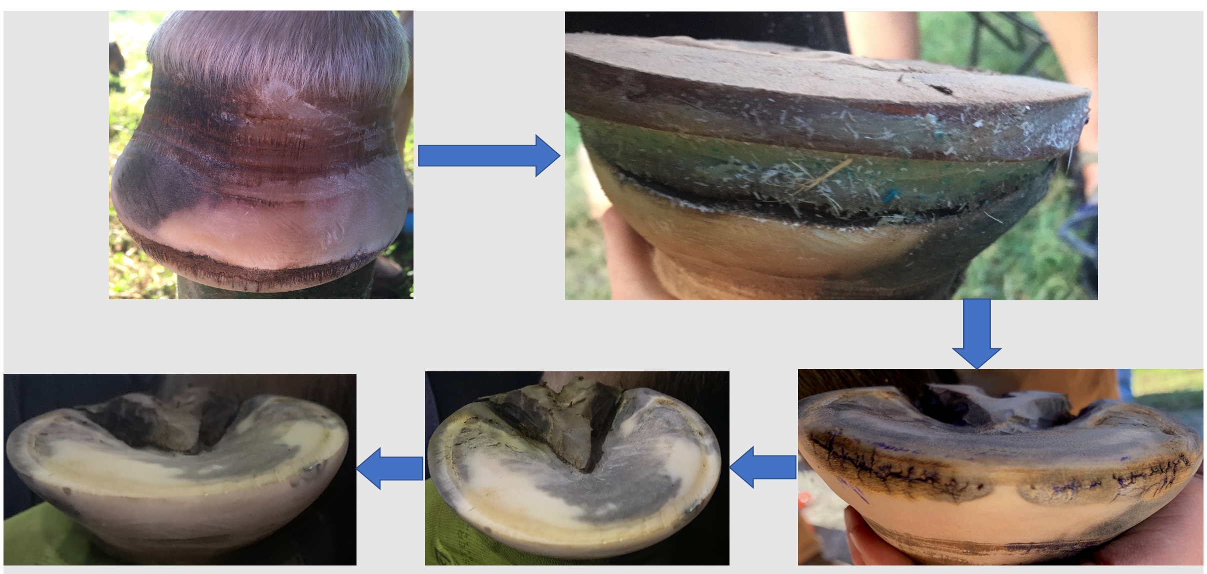

Figure 6: Intensity of trimming of the hoof wall deceased as lameness and white line (laminar tissue) decreased.

Once the shoes were set, an Equi-pak CS (copper sulfate) soft gel was used for stimulating the digital cushion. The gel was held in place using a fitted piece of mesh cut from a role of Equi-Mesh. This was positioned above the frog using two ropes that had been previously installed under the shoe before gluing (see figure 1). The gel was kept off the toe of the hoof with playdoh. This allowed only the frog to be covered with gel. Once the gel was poured in, it was allowed to set for 3-5min before the horse could bare weight. The gel only provides support for ½ to ¾ of the back of the hoof. This is from the heel to the apex of the frog (see figure 7).

Ultrasonography of the digital arteries was accomplished by washing the forefeet of the horses with water to remove contaminants. A portable ultrasound with a linear transducer (Ibex Pro, E.I. Medical Imaging, Loveland, CO) was used to obtain cross-sectional images. The hypoechoic area of the digital artery was measured. To enhance perception of the digital artery, an electric hair shaver was used to remove a 1-2-inch patch of hair proximal to the heel bulb and ventral to the ergot. Isopropyl rubbing alcohol and

Figure 7: Trimming and shoeing process for the front forefeet of laminitic horses.

Ultrasound:

ultrasound gel was used as needed on the ultrasound prob as conductive medium. Once the digital artery was identified the image was frozen and saved. Seven measurements were taken of the palmar digital artery area every session and averaged. Measurements were taken on days 63 (first trim), 118 (first shoeing), 163 (second shoeing), 237(third shoeing of experimental 1), and 262 (final shoeing).

Radiograph:

Lateral-medial radiographs were taken of the forefeet on days 57, 115, 162, and 261. Radiographs were obtained using the Bowie model PRX-90B of 50/60Hz (Toronto, Ontario Canada). The images were transferred to digital form using the ALLPRO imaging scan X trek, and the digital images were read and measured using the VetRay Vision 4.4.5 vet XP/2000 X-ray image processing program. All safety procedures were followed, such as lead jackets and monitoring badges, and the vicinity was cleared of all bystanders. The images were saved, and the degree of rotation was measured. A measuring program for laminitis was provided by the X-ray image processing. The cranial-dorsal surface of the coffin bone was measured against the cranial-dorsal surface of the hoof wall. The resulting angle measurements were recorded.

Blood Analyses:

For laminitic horses, blood was drawn on days 0, 68, and 276, but sound horses were only available for sampling on days 68 and 276. Samples were centrifuged within the hour and frozen at -20 C until shipment. Samples were analyzed by BET labs in Lexington, KY for ACTH, T_4, insulin, and cortisol.

Body Conditioning Score:

Three independent observers evaluated each horse for BCS on days 57, 115, 162, 237, and 261. Body condition scores were obtained using a scale of 1-9 (Henneke et al., 1983 see table 1). Normal active horses should range between 5-6 and conditions above 7 could be associated with progressing metabolic disorders (Henneke et al., 1983). The following six areas were felt with the hand to determine the size of fat deposits: the neck, the withers, the back, the tailhead, the ribs, and behind the shoulders.

Lameness exams:

Lameness exams were evaluated on days 57, 115, 162, 237, and 261 using the American Association of Equine Practitioners (AAEP). Lameness exams were conducted on soft and hard surfaces at different gates. Lameness scores for each horse were recorded by independent observers, and the scores of all observers was averaged.

Table 1: The Henneke body condition scoring (BCS) system was used to determine the body scores of each horse.

	Value	Description (Fat deposits in the neck, the withers, the back, the tailhead, the ribs, and behind the shoulders)
BCS	1	Extremely emaciated with poor slight deposit.
BCS	2	Emaciated with slight fat deposit.
BCS	3	Thin with some fat deposits on the ribs and tail head. Individual vertebrae easily visible.
BCS	4	Slight visibility of ribs and other structures.
BCS	5	Fat deposits conceal the ribs, the tailhead, and other body part but all blend smoothly together.
BCS	6	Fat becomes spongy around specified body areas, and a slight crease may be seen on the back.
BCS	7	Fat becomes soft and the ribs have noticeable fat fillings with a developing crease down the back.
BCS	8	A crease down the back might be seen and patchy or bulging fat is felt around body areas.
BCS	9	Extremely fat and is characterized by an obvious crease down the back, with large amounts of fat deposits.

Continual care:

The forefeet of the laminitic horses were routinely picked. Kopertox was added to the exposed part of the hoof sole and to the hoof wall to prevent thrush. Animals were fed twice daily and allowed physical activity, adequate sunshine, and turnout with a safe clean stall for inclement weather. Horses and ponies were able to interact with each other as in a healthy equine environment. The horses were also kept on their annual veterinarian exams, which included all core vaccinations (EWT, WEST NILE, and Rabies), dental care, and parasite control. All nutritional needs were met to maintain optimal health.

Statistical Analyses:

A two tailed t-test of equal variance with a critical value of 0.05 was used for analyzing BCS scores, lameness values, degree of rotation of the coffin bone, and digital artery area. The values for the rate of change of the entire study were used to analyze the BCS scores. For lameness scores and degree of rotation of the coffin bone the values from the first and final evaluations were used to give a comparison of change; a significant difference was expected at the beginning of the study and an insignificant difference at the end. Data from days 57-57.5 and 261-261.5 were compared for lameness scores. Data from days 57.5, 162, and 261 were used for degree of rotation, and data from days 63, 237, and 262 were used for digital artery area. Descriptive statistics was also used to determine the highest and lowest digital artery area values of each horse with the corresponding range and mode values. A one tailed t-test was used for the comparison of corticosterone values due to the assumption that laminitic horses would be higher. However, a two tailed t-test was used for T_4, Insulin, and ACTH.

CHAPTER III

RESULTS:

A comparison of the digital artery area, degree of rotation, body condition score (BCS), lameness score, and endocrine levels between two laminitic and two sound horses were used to determine the effects of therapeutic shoeing over a duration of 276 days. An overall decrease in the digital artery area, degree of rotation of the coffin bone, BCS values (body condition scores), lameness scores, and endocrine values were noted for both laminitic and sound equids. The larger decrease in digital artery area for the laminitic equids vs the sound was demonstrated by the increase in significance as the study progressed ($p = 0.50$, $p = 0.16$, $p = 0.06$, and $p = 0.09$ respectively). The degree of rotation of the right and left forelimb did decrease for both laminitic horses throughout the duration of the study returning to the near normal base line values. This resulted in a decrease in significant as the study progressed for the right and left forelimbs ($p = 0.15$, $p = 0.77$, and $p = 0.35$ right fore, and $p = 0.11$, $p=0.42$, and $p = 0.45$ left fore). Throughout the duration of the study, the BCS values fluctuate but did not significantly decreased ($p = 0.19$). Lameness scores were seen to decrease and return to normal value ranges. A significant difference did occur at the beginning of the study and an insignificant difference at the end ($p<0.001$ and $p = 0.15$ respectively). Cortisol values were found to be significant ($p=0.05$). The values for T_4, Insulin, and ACTH were not significant ($p=0.77$, $p=0.20$, and $p=0.63$ respectively).

Digital Artery Area:

The average digital artery area decreased for all equids (see figures 8 and 9). Measurements were taken on days 63 (first trim), 118 (first shoeing), 163 (second shoeing), 237 (third shoeing of laminitic 1), and 262 (final shoeing). However, a slight increase in digital artery area was seen during days 237 through 262 for both laminitic equids and sound 2 (see figure 8). Both laminitic equids expressed a larger change in digital artery area as expressed by the larger negative slope values (see figure 9 and table 2). The average digital artery area was not found to be significant at the beginning of the study indicating no difference in digital artery area (p=0.50). However, at the end of the study the average digital artery area for days 237 and 262 were marginally significant (p= 0.06 and p= 0.09 respectively). The return to marginally significant values is justified when the maximum, minimum, range, mode, and median values of the digital artery area are compared (see table 3).

Degree of Rotation of the Coffin Bone:

Measurements for the degree of de-rotation of the right fore hoof found in the sound and laminitic equids were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), and 261 (final shoeing). De-rotation of the coffin bone was experienced by both laminitic equids and sound 1 (see figures 10, 11, 14, and 15). However, rotation of the coffin bone was seen between days 162 through 261 for both laminitic equids and sound 1 (see figure 10, 14, and 15). Sound 2 did not experience any de-rotation, which is demonstrated by a slope of 0 (see figure 11). In comparison, a larger degree of de-rotation was experienced by both laminitic equids (see figure 11). This is demonstrated by the decrease slope value (see figure 11 and table 2). The degree of rotation at the beginning of the study was not significant (p=0.15). However, an increase in insignificance for the degree of rotation on days 162 and 261 demonstrated that the laminitic horses progressed toward values similar to the control's normal values (p=0.7705 and p=0.3530).

The degree of rotation in the left forelimbs of both laminitic equids decreased due to therapeutic shoeing (see figures 12, 13, 14, and 15). Measurements for these values were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), and 261 (final shoeing). Both laminitic equids experienced de-rotation of the coffin bone through days 57-162 but were seen to have rotation through days 162- 261 (see figure 12). Sound 1 also experienced the same progression, and a slight de-rotation of the coffin bone (see figure 12). The linear regression of the degree of rotation for both laminitic and sound equids showed an overall decrease (see figure 13 and table 2). The degree of rotation on day 57.5 at the beginning of the study was not significant (p=0.11). But the afore mentioned progression of values did decrease in significance through days 162 and 261 (p=0.42 and p=0.45 respectively).

The entire progression of the de-rotation of the coffin bone in both laminitic and sound equids is demonstrated in figures 14 and 15. These radiographs were taken and measured on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), and (261 final shoeing). The two laminitic equids experienced de-rotation but had slight increase in rotation on day 261 (see figure 14). A slight rotation of sound 1 was also noted (see figure 15). However, sound 2 stayed relatively constant (see figure 15).

Body Conditions Scores:

Body condition scores (BCS) decreased in all equids throughout the study (see figures 16 and 17), but the two laminitic equids were seen to have a greater BCS decrease when compared to the sound equids demonstrated by the decrease in slope values (see figure 17 and table 2). However, the overall change was not significant (p=0.20).

Lameness Scores:

The most obvious effects of treatment were seen in the lameness scores. Both sound equids had lameness scores of zero throughout the study (see figures 18, 19, and table 4). Laminitic 1's AAEP values steadily decrease throughout the study eventually returning to 0 (see figure 18, 19, and table 4), whereas laminitic 2's AAEP values initially decreased, then increase through days 237.5- 261, and decreased again through days 261- 261.5 (see figure 18 and table 4). Lameness scores were significantly different at the beginning of the study (p<0.001). However, at the end of the study there was no significant difference (p= 0.15).

Endocrine Values:

Endocrine values for T_4, cortisol, and ACTH for all equids were within the normal ranges, but the values decreased throughout the study (see table 5). Insulin was the only endocrine value that did not show a steady decrease as it fluctuated for both laminitic horses. In laminitic horses there was a greater reduction in cortisol concentration at the end of the study compared to Day 68, and this reduction was closer to significance (p=0.09) when compared to the sound horses (p=0.22). The only significant reducitons in hormones between Day 68 and Day 276 was a reduction in T4, but this occurred in both laminitic (p=0.03) and sound (p=0.04) horses.

Table 2: The linear regression of the rate of change experienced by each horse throughout the duration of the study. With corresponding P values of the data collected at the beginning of the study compared to P values of data collected at the end. The days that data was collected is indicated in parenthesis.

Linear regression (slope) of:	Sound 1	Sound 2	Laminitic 1	Laminitic 2	P Values for Beginning and End of Study (days)
Digital Artery Area (mm^2)	-0.0184	-0.0232	-0.0295	-0.0429	P= 0.50 (day 63) P= 0.06 (day 237) P= 0.10 (day262)
Degree of rotation of coffin bone Left Fore	-0.021	-0.005	-0.0564	-0.0207	P= 0.11 (day 57.5) P= 0.42 (day 162) P= 0.45 (day 261)
Degree of rotation of coffin bone Right Fore	-0.0129	0	-0.0525	-0.0325	P= 0.15 (day 57.5) P= 0.77 (day 162) P= 0.35 (day 261)
BCS Scores	-0.0012	-0.0044	-0.0074	-0.016	P= 0.20 (of BCS slope values)
Lameness Scores	0	0	-0.0148	-0.0025	P < 0.001 (day 57) P= 0.15 (day 261)

Table 3: Descriptive statistics for each horse's average digital artery area showing the maximum and minimum artery area, the rate of change (range), the mode, and median values.

Digital Artery Area (mm^2)	Sound 1	Sound 2	Laminitic 1	Laminitic 2
Maximum - Minimum	6.25 - 2.43	11.43 - 3.71	11.14 - 2.71	12.29 - 1.71
Range	3.82	7.71	8.43	10.57
Mode	2.43	7.86	N/A	2.86
Median	2.93	7.86	4.29	2.86

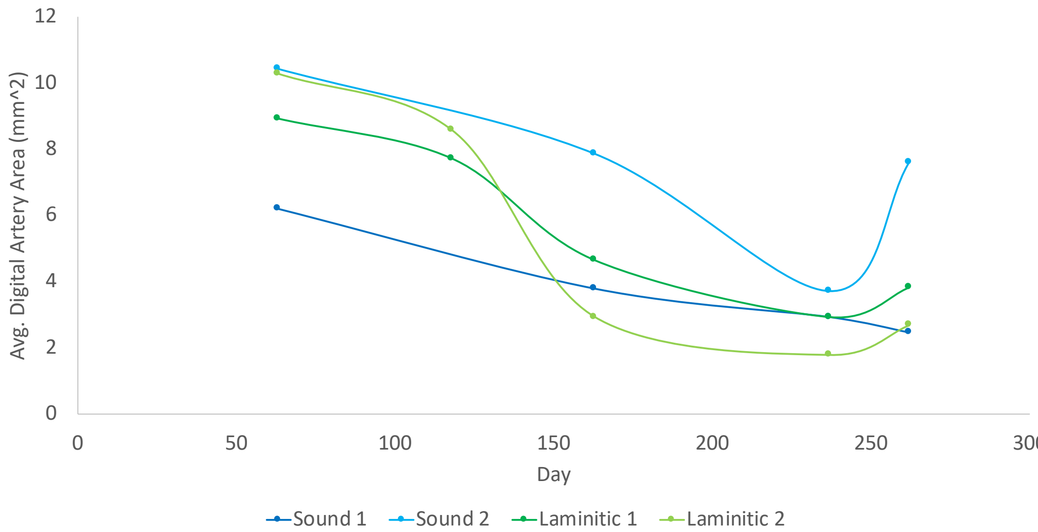

Figure 8: The average digital artery area of 2 sound equids and 2 laminitic equids. Measurements were taken on day 63 (first trim), 118 (first shoeing), 163 (second shoeing), 237 (third shoeing of experimental 1), and 262 (final shoeing).

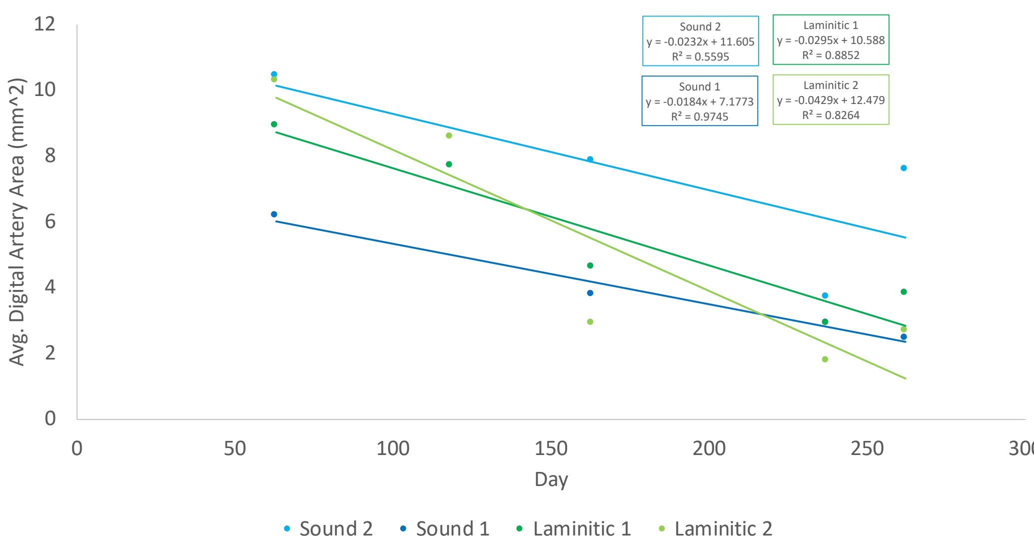

Figure 9: The linear regression of the average digital artery area of 2 sound equids and 2 laminitic equids. Measurements were taken on days 63 (first trim), 118 (first shoeing), 163 (second shoeing), 237 (third shoeing of experimental 1), and 262 (final shoeing).

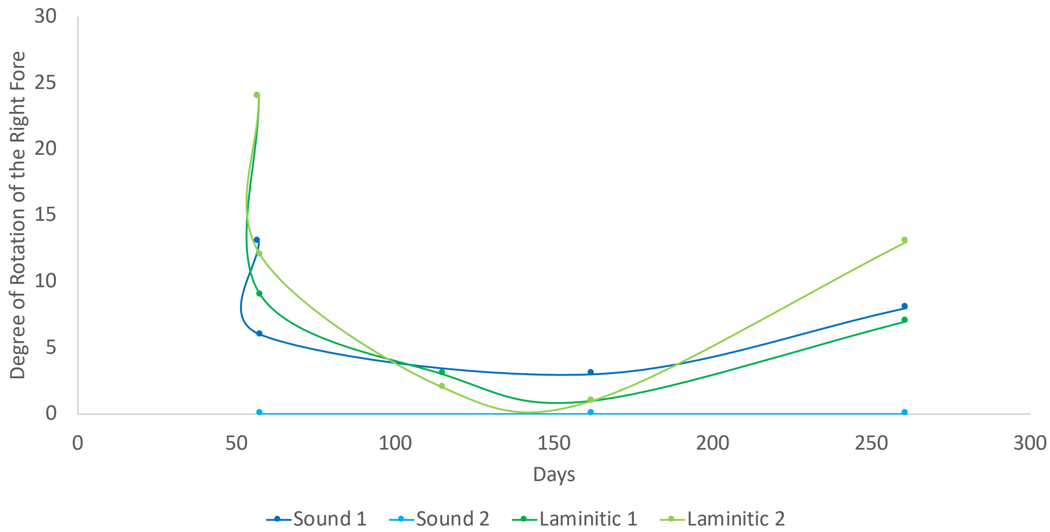

Figure 10: The degree of rotation obtained from radiographs of the right forelimb of 2 sound equids and 2 laminitic equids. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), and 261 (final shoeing).

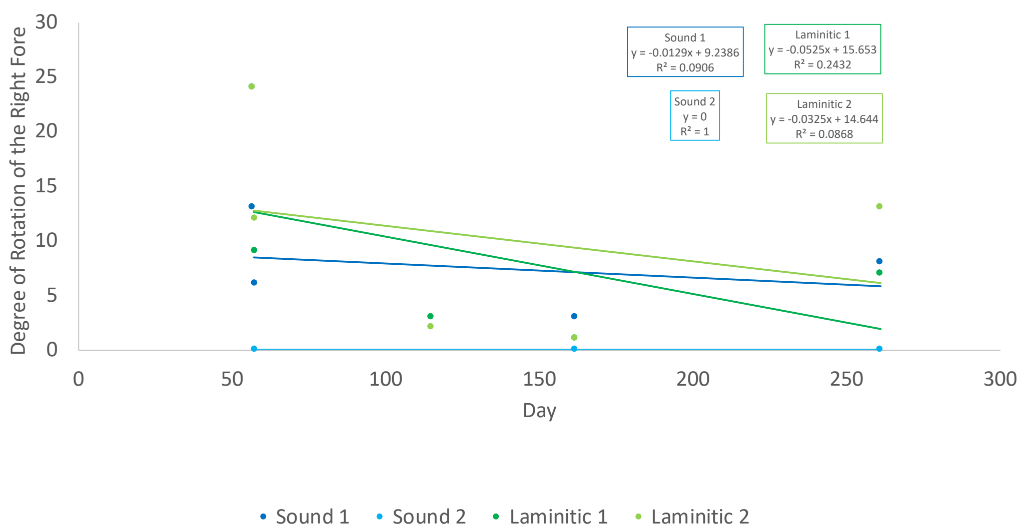

Figure 11: The linear regression of the degree of rotation obtained from radiographs of the right forelimb of 2 sound equids and 2 laminitic equids. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), and 261 (final shoeing).

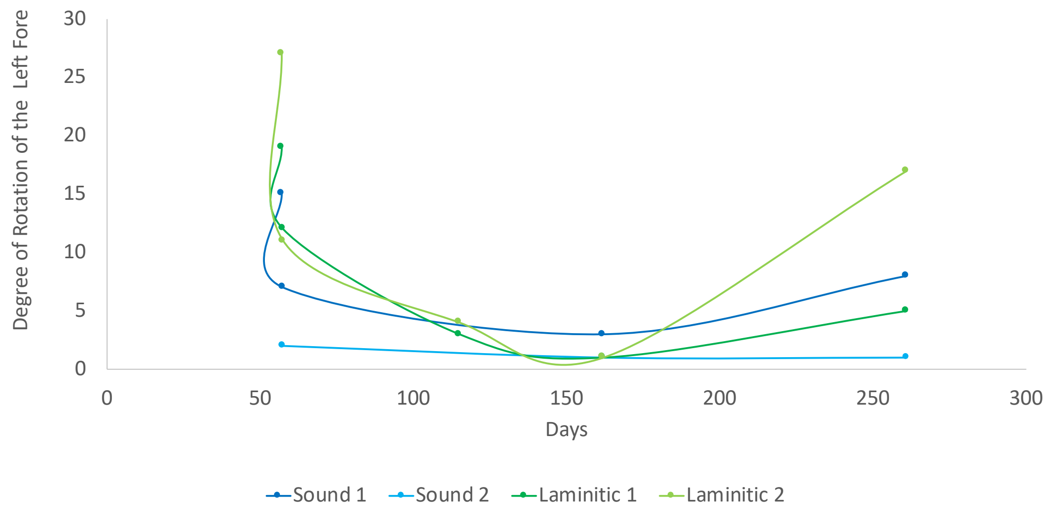

Figure 12: The degree of rotation obtained from radiographs of the left forelimbs of 2 sound equids and 2 laminitic equids. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), and (261 final shoeing).

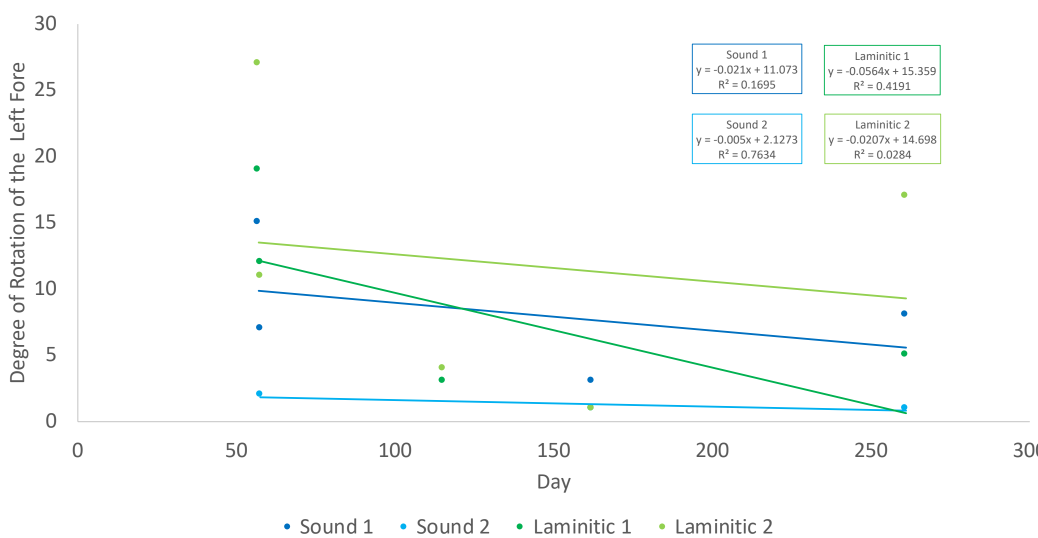

Figure 13: The linear regression of the degree of rotation obtained from radiographs of the left forelimbs of 2 sound equids and 2 laminitic equids. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), and (261 final shoeing).

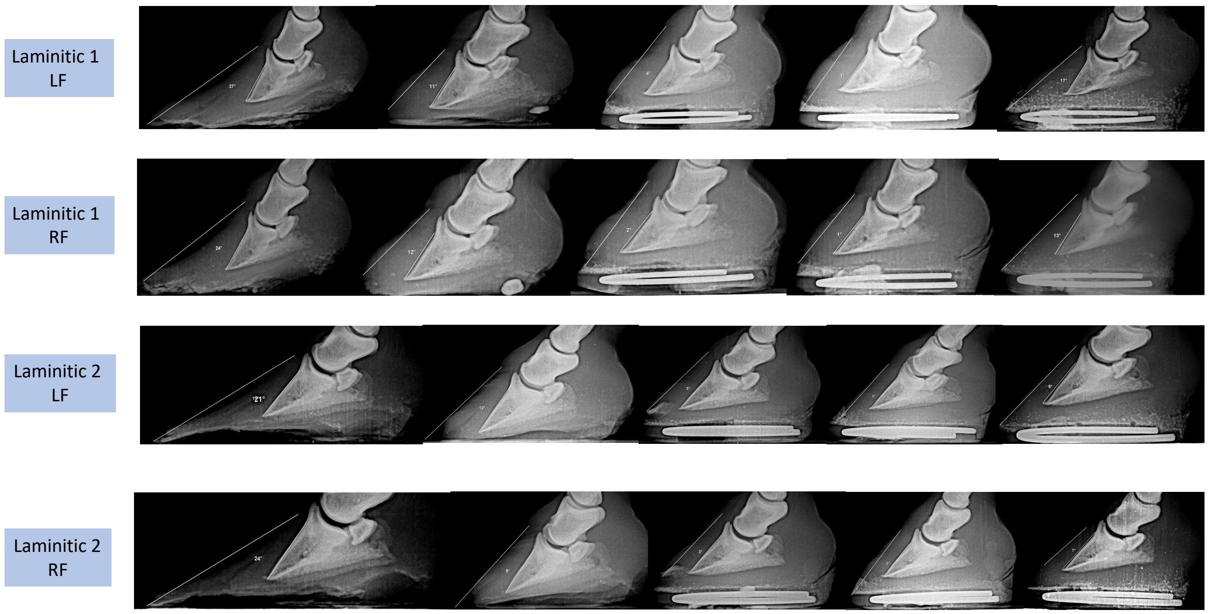

Figure 14: Radiograph images of the left and right forelimbs of the two laminitic equids with rotational measurements. Progressing from day 57 (first trim), 115 (first shoeing), 162 (second shoeing), and (261 final shoeing) from left to right.

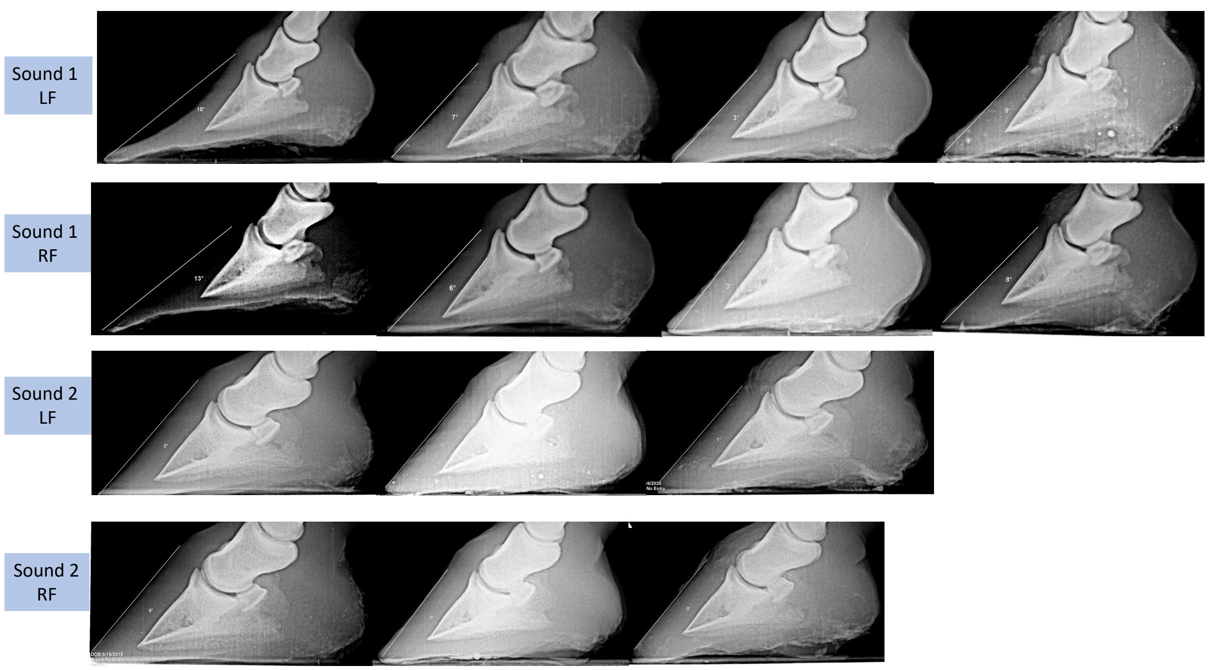

Figure 15: Radiograph images of the right and left forelimbs of the two sound equids with rotational measurements. Progressing from day 57 (first trim), 115 (first shoeing), 162 (second shoeing), and (261 final shoeing) from left to right.

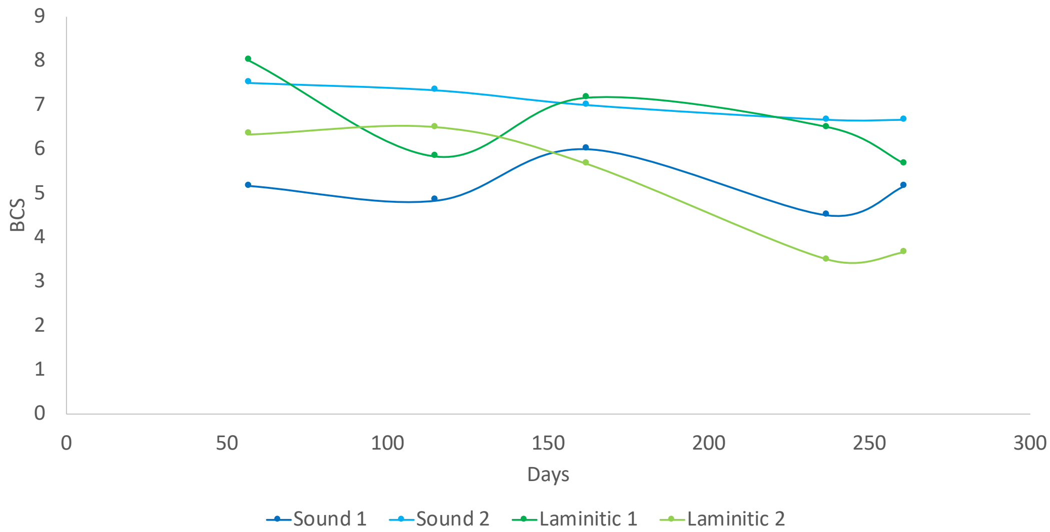

Figure 16: The progression of body condition scores (BCS) of two laminitic equids and two sound equids during therapeutic shoeing. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), 237 and (261 final shoeing).

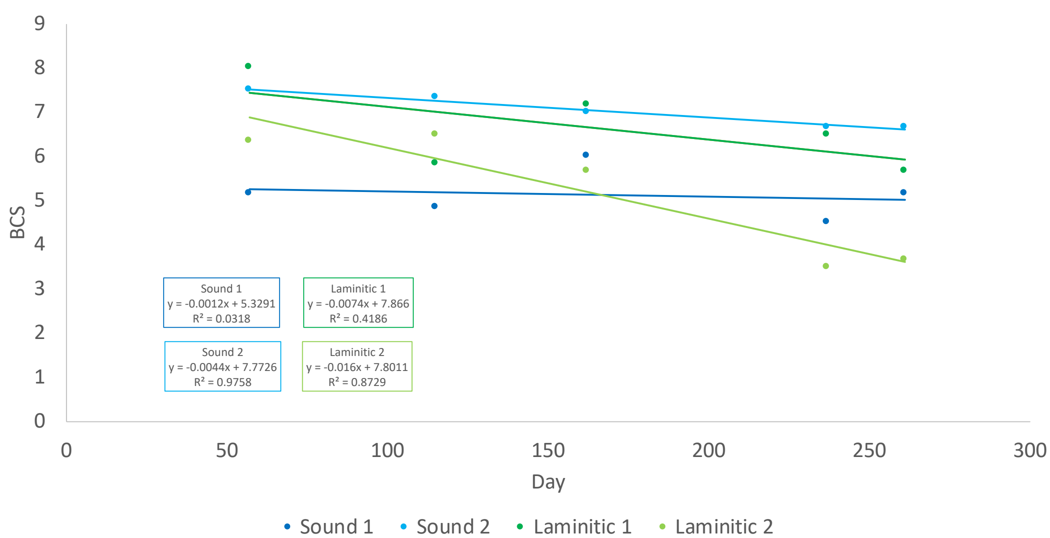

Figure 17: The linear regression of the progression of body condition scores (BCS) of two laminitic equids and two sound equids during therapeutic shoeing. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), 237 and (261 final shoeing).

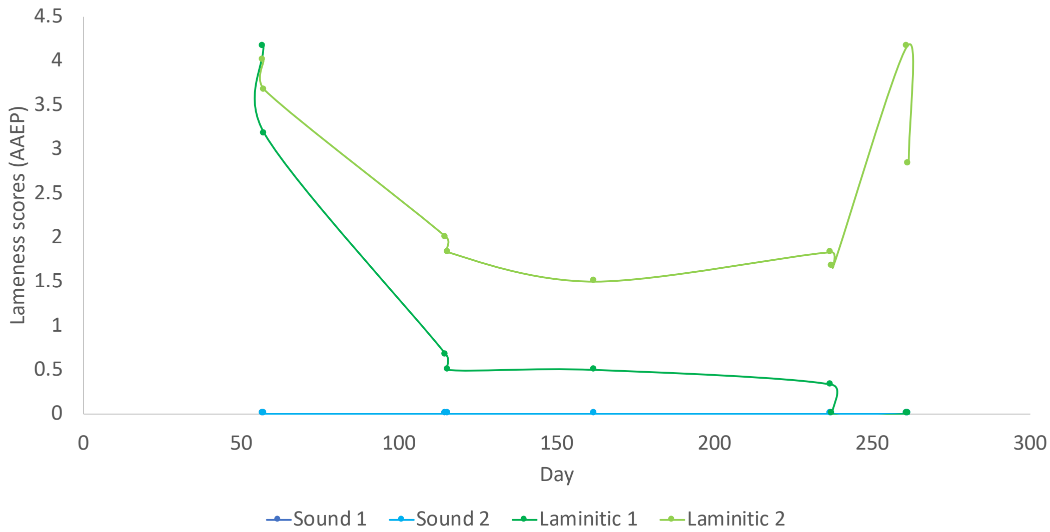

Figure 18: The progression of lameness scores of two laminitic equids and two sound equids during the use of therapeutic shoeing. Lameness was evaluated using the American Association of Equine Practitioners (AAEP) guidelines. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), 237 and (261 final shoeing).

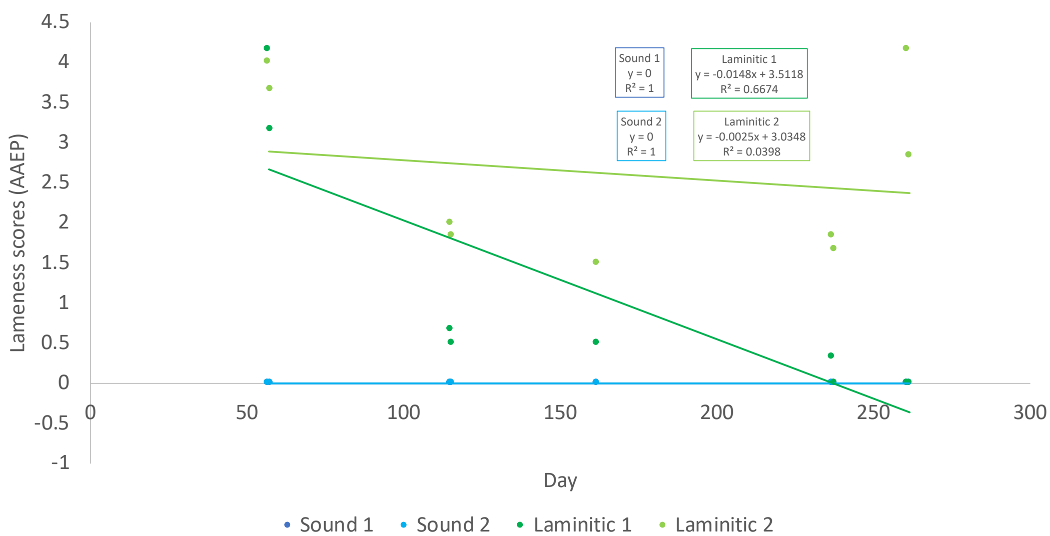

Figure 19: The linear regression of lameness scores of two laminitic equids and two sound equids during the use of therapeutic shoeing. Lameness was evaluated using the American Association of Equine Practitioners (AAEP) guidelines. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), 237 and (261 final shoeing).

Table 4: The lameness scores of two laminitic equids and two sound equids during the use of therapeutic shoeing. Lameness was evaluated using the American Association of Equine Practitioners (AAEP) guidelines. Measurements were taken on days 57 (first trim), 115 (first shoeing), 162 (second shoeing), 237 and (261 final shoeing).

Days	Sound 1 (AAEP)	Sound 2 (AAEP)	Laminitic 1 (AAEP)	Laminitic 2 (AAEP)
57	0	0	4.16666667	4
57.5	0	0	3.16666667	3.66666667
115	0	0	0.66666667	2
162	0	0	0.5	1.83333333
162.5	0	0	0.5	1.5
237	0	0	0.33333333	1.83333333
237.5	0	0	0	1.66666667
261	0	0	0	4.16666667
261.5	0	0	0	2.83333333

Table 5: The endocrine values of two laminitic equids and two sound equids were measured at the beginning of the study, before the first trim, and at the end during therapeutic shoeing.

	Laminitic 2	Laminitic 1	Sound 2	Sound 1
expected Values	T_4 ng/ml	12-25.		
Day 0	19.78	18.82		
Day 68	23.24	19.11	27	22.65
Day 276	5.3	3.97	9.97	4.52
expected Values	Insulin µI.U./ml	2-20.		
Day 0	59.99	107.51		
Day 68	35.91	22.55	20.6	15.89
Day 276	117.42	75.71	21.56	88.77
expected Values	Cortisol ng/ml	20-90		
Day 0	52.14	44.38		
Day 68	47.48	70.01	30.82	42.41
Day 276	38.51	29.02	23.26	34.35
expected Values	ATCH pg/ml	< 100		
Day 0	38.25	17.32		
Day 68	79.12	21.44	45.63	83.82
expected Values	ATCH pg/ml	< 30		
Day 276	4	10.1	6.6	16.9

CHAPTER IV

DISSCUSSION

Because therapeutic shoeing of the digital cushion should result in reduced laminar cell death, reduced hoof wall separation, increased blood flow to the laminar capillaries, and a decrease in the amount of pain. In addition, lameness scores, BCS values, endocrine values, and the degree of rotation of the coffin bone of laminitic horses were expected to be positively affected by stimulating the digital cushion. This study found that lameness scores decreased, body scores decreased slightly but were not found to be significant, and degree of rotation of the coffin bone decreased. There was no significant difference in T_4, insulin, and ACTH concentrations, but cortisol was significantly reduced indicating a reduction in pain.

Digital Artery Area:

The average digital artery area decreased for all equids. This may have been affected by the horses being removed from spring pasture and being transferred to a hay diet for 12 hours of every day. The horses were removed from pasture because over consumption of young grass had led to increased body weight and laminitis. The change in diet would lead to decreased amount of glucose intake, which in turn would lower insulin levels. High insulin levels are known to cause laminitis via vasoconstriction (Sillence et al., 2007; see also Huntington et al., 2009). A similar phenomenon was noted when a pasture rotation occurred. The artery area was seen to increase during the corresponding days (237 – 262). During the laminitic episode, the digital artery became vasodilated due to poor blood perfusion through the capillaries. It has been noted that laminitis can cause the blood supply in the hoof to cease or be significantly reduced (Coffman et al., 1970). Therefore, it was hypothesized that stimulating the digital cushion would result in an increase in blood flow. This was supported by the decrease seen in digital artery area of the laminitic ponies, resulting in marginally significant P values. The change from insignificant to significant values is due to the laminitic equids being compared to a sound horse. The sound horse had a naturally large digital artery area of around 7.86 mm^2 while the other sound pony was 2.93 mm^2. After therapeutic shoeing the laminitic ponies returned to digital artery values of around 2.52 mm^2 and 2.86 mm^2, which more closely resemble the sound pony. This is why an increase in significance was seen. Hence, therapeutic shoeing via stimulation of the digital cushion does reduce the digital artery area thereby increasing blood profusion in the hoof.

Rotation of The Coffin Bone:

There was visible de-rotation of the coffin bone in both laminitic equids. De-rotation of the coffin bone was also seen for sound 1 during the first trim. Trimming removes excess mechanical forces that are applied to the hoof wall, which can cause separation of the laminae tissue and rotation of the coffin bone. This is why the trimming and shoeing processes are of equal importance. Rotation of the coffin bone results in extreme pain, which can lead to increased cortisol levels, and aggravation of the laminitic cycle (see figure 2). However, de-rotation leads to decreased lameness scores and pain. Proper trimming and shoeing are known to result in de-rotation and decreased pain (Curtis et al., 1999). De-rotation continued to occur for both laminitic equids throughout the shoeing process but was seen to slightly increase in rotation towards the end. This increase was caused by the final trim being less aggressive. This is why therapeutic showing should be coupled with trimming in laminitic horses. Shoeing allows for a more aggressive trimming and hoof alignment due to shoes cushioning and supporting painful areas of the hoof. In conclusion, therapeutic shoeing does facilitate in de-rotation of the coffin bone which in turn decreases stress and pain allowing the horse to return to normal activity.

Body Condition Scores:

BCS values did not decreased significantly. However, the horses were able to return to more active lifestyles, which may in turn lead to further weight reduction. An increase in body size of horses past normal healthy body condition is directly correlated to laminitis (Ricciotti & FitzGerald, 2011). Horses that are kept at normal body weights are less likely to experience severe laminitic episodes. In conclusion, a horse that is suffering from a laminitic episode can experience pain reduction with increased activity levels through therapeutic shoeing.

Lameness Scores:

Lameness scores decreased for both treated horses. The severity of laminitis is directly correlated to increased lameness conditions expressed by horses (Hood et al., 2001). Laminitic 2 returned to soundness and full functional use. This may be attributed to the fact that laminitic 2 had experienced an acute laminitic episode. This same logic can be used for explaining the amount of decrease seen for laminitic 1. Laminitic 1 was diagnosed with chronic laminitis. Chronic laminitis results in extensive scaring of the laminitic tissues. This would have prevented proper laminar cell growth and de-rotation of the coffin bone. However, both equids did experience decreased pain and increased activity. Therapeutic shoeing is an effective way to reduce pain and lameness in laminitic horses.

Endocrine Values:

Cortisol was the only hormone that significantly decreased. T_4, insulin, and ACTH were not significantly different when compared to the controls. This was most likely due to small sample size and to the plethora of outlying factors that affect these hormones. However, the reduced cortisol demonstrates that the laminitic horses experienced pain reduction due to therapeutic shoeing. Cortisol is known to stimulate gluconeogenesis and ACTH production leading to aggravation of the laminitic cycle (Singh, 2003; see also Khani & Tayek, 2001; see figure 2). The production of cortisol is also known to be directly correlated with stress and pain (Rose et al., 1993). Due to therapeutic shoeing, the laminitic horses experienced a significant reduction in pain. This demonstrates that therapeutic shoeing can reduce pain which in turn reduced cortisol levels.

Shoes/Gel:

Polyflex Morrison Open Roller glue on shoes from No Anvil LLC, (Royal Palm Beach, FL) rubber shoes were found to be beneficial, because they allowed flexibility of the hoof wall and heel. This allowed the hoof to expand naturally. Furthermore, the shoes were not affixed by nailing, which decreased the probability of an abscesses. The ability of the hoof to expand and contract can prevent edema during laminitic trauma, which is of extreme importance for laminitic horses. Increased edema leads to aggravation of the laminitic cycle (see figure 2). The gel that was selected was chosen for its flexibility, but it was also required to be firm enough to apply pressure to the digital cushion. In addition to proper shoeing, a gel that mechanically stimulated the pumping of blood through the capillaries was necessary. Equi-pak CS (copper sulfate) soft gel was found satisfactory for this purpose. Furthermore, location specific application of gel supporting ½ to ¾ of the back of the hoof, the heel to the apex of the frog, leaving the toe exposed was highly beneficial. To the best of our knowledge, location specific gel support as applied in this study has not been tested. Most studies conducted have applied supportive gel to the entire sole of the hoof or with tapering of the gel as it extends over the toe (Steward, 2003; see also Curtis et al., 1999; O'Grady et al., 2008; Redden, 1997)

Ultrasonography:

Ultrasonography was used as a diagnostic and prognostic tool for evaluating the blood flow in laminitic horses. The average digital artery areas were expanded greatly in the laminitic equids during the beginning of the study. The digital artery areas returned to a more common value that corresponded to the median and mode values seen in the sound pony. Other studies also found the use of doppler ultrasonography to be useful for monitoring the rate of palmar digital blood flow (Aguirre, 2013; see also Wongaumnuaykul, et al. 2006). The ultrasound values were supported using radiographs, BCS scores, lameness scores, and endocrine values. It resulted in a non- invasive way to determine blood profusion in the hoof in contrast to venograms.

A venograms is a radiographed image of vessels perfused with diatrizoate sodium (Rucker, et al., 2006). Preparation for venograms requires anesthetizing of the medial and later palmer digital nerves and sedation of the horse, with a tourniquet applied to its pastern. Radiographs must be completed within 45 seconds after injected. The short time constraint is caused by diatrizoate sodium being hyperosmolar and diffusing into the surrounding tissue. However, this procedure is repeatable after a time wait. Venograms allow visual conception of circulation in the capillaries, arteries, and medial veins, but is extremely technique sensitive. Technique that is poor or inconsistent will result in skewed data that will not be plausible for comparison. Proper positioning of the horse is also crucial for successful images. Furthermore, venograms should also be conducted on a sound horse that can be used for comparison and for finetuning of the radiographs.

Conclusion and Future Studies:

The purpose of this study was to stimulate blood profusion through the capillaries of the laminitic hoof using flexible shoes and pads. Therapeutic shoeing via stimulation of the digital cushion resulted in decreased digital artery area thereby increasing blood profusion in the hoof. De-rotation of the coffin bone occurred in both laminitic equids and resulted in normalization of lameness scores. Cortisol levels were significantly reduced. Indicating reduction in pain and facilitation to normal activity. The use of ultrasonography resulted in a non-invasive prognostic and diagnostic tool for monitoring laminitis. The following procedure is recommended for treating laminitis: first the cause of laminitis should be determined and removed; second, any treatment that will result in the reduction of pain should be used; and third, an aggressive trimming and shoeing schedule that will prevent further de-rotation of the coffin bone should be planned.

Future studies should consider a comparison of digital artery area of horses of the same size and/or breed. This would result in greater accuracy for determining the effects of digital cushion stimulation. Artery size varies greatly when comparing a large horse to a pony or between different sized ponies to each other. For future studies horses should be grouped by size and breed. This could be used to construct a standard digital artery size value range of healthy horses. Ultrasound could be used as a noninvasive diagnostic and prognostic tool in laminitic cases. Future studies should also look at the effects of therapeutic shoeing on acute laminitic cases verses those on chronic laminitic cases as the degree of insult could affect the rate of improvement.

APPENDIX 1: IACUC APPROVAL

MARYVILLE COLLEGE INSTITUTIONAL ANIMAL CARE & USE COMMITTEE
Application for Use of Vertebrate Animals in Student Research

Provide information after each bold item
Student Name:
Charis Ramsey
Student Email Address:
Charis.ramsey@My.maryvillecollege.edu
Date:
4/22/19
Senior Study Advisor:
Dr. Drew Crain
Species to be used:
Equine
Age of animals:
9-12yr
Number of animals in study:
5
Duration of study:
1yr
Location of animals during the study (building and room):
Controled pasture turnout with freash water and stables

List personnel to call if problems with animals develop:

Name	Daytime Phone	Nighttime Phone	Emergency No.
Charis **Ramsey**	**(865)7480095**	**(865)7480 095**	**(865)74800 95**
Dr. Ramsey DVM	**(865)3351171**	**(865)3351 171**	**(865)33511 71**

What will happen to the animals at the end of the study? If euthanasia is required, state the specific methods.
Hopefully they will become pain free and return to normal activity.

(Do not write below line: For MC IACUC Use)

Maryville College IACUC Approval Number: 201907

Date Approved: 5/2/19

Signed: Dr. David e Unger

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