Supporting Limb Laminitis

James K. Belknap DVM, PhD, DACVS
Ohio State University College of Veterinary Medicine, Columbus, Ohio

Key Points

- Supporting limb laminitis (SLL) appears to have a unique pathophysiology compared to other types of laminitis; decreased perfusion likely to play a role in the disease process.
- Recent data (Univ. of Queensland) indicate that it may not be the excessive weight on the supporting limb that initiates the disease process in SLL, but more the lack of movement of the limb.
- According to our survey, the classic horse at risk of laminitis would be a large horse suffering moderate to severe pain from a septic synovial structure or fractured limb, with the first clinical signs of SLL (occurring 2-4 weeks post initiation of treatment for the original injury) being increased digital pulses on the supporting limb and a sudden increase in weight bearing on the originally affected limb.

Of the three primary categories of laminitis (sepsis-related, endocrinopathic, and supporting limb) the least is known regarding the pathophysiology, and therefore treatment of supporting limb laminitis (SLL). As the two main models to study laminitis for several decades were primarily models of sepsis-related laminitis (corn starch and oligofructose versions of carbohydrate overload), a large amount of data regarding not only the histopathologic changes but also the cellular signaling events is available for this type of laminitis. Although studies of endocrinopathic model were mainly limited to assessment of systemic abnormalities (especially those regarding insulin resistance and obesity) for many years, introduction of the hyperinsulinemia model and models on increased CHO consumption have resulted in a recent increase in research not only of the systemic events but also of laminar events which should lead to a rapid increase in our understanding of this common type of laminitis. There has been a veritable dearth of studies—both clinical and basic research—on supporting limb laminitis, with only one recent retrospective study of animals at risk, and inclusion of SLL in some other general studies on laminitis. There needs to be a combination of clinical studies (to fully assess risk factors for the disease process) balanced with basic research studies to determine effective management and therapeutic strategies for this devastating complication in the equine patient with decreased weight bearing in one limb.

The difficulty in developing a humane, consistent model for SLL has been a large impediment, primarily due to the fact that animals are much more variable temporally in the onset of the disease when exposed to similar factors putting them at risk of SLL. Although it may be impossible for humane reasons to replicate the time component when creating a model of SLL for humane reasons (impossible to have a model creating excessive weight bearing on one limb for long periods of time), we are beginning to obtain data on laminar events using short term models of weight bearing on one limb. One recent advantage is the remarkable advancement in research techniques to allow us to not only sample laminar interstitial fluid real time for determination of analytes with different physical forces placed on the foot (a collaboration of Drs. Andrew van Eps [University of Queensland] and Dean Richardson [Univ of Penn]), but also to rapidly perform an array of studies on cell signaling in laminar tissue at the gene expression and post-translational level (Belknap laboratory [Ohio State University]). In our laboratory, we have recently used a model which causes instability in one front foot (by placing an unstable shoe on the digit; abstract by Gardner et al. presented at this meeting) to cause the
animal to stand on the contralateral forelimb for 48 hours; we are studying laminar signaling in the supporting limb compared to other limbs in the foot. In preliminary studies, we have found a significant increase in a protein, hypoxia-inducible factor-1 alpha (HIF-A, well described to increase in concentration in hypoxic cells/ischemic tissues) in the supporting limb compared to the other digits. As HIF-1A can also be induced by inflammatory mediators (well known to increase in the laminae in sepsis-related laminitis), we also assessed inflammatory signaling and found no increase in laminar inflammatory mediators (thus indicating the increased laminar HIF-1A is due to hypoxia). Upon immunofluorescent staining with a HIF-1A antibody, we find that the laminar epithelial cells, the basal cells of which are the ones which dysadhere in laminitis, are the primary cell type expressing this hypoxia-inducible protein, and thus likely to be the cells suffering the most from hypoxia in SLL. In the UQ/UP study of metabolic changes occurring short term with excessive/unilateral weight bearing, the investigators have established a technique where they can place a microdialysis catheter in the laminar dermis between two primary epidermal laminae in the dorsal laminae for collection of interstitial fluid. Using this system, the investigators not only collected samples for metabolite concentrations, but also infused urea in order to assess urea clearance (indicator of perfusion). In preliminary results from this technique (unpublished data; personal communication with A van Eps), they have found that, compared with baseline samples from animals standing on all four limbs, laminar glucose and pyruvate concentrations increase whereas lactate/glucose ratios decrease rapidly when animals are walked. Additionally, urea clearance increases during walking, indicating increased laminar perfusion. Static limb load cycling (picking up the limb but no forward movement) caused the same pattern of changes noted with walking, but the magnitude of the changes were smaller. Interestingly, they did not detect any significant changes in metabolite concentrations or urea clearance when the animals were forced to undergo unilateral weight bearing for a short period of time (compared with baseline measurements of the animal standing on all four limbs). Furthermore, they also did not detect any changes when they administered vasodilatory agents such as ace promazine and KCl. These results indicate that the digital laminae undergo increased glycolysis with increased hypoxia in these digits. This is substantiated by recent results from our laboratory demonstrating increased HIF-1A with unilateral weight bearing. As it is likely that these hypoxia-related events are from a decrease in laminar blood flow, it is also likely that the waste products will accumulate in the intercellular milieu as there is likely impaired removal by the decrease in circulation. The lack of change of laminar metabolite concentrations with excessive weight bearing in the face of dramatic changes (indicating increased perfusion) with limb movement indicates that decreased motion may be as important if not more important than excessive weight bearing in initiating the cellular events that lead to laminar failure; this is consistent with the age old dogma that the “venous pump” in the digit enhances blood flow to and from the digit as the horse ambulates. The excessive weight bearing is likely to play a larger role once the laminar structural integrity is compromised, leading to the rapid descent of the distal phalanx which commonly occurs in SLL. Finally, the lack of change of metabolites or urea clearance with vasodilators in the UQ/UP study indicates that prophylactic therapy for the horse at risk of SLL may require physical manipulation of the digit and may not be possible with pharmaceutical agents.

Due to the relative paucity of clinical data on SLL, Drs. Gary Baxter, Andy Parks (both at University of Georgia) and I distributed a Qualtrics survey to obtain information from ACVS diplomates in equine practice on their experiences with SLL cases. The questionnaire was distributed to approximately 241 diplomates, from which we obtained 93 responses. Most
university referral hospitals were represented in the responses, as were many private referral hospitals and some private ambulatory practices. There was a broad range of clinical practice scenarios with the respondents regarding the amount of ambulatory/field practice they performed (approximately 50% performing 0-40% field practice, approximately 50% performing >40% field practice). The percent of case management pertaining to orthopedic surgery was also fairly well distributed between clinicians (17% claiming that 0-20% of their caseload was related to orthopedics, 32% claiming 21-40% of cases related to orthopedics, 25% claiming 41-60% of cases related to orthopedics, and 26% claiming that >60% of cases were orthopedics-related). The number of SLL cases seen per year by the respondents were fairly low, with the majority reporting 0-2 cases per year, 21% reporting 2-4 cases per year, and 6% reporting >4 cases per year. The most common types of cases in which SLL was observed were sepsis of synovial structures (25%) and both non-septic (22%) and septic fractures (19%), whereas the lowest incidence was reported for nerve injury (i.e. radial nerve paralysis, 6%) and with routine orthopedic procedures (i.e. pastern arthrodesis; 9%). The most common types of fracture cases stated by respondents to be associated with SLL were fractures complicated by sepsis (25%) and fractures with internal fixation (26%), whereas other fixation modalities including transfixation casts (15%) and simple casts (15%) were reported to have much lower incidence of SLL. Although laminitis was reported with all types of external coaptation that we queried, half limb casts and transfixation casts were reported to have a much higher incidence of SLL compared to other types including full limb cast, bandage casts, and splinting.

The vast majority of responses indicated moderate to severe lameness on the originally affected limb was most commonly associated with SLL (77% of responses), although minor lameness was reported to result in SLL by a small number of clinicians (13% of responses). When asked the shortest time period between initiation of treatment for the original injury and onset of SLL, 43% percent of clinicians reported that they had observed SLL in the first two weeks after the initiation of severe lameness in the opposite limb, with slightly less (35%) reporting 2-4 weeks being the shortest interval (very few-16% reported 4-8 weeks as the shortest interval). When asked the most common time period between onset of lameness in the opposite limb and onset of SLL, the 2-4 week time period was the most frequent response (41% of responses), followed by the 4-8 week period (32%), and the 0-2 week period (22%).

As we were interested in determining what clinicians feel are the earliest clinical signs to watch for, we asked them to write down the two most common signs noted at time of onset of SLL. The two most common responses were increased digital pulses in the supporting limb and a sudden increase in weight bearing on the originally affected limb (commonly noted to occur with no overall clinical improvement or to occur with an increase in heart rate); three other commonly noted signs were increased recumbency, increase in shifting weight between affected feet, and increased heart rate. The clinicians were also asked the frequency with which they used radiography to assess the supporting limb in the horse at risk of SLL. The majority of clinicians reported that they do not take radiographs of the supporting limb at routine intervals during the convalescence from the original injury; most only take radiographs when clinical signs of SLL appear.

The clinicians were asked several questions regarding foot management of the supporting limb (SL). Approximately 2/3 of respondents reported that they remove the shoe on SL at time of initiating therapy on a horse at risk of SLL. When asked the type of shoe/pad they applied to the SL foot at the initiation of therapy; the two most common applications were some type of cushioning of the entire sole (most commonly with a SoftRide but also with pads custom made
by the clinicians with impression material or foam), and elevation of the heel (most commonly with the NANRIC Ultimate combined with impression (cushion support) material). A smaller number of respondents apply a variety of steel or aluminum shoes to the supporting limb, most commonly with a pour in pad. A very small number of respondents apply a wooden shoe/clog to the supporting limb. Many respondents emphasized the need to try to “even out” the length of the SL with the originally affected limb. When asked if there were any types of digital management of the SL that were contraindicated, the heart bar shoe was far ahead of any other type of management as the most contraindicated technique. Three other types of digital management which “tied for second” as being contraindicated were 1) any shoe without sole support, 2) heel elevation, and 3) any shoes which increased toe depth or length (several respondents mentioned leaving shoes on with toe grabs as causing problems). A theme throughout the responses was that any drastic changes in palmar angle (negative or positive) were contraindicated. We also inquired to the perceived importance and type of bedding used. The majority of respondents (approx. 80%) felt that the type of bedding is important in management of the horse at risk of SLL, with shavings and sand being the most preferred bedding. A soft bedding composed of peat moss or tan bark was the third most commonly used bedding. The prominent theme was deep bedding, and covering the lower layer (sand or shavings) with straw, both being done to encourage the animal to lay down.

We asked several questions regarding therapeutic management of the horse at risk of SLL in addition to digital support, including the use of both pharmaceuticals and cryotherapy. In regards to pharmaceutical management of pain in horses at risk of SLL, phenylbutazone was the primary drug (and usually the only drug) used by the respondents; gabapentin, flunixin meglumine, a CRI of lidocaine, and epidurals (primarily morphine) for hindlimb pain were also mentioned. When asked of other treatments not related to analgesia that were used by the respondents to treat cases of SLL, pentoxifylline was prominent as the most commonly used drug, with respondents stating “none” being the second most common response. Other drugs mentioned (in order of number of responses) included ace promazine, doxycycline, aspirin, DMSO, and ulcer medications. Approximately half of the clinicians stated that they use cryotherapy (digital hypothermia) on their horses at risk of SLL, with a large range of the number of hours per day that they apply the treatment (the most frequent response was 20-24 hours/day). When asked the main factor which the clinicians feel influences whether or not an at risk case will develop SLL, the main answer (not unexpectedly) was the rapid return to normal (or close to normal) weight bearing of the originally affected/injured limb. We also assessed the clinician’s views on treatment options once a horse was diagnosed with SLL. The majority of clinicians (60%) responded that they do use cryotherapy on the laminitic foot, but they again varied in the time cryotherapy was applied each day (38% for 20-24 h/day, 19% for 12-19 h/day, 42% for 3-11 h/day). Regarding the use of slings, a small number of clinicians (10%) stated that they use them on animals at risk of SLL, 30% claimed they use them on horses with SLL, and 60% stated that they don’t use slings (half of these individuals used them in the past and do not use them now).

When asked the percentage of animals diagnosed with SLL that survive, the largest number of individuals stated that 0-20% survived, with only 4% stating that > 60% survived (46% of respondents for 0-20% survival, 27% for 21-40% survival, and 22% for 41-60% survival). When asked for the primary reason for euthanasia of SLL cases, the primary reason given was economics (combined with a poor prognosis), with the second reason being the severity of displacement of the distal phalanx (sinking being the most common displacement associated with
euthanasia, whereas rotation combined with sole perforation was second-most common). Humane issues (including most commonly the concern of unrelenting pain) was a major consideration in a large number of responses and was commonly combined with the above three reasons for euthanasia. When asked the most important factors regarding the horse which may allow a successful outcome, the primary response was weight of the horse, with temperament of the horse (especially the willingness to lie down) the second most important factor listed. The severity of the initial injury and distal limb/foot conformation were also well represented in the answers.