Vascular distribution of contrast medium during intraosseous regional perfusion of the distal portion of the equine forelimb

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Objective—To describe the vascular distribution pattern of contrast medium during intraosseous regional perfusion (IORP) of the distal portion of the equine forelimb.

Sample Population—13 cadaveric forelimbs from 12 horses without forelimb diseases.

Procedures—Serial lateromedial radiographic views were taken of the distal portion of 10 heparinized cadaveric forelimbs at 0, 1, 2, 6, 15, and 30 minutes during IORP of the third metacarpal bone (MCIII) by use of iodinated contrast medium and a tourniquet placed over the proximal portion of MCIII. Vascular regions of interest (ROI) were created for each radiograph. Reviewers identified the presence or absence of contrast medium–induced opacified vessels in all ROI on radiographs. This information was summarized to identify vessel-filling patterns over time. Vessel identification was verified by use of computed tomography angiography and latex perfusion studies on the distal portion of separate cadaveric forelimbs.

Results—During IORP, contrast medium filled the medullary cavity of the MCIII; exited via transcortical vessels; and diffused distally to the remaining arteries and veins of the forelimb, distal to the tourniquet. Maximum vessel and soft tissue opacification occurred in most specimens at 6 and 30 minutes, respectively. Serial radiography vessel patterns matched those of computed tomography images and dissected specimens.

Conclusions and Clinical Relevance—IORP provides a repeatable pattern of vascular distribution in the distal portion of the equine forelimb. To our knowledge, our study provides the first documentation of arterial perfusion by use of IORP; results of previous reports indicate that IORP delivers medications to only the venous vessels of the perfused forelimb. (Am J Vet Res 2006;67:1445–1452)

Orthopedic infection (ie, septic arthritis and osteitis-osteomyelitis) can be a devastating and life-threatening condition in the horse.1,5 Sources of infection can be hemogenous, traumatic, and iatrogenic.2 Synovial infections may involve numerous joints in foals through hemogenous spread. In adults, structures of the distal portion of the limb, including the navicular bursa, distal interphalangeal joint (coffin joint), digital tendon sheath, metacarpophalangeal and metatarsophalangeal joints (fetlock joints), proximal interphalangeal joint (pastern joint), carpus, and tarsus, are frequently involved.6 Postoperative orthopedic infection rates may be as high as 53% following clean-contaminated surgical procedures.1 Bone infections appear to carry a worse prognosis, compared with synovial infections.7

Recommended treatments include systemic treatment with antimicrobials with debridement of infected tissues and lavage of infected synovial structures.1–5 Local treatments are advocated to deliver high concentrations of antimicrobials to the site of infection. These include intra-articular administration of antimicrobials,6,9 implantation of antimicrobial-impregnated materials,10,11 continuous antimicrobial infusion systems,12 and regional limb perfusion techniques.13–20

Regional limb perfusion techniques include IORP and IVRP. With these methods, antimicrobials are administered to the tissues of the limb via the medullary cavity (during IORP)13–18 or a venous vessel (during IVRP).13–20 A tourniquet applied proximal to the site of infection limits the systemic distribution of the antimicrobial.14 Both methods have been shown to establish high concentrations of antimicrobials in the soft tissues, synovial fluid, and bone of the distal portion of the equine limb.13–15,17,20

Recent reports13,14,20 have compared the effectiveness of IORP versus IVRP. In 1 study,24 injection of technetium Tc 99m pertechnate with either technique resulted in similar amounts of radionuclide uptake in the distal portion of the equine forelimb, suggesting that both methods are equally effective. However, results of similar studies13,15 measuring antimicrobial concentrations suggest that higher concentrations are achieved in synovial fluid following IVRP. For this reason, IVRP appears to be a favored technique. Yet, clinical conditions such as local edema, infection, or vas-
cular injury may preclude repeated IV injections or catheterization. In these instances, IORP may be a suitable alternative.

Why differences exist between the 2 techniques is unknown. It may be that the vascular distribution pattern following IORP is different than that following IVRP. Angiographic studies on IVRP and CTA have been described for the distal portion of the equine limb. Contrast studies performed following IORP of the equine tarsus and carpus indicate that the tourniquet limits distribution of perfused contrast medium to the dorsal digital pedis artery and vein, dorsal MCIII periosteal vessels, palmar metacarpal vessels, dorsal MCIII periosteal vessels, proper palmar digital veins, proper palmar digital arteries, dorsal vessels of the proximal phalanx, coronary vein and dorsal branch (vein) of the middle phalanx, bulbar branch artery and vein, dorsal vascular plexus of laminar corium, terminal arch vessels, solar marginal vessels, bulbar plexus, and parietal plexus.

One investigator (GJK) prepared a questionnaire. It was asked reviewers (JCJ and LEF) to identify all ROI on each radiograph. It then asked the reviewer to assign a score of 1 if the ROI was present and a score of 0 if the ROI was absent on the basis of whether contrast medium, the same computed tomography scan was repeated. Images were viewed by use of a soft tissue window. Occluded vessels were identified and named by a consensus opinion between 2 reviewers (LEF and GJK).

IORP with latex and dissection—Intraosseous regional perfusion was performed on 2 prepared specimens by use of the same technique as in the SR study, except 0.15 mL of blue latex/kg of body weight was used as the contrast medium. The latex was allowed to set according to recommendations of the manufacturer. The specimen was frozen at –18°C until used. While frozen, 1 forelimb was sectioned in a transverse plane in 2.4-cm increments by use of a band saw. The other forelimb was thawed and dissected to identify perfused vessels. This forelimb was then sectioned in a sagittal plane. Latex-filled vessels were identified and named by a consensus reached between 2 reviewers (LEF and GJK).

SR analysis—Based on the vessels identified in SR, CTA, and latex-dissected specimen studies, 13 vascular ROI were selected on lateromedial radiographic views for SR. A vascular template was prepared, highlighting these 13 ROI (Figure 1). They included the following: medullary cavity of MCIII, palmar metacarpal vessels, dorsal MCIII periosteal vessels, proper palmar digital veins, proper palmar digital arteries, dorsal vessels of the proximal phalanx, coronary vein and dorsal branch (vein) of the middle phalanx, bulbar branch artery and vein, dorsal vascular plexus of laminar corium, terminal arch vessels, solar marginal vessels, bulbar plexus, and parietal plexus.

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ROI. The total number of present scores was counted for ROI of every specimen at every time interval. This total was divided by the number of specimens to provide the percentage of contrast medium–induced opacified vessels in each of the ROIs.

All radiographs for 1 specimen were organized in a series. Radiographs in each series were arranged in chronologic order, corresponding to time 0, 1, 2, 6, 15, and 30 minutes of perfusion. One questionnaire was completed for each series. Reviewers were then asked to identify which radiograph in each series had maximum vessel opacification. They were also asked to identify which radiograph in each series had maximum soft tissue opacification. Reviewers were not blinded to treatment. Reviewers assigned each of the ROI a score and a maximum opacification score by consensus.

Results

Anatomic evaluations—The vascular patterns identified on SR (Figure 1) were consistent and repeatable with every specimen following IORP, regardless of horse or left or right forelimb. These patterns were consistent with the CTA images and dissected specimens. All named vessels were identified according to established anatomic terms, when available.30-33 When discrepancies existed in the literature for the name of an anatomic structure, the most descriptive term was chosen. Although minor variations existed in vessel appearance and branch location among specimens, this did not preclude vessel identification. Smaller, unnamed vessels had more variation, but these vessels were not included in the ROI, and this did not affect the SR analysis.

Overall, every named vessel in the equine forelimb distal to the tourniquet was opaque following IORP. This included veins and arteries. Serial radiography was the least detailed method of identifying these vessels, compared with CTA and latex-dissected specimens, but it provided a consistent and repeatable method of evaluating these structures over time. Identification of superimposed major vessels was challenging with SR alone. However, once these vessels were confirmed by use of dorsoventral radiographic views, CTA, and latex-dissected specimens, identification of named vessels was not problematic.

Computed tomography angiography provided detailed images of the vascular anatomy of the distal portion of the equine forelimb (Figure 2). No vessels were opaque prior to perfusion. Following perfusion, contrast medium was identified in the medullary cavity of MCIII and the transcortical vessels of the MCIII, distal to the tourniquet. All named vessels and many unnamed vessels were opaque. This included all vessels used in the ROI for SR analysis. No contrast medium was observed in the medullary cavity of the proximal or middle phalanx. Contrast medium was identified in the vessels of the solar foramen, solar marginal vessels, and vascular plexus of the laminar corium of the distal phalanx.

In the dissected specimens, blue latex was identified in all the vessels identified on CTA and SR. Latex filled the medullary cavity of MCIII (Figure 2). Blue latex was evident in the cortex of MCIII in all areas except directly underneath the tourniquet and at the articular margins, where it was sparse (Figure 3). Large vessels under the tourniquet were not filled with latex. Minimal latex was present in the vessels of the periosteum under the tourniquet. Latex was observed in the lumen of the medullary cavity underneath the tourniquet. Latex was also observed in the cortex and periosteal vessels of MCIII proximal to the tourniquet in each specimen, the tourniquet was situated over the level of the nutrient foramen of MCIII. In this location only, the emissary vein was filled with blue latex but the artery was not. Vessels draining the forelimb proximal to the tourniquet and connected to these proximal periosteal vessels and emissary vein were filled with latex. The periosteal vessels of MCIII distal to the tourniquet were uniformly filled with latex, as were the large distal metaphyseal vessels and palmar metacarpal vessels distal to the tourniquet (Figure 4). These latex-filled vessels communicated with the major vessels of the distal portion of the forelimb, including the proper palmar digital arteries and veins. All grossly visible arteries and veins communicating with these major vessels distal to the tourniquet were filled with latex. Latex was observed in the vessels of the plexus of the laminar corium, vessels of the digital flexor tendons and suspensory ligament, collateral ligaments of each joint, and ligaments of the proximal and distal sesamoid bones. No latex was observed in the...
medullary cavity of the proximal or middle phalanx or within the bone of the distal phalanx or the sesamoid bones. No latex was observed free in any synovial compartment but was visible within the vessels of every synovial capsule distal to the tourniquet. The latex-perfused specimen cut in transverse slices had identical filling patterns to the corresponding CTA images.

Perfusate diffusion was determined to be similar between specimens from an 11-year-old horse (Figure 2) and a 7-year-old horse (Figures 3 and 4).

Subjectively, perfusate was observed to be low in the distal epiphysis of MCIII in both specimens. It is not possible to determine from this information whether age of a horse has an influence on distribution pattern.

SR analysis—A total of 59 radiographs were used in SR analysis. One radiograph was excluded because of an experimental error. Mean infusion volume was 72.3 mL (range, 59.3 to 96.2 mL). The SR analysis questionnaire was completed successfully for all available radiographs. Regions of interest filled in order from proximal to distal. None of the ROI had opacified vessels at time 0. All ROI had completely opacified vessels by 15 minutes (Figure 5).

Regions of interest 1, 2, and 3 had 100% opacification of vessels by 1 minute. Regions of interest 4, 5, and 6 had 60%, 80%, and 70% opacification of vessels by 1 minute, respectively; they had 100%, 89%, and 100% opacification of vessels by 2 minutes, respectively. Regions of interest 7, 8, and 9 had 78%, 67%, and 44% opacification of vessels by 2 minutes, respectively. Meanwhile, ROI 10, 11, 12, and 13 had 78%, 67%, 22%, and 0% opacification of vessels by 2 minutes, respectively. All vessels were opaque by 6 minutes, with the exception of those in region 13, which had 90% opacification of vessels by 6 minutes.

In 8 of 10 specimens, all vessels appeared maximally opaque at 6 minutes. Vessels in the remaining 2 specimens appeared to be maximally opaque at 15 minutes. In 8 of 10 specimens, it appeared that maximum soft tissue opacification occurred at 30 minutes. In the remaining 2 specimens, maximum soft tissue opacification appeared to occur at 15 minutes.

Experimental errors—For 1 specimen during SR, a radiograph was double exposed. Double exposure occurred while obtaining the radiograph for the 6-minute assessment, during which time it was superimposed over the radiograph obtained at 2 minutes. Because the 2 radiographs were taken identically and no difference in positioning occurred, the information was determined to be valid for the 6-minute assessment. Consequently, information for the 2-minute radiographic assessment was lost. During radiography of another specimen at time 0, a small amount of contrast medium had diffused into the medullary cavity prior to the initiation of perfusion, giving an aberrant positive score for that region.

Leakage of contrast medium occurred from 2 sources in every specimen. One source was from around the intraosseous cannula. This leakage was considered minor (<5 mL). It was determined that the
Others have studied the distribution of contrast medium during IORP. Investigators have evaluated the angiography of the distal portion of the equine forelimb by use of IVRP and CTA. Others have studied the distribution of contrast medium following IORP of the equine tarsus and carpus. Results of these studies have indicated that IORP distributes contrast medium to the superficial venous system isolated by a tourniquet. To our knowledge, our study is the first to evaluate angiography of the distal portion of the equine forelimb following IORP. Ours is also the first study to document the presence of contrast medium in arteries of the distal portion of the forelimb with this technique.

Results of our study indicate that a consistent pattern of distribution of contrast medium exists from the medullary cavity to the local tissues following IORP. Contrast medium enters the medullary cavity of the MCIII through the intraosseous cannula and distributes through the cortical bone proximal and distal to the tourniquet. The periosteal and metaphyseal vessels collect this medium and deliver it to the major veins and arteries of the forelimb. With time and increasing volume, this medium diffuses to the remaining vessels, distal to the tourniquet. It is of particular interest that arteries and veins fill simultaneously in a proximal to distal direction. Therefore, it was evident that the null hypothesis was not totally demonstrated; it was predicted that only veins would fill with contrast medium following IORP.

Time for diffusion to occur was also evaluated in our study. At 6 minutes, nearly all vessels distal to the tourniquet were opaque. Gradually, this contrast medium exited the vessels and distributed to the surrounding soft tissues. In our study, maximum soft tissue opacification by contrast medium occurred at 30 minutes.

The circulation of mammalian long bones has been described as centrifugal. Arterial blood enters the medullary cavity via metaphyseal arteries and the nutrient artery. Venous blood exits through free-flowing, nonexpansile vascular channels across all surfaces of the cortical bone as well as metaphyseal veins at either end of the bone. Large emissary veins drain medullary contents via the nutrient foramen. Results of our study indicate that IORP contributes to this centrifugal flow out of the bone.

In our study, contrast medium was observed in the arteries distal to the tourniquet. This suggests that the tourniquet may exert a unique pressure difference, encouraging retrograde diffusion of a substance out of the medullary cavity via arterial channels as well as normograde diffusion via venous channels. Once in the superficial vasculature, contrast medium distributed normograde via arterial vessels to distal capillary beds. It also traveled retrograde via venous vessels to the same capillary beds. The result was a complete perfusion of the vessels distal to the tourniquet.

It was unexpected that contrast medium would drain from the transected surface of each specimen. No leakage was observed through vessels underneath the tourniquet. However, the dissected specimens clearly demonstrated that contrast medium travels proximal
to the tourniquet via the medullary cavity and then exits via transcortical vessels near the proximal portion of MCIII. A pneumatic tourniquet was used in our study. The tourniquet was applied in the same manner by the same investigator (GJK) and inflated to the same pressure in each specimen.

The influence of the tourniquet during IORP has been clearly demonstrated by previous investigators. During IORP and IVRP of the distal portion of the equine forelimb with technetium Tc 99m pertechnate, it was found that a tourniquet is essential to prevent rapid systemic redistribution of the radionuclide. Furthermore, placement of a tourniquet for 30 minutes was essential to maintain high radiouclide counts in tissues of the distal portion of the forelimb, even after tourniquet removal. These authors concluded that technetium Tc 99m pertechnate diffused into the extracellular space during the 30-minute perfusion. These conclusions are consistent with the results of our study, where soft tissue opacification was observed in the later stages of perfusion. Maximum soft tissue opacification occurred in most specimens at 30 minutes. No radiographs were obtained beyond 30 minutes; therefore, further studies are necessary to determine what effect longer durations of tourniquet application have on this distribution pattern.

No diffusion of latex into the surrounding soft tissues was detected. The latex used in our study was a commercial, radiopaque product intended for use in microvascular perfusion studies. However, the degree of radiopacity provided by this product was not adequate for the angiography portions of our study. In liquid form, this product has a viscosity of 25 centipoise. The iodinated contrast medium used in our study has a viscosity of 7 centipoise at 25°C. It diffuses rapidly from the vascular to the extravascular space in non-neural tissue.

Because the latex does not extravasate, the exact pattern of diffusion of the latex product may not be identical to that of the contrast medium. However, the latex product was felt to be a suitable choice for the dissected specimens in our study because before it sets, it is a liquid that distributes throughout the vessels to the level of capillaries. Once it sets, it forms a solid, highly visible contrast medium that is easily identified during dissection. It was decided that for the purpose of identifying the vessels perfused during IORP, the 2 substances would be comparable. Further studies are necessary to determine what affect the viscosity and molecular size of medications used in IORP has on their distribution to local tissues.

In our study, only grossly and radiographically visible vessels were identified on dissected specimens, SR images, and CTA images. Previous investigators have determined that following IORP, bone synovial fluid, and synovial membrane concentrations of aminoglycosides distal to the tourniquet far exceeded recommended minimum inhibitory concentrations for susceptible bacteria commonly implicated in equine orthopedic infections. Whitehair et al used histologic methods to identify India ink within the venous system of the joint capsule, extensor carpi radialis tendon, and venules of the synovial villi of the equine carpus following IORP of the proximal metacarpus. With a similar technique but perfusing with iodinated contrast medium, these same investigators also demonstrated that contrast medium was present in the carpal bones following IORP of the carpus.

In our study, it was observed that no contrast medium entered the medullary cavity of the bones distal to the MCIII. The reasons for this are not obvious. It may be that the pressures generated in the vascular space during IORP were insufficient to overcome the resting intramedullary pressures of these bones. Therefore, contrast medium diffuses to other vascular locations preferentially. A difference may exist in the vascular distribution between cadaveric forelimbs and living subjects. It may be that the radiography methods used in our study were not sensitive enough to identify contrast medium within bone. Indeed, a study by other investigators who used smaller volumes of perfusate has demonstrated that high concentrations of aminoglycosides are achieved in the bone of the proximal, middle, and distal phalanges following IORP of the MCIII.

Numerous variations in technique of IORP have been reported. Published regional perfusion volumes vary considerably and are based on empirical data only. To reduce the amount of variation between individuals, Mattson et al report a perfusate volume based on body weight (0.1 mL/kg). This principle was adopted in our study. A volume of 0.15 mL/kg was used in our study. This higher volume was used to approximate the upper level of the reported volume range. Further studies are required to determine what effect volume has on the distribution of contrast medium following IORP as well as what volume is optimal for a therapeutic effect.

Effects of other variables on IORP distribution pattern have not been studied. Such variables include the age of the horse, concentration of medications administered, rate of delivery, pressure of infusion, location of the tourniquet placement, and location of intraosseous cannula placement. A wide range in ages of horses was used in our study. No obvious difference in distribution pattern was observed between the ages of 2 and 25 years, but further investigation into this subject is warranted. The concentration of contrast medium and latex used in our study was based on recommendations of the manufacturer for vascular perfusion studies. Rate of delivery in our study was set at 10 mL/min. This was to approximate clinical conditions. Maximum infusion pressure was based on a previous study. Location of tourniquet was based on recommendations from previous studies and on the available room between the carpus and the intraosseous cannula.

Location of intraosseous cannula placement was unique in our study. Previous investigators have removed placing the catheter in the dorsolateral cortex of MCIII, at the junction of the middle and distal third of this bone. To ensure that the infusion went directly into the medullary cavity, we placed it in the middle of MCIII. In our study, the intraosseous cannula was placed medial to the common digital extensor tendon to avoid soft tissue complications with the lat-
eral digital extensor tendon. The dorsal cortex of the MCIII is thicker than in other areas; therefore, the cannula was placed as dorsal as possible to ensure a secure fit of the intraosseous cannula and to minimize leakage from the bone-catheter interface.

Leakage from the intraosseous perfusion site is a commonly described, albeit minor complication during IORP. Poor catheter fit has been attributed to this complication. Cyanoacrylate ester and the use of an intraosseous cannula have been suggested to minimize this leakage. A custom-made intraosseous cannula was used in our study for this reason. In our study, most of the leakage occurred, not from the catheter-bone interface, but from the incised soft tissues around the infusion portal (ie, skin, subcutaneous tissue, and periosteum).

A major limitation of our study was the use of cadaveric forelimbs as specimens. Cadaveric forelimbs were chosen to minimize variability between specimens, allowing identical serial radiographic views to be taken and later compared. Although the pattern of distribution of contrast medium was consistent among specimens, it remains to be seen if this pattern is repeatable in living horses and is consistent. The influence of injury and disease of the distal portion of the forelimb on this distribution pattern is also an important area for future investigation.

In conclusion, IORP by use of contrast medium in the distal portion of the equine forelimb produces a consistent and repeatable pattern of distribution. This distribution is in a centripetal direction from the medullary cavity to peripheral vessels distal to the tourniquet, including veins and arteries. Although studies with living horses are necessary to further validate this technique, the results of our study support the use of IORP to deliver medications to the tissues of the distal portion of the equine forelimb.

References