Lung region and racing affect mechanical properties of equine pulmonary microvasculature

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Stack A, Derksen FJ, Williams KJ, Robinson NE, Jackson WF. Lung region and racing affect mechanical properties of equine pulmonary microvasculature. J Appl Physiol 117: 370–376, 2014. First published June 12, 2014; doi:10.1152/japplphysiol.00314.2014.—Exercise-induced pulmonary hemorrhage is a performance-limiting condition of racehorses associated with severe pathology, including small pulmonary vein remodeling. Pathology is limited to caudodorsal (CD) lung. Mechanical properties of equine pulmonary microvasculature have not been studied. We hypothesized that regional differences in pulmonary artery and vein mechanical characteristics do not exist in control animals, and that racing and venous remodeling impact pulmonary vein mechanical properties in CD lung. Pulmonary arteries and veins [range of internal diameters 207–386 ± 67 μm (mean ± SD)] were harvested from eight control and seven raced horses. With the use of wire myography, CD and cranioventral (CV) vessels were stretched in 10-μm increments. Peak wall tension was plotted against changes in diameter (length). Length-tension data were compared between vessel type, lung region, and horse status (control and raced). Pulmonary veins are stiffer walled than arteries. CD pulmonary arteries are stiffer than CV arteries, whereas CV veins are stiffer than CD veins. Racing is associated with increased stiffness of CD pulmonary veins and, to a lesser extent, CV arteries. For example, at 305 μm, tension in raced and control CD veins is 27.74 ± 2.91 and 19.67 ± 2.63 mN/mm (means ± SE; P < 0.05, Bonferroni’s multiple-comparisons test after two-way ANOVA), and 16.12 ± 2.04 and 15.07 ± 2.47 mN/mm in raced and control CV arteries, respectively. This is the first report of an effect of region and/or exercise on mechanical characteristics of small pulmonary vessels. These findings may implicate pulmonary vein remodeling in exercise-induced pulmonary hemorrhage pathogenesis.

EXERCISE-INDUCED PULMONARY hemorrhage (EIPH) is defined as the presence of frank blood (of pulmonary origin) in the airways after a bout of intense exercise (28, 30, 32). The condition has been reported in several athletic species, including humans (12), racing dogs (10), and camels (1); however, it is most commonly described in horses (6, 32). The incidence rate of EIPH in racehorses exceeds 75% (6, 34) when diagnosed by tracheo-bronchoendoscopic examination within 30–90 min of exercise (16). This highly prevalent condition is associated with impaired racing performance in Thoroughbred horses (17).

EIPH pathology is most severe and most common in caudodorsal (CD) lung regions, while the cranioventral (CV) lung is spared (28–31, 42, 43). The CD lung is also the region to which blood flow is preferentially distributed in the horse, both at rest (18) and to an even greater degree during exercise (4). The distribution and severity of the EIPH lesion matches the distribution of pulmonary blood flow (43).

Remodeling of small (100–200 μm outer diameter) intralobular pulmonary veins is a consistent histological feature of the EIPH lesion (42, 43) and is characterized by accumulation of adventitial collagen and, in more severely affected veins, hypertrophy of the tunica media (42). Pulmonary arteries and larger pulmonary veins are not affected in a similar manner. Venous remodeling, along with other EIPH-associated histopathological changes, such as interstitial fibrosis and hemosiderin formation, is limited to the CD lung (42, 43). In randomly sampled sections of EIPH-affected lung, the entire spectrum of lesions never occurs without colocalized venous remodeling, although venous remodeling occurs on its own (43). This suggests that venous remodeling is an early and key feature of the EIPH lesion and may be central to the pathogenesis of the disease.

Little is known about regional differences in mechanical characteristics of pulmonary microvasculature in horses or indeed in any other species. To further understand the pathogenesis of EIPH, a region-specific condition, investigations into regional differences in vascular biology are warranted.

It has been reported that pulmonary vascular remodeling, including collagen deposition, alters the mechanical properties of vessels (21, 38, 40). If pulmonary vein remodeling, such as that observed in EIPH-affected lungs (42, 43) affects wall mechanics, this will have functional ramifications on upstream capillaries. Pulmonary capillary stress failure has been described in the lungs of horses with EIPH (41) and is widely considered to be the source of airway hemorrhage, occurring secondary to dramatic increases in pulmonary vascular pressures in the exercising horse. Pulmonary capillary pressures (which are determined by arterial and venous pressures) are estimated to range between 72 (22) and 83 (26) mmHg during galloping, and transmural pressures in excess of 75 mmHg exceed the breaking strength of equine pulmonary capillaries (5). Remodeled veins are thick-walled compared with normal, unaffected veins, and in some cases have reduced luminal area (9). Should these changes reduce venous compliance (i.e., increase venous wall stiffness), it follows that, during strenuous exercise, pulmonary capillary pressure will increase yet further and potentially augment EIPH.

The purpose of the study reported here was to test two hypotheses. First, mechanical properties of small pulmonary arteries and veins do not differ by region (CV compared with CD) in control, unraced horses. Second, pulmonary veins, but
not arteries, from horses that have a recent racing history have increased wall stiffness compared with veins from horses that have never raced, and this change is limited to veins in the CD lung, the site of venous remodeling. Wire myography (15) was utilized to evaluate vessel mechanics in these experiments as the equipment is custom designed for small-diameter vessels, such as those of interest in this study.

Our data demonstrate regional differences in vessel wall stiffness in both pulmonary arteries and veins from control, unraced horses. Furthermore, CD veins from raced horses are stiffer than those from control, unraced horses. This finding establishes the first link between descriptions of pulmonary vein remodeling (42, 43) in the horse lung and the physiological effects this change is proposed to exert on the pulmonary vasculature during exercise.

MATERIALS AND METHODS

Animals. For this study, eight control horses and seven raced horses were acquired by donation. Control horses [3 geldings, 5 sexually intact females, 6.6 ± 0.6 yr (age ± SE)] were of various breeds (2 Arabians, and 1 each of Thoroughbred, Standardbred, paint, Quarterhorse, Haflinger, and crossbred) and did not have a race history. Race-trained horses [3 geldings, 1 sexually-intact male, and 3 sexually intact females, 6.3 ± 0.6 yr (age ± SE)] were all Thoroughbreds with a race record. The time period between the last race and euthanasia was 305 ± 77 days (mean ± SD). Raced horses had, on average, 22 ± 18 race starts (mean ± SD, range: 1–54 race starts) and were donated for reasons other than severe EIPH (predominantly career-limiting sections (4c m3) were immediately harvested from both the CD and CDV regions of lungs of raced horses was placed in 10% formalin for fixation and histological assessment. Pulmonary arteries were identified based on anatomic/dissection criteria. Pulmonary arteries were thick walled (compared by both an internal and external elastic lamina (27). In contrast, pulmonary veins had less smooth muscle in the tunica media, a single identified based on a relatively substantial tunica media that was bounded by both an internal and external elastic lamina (27). In contrast, pulmonary veins had less smooth muscle in the tunica media, a single distinct external elastic lamina between the tunica media and tunica adventitia (27) and an absent internal elastic lamina between the tunica intima and tunica media (35, 39) (Fig. 1).

Tissue acquisition. Horses were administered intravenous heparin sodium (50,000 IU/horse) ~15 min before euthanasia, which was carried out with pentobarbital sodium (90 mg/kg iv). Lung tissue sections (~4 cm3) were immediately harvested from both the CD and CV regions of the caudal (diaphragmatic) lobe of both left and right lungs. Lung tissue was placed in chilled normal saline (0.9% sodium chloride) solution for transportation to the laboratory. Additional tissue from CD regions of lungs of raced horses was placed in chilled Ca2+-free physiological saline solution (PSS) containing (in mM) 140 NaCl, 5 KCl, 1 MgCl2, 10 HEPES, 10 glucose (pH 7.4, 295 mosM). A low-calcium environment was chosen to minimize vasospasm that can occur during vessel manipulation.

Sections of pulmonary veins and arteries ranging in length from 0.34 to 1.39 mm and between 100- and 400-μm diameter were carefully dissected from tissue based on the following anatomic criteria: intralobular pulmonary veins that course completely alone in the parenchyma (42); pulmonary arteries were collected from bronchovascular triads. Within a triad of pulmonary artery, vein, and conducting airway, pulmonary arteries were easily distinguishable from the vein in the same bundle. They were stiff walled (compared with veins) and always immediately adjacent to a conducting airway, while veins in the bundle were more distant from the airway (35). Individual vessels were kept in Ca2+-free PSS at 4°C for up to 24 h until mounted on the myograph.

Wire myography. Vessels were mounted as a cylinder on two stainless steel 40-μm diameter wires, and the wires secured (one to a micrometer screw and the other to a force transducer) in a four-chamber myograph (DMT, Aarhus, Denmark). Each chamber contained 5 ml of Ca2+-free PSS, and all vessels were submerged throughout the experiment. The bath fluid was heated slowly to 37°C, and air was bubbled gently through the fluid continuously. Vessel length was recorded using a previously calibrated stereomicroscope, and the micrometer reading at which the wires were barely touching and parallel to one another was recorded. The myograph force transducer was used in conjunction with a PowerLab (ADInstruments, Colorado Springs, CO) data acquisition unit and LabChart (ADInstruments, Colorado Springs, CO) software platform.

Wires were then separated by use of the micrometer until the transducer registered a small (<0.05 mN) but sustained force. The micrometer reading was again recorded, and this was designated an individual vessel’s start point. Vessel diameter was calculated and recorded at this point. From that point, wires were separated from one another in 10-μm increments. The peak force achieved at each micrometer adjustment was recorded, and, once a plateau in force was attained, the wires were separated again for the next force measurement. Vessels were stretched in this stepwise manner until stretching resulted in no further increase, or a decrease in recorded force, which was interpreted as vessel failure.

Vessel histology. Once length-tension data acquisition was complete, a subset of vessels was fixed in situ on the myograph wires in 10% neutral buffered formalin. Following fixation, the vessels were removed from the wires and mounted orthogonal to the long axis in Histogel (American MasterTech, Lodi, CA) specimen processing gel. The gel-embedded vessel was then embedded in paraffin for sectioning. Six-micrometer sections were placed on glass slides and stained with hematoxylin and eosin and Verhoeff-Van Gieson. These stained sections were used to confirm vessel identity as a pulmonary artery or a pulmonary vein. Slides were reviewed by a board-certified veterinary pathologist (KJW), who was blinded to the identity of the vessel based on anatomic/dissection criteria. Pulmonary arteries were identified based on a relatively substantial tunica media that was bounded by both an internal and external elastic lamina (27). In contrast, pulmonary veins had less smooth muscle in the tunica media, a single distinct external elastic lamina between the tunica media and tunica adventitia (27) and an absent internal elastic lamina between the tunica intima and tunica media (35, 39) (Fig. 1).
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Table 1. Mean vessel diameters at start point

<table>
<thead>
<tr>
<th>Vessel Type</th>
<th>Region</th>
<th>Horse Status</th>
<th>n</th>
<th>Diameter at Start, μm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vein</td>
<td>CD</td>
<td>Control</td>
<td>9</td>
<td>217.5 ± 25.21</td>
</tr>
<tr>
<td>Artery</td>
<td>CD</td>
<td>Control</td>
<td>10</td>
<td>280.0 ± 38.81</td>
</tr>
<tr>
<td>Vein</td>
<td>CV</td>
<td>Control</td>
<td>7</td>
<td>207.3 ± 30.83</td>
</tr>
<tr>
<td>Artery</td>
<td>CV</td>
<td>Control</td>
<td>9</td>
<td>314.5 ± 37.42</td>
</tr>
<tr>
<td>Vein</td>
<td>CD</td>
<td>Raced</td>
<td>15</td>
<td>223.8 ± 15.35</td>
</tr>
<tr>
<td>Artery</td>
<td>CD</td>
<td>Raced</td>
<td>10</td>
<td>386.3 ± 29.28</td>
</tr>
<tr>
<td>Vein</td>
<td>CV</td>
<td>Raced</td>
<td>8</td>
<td>211.9 ± 34.68</td>
</tr>
<tr>
<td>Artery</td>
<td>CV</td>
<td>Raced</td>
<td>10</td>
<td>330.3 ± 27.2</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of vessels. Start point is defined as the smallest diameter at which a vessel maintains a small (<0.05 mN) but sustained wall tension. CD, caudodorsal; CV, cranioventral.

Lung histopathology. Fixed lung tissue samples from the CD regions of six of the seven raced horses underwent routine processing and embedding in paraffin for histological examination. Following sectioning, tissues were stained with hematoxylin and eosin and Verhoeff-Van Gieson and evaluated by KJW for the presence and severity of EIPH vascular pathology using previously described criteria (42).

Data analysis. Variability between vessels was similar to variability between animals; therefore, in this study, the sampling units are individual vessels and not horses.

Vessel internal diameters at the start point were calculated as follows: vessel internal circumference at that point divided by \( \pi \). Vessel internal circumference was calculated as twice the distance between the wires, plus the wire circumference, plus twice the wire diameter (44). The effect of vessel type (artery or vein) and region (CD or CV) on diameter at the start point was analyzed within racing status (control or raced) using a two-way ANOVA with Bonferroni’s multiple-comparisons test (GraphPad Prism 6, GraphPad Software, La Jolla, CA).

Change in vessel internal diameter from that vessel’s diameter at start point (as previously defined) was referred to as length and expressed in micrometers. Length for each vessel was plotted against the change in vessel internal diameter from that vessel’s diameter at start point, or length. Length-pressure data from arteries and veins were compared between racing status (control and raced) within each region (CD and CV) using a two-way ANOVA with Bonferroni’s multiple comparisons test (GraphPad Prism 6, GraphPad Software, La Jolla, CA).

RESULTS

From control horses, 9 veins and 10 arteries were harvested from CD lung regions, and 7 veins and 9 arteries from CV lung. From raced horses, it was 15 veins and 10 arteries from CD lung regions, and 8 veins and 10 arteries from CV lung. Seventy-eight vessels were included in all subsequent statistical analyses.

Vessel diameters. Vessel diameters are shown in Table 1. Diameters did not differ between arteries and veins from CD and CV lung in both control and raced horses with the following exception: arteries from the CD lung region were larger in diameter than veins from both CD and CV lung region of raced horses.

Vessel identification. Histology was performed on 29 of the 78 vessels that were studied. All vessels that were identified during dissection as either an artery or a vein had that identity confirmed by use of histology (Fig. 1).

Length-tension data. When data from the CD and CV vessels were combined, pulmonary veins (\( n = 16 \) and \( n = 23 \) for control and raced, respectively) were stiffer (as demonstrated by a steeper length-tension curve) than pulmonary arteries (\( n = 19 \) and \( n = 20 \) for control and raced, respectively). This observation was consistent in both control and raced horses (Fig. 2, A and B, respectively) (\( P < 0.0001 \)).

In control horses, pulmonary veins from the CV lung were stiffer than those from the CD lung (\( P < 0.0001 \)), whereas pulmonary arteries from CD lung were stiffer than arteries from CV lung (\( P < 0.0001 \)) (Fig. 3, A and B, respectively). This regional pattern of differences in vessel stiffness was maintained in vessels from raced horses (Fig. 3, C and D).

Vessels from raced horses were compared with vessels from control horses within lung region. CV veins and CD arteries were not affected by race training (\( P = 0.8078 \) and \( P = 0.4317 \), respectively) (Fig. 4, B and C, respectively). However, CD veins from raced animals were significantly stiffer than those from control animals (\( P < 0.0001 \)) (Fig. 4A). CV arteries from raced horses were also significantly stiffer than those from control horses (\( P = 0.0014 \)) (Fig. 4D).

Fig. 2. Length-tension plots for arteries and veins from control, unraced (A) and raced (B) horses. Values are means ± SE. In both control and raced horses, veins are stiffer than arteries. \( P < 0.05 \) is considered significant.

![Image](http://jap.physiology.org/.../Downloaded.png)
**Length-pressure data.** Tension values were converted to equivalent transmural pressure values encompassing in vivo physiological pressure ranges experienced by horses at rest and during exercise: 0–120 mmHg for arteries, and 0–80 mmHg for veins. Length-pressure data in these ranges were compared between control and raced horses within lung region. CV veins and CD arteries were not affected by race training ($P = 0.9416$ and $P = 0.0552$, respectively) (Fig. 5, B and C, respectively). However, CD veins and CV arteries from raced animals underwent a significantly smaller change in internal diameter over a physiological pressure range than vessels from control animals ($P < 0.0001$) (Fig. 5, A and D, respectively).

**Lung histopathology.** Venous remodeling and lung pathology consistent with EIPH changes were detected in all CD lung sections examined from raced horses. The venous remodeling was consistent with that previously described in association with EIPH (42, 43). Briefly, these changes consisted of mild to moderate increases in adventitial collagen surrounding small veins, along with small numbers of hemosiderophages, indicating prior hemorrhage and erythrophagocytosis by the alveolar macrophages.

**Fig. 3.** Length-tension plots for caudodorsal (CD) and cranioventral (CV) veins (A and C), and for CD and CV arteries (B and D) from unraced horses (A and B) and from raced horses (C and D). Values are means ± SE. In both control and raced horses, veins from CV lung are stiffer than veins from CD lung, and arteries from CD lung are stiffer than arteries from CV lung. $P < 0.05$ is considered significant.

**Fig. 4.** Length-tension plots of vessels from control and raced horses. Data are from CD (A and C) and CV (B and D) veins (A and B) and arteries (C and D). Values are means ± SE. Veins from the CD region of lungs of raced horses are stiffer than those from unraced, control horses. Arteries from the CV region of lungs of raced horses are stiffer than those from unraced, control horses. $P < 0.05$ is considered significant.
DISCUSSION

To the authors’ knowledge, this is the first published account of the effect of lung region and/or exercise on pulmonary microvascular mechanical properties in any species to date. Study of these factors in equids is particularly important to better understand EIPH pathogenesis.

The predominant tissue types that determine a vessel’s mechanical characteristics are collagen and elastin (7, 37). Elastin contributes most resistance to stretching at lower tension values, whereas collagen provides most resistance at higher tension values (7, 37). Collagen is minimally distensible and has an elastic modulus that is ~400 times that of elastin (7).

In both control and raced horses, pulmonary veins are stiffer walled than pulmonary arteries, and we propose that this difference is due to the greater proportion of collagen in vein walls compared with arteries. This particular finding has been documented in other species. In the dog, intraparenchymal pulmonary veins are less distensible in response to increases in intravascular pressure than equivalently sized pulmonary arteries (24). Larger pulmonary veins are also less distensible than pulmonary arteries in both rabbits (8) and humans (3, 23).

Mechanical properties of small-caliber pulmonary vessels, such as those evaluated in this study, are not well described in the literature to date, and, to the best of the authors’ knowledge, published data regarding regional differences in mechanical properties of pulmonary arteries and veins of this size range in any species do not exist. In both control and raced horses, CD arteries are stiffer walled than CV arteries. Due to the absence of similar observations in other species, this finding is unexpected, and any proposed rationale for this observation at this time remains speculative. However, in light of what is known about pulmonary blood flow distribution patterns that are observed in the horse (18) and in other mammals (13, 14), stiffer-walled pulmonary arteries in CD lung may represent an adaptive response to normal preferential distribution patterns of blood flow to this region, which in turn is largely due to the anatomy of the pulmonary vascular system (19). This change may also serve to protect pulmonary capillaries in this region from a higher-flow state during intense exercise.

In both control and raced horses, CV veins are stiffer walled than CD veins. Considering an example from the equine systemic circulation, veins within the foot (i.e., laminar veins) are exposed to the highest intravascular pressures in the limb due to gravitational forces and are thick-walled (2) structures that are difficult to discern from laminar arteries (20). It is possible that pulmonary veins from the CV lung are stiffer walled than their CD counterparts due to a similar adaptive response to the hydrostatic pressure difference between the dorsal and ventral lung.

Although vessel mechanics play a role in influencing blood flow distribution, vessel reactivity must also be considered a key determinant of pulmonary blood flow. Interestingly, a small number of studies report regional differences in pulmonary vessel reactivity, both in the horse (33) and in the pig (11, 36). Larger dorsal arteries in both pigs (36) and horses (33) demonstrate enhanced endothelial-mediated vasorelaxation compared with vessels from ventral regions. Regional patterns of vessel mechanical properties, along with vascular reactivity, merit further and more detailed investigation.

An important finding of this study was that CD veins from raced animals were significantly stiffer than those from control animals. This increase in stiffness is most likely a consequence of venous remodeling in raced horses. We previously reported that small pulmonary veins in CD, but not in CV, lung remodel in EIPH-affected horses, while equivalently sized pulmonary arteries are largely unaffected in both regions (42). EIPH-
associated venous remodeling is typified by extensive adventitial collagen expansion (42), resulting in reduced lumen area (9). In studies performed on the pulmonary vasculature of other species, remodeling is also associated with altered mechanical properties (21, 38, 40).

An increase in stiffness of pulmonary veins has important physiological consequences. Increased vein stiffness will decrease pressure-induced distension of the veins and increase resistance to blood flow, particularly during exercise. This, in turn, should increase pressure in upstream pulmonary capillaries. If pressure increases exceed the reported breaking strength of these vessels [transmural pressure 75 mmHg (5)], stress-failure (41) of capillary walls can occur, resulting in EIPH.

Despite the difference between length-tension curves of pulmonary arteries harvested from CV lung in raced and unraced horses being small, this difference was statistically significant. The observation that CV pulmonary arteries were stiffer in raced horses was unexpected, as vascular pathology in CV lung is not reported in existing literature on the topic (30, 31, 42). As extensive EIPH pathology in this region is not observed, it is possible that mild arterial remodeling changes have been overlooked in past studies, and further, more detailed studies of the vasculature of this region are warranted based on this observation. It is plausible that stiffening of CV pulmonary arteries in response to race training is somewhat protective of capillaries in that region, and that, through this mechanism, this observation may also explain (at least in part) the regional nature of the EIPH lesion.

Alterations in vessel stiffness, as determined by analysis of length-tension curves, are a direct result of changes in vessel wall structural components (23). In this study, we evaluated tension over a wide range, from zero stress to tension values approaching vessel breaking point. In light of previous studies in EIPH-affected horses that report collagen deposition in remodeled vein walls (9, 42, 43), it is most likely that the observed increase in vessel stiffness is due to an increase in wall collagen content. In this study, all vessels were stretched to near-breaking point, which distorted vessel wall anatomy greatly. For this reason, morphometric analyses of the vessels were not performed, and, therefore, we do not provide data quantifying collagen deposition in affected vessels. Studies using a reduced range of tension application to correlate collagen content and mechanical properties are warranted.

Vessel mechanics were analyzed over a large range of wall tensions, which undoubtedly exceeds any wall tension changes experienced during exercise in vivo. Extrapolation of the effect of mechanical changes over such a large wall tension range on vessels in the living horse at rest or during exercise is difficult, and predicted effects, if any, should not be overstated. In an effort to address this, we converted tension values to equivalent transmural pressure values using the law of Laplace and evaluated length-pressure relationships over a range encompassing in vivo physiological pressure ranges experienced by horses at rest and during exercise: 0–120 mmHg for arteries, and 0–80 mmHg for veins (25). This analysis demonstrated an identical pattern of significant effects of racing (stiffening of CD veins and CV arteries) to that found in the larger (supraphysiological) range of vessel wall tensions. It is reasonable to extrapolate the effect of these data to vessels in vivo, and these findings lend further support to the hypothesis that pulmonary venous remodeling in the CD lung, which in this study manifests as an increase in vessel wall stiffness, may be a component of EIPH pathogenesis.

Previous reports of EIPH pathology have utilized horses with career-limiting EIPH (31, 42, 43) and correspondingly severe pulmonary pathological changes. In contrast, raced horses used in this study were retired from racing for reasons other than EIPH. Interestingly, and despite an absence of severe EIPH clinical history, these horses had mild to moderate EIPH pathology, suggestive of underlying prior pulmonary hemorrhage. Consistent with previous reports (42, 43), CD veins of raced horses in this study were remodeled. The data presented in this paper expand this observation by demonstrating that this remodeling is associated with increased vein wall stiffness. These alterations in vessel mechanics further substantiate the contention that remodeling of the pulmonary venous system of the equine lung is an early response to strenuous exercise. The authors propose that this remodeling may have a role in the pathogenesis of EIPH (43), although it is acknowledged that the experiments described in this study were not designed to ascertain whether alterations in pulmonary vein stiffness contribute to EIPH, or whether the changes come about because of EIPH earlier in these horses’ racing careers. Further support for a relationship between histological remodeling changes and increased vein stiffness is provided by the observation that the mechanical properties of CV veins and CD arteries, vessels that are not reported to remodel in EIPH-affected horses (42, 43), were unaffected by racing.

In conclusion, the findings of this study indicate, for the first time, that regional differences in vessel mechanics exist in the unraced horse, and that changes in pulmonary vein wall structure occur in horses that have undergone race training. Furthermore, these changes occur before the development of severe, career-limiting EIPH. Altered vessel mechanics are detectable within a physiologically applicable range of vessel wall tensions. Therefore, this finding may have important consequences in the exercising horse. Increased vein wall stiffness increases pulmonary capillary pressures, particularly during exercise, thereby augmenting EIPH. These data highlight pulmonary vein remodeling as a lesion of interest in EIPH pathogenesis and suggest that pulmonary veins could be an interesting therapeutic target in future approaches to EIPH management.

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GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

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