Doppler renal resistivity index in horses: a systematic review

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Abstract

The renal resistivity index is a tool to evaluate the hemodynamics through arterial resistance. Considering perfusion as one of the first aspects to be affected upon kidney injury, alterations in renal blood flow could be especially important for the early detection of kidney damage. The aim of this systematic review was to retrieve published studies on equine renal resistivity index (RI) in order to develop a standardized method of renal ultrasound examination through a transabdominal approach as well as to evaluate current reference range for renal RI value in horses. An electronic search in Science Direct, PubMed, Scopus and Web of Science databases was performed in February 2023 using the terms “RI” OR “resistivity index” OR “IP” OR “pulsatility index” AND (kidney OR renal) AND (equine OR horse) in titles, keywords and abstracts. The studies were screened based on inclusion criteria and variables of interest were extracted. To assess the methodological quality, the SYRCLES’s risk of bias tool was used. From the search, a total of 134 studies were identified and five of them were considered eligible. The selected studies had been conducted in healthy non-sedated horses through transabdominal technique. The upper limit of normality for renal RI was 0.58 ± 0.06 for the right kidney of untrained horses, which is considerably lower than the value of 0.70 currently used for humans, cats and dogs. There were heterogenous outcomes among studies, where two out of the five demonstrated difference between RI value of left and right kidneys and one out of the five showed increased renal RI value in the elderly compared to foals and adult animals. Data of RI in horses is still scarce; a normality standard for renal RI studies in horses would greatly improve comparison and good quality results to allow clinical application.

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**Keywords:** horse, ultrasonography, kidney, resistivity index

**Introduction**

The kidneys are vital organs once they are responsible for homeostasis as they play a main role in the hydric, acid-base and electrolyte balance, help controlling blood pressure, and having endocrine function as well [1]. Although renal diseases are reported as being uncommonly diagnosed in horses, there are several published reviews and case reports on different renal diseases [2-6] suggesting otherwise. A study on the prevalence of acute kidney injury (AKI) in hospitalized horses found that 14.8% of studied horses developed AKI [7]. Further, Knottenbelt e Pascoe [8] have noted that kidney injuries are frequently found in post-mortem examinations in horses and so, we are probably dealing with a scenario where kidney diseases are underdiagnosed.

Considering such possible underdiagnosed kidney damage and the difficulties on treatment of kidney disease, it is very important to establish an early diagnosis due to its major impact on the body. There are several hematological and urinary exams available nowadays, but it is known that renal injuries up to 75% can be compensated by nephrons and possibly no relevant alterations would be seen in those exams [9]. In that sense, when kidney injuries are detected using these methods, effective treatment might be unattainable.

In human medicine, ultrasonography is being widely used as a tool to enhance the early diagnosis of renal damage. It is an easy and non-invasive exam that provides information about the morphology, shape, length, echogenicity and even hemodynamics of the kidneys [10, 11].

On top of the well-known B mode, the Doppler ultrasound can detect alterations of reflected sound waves frequency when the object hit by the wave is in movement and, by an equation, the velocity of that object can be obtained [12]. The color Doppler shows the presence and direction of the object towards the probe, it is majorly represented by the blue and red colors, largely used for blood flow evaluation [13]. Furthermore, the pulsed Doppler is responsible for reading the sound pulses and generating a spectral wave that shows their number within the same frequency [12], being represented as velocity X time. Two indexes can be calculated from the information acquired from the spectral wave, the resistivity index (RI) and the pulsatility index (PI). These indexes stand for (1) RI ([peak systolic velocity – final diastolic velocity]/peak systolic velocity) and (2) PI ([peak systolic velocity – final diastolic velocity]/average velocity), according to Novellas et al. [14]. The RI and PI give information about perfusion of the organ and its vascular resistance [15,16].

Measurements of renal RI and PI are already being described in humans as a method to investigate and follow the progression of various diseases, not only related directly to the kidneys [17], as well as a valuable technique to evaluate the successfulness of renal transplantations [18]. In small animals, it has been reported that RI and PI would be advantageous to evaluate chronic renal disease in cats [19], kidney damage from inflammatory disease in cats [20], acute renal disease in dogs and cats [21], cardiorenal syndrome in dogs [22] and a number of other conditions. In addition, there are numerous studies regarding the normal range for each species [14,23,24].

For horses, however, there are only few studies in respect to RI, consequently, limiting its clinical use. This review aimed to evaluate standard RI values of normality in horses and analyze published studies concerning their methodology, appraise and compare their results. In addition, we were able to critically review possible limitations, difficulties and methodological flaws in the selected studies along with pointing achievable future directions on the subject.

**Materials and methods**

The present systematic review was conducted according to the premises of PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses [25].

**Search strategy**

PubMed, Science Direct, Web of Science and Scopus were the databases chosen for this research. An extensive
search was driven applying the following terms: RI OR “resistivity index” OR IP OR “pulsatility index” AND (kidney OR renal) AND (equine OR horse) in titles, keywords and abstracts. There were no limitations upon language, year or country of publication and the last search was performed on February 9, 2023.

Eligibility criteria

The studies screened in the searching were selected if they accomplished the following features: (1) horses were the animal model, (2) conducted in renal vessels, (3) at least the RI was measured. Further, the studies were excluded if they were: (1) in another species other than equine, (2) not performed in the kidneys, (3) book chapters, (4) not mentioning RI or PI.

Data extraction

Extraction was carried out by the same people and the variables considered as being of interest were listed in an Excel table. Extracted data were grouped according to articles information (authors, year and country of publication), experimental model (horses’ breed, age, body weight and sex), methodology (animal grouping, sedated or non-sedated, athletes or not athletes, comparing or not left and right kidney, comparison between age groups, artery of interest), technical information (type of equipment and probe, frequency of the last, wall filter, sample volume) and the values obtained for RI and PI.

Risk of Bias assessment

The quality assessment of the included studies was checked using the SYRCLE’s risk of bias tool for animal studies [26]. This method is based on ten signaling questions that can be adapted according to the reviewer and the papers being reviewed so the analyses can be more accurate.

Results

Selected studies

From the initial search, 134 studies were identified. The screening phase consisted of reading the titles and abstracts and evaluating if they match the previously cited inclusion criteria, stage at which 14 studies were selected. A great number of studies were not included because they were based on other animals rather than horses or because they were not performed in kidneys. The selected records were downloaded and fully read. One study was not available online, so it was necessary to email the author, having a copy promptly sent. Finally, after exclusion of duplicates and of one paper that did not address renal arteries [27], five studies were included in the present systematic review. All steps from identification to inclusion were taken by two examiners and there were no disagreements. It was not necessary to use a specific program or software to evaluate data due to the small number of eligible studies. The flow diagram on Figure 1 demonstrates how the process of selecting the articles was conducted.

Figure 1 - Flow diagram showing the sequency of how studies were selected to systematic review, according to PRISMA.

Study characteristics

Two out of the five eligible studies were published in the 2010s [11,28], two in the 2020s [29,30] and one is dated back in the 1990s [31]. From those, two were carried out in Poland [28,30], two in Italy [11,29] and one in Australia [31].

According to the findings of this systematic review, Hoffmann and colleagues [31] were the first research group to publish about RI measurement in horses. They considered a group of 11 healthy animals, being five of them sedated to ensure good ultrasonographic access to the intrarenal arteries and seven of them not sedated so the pyleorenal arteries were assessed. Although there were sedated horses in the study, only the healthy non-sedated group was included in this review. The aim of this pioneer research was to establish a reference range for peak systolic and end diastolic velocities and for RI in the equine.
Furthermore, Macri et al. [11] included 13 healthy Thoroughbred horses aiming at determining a reference range for arterial renal RI in healthy non-sedated horses and to compare the results of right and left kidneys, mares and geldings as well as trained and untrained animals. Siwinska and peers [28] selected 45 Warmbloods horses and compared the renal RI among animals’ age groups (15 foals, 15 adults and 15 elderly), between the left and right kidneys, likewise the influence of age, body weight, heart rate and blood pressure on the intrarenal arteries RI. They also assessed repeatability by performing a second ultrasound two hours after the first measurements.

In addition, Freccero et al. [29] aimed to obtain the renal RI value of each kidney from 33 horses and nine donkeys, along with their breeds, age, body mass and body condition and compare all this information within itself. Since this systematic review is considering only horses, the data including donkeys were excluded. Lastly, Siwinska and colleagues [30] obtained the renal RI of 30 healthy horses (proven healthy throughout complete clinical and laboratorial evaluation and urinary tract ultrasonographic examination), 11 horses diagnosed with acute kidney injury (AKI) and 30 horses under risk of developing AKI (10 horses with colic/gastrointestinal diseases; 10 horses on phenylbutazone - 2.2 mg/kg twice a day orally for 10 days; 10 horses on gentamicin - 6.6 mg/kg intravenously for 5 days). She and her group aimed to determine if animals with AKI would show a higher renal RI, as well as, to measure renal RI in horses at risk for AKI and investigate if potential nephrotoxic agents could impact renal RI. They compared the RI data from right and left kidneys between groups and checked for correlation between renal RI and blood and urine parameters. Also, the group evaluated the sensitivity and specificity of renal RI to AKI detection.

It is crucial to establish that for this systematic review only the healthy non-sedated group of each study was considered, so the baseline characteristics and methodological features could be reliably compared between papers. The Table 1 summarizes the characteristics of the included information from the studies included in the review.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Breed</th>
<th>Number of animals</th>
<th>Grouping</th>
<th>Body weight</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffmann et al., 1997</td>
<td>Australia</td>
<td>Thoroughbreds</td>
<td>7</td>
<td>Non-sedated</td>
<td>NR</td>
<td>15 ± 4.6 years</td>
</tr>
<tr>
<td>Macri et al., 2015</td>
<td>Italy</td>
<td>Thoroughbreds</td>
<td>13</td>
<td>Male (5) Female (8)</td>
<td>420 – 500kg</td>
<td>3 – 24 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Standardbreds</td>
<td></td>
<td>Trained (5) Untrained (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Siwinska et al., 2019</td>
<td>Poland</td>
<td>Warmbloods</td>
<td>45</td>
<td>Foals (15) Adults (15) Elderly (15)</td>
<td>205 ± 38.8kg 558.4 ± 95.3kg 542.6 ± 74.6kg</td>
<td>Up to 6 months 4 – 10 years Above 18 years</td>
</tr>
<tr>
<td>Freccero et al., 2020</td>
<td>Italy</td>
<td>Trotters Thoroughbreds</td>
<td>33</td>
<td>Adults (18) Elderly (15) Trotters (23) Other breeds (10)</td>
<td>Horses: 370 – 645kg</td>
<td>Horses: adults up to 15 years and elderly above 15 years</td>
</tr>
<tr>
<td>Siwinska et al., 2021</td>
<td>Poland</td>
<td>Warmbloods</td>
<td>30</td>
<td>Healthy (15F/15M)</td>
<td>Healthy: 554 ± 80kg</td>
<td>Healthy: 14.7 ± 8.4 years</td>
</tr>
</tbody>
</table>

Table 1 - Characterization of studies (n = 5) selected to the systematic review

Abbreviations: NR not reported, F female, M male, AKI acute kidney injury.
Ultrasonographic examination

In view of renal ultrasonography, all studies reported the performance of the transabdominal approach with the horse standing and none of them have selected the transrectal access. All studies also have described the preparation of the animals prior to the examination (Table 2). This stage was very similar between studies and consisted of clipping or shaving the hair coat over the 14th or 15th to the 17th intercostal space (ICS) and the paralumbar fossa on the right side and over the 15th or 16th to the 17th ICS and the paralumbar fossa on the left side. Siwinska et al. [28,30] opted for washing the horses’ skin with chlorhexidine and rinsing with alcohol, drying and applying water-soluble coupling gel while Freccero et al. [29] chose to use alcohol and coupling gel, similarly Hoffmann et al. [31] and Macri et al. [11] applied only ultrasound gel. Concerning the technical information about the ultrasound machine and settings (Table 2.2), the five studies have reported the type of probe and its range of frequency, the sample volume (SV) and the wall filter (WF), except for Macri et al. [11] that did not demonstrate data on the last two and for Hoffmann et al. [31] that reported only the WF. Freccero et al. [29] have additionally presented information about the pulse repetition frequency (PRF). Siwinska et al. [30] used the same ultrasound protocol as Siwinska et al. [28].

In order to avoid stressing the animals, Siwinska et al. [28] had the foals included in their experiment kept together with mares during the examination, also adults and elderly horses were examined near or in front of their stalls. Freccero et al. [29] had the animals restrained in a handling box that horses had already been acclimated. It is important to minimize stress as it can affect the waveforms, and thus the RI value [35].

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient preparation</th>
<th>US characteristics</th>
<th>Equipment settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffmann et al., 1997</td>
<td>Hair shaving and coupling gel</td>
<td>Opus 1 (Ausonics International). Split-crystal mechanical sector probe. 2.5MHz for B-mode and 1.9MHz for continuous wave Doppler</td>
<td>WF of 50Hz</td>
</tr>
<tr>
<td>Macri et al., 2015</td>
<td>Hair clipping and coupling gel</td>
<td>MyLab 50 Vet (Esaote, Italy). 1.9MHz to 3.0MHz phased-array probe.</td>
<td>NR</td>
</tr>
<tr>
<td>Siwinska et al., 2019</td>
<td>Hair clipping, skin washing with chlorhexidine soap and alcohol, use of coupling gel</td>
<td>MyLab 30 Gold Vet (Esaote). 1MHz to 5MHz convex probe.</td>
<td>SV set at 5 to 10mm and decreased to small as possible WF of 50 or 100Hz</td>
</tr>
<tr>
<td>Freccero et al., 2020</td>
<td>Hair clipping, alcohol and coupling gel</td>
<td>MyLab 30 Gold (Esaote, Italy). Multifrequency curvilinear probe 3.5MHz to 5MHz.</td>
<td>SV set at 2mm WF of 50Hz PRF set lowest possible values</td>
</tr>
<tr>
<td>Siwinska et al., 2021</td>
<td>Hair clipping, skin washing with chlorhexidine soap and alcohol, use of coupling gel</td>
<td>MyLab 30 Gold Vet (Esaote). 1MHz to 5MHz convex probe.</td>
<td>SV set at 5 to 10mm and decreased to small as possible WF of 50 or 100Hz</td>
</tr>
</tbody>
</table>

Table 2 - Characterization of patient preparation and ultrasound machine and settings of the studies included (n = 5) in the systematic review. Abbreviations: US ultrasonography, ICS intercostal space, PL paralumbar,
NR not reported, WF wall filter, SV sample volume, PRF pulse repetition frequency

**RI measurements**

All five studies included in this review reported data on RI measurements in healthy horses and none of them reported PI values. A total of 128 healthy horses were assessed in the studies; data collected are presented in Table 3. Among the five studies, one has reported a mean value for both kidneys whereas the other four have presented the values for left and right kidneys separately. Only Hoffmann et al. [31] has used pyelorenal arteries, all other authors have chosen intrarenal arteries, being those the arcuate and/or interlobar. All writers presented the RI values as mean and standard deviation. The higher value measured across studies was $0.58 \pm 0.06$ for the right kidney of untrained horses [11] and the lowest value was $0.46 \pm 0.04$ for the left kidney of foals [28]. Hoffmann and colleagues [31] accepted horses’ RI normality value as being of the same order of humans, cats and dogs, in which 0.70 is considered to be the upper limit.

As a method to calculate a more reliable RI value, Hoffmann et al. [31] reported that at least seven continuous-spectral waves consisting of peak systolic and end diastolic velocities were attempted. Macrì and colleagues [11] repeated measurements three times on each kidney and Siwinska et al. [28,30] have acquired three adequate waveforms. Lastly, Freccero and peers [29] have selected at least one 8-second spectral tracing from each kidney.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Reference</th>
<th>Artery of interest</th>
<th>Artery of interest</th>
<th>Grouping (n)</th>
<th>Grouping (n)</th>
<th>RI</th>
<th>RI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffmann et al., 1997</td>
<td>Hoffmann et al., 1997</td>
<td>Pylorenal</td>
<td>Pylorenal</td>
<td>Non-sedated</td>
<td>Non-sedated</td>
<td>0.512 ±</td>
<td>0.512 ±</td>
</tr>
<tr>
<td>Macri et al., 2015</td>
<td>Interlobar and arcuate</td>
<td>Male (5)</td>
<td>Male (5)</td>
<td>0.50 ± 0.05</td>
<td>0.50 ± 0.05</td>
<td>0.48 ± 0.06</td>
<td>0.56 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>Interlobar and arcuate</td>
<td>Female (8)</td>
<td>Female (8)</td>
<td>0.50 ± 0.06</td>
<td>0.50 ± 0.06</td>
<td>0.48 ± 0.06</td>
<td>0.56 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>Interlobar and arcuate</td>
<td>Untrained (5)</td>
<td>Untrained (8)</td>
<td>0.52 ± 0.04</td>
<td>0.52 ± 0.04</td>
<td>0.48 ± 0.06</td>
<td>0.55 ± 0.01</td>
</tr>
<tr>
<td>Siwinska et al., 2019</td>
<td>Interlobar or arcuate</td>
<td>Foals (15)</td>
<td>Foals (15)</td>
<td>0.46 ± 0.04</td>
<td>0.46 ± 0.04</td>
<td>0.52 ± 0.05</td>
<td>0.52 ± 0.05</td>
</tr>
<tr>
<td></td>
<td>Interlobar or arcuate</td>
<td>Adults (15)</td>
<td>Adults (15)</td>
<td>0.48 ± 0.05</td>
<td>0.48 ± 0.05</td>
<td>0.48 ± 0.05</td>
<td>0.47 ± 0.05</td>
</tr>
<tr>
<td></td>
<td>Interlobar or arcuate</td>
<td>Elderly (15)</td>
<td>Elderly (15)</td>
<td>0.52 ± 0.05</td>
<td>0.52 ± 0.05</td>
<td>0.52 ± 0.05</td>
<td>0.52 ± 0.05</td>
</tr>
<tr>
<td>Freccero et al., 2020</td>
<td>Arcuate</td>
<td>Adults (18)</td>
<td>Adults (18)</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>Arcuate</td>
<td>Elderly (15)</td>
<td>Elderly (15)</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>Arcuate</td>
<td>Trotters (23)</td>
<td>Trotters (23)</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>Arcuate</td>
<td>Other breeds (10)</td>
<td>Other breeds (10)</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
<td>0.51 ± 0.01</td>
</tr>
<tr>
<td>Siwinska et al., 2021</td>
<td>Interlobar or arcuate</td>
<td>Healthy (15F/15M)</td>
<td>Healthy (15F/15M)</td>
<td>0.50 ± 0.05</td>
<td>0.50 ± 0.05</td>
<td>0.50 ± 0.05</td>
<td>0.50 ± 0.04</td>
</tr>
</tbody>
</table>
Table 3 - Characterization of resistivity index of healthy horses’ groups of the studies (n = 5) included in the systematic review.

Abbreviations: RI resistivity index, LK left kidney, RK right kidney, F female, M male.

Other findings
Macrì et al. [11] and Freccero et al. [29] reported differences in the RI values from right and left kidneys of the horses evaluated in their study. No study has found difference in the RI values related to gender. Siwinska et al. [28] assessed repeatability in their study and found a high correlation between measuring time-points. She and her group also noted a higher RI value among the elderly horses compared to adults and foals. They have also shown that RI is affected by the pulse pressure. All studies have considered the renal ultrasonographic examination for obtaining RI value as time consuming, dependent on the horse’s willing to cooperate and dependent on the operator’s experience to perform the exam.

Risk of Bias
The risk analysis applied in this systematic review was adapted from the SYRCLE tool [26] and the results are demonstrated in Table 4 below.

Concerning selection bias, allocation concealment was not included due to the types of studies. For allocation sequence, it was considered a high risk for all five studies [11,28,29,30,31] as the authors have selected animals after taking laboratorial tests to ensure horses’ good health and so it cannot be considered as random allocation. In regard to baseline characteristics, Hoffmann et al. [31] did not describe in details the animals’ conditions prior to ultrasound examinations as the other four studies [11,28,29,30] did, so to his study the risk was considered as unclear and to the others it was considered as low risk.

The performance bias of animal housing and management was addressed as high risk for one study [31] that did not report any data on this matter, as unclear risk for two studies [29,30] that informed incomplete data and as low risk to two studies [11,28] that described in details the housing, feeding, management, handling and exercising routine of the horses. Another source of bias was the outcome assessor and its randomness. In this matter, the experience level of the evaluator was assessed and whether it was the same person to perform the examinations in all horses during the research. The study that did not report any information was considered as high risk, if there was at least one information available, it was considered as unclear risk and as low risk if there was enough data.

Regarding the risk of incomplete outcome data, we assessed it by analyzing if the study has demonstrated the expected results, if all proposed RI measurements were concluded and if they were achieved in both kidneys and in all horses. Furthermore, to evaluate the risk of selective outcome reporting, we analyzed if the study reported data about all proposed outcomes and methods of animal evaluation, if they mentioned the ethical committee protocol or equivalent and if it was clear whether all expected results were demonstrated. For both previously cited risks, the studies were considered as high risk if they did show any of the cited characteristics, as unclear if they reported a few information and as low risk if they presented all information needed.

Other high risks assigned to the retrieved articles were related to a small sample number [11,31], one-time observation on renal RI [11,29,30,31] and to not performing blood pressure measurement [11,30], as this parameter is known to potentially interfere with the renal RI value.

<table>
<thead>
<tr>
<th></th>
<th>HOFFMANN, 1997</th>
<th>MACRÌ, 2015</th>
<th>SIWINSKA, 2019</th>
<th>FRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection bias</td>
<td>Allocation sequence</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Baseline characteristics</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Performance bias</td>
<td>Animal housing and management</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Detection bias</td>
<td>Outcome assessor</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Table 4 - Assessment of methodological quality of reviewed reports. Symbols were addressed to each bias regarding the five evaluated studies, standing for high risk (- red), unclear risk (? yellow) and low risk (+ green). MUST BE COLORED

<table>
<thead>
<tr>
<th>Bias</th>
<th>Hoffmann, 1997</th>
<th>Macrì, 2015</th>
<th>Siwinska, 2019</th>
<th>Freccero, 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attrition bias</td>
<td>-</td>
<td>?</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Reporting bias</td>
<td>Selective outcome reporting</td>
<td>?</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td>Other sources of bias</td>
<td>Small sample number</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Single moment of evaluation</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Blood pressure measurement</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Discussion

Despite B mode ultrasound being largely used in the equine veterinary practice, its relevance to renal evaluation is limited as morphology does not always relate to function [32]. On the other hand, the noninvasive Doppler sonography is able to provide data in respect to renal blood flow and vascular resistance [16]. The RI derives out of the information given in the Doppler arterial waveforms and reflects the hemodynamics of the targeted tissue [12,33], which in turn, can reflect its function and, as so, an impaired function [17].

Although the RI is still not extensively used in veterinary medicine, it is being considered as an important tool to assess renal microcirculation in physiological and pathological situations [34], most widely considered today for dogs and cats [14,20,22,24]. However, a number of elements can influence renal RI, such as arterial characteristics (i.e. aortic stiffness), and systemic hemodynamics factors (i.e. pulse pressure, hydration status) [17,33,34]. It is crucial to keep that information in mind when undertaking a RI study.

Although renal RI relevance in humans and other animal species have been demonstrated, the lack of information for equines and its physiological range of value, motivated this systematic review. A compilation of renal RI values obtained from healthy horses in five eligible studies was made, as well as a description of study methodology, equipment adjustments, technical information and patient preparation. All information acquired was analyzed in order to develop a standardized method to perform renal Doppler ultrasonography and to evaluate the reference range for renal RI values in horses. Unfortunately, due to the limited number of studies and the methodological variation between them, a meta-analysis was not possible. This impaired the evaluation of the reference range, making it clear that more studies are still needed in horses.

Regarding patient preparation, the five selected studies [11,28,29,30,31] described this step minutely and were consentaneous about hair clipping, use of coupling gel and the location of examination. Also, Siwinska et al. [28] and Freccero et al. [29] described important strategies to minimize stress, as it can affect the waveforms, and thus the RI value [35], which should be observed in future studies.

The transabdominal approach was a successful method in all studies, using a 2 to 5MHz frequency curvilinear probe [11,28,29,30,31]. It has been already described that this frequency range is more suitable for abdominal ultrasound imaging in horses [36], shown by these 5 studies to be also suitable for Doppler ultrasound and, thus, RI measurements. For ultrasound examination, all operators first performed the B mode evaluation of the kidneys, used the color Doppler to set the artery and then got the Doppler waveforms on spectral Doppler. Another important information concerns equipment settings as reason for better image resolution, lowering occurrence of artifacts and, thus, providing a more reliable result. In this light, pulse repetition frequency and wall filter should be set as lower as possible to avoid aliasing [37] and wall artifacts or clutter [38,39], respectively. Sample volume size should be adjusted to artery diameter and positioned in the vascular lumen [35], but it is still not standardized for horses. These aspects described in the works included in this review should also be observed in future studies.

Some authors [28,30,31] have found it difficult to retrieve a good quality image from left kidney in comparison to right kidney. Siwinska et al. [28] have attributed this difficulty to the anatomical location of the organ,
that lays under the spleen and is surrounded by intestinal components. The target arteries (arcuate and interlobar) was the same in four studies [11,28,29,30], only Hoffmann and others [31] used the pyelorenal artery due to the equipment they had available. The ideal vessel for RI measurement is still not well described for horses; however, it has been demonstrated that lower caliber arteries suffer more from flow changes, thus producing a greater variation in the RI value [14,40]. Also, it has been reported that it is necessary to acquire three to five RI measures to properly get a RI definitive value [41]. Two of the reviewed studies [11,31] did not mention if they managed to get all desired waveforms and the other three [28,29,30] have reached a lower number that they expected. Yet, all five studies considered RI values to be reliable. Based on studies in other species, we strongly suggest future works to acquire at least 3 waveforms when conducting RI analysis and that future studies may be done with such objective.

Macrì et al. [11] and Freccero et al. [29] have reported different RI values for right and left kidneys, as showed in Table 3. However, the other three studies [28,29,30] did not show RI disparity, corroborating with cats, dogs and humans' findings [14, 18, 20]. No explanation is yet available for these divergent values between kidneys, and so more research addressing this specific question is still needed.

Siwinska et al. [28] found a higher RI value in the group of elderly horses (0.52 ± 0.05 vs 0.48 ± 0.05 in adults; 0.52 ± 0.05 vs 0.47 ± 0.05 for right kidney and 0.46 ± 0.04 for left kidney in foals). For humans, changes in the RI value according to age have been described, being higher in infants and in the elderly population [44-47]. For dogs, the age seems to influence the renal RI value as well, mostly during the first three weeks of life, being higher in this period and then slowly decreasing until adult values at 12 weeks [49]. RI changes according to age are still unclear in cats [20] and should still be a subject of study in horses.

Regarding the expected range of value for each species, it can be noticed that they diverge from equine findings; for equine, the RI values are mostly under 0.60 while for the other mentioned species the upper limit is considered to be 0.70 [18,24,42]. For humans, a normal renal RI value of 0.60 ± 0.01(mean and SD) and a threshold of 0.70 is being accepted nowadays [43,44]. For cats, the normal renal RI values range has been reported to be between 0.64 and 0.72 [20]. Further, the mean renal RI for dogs found in a study with 27 healthy animals was 0.62 ± 0.04 [48] and the considered upper limit is the same as for humans [22].

Although at first it was not considered for appraisal by this systematic review, Siwinska et al. [30] also evaluated two other groups that can be interesting for our objectives: animals at risk of developing acute kidney injury (AKI) and animals with clinical AKI. Siwinska and her colleagues identified that even in the nonhealthy categories, the renal RI values did not reach or pass 0.70, the RI value used for humans and small animals, which brings the question whether this upper limit is suitable for the equine species. In this regard, more studies on the theme are still necessary to determine a reliable renal RI reference range for horses.

Siwinska et al. [28] have analyzed their results in correlation to a number of physiological parameters, such as age, heart rate, body weight and blood pressure. They found no interaction among the RI and cited parameters, however, there was an association between pulse pressure and the obtained renal RI values. Therefore, for future studies, researchers may include the measurement of pulse pressure in order to perform a better evaluation of the renal RI results. Freccero et al. [29] compared renal RI values to physiological parameters as well, being age, breed, body weight and body condition and also did not find any correlation.

Conclusions and future directions

Although renal RI has been established over the years as an efficient tool in human medicine and has been a matter of interest for more than a decade in regard to small animals, its usefulness in the equine medicine is still not demonstrated. It is crucial that a variety of studies still need to be conducted to ensure that renal RI has clinical utility in horses. Determining a normal range for equine renal RI is still necessary in a larger population, including comparisons with horses proven to present kidney disease, once all studies enrolled in this systematic review found a RI value between 0.50 and 0.64 (mean values) in the 128 examined animals, much lower than the upper limit considered for humans, cats and dogs of 0.70.

As future directions, we suggest a few patterns to be followed during transabdominal renal ultrasound
examination. For animal preparation, hair clipping and use of coupling gel are very important, but if it is not possible to trim the horse, the haircoat should be abundantly rinsed with alcohol. A curvilinear probe is more suitable for the exam and the frequency range should be between 2 and 5MHz. The wall filter should be set at 50Hz, a sample volume of 2 to 4mm should be preferred and a lower as possible pulse repetition frequency should be set. In order to locate the artery to be assessed, the color or power Doppler must be employed. All this information should be included on the description of the material and methods. It is crucial that at least three waveforms are acquired from each kidney, so the RI value could be more reliable. The RI value can be presented as mean and standard deviation, separating right and left kidney as there is still doubt that difference exist and since upon disease, kidneys can be differently affected. Lastly, as the pulse pressure have been shown to influence the RI results, it should also be measured and taken into consideration when evaluating the kidneys. We believe and hope that in a short future other works on the topic will be presented and further evaluation will be made.

References


