# Equine aortic regurgitation: The search for objective repeatable and reproducible indicators of severity

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Guest Editorial

# Equine aortic regurgitation: The search for objective repeatable and reproducible indicators of severity

In a recent issue of The Veterinary Journal, Ven et al. (2016) describe a retrospective study to evaluate objective ultrasonographic indicators that are associated with differing degrees of regurgitation through the aortic valve. Aortic regurgitation (AR) is arguably one of the most important and clinically significant valvular disorders that we see in the horses. Lesions of the aortic valve are common in the horse and the majority are due to degenerative valvular disease, likely due to the high blood pressures under which these valves operate (Smetzer et al., 1966; Else and Holmes 1972). A relative minority of cases occur due to other pathologies such as endocarditis, tearing of the leaflets, secondary to large VSDs or due to congenital primary valvular lesions (Reef et al., 1987). Whatever the cause, accurate assessment of disease severity that is repeatable and reproducible amongst clinicians, as well as sensitive to progression, is essential.

The particular significance of AR to equine cardiologists is the increased risk of sudden cardiac death in some horses. Although most lesions causing AR deteriorate slowly with minimal impact on the ability to ride the horse or its performance, those horses with moderate to severe AR are at increased risk of sudden cardiac death due to ventricular arrhythmia (Reef et al., 2014). Although rare, this has high individual impact and importance and clinicians attending these cases therefore agonise about accurately assessing severity and reproducibly monitoring progression of disease. Reaching such lofty aims can often be challenging (Reef et al., 2014). Given the importance and relatively high prevalence of AR amongst cardiac disease in the older general riding horse population (Stevens et al., 2009; Ireland et al., 2012), a population apparently on the increase, it is perhaps surprising that

there has been relatively little published evidence critically assessing methods of determining AR severity.

Perhaps the lack of published guidance relates to the lack of a perceived reference standard, or reference point, with which to compare techniques for assessing severity. Many of the methods currently employed in horses are either subjective, based on findings from a limited number of cases, or are only useful for categorising very severe disease which is often obvious clinically. Auscultation is rarely useful in AR since many murmurs presented for evaluation are musical and the audible grade does not necessarily relate to the severity of regurgitation. While clinical clues such as the age and type of horse, subjective or objective assessment of pulse pressures and exercising electrocardiograms can help determine the likely severity and/or risk of progression, these factors are often only of indirect help and/or subjective. The current reference point in humans, cardiac MRI, is currently not available for horses for technical and logistical reasons. More invasive cardiac catheterization techniques that may also serve as useful reference points are beyond what most equine clinicians would deem normal clinical practice and unlikely to be popular with clients, thereby posing difficulties for conduct in the field. In theory then, the direct visual and functional assessment of the heart offered by echocardiography should give equine clinicians the most direct information on severity and should allow us to reap rewards in terms of diagnosis and prognosis. When assessing AR severity, the echocardiographer has three main aims: (1) the evaluation of valve leaflet structure and function; (2) estimation of the severity of the regurgitant volume; and (3) the evaluation of the haemodynamic impact of any regurgitation on heart structure and function, in particular that of the left ventricle. In the hands of experienced equine echocardiographers such methods have acceptable intra-operator variability, but reproducibility between different operators and different ultrasound machines

can be poor. Looking for relatively easy to measure objective echocardiographic indicators of severity that have high repeatability and reproducibility is therefore warranted.

The study by Ven et al. (2016) therefore is welcomed as a step along the road to providing objective guidance for evaluating this important cardiac disease. This group evaluated dimensions of the cardiac chambers and large outflow vessels along with changes to blood flow in association with grades of severity from zero regurgitation to severe regurgitation. The severity was categorised by a combination of subjective and objective methods that would be deemed 'normal clinical practice'. Of course, studies such as this that are based on grades of clinical dysfunction are only as good as the criteria under which the grades are defined. In using semi-subjective criteria for grading AR severity, the authors admit this as a significant potential flaw. Nevertheless, there is a need to use something and it would be very easy to be paralysed into inactivity for want of what was deemed a more appropriate reference point. The fact is that there are no other easily available non-invasive reference points currently available.

In human medicine, criteria for assessing aortic valve regurgitation by echocardiography are determined by consensus from associations such as the American Association of Echocardiography and the European Association of Cardiovascular Imaging (Lancellotti et al., 2013). Some of these criteria are difficult if not impossible to reproduce in horses due to the significant limitation in equine echocardiography of only obtaining parasternal views. While we can 'piggy back' on the experience in humans, since key aspects of evaluation of regurgitation severity are similar, nevertheless we must deduce our own methods specific to equine patients. Techniques for assessing regurgitant flow, such as the flow convergence (PISA) method, or measuring the vena contracta, are unexplored in

equine valvular regurgitation and are worthy of investigation. Furthermore, advances in ultrasonographic imaging may aid our search for more accurate assessment of regurgitation through all valves, including the aorta. Innovations such as harmonic imaging have improved 2D image quality, and evaluation of the large and easily visible aortic valve is particularly rewarding in horses. Innovations such as speckle tracking echocardiography that allow angle independent determination of myocardial strain may provide some benefit in determining left ventricular function in response to aortic regurgitation (Schwarzwald et al., 2009). Furthermore, technologies such as real-time 3D echocardiography (3DE) may provide better pre-mortem definition of pathology of the aortic valve along with assessment of volume overload associated with AR (Lang et al., 2012). Of particular interest with regards 3DE is the ability to more accurately assess left ventricular volume. Techniques based on 2D echocardiography only allow an estimation of volume, based on geometric assumptions of left ventricular shape. Indeed, Ven et al. (2016) evaluated two methods for estimating LV volume based on 2-D images: the bullet method and the apical area length method, and the former was associated with increasing severity of AR. Three-dimensional echocardiography offers more accurate assessment of chamber volume when compared to cardiac MRI and is increasingly recommended as the technique of choice in humans (Lang et al., 2015). Given the findings from human medicine, it is likely that the technique will be useful for horses should the measurements be repeatable and reproducible.

Whether such extra information from these novel technologies and indicators such as those described by Ven et al. (2016) will offer a clinical advantage over 2D imaging has yet to be determined. Moreover, whether the indicators associated with increasingly subjective degrees of severity, such as those determined by Ven et al. (2016), are of use for accurately categorising horses with AR in a prospective manner remains to be seen. The challenge

going forward is to determine whether these measures accurately reflect clinical disease severity and likely prognosis. For this, a model using these indicators would need to be tested prospectively in a larger cohort of clinical cases with follow up, preferably all the way to post-mortem.

For those with enthusiasm for and interest in equine cardiac disease, the continued development of equine echocardiography, paralleling advances and novel technologies offered to human echocardiographers, will surely bring benefits to our understanding of diseases such as equine aortic regurgitation.

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**References**

Else, R.W. and Holmes, J.R., 1972. Cardiac pathology in the Horse I: Gross pathology. Equine veterinary Journal 4, 1-8.

Ireland, J.L., Clegg, P.D., McGowan, C.M., McKane, S.A., Chandler, K.J. and Pinchbeck, G.L., 2012. Disease prevalence in geriatric horses in the United Kingdom: Veterinary clinical assessment of 200 cases. Equine Veterinary Journal 44, 101–106.

Lancellotti, P., Tribouilloy, C., Hagendorff, A., et al., 2013. Recommendations for the echocardiographic assessment fo native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. European Heart Journal 14, 611-644.

Lang, R.M., Badano, L.P., Tsang, W., Adams, D.H., Agricola, E., Buck, T., Faletra F.F., Franke, A., Hung, J., de Isla, L.P., et al., 2012. EAE/ASE Recommendations for image acquisition and display using three-dimensional echocardiography. Journal of the American Society of Echocardiography 25, 3-46.

Lang, R.M., Badano, L.P., Mor-Avi, V. Afilalo, J., Armstrong, A., Ernande, L., Flachskampf, F.A., Foster, E., Goldstein, S.A., Kuznetsova, T., et al., 2015. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the

American Association of Echocardiography and the European Association of Cardiovascular Imaging. Journal of the American Society of Echocardiography 25, 3-46.

Reef, V.B. and Spencer, P., 1987. Echocardiographic evaluation of equine aortic insufficiency. American Journal of Veterinary Research 48, 904-909.

Reef, V.B., Bonagura, J., Buhl, R,, McGurrin, M.K., Schwarzwald, C.C., van Loon, G., Young, LE., 2014. Recommendations for management of equine athletes with cardiovascular abnormalities. Journal of Veterinary Internal Medicine 28, 749-61.

Schwarzwald, C.C., Schober, K.E., Berli, A.-S.J., Bonagura, J.D., 2009. Left ventricular radial and circumferential wall motion analysis in horses using strain, strain rate and displacement by 2D speckle tracking. Journal of Veterinary Internal Medicine 23, 890-900.

Smetzer, D.L., Bishop, S., Smith, C.R., 1966. Diastolic murmur of equine aortic insufficiency. American Heart Journal 72, 489-497.

Stevens, K.B., Marr, C.M., Horn, J.N.R., et al. 2009. Effect of left sided valvular regurgitation on mortality and causes of death among a population of middle-aged and older horses. Veterinary Record 164, 6–10.

Ven, S., Decloedt, A., Van der Vekens, N., De Clercq, D., van Loon, G., 2016 Assessing aortic regurgitation severity from 2D, M-mode and pulsed wave Doppler echocardiographic measurements in horses. The Veterinary Journal Setters to insert doi number.