Proceedings of the November Meeting of the Veterinary Cardiovascular Society

BSAVA Affiliated group

Friday and Saturday 13th and 14th November 2015

Proceedings produced and sponsored by:

Officers of the society

Chair	Proceedings Editor
Mark Patteson MA VetMB DVC PhD MRCVS HeartVet Consultants Ltd 40 The Street, North Nibley, Dursley, Gloucestershire, GL11 6DW chairperson@vcs-vet.co.uk	Jordi López-Alvarez LltVet DipECVIM-CA (Cardiology) PhD MRCVS Davies Veterinary Specialists, Manor Farm Business Park Higham Gobion Hertfordshire SG5 3HR proceedings@vcs-vet.co.uk

Joint Secretaries		Treasurer
Jo Cottee BvetMed MRCVS Bowden Gen, Hodsoll St, Wrotham, Sevenoaks, Kent, TN15 7LH secretary@vcs-vet.co.uk	Paul Wotton BVSc PhD DVC MRCVS University of Glasgow 464 Bearsden Road, Glasgow, G61 1QH	Jan Cormie BVMS CertVC MRCVS Ty Pen-y-Coed, Glangrwyney, Crickhowell, Powys NP8 1EW treasurer@vcs-vet.co.uk

Programme Veterinary Cardiovascular Society meeting

BURLEIGH COURT, LOUGHBOROUGH
Friday 13th NOVEMBER 2015

8:30 -9:30	**REGISTRATION**	Page
9:30-10:10	Atrial fibrillation: the human perspective ***Martin Lowe**, University College London Hospital, Great Ormond Street Hospital*	8
10:15-10:55	Atrial fibrillation: the canine perspective ***Anna Gelzer**, University of Liverpool*	9-15
11:00-11:30	**COFFEE BREAK**	
11:30-12:15	Atrial fibrillation: the equine perspective ***Gunter van Loon**, University of Ghent, Belgium*	16-18
12:20-12:40	SA Case presentation: Dissimilar atrial rhythms ***Julia Sargent**, Royal Veterinary College and Southern Counties Veterinary Specialists*	19
12:45-13:05	ACVIM 2014 equine abstracts ***Liz Finding**, Royal Veterinary College*	15
13:10-14:10	**LUNCH BREAK**	
14:10-14:45	Ventricular arrhythmias: what worries me in small animals? ***John Bonagura**, Ohio State University*	21-22
14:45-15:20	Ventricular arrhythmias: what worries me in horses? ***Colin Schwarzwald**, University of Zurich, Switzerland*	23-30
15:20-15:50	Ventricular arrhythmias: what worries me in people? ***Martin Lowe**, University College London Hospital, Great Ormond Street Hospital*	15
15:50-16:20	**COFFEE BREAK**	
16:20-17:20	ECG Panel (John Bonagura, Martin Lowe, Anna Gelzer, Gunther van Loon)	
17:20-18:10	AGM (VCS members only)	19
19:00-19:45	Pre-dinner drinks in sponsor's area	
From 19:45	**SOCIAL DINNER**	

Programme Veterinary Cardiovascular Society meeting

BURLEIGH COURT, LOUGHBOROUGH
Saturday 14th NOVEMBER 2013

8:30-9:00	**BREAKFAST + registration for day attendees**	
9:00-9:40	Interventional arrhythmia management in people: where next? ***Martin Lowe**, University College London Hospital, Great Ormond Street Hospital*	8
9:45-10:20	Accessory Pathways: the veterinary practitioner's view ***Chris Fellows**, Lakes Cardiology Service*	9-15
10:25-11:00	Calcium mismanagement in arrhythmogenesis and heart failure ***Liz Bode**, Royal (Dick) School Veterinary Studies, Edinburgh*	
11:00-11:30	**COFFEE BREAK**	
11:30-12:00	SA Case presentation: EP study and radiofrequency ablation ***Pedro Oliveira**, Davies Veterinary Specialists*	16-18
12:00-12:35	ECVIM 2015 Update ***Rachel Blake and Dave Sewell***	19
12:35-13:05	Sleeping respiratory rate in dogs and cats with clinically controlled congestive heart failure ***Luca Ferasin**, CVS Referrals*	
13:05-14:05	**LUNCH BREAK**	
14:05-14:35	4D echo in horses: clinical tool? ***John Keen and Karen Blissitt**, Royal (Dick) School Veterinary Studies, Edinburgh*	21-22
14:40-15:05	Tissue Doppler and speckle tracking in horses: scientific tool or real-world technique? ***Annelies Decloedt**, University of Ghent, Belgium*	
15:10-15:45	ACVIM 2015 Update ***Brigite Pedro and Jorge Prieto-Ramos***	
15:45-16:15	**COFFEE BREAK**	
16:15-17:00	Future modalities in echo. What's worth doing ***John Bonagura**, Ohio State University*	45
17:00	**CLOSE**	

The Veterinary Cardiovascular Society gratefully acknowledges the support of all our sponsors (in alphabetical order)

Platinum Sponsors

Ceva Animal Health Ltd

Tel: +44 (0) 1494 781 510
E-mail: cardio-group@ceva.com
Website: www.ceva.co.uk

Vetoquinol

E-mail: office@vetoquinol.co.uk
Website: www.vetoquinol.co.uk
Tel: +44 (0) 1280 814 500

Gold Sponsor

Boehringer Ingelheim Vetmedica

Ellesfield Avenue, Bracknell, Berkshire
RG12 8YS
Tel: +44 (0) 1344 746 959
E-mail: Vetmedica.uk@boehringer-ingelheim.com

Silver Sponsors

Elanco Animal Health

Phone: +44(0)1256 353131
Email: lancoCAH.uk@elanco.com
Technical enquiries:
elancovets@elanco.com
Address: Lilly House. Priestley Road, Basingstoke. RG24 9NL.

Horserace Betting Levy Board

5th Floor, 21 Bloomsbury Street,
London WC1B 3HF
Tel: +44 (0)20 7333 0043

KRUUSE UK Ltd

12 Sherburn Network Centre,
Lancaster Close
Sherburn in Elmet
North Yorkshire, LS25 6NS
Tel: +44 (0) 1977681523
Fax: +44 (0) 01977 683537
www.kruuse.com

Bronze Sponsors

BCF Technology Ltd

3 Tailend Court, Starlaw Road
Livingston, EH54 8TE
Scotland, UK
Tel: +44 (0) 1506 468 941
E-mail: www.bcftechnology.com

Holter Monitoring Service

26 Bridge Street
Dollar
FK14 7DE
E-mail: info@holtermonitoring.co.uk
Webiste:www.holtermonitoring.co.uk

Imotek International Ltd

West Newlands Industrial Estate,
Huntingdon,
Cambridgeshire. PE28 3FF
Tel: +44 (0) 1487 843 193
Email: sales@imotek.com

Pie data (UK) Ltd

4 Mill Court, Spindle Way,
Crawley,
West Sussex, RH 10 1TT
Tel: +44 (0) 1293 510231
Fax: +44 (0) 1293 510234
Email: sales@pie-data.com
www.pie-data.com

Spacelabs Healthcare

1 Harforde Court
John Tate Road
Hertford
SG13 7NW
Tel: +44 (0) 1992 507700
Email- uksales@spacelabs.com
www.spacelabshealthcare.com

UKTS ltd.
UK Taxation Services
221 High Street
Blackwood
NP12 1AL
Website: www.ukts.co.uk

Speakers:

Martin Lowe BSc MB BS PhD FRCP

Martin Lowe is a consultant cardiologist and electrophysiologist specialising in the treatment of arrhythmias in adults and children with catheter ablation and pacemaker / defibrillator implantation. Having qualified from St George's Hospital. London, he trained in London and Cambridge, before undertaking a research fellowship at The Mayo Clinic, USA. He is currently based at the new Barts Heart Centre, London, and Great Ormond Street Hospital, London. Current research interests include ablation strategies in those with arrhythmias accompanying cardiomyopathy or congenital heart disease, risk stratification in patients and families predisposed to sudden cardiac death, and multisite pacing in heart failure patients.

Anna Gelzer Dr. med.vet. PhD DACVIM and DECVIM-CA MRCVS

Anna Gelzer earned her veterinary degree at the University of Bern, Switzerland in 1992, followed by a Masters degree at the University of Bern in collaboration with Novartis, Cardiovascular Biology, Basel, Switzerland. She completed a small animal internship at the University of Georgia, GA in the USA, and a residency in cardiology at Cornell University. Dr. Gelzer received board certification from the American College of Veterinary Internal Medicine, ACVIM in cardiology (1998) and also the European College of Veterinary Internal Medicine, ECVIM - Companion Animal (Cardiology, 1999). She has been faculty a member at Cornell University, University of Liverpool and recently joined the University of Pennsylvania. Her special interest focuses on arrhythmias and cardiac electrophysiology.

Gunther van Loon DVM PhD DECEIM Assoc. Member ECVDI

Gunther van Loon graduated from Ghent University, Belgium, in 1992 and has worked at Ghent University, Department of Large Animal Internal Medicine, ever since. In 2001 he finished his PhD on "Atrial pacing and experimental atrial fibrillation in equines". In 2004 he became Diplomate of the European College of Equine Internal Medicine and in 2011 Associate Member of the European College of Veterinary Diagnostic Imaging. In 2015, he received from the World Equine Veterinary Association the "Merial Applied Equine Research Award" for his research in the field of equine cardiology. He is Professor in Large Animal Internal Medicine at Ghent University and his major interests are cardiology (arrhythmias, electrophysiology, cardiac pacing, echocardiography, TDI, 2D ST, biomarkers), and thoracic and abdominal ultrasound.

Julia Sargent BVSc MVetMed MRCVS

Julia graduated from the University of Bristol veterinary school in 2006, and then spent three years as a small animal vet in general practice. In 2009 she began her cardiology training as a cardiology intern at Southern Counties Veterinary Specialists. She next completed rotating and specialist internships at the Royal Veterinary College before starting her Cardiology residency training and master's degree in veterinary medicine. She has now rejoined the team at SCVS and continues as a part time clinical research fellow at the RVC.

Liz Finding BVetMed(Hons) CertVA MVetMed DACVIM MRCVS

Liz graduated from the RVC in 2005 and initially completed an internship in the Equine Referral Hospital at the RVC before working for 3 years in equine general practice in Cambridgeshire. She returned to the RVC to complete a residency in equine internal medicine and gained her ACVIM Diploma in Large Animal Internal Medicine. She is currently studying (still at the RVC!) for a PhD investigating the role of endothelial dysfunction in the predisposition to equine laminitis. She teaches on the cardiorespiratory module of the BVetMed at the RVC and teaches cardiac anatomy at Nottingham.

John Bonagura DVM MS DACVIM (Cardiology, Internal Medicine)

John Bonagura is Professor of Veterinary Clinical Sciences in Cardiology & Interventional Medicine Service at the Ohio State University College of Veterinary Medicine. John has been Visiting Research Fellow at the University of Edinburgh and served as Gilbreath-McLorn Endowed Professor of Veterinary Cardiology at the University of Missouri. His publications number over 200 scientific papers and book chapters, he is co-author of a Colour Atlas of Veterinary Cardiology, and he edits Kirk's Current Veterinary Therapy. He is a three-time recipient of the Norden award for distinguished teaching and has been designated an Ohio State University campus Distinguished Teacher. Dr Bonagura is a recipient of the BSAVA International Bourgelat award, the Doctor Honoris Causa of the Universitat Autonòma de Barcelona, The Kirk Lifetime Achievement Award from the ACVIM, Faculty Achievement Award of the American Association of Veterinary Clinicians, and distinguished Alumnus awards from the Ohio State University and the Animal Medical Center in New York.

Colin Schwarzwald Prof Dr.med.vet. PhD DACVIM & DECEIM

Colin C. Schwarzwald graduated in 1997 from the University of Zurich School of Veterinary Medicine. Between 1998 and 2001 he completed an internship at the Equine Hospital of the University of Zurich and worked on his doctoral thesis to attain the Dr.med.vet. degree. Between 2001 and 2004 he completed an ACVIM Large Animal Internal Medicine residency program at The Ohio State University. Concurrently, from 2001 to 2006, he was also enrolled in a PhD program and conducted several research projects in the field of equine cardiology, in cooperation with Dr. John Bonagura, Dr. Robert Hamlin, Dr. William Muir, and several members of the cardiology section. In 2006 he moved back to the Vetsuisse Faculty of the University of Zurich, where he was employed as a Senior Lecturer in Equine Internal Medicine Section. In 2009 he completed his 'Habilitation' titled 'Advances in equine cardiology'. In 2012 he was appointed to a full professorship in Equine Internal Medicine. He is currently the director of the Clinic for Equine Internal Medicine at the Vetsuisse Faculty of the University of Zurich. His academic and clinical interests include large animal

and comparative cardiology, with emphasis on echocardiography, cardiac electrophysiology, cardiovascular pharmacology, and cardiac biomarkers.

Chris Fellows BVMS CertVC MRCVS

Chris qualified at Glasgow Veterinary School in 1990 and went into small animal practice in Leeds where he gained his certificate in veterinary cardiology in 1995. After a short stint back at Glasgow in the cardiology department (covering for Chris Little doing his studies on vagal tone…) he moved the Lake District where he set up his own small animal practice in Ulverston. In 2010 Chris sold his practice to take up cardiology work full time and now runs "Lakes Cardiology Services", a peripatetic cardiology service for practices in the North of England. He is recognised by the RCVS as an advanced practitioner in Veterinary Cardiology, and has just taken up a part time post at Manchester University as an honorary research fellow. He has a particular interest in electrophysiology although is aware he unlikely ever to get to do any in veterinary practice!

Liz Bode BVSc PhD MRCVS

Liz graduated from The University of Liverpool in 2006 and began her veterinary career in a mixed practice in East Yorkshire. Following this she undertook a small animal rotating internship at The Queen's Veterinary School Hospital, University of Cambridge. This sparked an interest in research and in September 2009 she began a British Heart Foundation funded PhD at The University of Manchester. Her PhD focused on calcium homeostasis within the aged and failing ventricle and she was awarded her doctorate in 2013. After a further year in a small animal practice in Cheshire she joined the Hospital for Small Animals of the Royal (Dick) School of Veterinary Studies as a Senior Clinical Training Scholar in Cardiopulmonary Medicine.

Pedro Oliveira DVM MRCVS DECVIM-CA (Cardiology)

Pedro qualified from Porto University (Portugal) in 2005 and obtained the ECVIM-CA cardiology diploma in 2012. He worked in a number of European referral centres before joining Davies Veterinary Specialists in October 2012 where he is head of the cardiology service. He has a particular interest in interventional cardiology and the study of arrhythmias. In the past year he has established an electrophysiology laboratory for diagnosis and treatment of arrhythmias at Davies Veterinary Specialists.

Rachel Blake MVB MRCVS

Rachel graduated from the University College Dublin School of Veterinary Medicine in 2012. She went on to complete a rotating small animal internship at Mississippi State College of Veterinary Medicine. While in the USA, she also completed cardiology externships at North Carolina State University and at Advanced Veterinary Care Center in Los Angeles. She then worked in a busy first opinion small animal practice near Manchester for almost 2 years before joining the Royal (Dick) School of Veterinary Studies in May 2015 as a Resident in Cardiopulmonary Medicine.

David Sewell BVM&S BSc CertVC MRCVS

David graduated from the University of Edinburgh in 2003 with a BVM&S and an intercalated honours degree in veterinary science. He has been in small animal practice for over 12 years and completed an RCVS certificate in veterinary cardiology in 2011. He is currently working at Highcroft veterinary group in Bristol as a cardiologist and general practitioner.

Luca Ferasin DVM PhD CertVC PGCert(HE) DECVIM-CA (Cardiology) MRCVS

Dr Ferasin graduated with honours in 1992 from Bologna University. After 3y research in endocrinology in Cambridge he was awarded his PhD in 1996. Following 3y as Assistant Professor at Padua University, he moved to Bristol University, where he taught cardio-respiratory medicine of the dog and cat for 7 years. In 2005-2007 was Associate Professor in Cardiology at the University of Minnesota. Since 2008 he run his own cardiology consultancy company, comprising a mix of private clinical referral work, telemedicine and post-graduate teaching. In March 2014 he joined CVS/Wey Specialist Referrals, in Surrey. He obtained RCVS certificate in cardiology in 2001, certificate in Teaching & Learning in Higher Education in 2002, ECVIM diploma (cardiology) in 2004 and certificate in Business & Professional Studies in 2011. He vastly contributed to the veterinary literature with articles, abstracts, and book chapters.

John Keen BVet Med PhD Cert EM(Int Med) DECEIM MRCVS

Following graduation from the RVC in 1996, John spent 4 years in mixed and then predominantly equine practice before being appointed the RCVS Clarke and Sparrow Resident in Equine Studies at the 'Dick' Vet in 2000, where he has remained ever since. John is currently a senior medicine clinician in the equine hospital and Director of the Equine Hospital and Practice. He has gained his Certificate in Equine Internal Medicine, MSc by research and a PhD investigating the pharmacology and physiology of digital laminar microvasculature. He was awarded the European Diploma in Equine Internal Medicine in 2007 and has gained RCVS and European specialist status in equine internal medicine. Clinical and research interests include all aspects of internal medicine, but with particular emphasis on cardiovascular disease, metabolic and endocrine disease and the potential links between these disorders.

Karen Blissitt BVSc PhD DVA DECVAA MRCVS

Karen Blissitt graduated BVSc from the University of Liverpool in June 1982. After 3 years in general practice she joined the R(D)SVS Edinburgh where she is currently a senior lecturer. She was awarded her PhD in 1993 for her work echocardiographic studies of valvular and ventricular function in horses, which was funded by the HBLB. Karen obtained her DVA in 1995 and her DipECVAA in 1997. Her research interests include transoesophageal echocardiography for assessing ventricular function in anaesthetised horses, recovery quality after general anaesthesia in horses, sudden cardiac death in racing Thoroughbreds and 3D echocardiography. With Dr Lesley Young, she presents the BEVA practical cardiology and ultrasound courses. Karen is married to Martyn and has two children Edward and Grace.

Annelies Decloedt

After graduation as an equine veterinarian in 2008, Annelies completed a PhD at Ghent University in equine echocardiography (tissue Doppler imaging and two-dimensional speckle tracking for quantification of left ventricular function). Since 2012, she works as a postdoctoral research fellow of the Research Foundation Flanders, investigating the influence of pulmonary hypertension and exercise training on right ventricular function. In 2015, she was appointed as part-time professor in veterinary clinical and communicative skills at Ghent University. Her areas of major professional interest are equine cardiology, ultrasound and exercise physiology.

Brigite Pedro DVM MRCVS

Brigite Pedro graduated from the University of Porto (Portugal) in 2008. She completed a general internship at the VRCC (Essex, UK) in 2010. In the same year she was awarded with a Leonardo da Vinci scholarship, which funded her internship in Cardiology at the University of Liverpool (UK) where she also started a cardiology residency program in 2012. In 2013 she obtained a master degree in Cardiovascular Pathophysiology, after presenting a final thesis “Left ventricular mechanics in Great Danes”. In 2015 she completed her residency training and she is now working as a lecturer at the University of Liverpool.

Jorge Prieto-Ramos DVM MRCVS

Jorge graduated from University of Zaragoza in Spain in 2009. Following Veterinary School Jorge visited and worked in Universities in Nicaragua and Mexico and private practice in England. He completed a rotating Internship in a referral hospital in Barcelona and after that he got experience working in general practice. He spent 3 months as a cardiology intern at the Royal (Dick) School of Veterinary Studies in Edinburgh. Jorge completed a Residency in Cardiology in the Small Animal Hospital of the University of Glasgow in September 2015. At the moment he is working as a Cardiology Clinician at Glasgow Veterinary School for a short period of time.

Atrial fibrillation: the human perspective

Martin Lowe
University College of London, UK

TALK SPONSORED BY:

Atrial fibrillation: the canine perspective

Anna Gelzer
Small Animal Teaching Hospital, University of Liverpool, UK

TALK SPONSORED BY:

Atrial fibrillation (AF) is the most common cardiac arrhythmia in dogs, with a higher incidence in large-breed, male dogs and rare in dogs less than 12 months of age. In AF, the electrical impulses that are normally generated by the sinoatrial node are "overdriven" by disorganized electrical impulses that originate in the atria and pulmonary veins, leading to conduction of irregular impulses to the AV node and ventricles (ventricular response). AF occurs most often secondary to underlying structural heart disease, associated with pathological left and/ or right atrial enlargement and is associated with decreased survival. Clinical signs depend on the presence and severity of underlying heart disease. Dogs with congestive heart failure (CHF) and AF may present with coughing, dyspnoea, ascites or weakness due to advanced stages of dilated cardiomyopathy, AV valve insufficiency or cardiac enlargement due to left to right shunting. In some giant-breed dogs, AF may be an incidental finding with no clinical signs pertaining to the cardiovascular system and no demonstrable heart disease at the time of first diagnosis of AF, thus termed "lone AF". These dogs' heart rate (HR) may not be elevated at rest but can be increased during excitement or stress. This type of AF might represent a primary disorder, similar to spontaneous AF in humans and horses, where critical atrial mass and high vagal tones precipitate the development of AF. However, it has been demonstrated in some of these dogs that myocardial failure develops over subsequent months to years, suggesting that AF is a harbinger of a cardiomyopathy.

There are 2 therapeutic strategies for the treatment of AF: (1) restore and maintain sinus rhythm with electric or pharmacologic cardioversion (rhythm control), or (2) control the ventricular rate by slowing conduction across the AV node with antiarrhythmic drugs (rate control), allowing AF to persist. Reasons for restoration of sinus rhythm in dogs include avoidance of tachy-cardiomyopathy, improved left ventricular function and a reduction in clinical signs. However, most dogs fail pharmacologic cardioversion or do not maintain sinus rhythm for very long after electric cardioversion because of advanced myocardial pathology. Clinical trials in humans, comparing rate control with rhythm control therapy, propose that rate control is at least as efficacious as rhythm control in most patients and a trend towards lower mortality in the rate control group was found. Therefore, improvement of clinical

signs as primary therapeutic goal in dogs with fast AF and significant underlying heart disease is usually achieved by rate control.

In dogs with AF, the brief in-clinic ECG overestimates the HR obtained by a 24h Holter significantly. Verifying whether a dog has fast AF and thus may require rate slowing therapy, as well as determining the efficacy of pharmacological rate-control is most accurately determined by 24h Holter monitoring in the home environment. This allows HR monitoring outside the hospital setting, which is often associated with stress and secondary tachycardia. However, dogs with an in-clinic ECG HR < 155 bpm most likely have "slow AF" (less than 140 bpm on average over 24h), while dogs with a HR > 155 bpm recorded in the clinic setting probably require (additional) rate control therapy.

Rate control:

Digoxin prolongs AV node conduction via a vagomimetic effect. Monotherapy achieves only modest reduction in HR in dogs with rapid AF. This is similar to findings in people and horses with AF, where increased sympathetic tone during exercise or CHF, overrides the vagal effects of digoxin resulting in frequent "break-through" episodes of rapid HR. The combination of digoxin with the calcium channel blocker diltiazem yields a good reduction in ventricular response, superior to diltiazem monotherapy.

Digoxin: 0.003 – 0.004 mg/kg PO q 12 hours for large and giant breeds of dogs (or 0.22 mg/m^2 divided bid). To avoid toxicity, digoxin serum concentrations should always be measured 5 – 7 days after starting digoxin therapy at "trough" levels (6-8h hours post pilling). Ideal trough level should be 0.5 – 1.0 ng/ml (most labs list the range as 1.0 – 2.5 ng/ml), but many dogs show signs of toxicity at serum levels above 1.0 ng/ml. Signs of digoxin toxicity include lethargy, inappetance, vomiting / diarrhoea. Occasionally pro-arrhythmic effects are seen (1st degree AV block, ventricular arrhythmias). Elimination half-life in dog: 14-56 hours; if digoxin toxicity is suspected, stop digoxin for several days, and then start up again at a lower dose. Consider reducing the dose of digoxin (highly protein-bound) in the presence of cachexia, ascites or obesity, hypoproteinaemia, hypokalaemia (digoxin competes with K+ at Na+K+ATPase pumps), hypothyroidism, renal dysfunction (reduced excretion); Doberman's seem more prone to GI side effects thus 0.25mg BID should not be exceeded in this breed.

Calcium channel antagonists slow the ventricular response to AF by prolonging conduction across the AV node. Effect on heart rate occurs within a few hours of oral dosing. Only mild effects on contractility, when given at prescribed doses.

Diltiazem: 2 -3 mg/kg PO q8 hours (modified release formulation of diltiazem); or 3 mg/kg PO q12 hours (extended release (XR) formulation [capsules in the UK]; For unstable dogs with HR >250 bpm consider diltiazem IV bolus (0.10-25mg/kg IV up to 3 times) and/or constant rate infusion (2-6 ug/kg/min). Diltiazem PO can be added to digoxin, at the standard doses.

Beta blockers directly slow conduction across the AV node. Due their negative inotropic

effects they are not well tolerated in the setting of poor systolic function (dilated cardiomyopathy) and should not be used in patients with unstable CHF. They can also be given in combination with digoxin, but should not be added to a calcium channel blocker to avoid excessive bradycardia. As many dogs with AF have impaired systolic function and / or CHF, beta blockers are not usually my preferred choice. In people, beta-blockers are of no additional benefit in patients with heart failure and reduced ejection fraction, if they also have AF.

Atenolol: 0.5-2mg/kg q12-24 h, start at a low dose, and up-titrated as needed.

In patients with AF and significant ventricular arrhythmias, sotalol (1-2 mg/kg PO q 12h), a drug with combined K and beta blocker properties may be used cautiously for rate control and suppression of ventricular arrhythmias This drug can also be combined with digoxin.

Rhythm control- cardioversion:

Dogs with a slow ventricular rate (lone AF) can pose a dilemma for the clinician. The option of restoring sinus is intuitively appealing, granted a long-term AF free interval follows the episode. In my experience dogs that undergo cardioversion tend to revert to AF fairly soon thereafter. Furthermore, there is no data proving that dogs with slow AF have a higher morbidity and mortality than dogs that are converted to sinus rhythm.

Electrical (DC) cardioversion aims to convert AF to normal sinus rhythm with a defibrillator and external paddles or patch electrodes. It requires a short general anesthesia and hospitalization, and in addition, maintenance of sinus rhythm may also necessitate long-term antiarrhythmic medication (amiodarone) and serial follow-up evaluations, similar to the required aftercare of dogs on rate control therapy.

Medical cardioversion is rarely achieved in dogs: Amiodarone (loading dose: 10mg/kg q 12 h for 1 week, then reduce to 10mg/kg q 24h for maintenance) may convert AF to sinus rhythm, but is more commonly used as pre-treatment to DC cardioversion, and kept on board to prevent recurrence of AF post DC cardioversion. It has a high incidence of toxicity/ adverse side effects (hepatotoxicity), and a long half life (3 days) in the dog; after cessation of the drug, significant myocardial concentrations can persist for up to 3 weeks.

References

1. Bonagura, J.D., Ware, W.A. (1986) Atrial fibrillation in the dog: Clinical findings in 81 cases. JAAHA 22, 111-120

2. Collet, M. (2000) A retrospective study of 14 cases of chronic atrial fibrillation without evidence of initial underlying cardiac disease in dogs. Pratique de Medecine et Chirurgie des Animaux de Compagnie 10, 167–176.

3. Menaut, P., Bélanger M.C., Beauchamp G., et al. (2005) Atrial fibrillation in dogs with and without structural or functional cardiac disease: A retrospective study of 109 cases. JVC 2, 75-83

4. Gelzer, A.R., Kraus, M.S., Rishniw, M., et al. (2009) Combination therapy with digoxin and diltiazem controls ventricular rate in chronic atrial fibrillation in dogs better than digoxin or diltiazem monotherapy: a randomized crossover study in 18 dogs. JVIM 23, 499-508

5. Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, Kellen JC, Greene HL, Mickel MC, Dalquist JE, Corley SD (2002); Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. NEJM 347(23):1825-33.

6. Kotecha D, Holmes J, Krum H, et al. 2014. Efficacy of ß blockers in patients with heart failure plus atrial fibrillation: An individual-patient data meta-analysis. Lancet, 384(9961):2235-43.

7. Gelzer AR, Kraus MS, Rishniw M. (2015) Evaluation of in-hospital electrocardiography versus 24-hour Holter for rate control in dogs with atrial fibrillation. JSAP. 56(7):456-62.

8. Pedro B, López-Alvarez J, Fonfara S, Stephenson H, Dukes-McEwan J. (2012) Retrospective evaluation of the use of amiodarone in dogs with arrhythmias (2003 to 2010). JSAP 53(1):19-26.

9. Bright JM, Martin JM, Mama K. (2005) A retrospective evaluation of transthoracic biphasic electrical cardioversion for atrial fibrillation in dogs. JVC 7(2):85-96..

Atrial fibrillation: the equine perspective

Gunter van Loon
Dept. of Large Animal Internal Medicine, Fac. of Veterinary Medicine,
Ghent University, Belgium

Abstract

Atrial fibrillation (AF) is a common arrhythmia in horses and often occurs in the absence of (detectable) predisposing disease (lone AF). It does not cause any signs at rest but is often associated with reduced performance in athletic horses. Epistaxis, or on rare occasions even weakness, collapse or even sudden death may occur during exercise. Treatment of lone AF horses is rewarding as successfully converted horses do return to their previous level of exercise. However, recurrence rate, which is independent of the treatment procedure used, is about 35-40%. Medical or electrical cardioversion can be used. Medical treatment is generally performed with repeated administration of quinidine orally until conversion or toxicity occurs. Intravenous administration of amiodarone has also been reported but had lower efficacy. Electrical cardioversion under general anaesthesia is performed after positioning of cardioversion electrodes in the left pulmonary artery and the right atrium. Synchronised biphasic shocks are delivered and cardioversion is usually obtained around 150-250 Joules. Transvenous electrical cardioversion has a high success rate (> 90%) and might be effective in horses that failed to convert on quinidine.

Introduction

Atrial fibrillation (AF) represents the most important cardiac rhythm disorder affecting performance in horses. The prevalence in horses is probably about 0.5% with no clear gender or age predilection. Atrial fibrillation is an atrial tachyarrhythmia that is frequently found in the absence of other (detectable) cardiac pathology, especially in large breeds. In ponies, AF is only encountered as a result of severe cardiac disease.

Mechanisms and pathophysiology

Different theories have been described explaining initiation and perpetuation of AF in other species and they most likely apply to horses as well. The well-known multiple wavelet model assumes that during AF multiple electrical wavelets move chaotically through the atrial myocardium. In order for AF to be self-sustained, a critical number of wavelets must co-exist in the atria.

Atrial fibrillation occurs when both a trigger to start the arrhythmia and a substrate to maintain it, are present. The trigger can be one or more atrial premature beats, a rapidly firing focus or small reentry sites (spiral waves or rotors) that initiate reentry. These triggers occur because of increased myocardial excitability, myocardial damage or stretch,

electrolyte disorders, or systemic disease. In human medicine, these triggers have been shown to originate mainly from myocardial sleeves that invade the pulmonary veins which makes them an important target for prevention of AF recurrence. Similar mechanisms are likely to play a role in horses, as myocardial sleeves have been demonstrated in horse pulmonary veins. Once initiated, the perpetuation of AF depends on the suitability of the substrate, the atrial myocardium. Factors in favour of AF are a large atrium, short refractory period, dispersion of refractoriness, slow conduction velocity and structural obstacles for conduction (such as anatomical structures or structural lesions such as fibrosis). Strenuous exercise leading to elevated left atrial pressures (more in horses than in other species), may lead to a higher burden of atrial stretch-related premature beats (triggers). High vagal tone, large atria and a short refractory period in relation to atrial size, makes the equine atria an almost perfect substrate for sustained, lone (primary) AF. Underlying cardiac disease further increases this risk (secondary AF).

Occasionally, AF is short-lived and terminates spontaneously, usually within the first 24-48 hours, which is called paroxysmal AF. This form of AF has been shown to be a cause of reduced performance in slowly finishing Thoroughbreds. Probably strenuous exercise triggers initiation of AF by stretching the atrial myocardium, leading to atrial premature beats and electrophysiological changes that are exacerbated by electrolyte disturbances, while the myocardium is not suited for maintenance of AF due to its size, structure or electrophysiological properties.

In most horses, however, once initiated, AF does not terminate spontaneously because of the size and properties of the atrial myocardium. In addition, experimental work has shown that immediately after AF occurrence, shortening in refractory period and loss of contractile function occur, both leading to further stabilisation of the arrhythmia. As a result, AF generally becomes persistent and will never terminate without treatment.

During AF, a continuous and chaotic, self-sustained electrical activity is present in the atria at a ‘rate’ of about 375±/50min. Due to the high vagal tone in horses, the atrioventricular node blocks most of these electrical pulses and the final ventricular rate remains normal at rest. Within days to weeks after initiation of AF, atrial contractile function is almost completely lost, a process which appears reversible after restoration of sinus rhythm. Although the atrial contraction contributes up to 20% to ventricular filling, loss of atrial contractility is not related to clinical signs at rest because passive filling is sufficient to maintain cardiac output. During exercise, when heart rate increases, the atrial contribution to filling becomes more important and may reduce cardiac function. More importantly, exercise results in a predominance of sympathetic tone, whereby the atrioventricular node will suddenly conduct a high number of pulses to the ventricles, resulting in a disproportionate tachycardia during exercise. Heart rates well over 250/min are often encountered during exercise. Especially during vigorous exercise, this disproportionate tachycardia will affect exercise capacity, even if no underlying cardiac disease is present. Mean maximal heart rates during exercise of over 220 beats per minute are regarded as an

indication for cardioversion even if overt clinical signs are absent.

In addition, some AF horses present short runs of broad QRS tachycardia with an R-on-T-like phenomenon during sudden stress or exercise. This might be caused by aberrant conduction due to bundle branch block during rapidly conducted impulses over the atrioventricular node, although ventricular ectopy might be the cause as well. Such broad QRS tachycardia is regarded as a risk factor for weakness, collapse or even sudden death. Indeed, during such a rhythm, a marked ventricular dyssynchrony is often present which has a major impact on cardiac output. In addition, broad QRS tachycardia is a risk factor for deterioration into ventricular fibrillation. Typically, the R-on-T-like phenomenon is no longer found after successful conversion to sinus rhythm.

Clinical presentation

Clinical signs depend on whether or not concurrent cardiac or non-cardiac disease is present. Horses with cardiac failure that suddenly develop AF will experience an increase in heart rate (usually around 60-70 bpm) with an aggravation of clinical signs.

Horses that have atrial fibrillation without underlying cardiac lesions usually present with a history of reduced performance at high level exercise (e.g. racehorses, but also high level jumping and dressage horses). Epistaxis may occur during exercise. More rarely, a brief period of distress, weakness or even collapse may be observed during fast work. Because of the influence on performance, diagnosis is often made in an early stage in racehorses. In jumping or dressage horses, AF results in moderate reduction in performance, which makes that veterinary attention is sometimes sought in a later stage, delaying diagnosis of the arrhythmia. In non-competing horses, clinical signs may be absent and AF may be an incidental finding. Some owners do report subtle changes in the behaviour of their horse when AF (re)occurs. The author has seen more narcolepsy symptoms in AF horses compared to the general clinic population but it is unclear if there is any relation between the two.

On auscultation of the heart, AF is characterised by an irregularly irregular rhythm with a loud first heart sound. Careful auscultation will easily distinguish between AF and 2nd degree atrioventricular block because during AF the rhythm is more irregular, the first heart sound is louder, an unexpected early beat will always be heard and an atrial sound is absent, also during a long pause. Additionally, after slight excitation of the horse, the arrhythmia remains present in case of AF while the rhythm will become (temporarily) regular if it was a 2nd degree AV block. One should carefully interpret auscultation immediately after exercise because at high heart rates the AF irregularity in RR intervals is less pronounced due to the shortened diastolic time. In addition, post-exercise sinus arrhythmia commonly occurs in normal horses. Horses with secondary AF might present clinical signs related to the predisposing disease. However, the horse with lone AF should not present signs of heart disease at rest. Arterial pulse quality is variable. Inspection of the jugular veins might show an intermittent filling of the veins during a long diastolic pause. This should be distinguished from any pathological pulsation of the veins as seen in case of right-sided heart failure.

Diagnosis of AF must be confirmed by ECG, which will show normal QRS morphology with irregularly irregular RR intervals, undulations of the isoelectric line ('f" waves) and absence of P waves. The f waves frequently shift from coarse to fine undulations. Due to aberrant conduction, a shortly coupled (normal) QRS complex might show a changed T wave morphology, whereby QRS and T polarity become opposite. This should not be mistaken for a ventricular premature beat.

Ventricular premature beats, however, are found in a number of AF horses either at rest or during exercise. In the absence of electrolyte disorders or systemic disease, they might indicate underlying, myocardial disease, rather than a consequence of AF. Whatever the cause, presence of ventricular premature beats warrants further investigation (ultrasound, troponin, post-cardioversion ECGs).

Treatment

Atrial fibrillation per se is not a life threatening disease and horses at rest, broodmares, etc. have a normal life expectancy. Treatment of these animals is generally not required.

During the first 48-72 hours after initiation of AF, especially in racehorses, no anti-arrhythmic treatment should be given as spontaneous conversion to sinus rhythm may occur. Electrolyte disorders must be corrected.

If AF lasts for more than 72 hours it will generally not convert spontaneously and thus become persistent AF. In these horses a full cardiac exam, including cardiac ultrasound, should be performed to search for a predisposing disorder, such as atrial dilatation, atrioventricular valve regurgitation, atrial myocardial disease or other underlying disease. Mild to moderate mitral regurgitation is often found and is known to be a risk factor for AF recurrence. If severe predisposing disease is found, treatment of AF should be questioned because of the higher risk of treatment, the lower success rate of treatment and the higher recurrence rate after successful cardioversion.

Most frequently, horses present with lone AF and a history of reduced performance. In these animals one should attempt to restore sinus rhythm as they generally return to their previous athletic ability after restoration of sinus rhythm. But even when horses in training do not show any clinical signs, advice is given to treat AF especially when an exercise test shows mean maximal heart rates over 220 beats per minute or abnormal ventricular rhythms. In case the owner declines treatment but still wants to ride the horse, AF is considered a risk factor and ECG recordings during representative exercise tests should at least be free of the above mentioned findings.

Cardioversion of AF can be achieved pharmacologically or electrically.

Pharmacological treatment

Quinidine sulphate

Quinidine sulphate (QS) administration through a nasogastric tube is the most widely used pharmacological treatment for AF in horses. However, in many countries the product has become expensive or is being taken off the market.

Quinidine is a class IA anti-arrhythmic drug that is supposed to prolong action potential duration by blocking sodium channels, which may lead to AF termination. QS induces hypotension by a negative inotropic effect and alpha-adrenergic blockade. Due to its vagolytic effects atrioventricular conduction increases, which results in an increased ventricular rate during treatment. For these reasons, treatment should be performed in a quiet environment, and the horse should remain in its stall during treatment. These side effects also explain why horses with AF and cardiac failure should not receive QS treatment. Permanent venous access must be available for administration of drugs. A continuous telemetric ECG facilitates immediate detection of unwanted cardiac effects of the drug.

A test dose of 10 mg/kg QS (rarely given) or the first full dose is used to check for idiosyncratic reactions, although these rarely occur. Treatment begins with administration of 22 mg/kg of QS via a nasogastric tube. The drug should not be given directly into the mouth because it is irritating to mucosa. The 22 mg/kg dosage is repeated every 2 hours to a maximum of 6 doses per day. Many horses do not tolerate 6 doses, however. The aim of the treatment is to titrate the drug to the therapeutic plasma concentration (2-5 µg/ml) but drug monitoring is generally not available. When side effects start to occur, the dosing interval is often adjusted based on clinical signs, or is set to a 6-hour interval, which is about the half-life of quinidine. The longer plasma levels are kept in the therapeutic range, the more likely successful cardioversion will be achieved. Treatment should be terminated when sinus rhythm is restored or when the QRS duration prolongs by 25% or when severe side-effects occur.

Side-effects are encountered very frequently and one should distinguish between common, non-problematic signs such as depression, nasal oedema, and mild tachycardia, and more severe reactions that require termination of treatment including colic, diarrhoea, laminitis, ataxia, hypotension, collapse, or a sustained ventricular rate exceeding 120/min. Emergency treatment includes fluid therapy and intravenous isotonic sodium bicarbonate (1 mEq/kg) to increase protein binding of free quinidine. When tachycardia occurs, one should distinguish between supraventricular tachycardia, which is the most common, and ventricular tachycardia. Because of the absence of P waves and because the quinidine treatment is associated with a mild widening of the QRS complex, differentiation might be challenging. Supraventricular tachycardia can be treated with digoxin (2.2 µg/kg IV), and, if unsuccessful, with propranolol (0.03 mg/kg IV). If no severe signs of hypotension are present, administration of an alpha2-adrenergic agonist such as detomidine is often effective to slow down the supraventricular rate immediately. Ventricular tachycardia can be treated with

magnesium sulphate (4 mg/kg every 2 minutes up to a total of 50 mg/kg). If ventricular tachycardia appears unstable lidocaine should be administered (0.25-0.5 mg/kg IV q 5-10 minutes to total dose of 2-4 mg/kg). Hypotension can be managed by IV administration of crystalloids and phenylephrine (0.1-0.2 µg/kg/min up to 0.01 mg/kg).

It has been recommended that, if cardioversion is not achieved by the second day of treatment, the QS treatment should be combined with oral digoxin to slow down AV nodal conduction. However, one should be aware that both drugs are protein bound and that their concurrent use increases effective plasma levels of both agents, increasing the risk of adverse effects. In addition, from an electrophysiological point of view, digoxin would be expected to also have AF promoting effects.

When sinus rhythm cannot be restored after a first attempt, a second QS treatment with a few days interval might be successful. Overall success rate of QS treatment in (race)horses with lone AF is around 85%.

Quinidine gluconate

Intravenous administration of quinidine gluconate has been reported for recent-onset AF (3-7 days duration). Slow IV administration of 1-1.5 mg/kg is repeated every 10 minutes until cardioversion, QRS widening of more than 25% over baseline, toxic side effects occur or a total dose of 12 mg/kg is administered. However, this treatment protocol, although more convenient, carries an increased risk of side effects. Quinidine gluconate is not available in most countries.

Flecainide

Flecainide is a class IC anti-arrhythmic drug that depresses the upstroke of the action potential by blocking sodium channels. This drug is known to have pro-arrhythmic properties especially in the presence of structural heart disease.

In horses with chronic AF, IV administration of 0.2 mg/kg/min flecainide acetate during 10 minutes has a low efficacy and can induce potentially life-threatening ventricular arrhythmias. However, even in recent-onset, lone AF, this treatment protocol has led to fatal ventricular fibrillation. Also oral administration of flecainide has led to sudden death. The author therefore recommends that flecainide should not be used at all in horses.

Amiodarone

Amiodarone is a class III anti-arrhythmic drug that prolongs repolarization predominantly by blocking potassium channels. In human medicine, the drug is used as an IV infusion for acute treatment or as an oral formulation for chronic administration.

In horses, bioavailability of oral amiodarone is low but intravenous amiodarone administration has been used to treat chronic AF. The described treatment protocol consisted of a loading dose over one hour, followed by a continuous infusion over 1 to 3

days, but resulted in only a moderate conversion rate (50%). Amiodarone administration over more than 36 hours was associated with an increased risk for side effects that included diarrhoea and hind limb weakness.

Propafenone

Intravenous treatment with propafenone, at 2 mg/kg over 15 minutes, followed by 7µg/kg/min over 2 hours, was reported not be effective in treating AF in horses. It has been suggested that 2 mg/kg propafenone orally TID, might convert AF in some horses, but no published data available.

Non-pharmacological treatment: electrical cardioversion

In human medicine, electrical cardioversion using a direct current (DC) shock is a commonly used approach to convert atrial as well as ventricular fibrillation. Although the exact mechanisms are not fully understood, the DC shock probably causes complete depolarisation of the myocardium, bringing it into a refractory state, thereby blocking all fibrillation waves and creating the chance for normal sinus rhythm to resume. A critical amount of myocardium needs to be depolarized which can only be obtained by a sufficiently large current flow through the atria. The latter depends on the kind and location of the electrodes (electrode surface area, interelectrode distance and impedance, position of the electrodes in relation to the atria), and the applied energy. Besides the energy level (Joules), it is known from human medicine that the DC waveform morphology also plays an important role, whereby biphasic waves are more effective than monophasic waves. It is crucial not to deliver the DC shock on the T wave, as this is likely to be fatal due to induction of ventricular fibrillation. Shock delivery should therefore always be synchronized with the R wave. Correct R wave detection must always be verified before shock delivery as the T wave might occasionally be falsely detected as R wave by the defibrillator. Because shock delivery might result in temporary bradycardia or asystole due to impaired atrioventricular nodal conduction, ventricular backup pacing during electrical cardioversion in horses is recommended. As electrical cardioversion is painful, general anaesthesia is always required.

Transthoracic electrical cardioversion

Transthoracic electrical cardioversion of AF implies shock delivery between paddle electrodes placed on the skin at each side of the thorax. Because of the large size of the equine thorax with the atria covered by the insulating lungs, the final current flow through the atria, and thus efficacy, is very low, even when high energy levels are used. This technique is not recommended in adult horses.

Transvenous electrical cardioversion

Placement of the electrodes near or in the atria, results in a much higher amount of current flow through the myocardium. This approach is used during transvenous electrical cardioversion and has proven to be very efficacious in horses with AF. In the standing horse,

2 cardioversion catheters, with large surface area electrodes at the tip, are introduced via the jugular vein. Each catheter is then positioned using ultrasonography, radiography and/or pressure tracings from the catheter. To encompass as much atrial myocardium between both electrodes as possible, one electrode is manoeuvred into the proximal left pulmonary artery while the other is placed in the right atrium. Subsequently, after induction of general anaesthesia and verification of catheter position, synchronized shocks are delivered. Starting at about 125 J, energy level is stepwise increased until a maximum of 360 J. Using biphasic waves, mean energy level to obtain cardioversion in horses with AF is reported to be around 160 J.

Aftercare

Successfully converted horses

After successful pharmacological or electrical cardioversion, depending on the duration of AF, the horse should be rested. Experimental work suggests that it takes about 4 to 6 weeks for the atrial refractoriness and contractile function to fully recover from chronic (6 months) AF, while it takes about 1 day for recent-onset (1 week) AF. The author recommends a resting period between 1 and 6 weeks depending on the estimated AF duration. Ideally, 2D and TDI ultrasound should indicate restoration of atrial contractile function before returning to full training. Twenty-four hour ECG monitoring a few days after cardioversion may be useful to detect the burden of atrial premature beats, which are known to trigger AF recurrence. In horses with a high number of atrial premature beats, the resting period should be prolonged and anti-inflammatory treatment with corticosteroids may be considered. Sotalol orally at 2 mg/kg BID is used by the author to decrease the risk for early recurrence of AF during the recovery period.

Successfully converted horses without underlying cardiac disease have a good prognosis and usually return to their previous level of performance. Recurrence rate of lone AF is expected to be unrelated to the cardioversion technique used and is reported to be around 35-40%. Risk factors for recurrence are mitral regurgitation, large atrial size, short atrial refractory period, abnormal atrial contractile function and a previous AF episode. Owners should be advised to check cardiac rhythm frequently in order to detect recurrence of AF.

Non-converted horses

If conversion cannot be obtained and the horse is not intended to perform, no further action is needed. Lone AF in non-performing horses does not usually cause clinical signs and does not progress to heart failure. High level performance should not be expected from AF-affected horses: these horses generally do not perform well and strenuous exercise might even be associated with epistaxis, ataxia or collapse. If only light or moderate work is demanded, a thorough exercise test with continuous ECG monitoring is necessary to identify any other exercise related arrhythmias, tachycardia or clinical signs. AF is considered a potential risk factor if mean maximal heart rates exceed 220/min or if abnormal ventricular

rhythms occur during exercise.

Horses with AF secondary to significant underlying cardiac disease need to be rested with supportive treatment. Digoxin might be beneficial to limit ventricular response rate. Anecdotal evidence suggests that some of these horses might benefit from angiotensin converting enzyme inhibitor therapy but no objective data are available.

Supplemental readings

De Clercq, D., van Loon, G., Schauvliege, S., Tavernier, R., Baert, K., Croubels, S., De Backer, P., Deprez, P., 2008. Transvenous electrical cardioversion of atrial fibrillation in six horses using custom made cardioversion catheters. Vet. J. 177, 198-204.

De Clercq D, van Loon G, Tavernier R, et al. Atrial and Ventricular Electrical and Contractile Remodeling and Reverse Remodeling Owing to Short-Term Pacing-Induced Atrial Fibrillation in Horses. J Vet Intern Med 2008; 22:1353-1359.

De Clercq, D., Decloedt, A., Sys, S.U., Verheyen, T., Van Der Vekens, N., van Loon, G., 2014. Atrial fibrillation cycle length and atrial size in horses with and without recurrence of atrial fibrillation after electrical cardioversion. J. Vet. Intern. Med. 28, 624-629.

Decloedt A, Schwarzwald C, De Clercq D, Van Der Vekens N, Pardon B, Reef VB and van Loon G. Risk factors for recurrence of atrial fibrillation in horses after cardioversion to sinus rhythm. J Vet Intern Med. 2015; 29:946-953.

Decloedt, A., Verheyen, T., Van der Vekens, N., Sys, S., De Clercq, D., van Loon, G., 2013. Long-term follow-up of atrial function after cardioversion of atrial fibrillation in horses. Vet. J. 197, 583-588.

Reef VB. Arrhythmias. In: Marr CM, ed. Cardiology of the horse. London: Saunders W. B.; 1999:179-209.

Reef, V.B., Bonagura, J., Buhl, R., McGurrin, M.K., Schwarzwald, C.C., van Loon, G., Young, L.E., 2014. Recommendations for management of equine athletes with cardiovascular abnormalities. J. Vet. Intern. Med. 28, 749-761

McGurrin MKJ, Physick-Sheard PW, Kenney DG. Transvenous electrical cardioversion of equine atrial fibrillation: Patient factors and clinical results in 72 treatment episodes. J Vet Intern Med 2008; 22:609-615.

van Loon G. Atrial pacing and experimental atrial fibrillation in equines. In: Dept. of Large Animal Internal Medicine. Merelbeke: Ghent University, Belgium; 2001:258.

van Loon G., Patteson M. Electrophysiology and arrhythmogenesis. In: Marr CM, Bowen M. ed. Cardiology of the horse, 2nd Edition. London: Saunders W. B.; 2010:59-73.

van Loon, G., De Clercq, D., Tavernier, R., Amory, H., Deprez, P., 2005. Transient complete atrioventricular block following transvenous electrical cardioversion of atrial fibrillation in a horse. Vet. J. 170, 124-127

Verheyen, T., Decloedt, A., Van der Vekens, N., Sys, S., De Clercq, D., van Loon, G., 2013. Ventricular response during lungeing exercise in horses with lone atrial fibrillation. Equine Vet. J. 45, 309-314.

Dissimilar atrial rhythms

Julia Sargent
The Royal Veterinary College, London
Southern Counties Veterinary Specialists

TALK SPONSORED BY:

Dissimilar atrial rhythms are characterised by the presence of two separate supraventricular rhythms discharging independently. A unilateral ectopic rhythm is present that is independent to the basic rhythm and demonstrates both entrance and exit block. None of the ectopic impulses result in ventricular depolarization and the rhythm does not disturb the basic rhythm. This should be differentiated from artifact and atrial parasystole, in which the discharging ectopic focus is conducted to the ventricles whenever it occurs outside of the refractory period of the basic rhythm.

Although rare, there are at least three case reports of dissimilar atrial rhythms in the veterinary literature. In this session we examine the electrocardiographic and echocardiographic findings from a dog with an unusual surface ECG.

References:

1. Karch MR, Ndrepepa G, Schneider MA, Weber S, Schreieck J, Schmitt C. Single chamber atrial fibrillation involving only the left atrium: implications for maintenance and radiofrequency ablation therapy. Pacing and clinical electrophysiology: PACE. 2003; 26:883-891.
2. Kovacevic A, Sastravaha A. Clinically silent atrial dissociation in a dog. Journal of veterinary cardiology: the official journal of the European Society of Veterinary Cardiology. 2007; 9:135-137.
3. Martinez EE, Pontes S, dePaola AA, Gomes JA. Segmental atrial fibrillation resulting in chronic atrial dissociation. A case report. Journal of electrocardiology. 1991; 24:185-190.
4. Mekhamer YE, Kittleson MD. ECG of the month. Generalized cardiomegaly and an enlarged left atrium in a dog. Journal of the American Veterinary Medical Association. 1989; 194:1198-1199.
5. Nakai H, Takeuchi M, Nishikage T, Nagakura T, Otani S. The mitral L wave: a marker of advanced diastolic dysfunction in patients with atrial fibrillation. Circulation journal: official journal of the Japanese Circulation Society. 2007; 71:1244-1249.
6. Ndrepepa G, Zrenner B, Schreieck J, Karch MR, Schneider MA, Schomig A, Schmitt C. Left atrial fibrillation with regular right atrial activation and a single left-to-right electrical interatrial connection: multisite mapping of dissimilar atrial rhythms. Journal of cardiovascular electrophysiology. 2000; 11:587-592.
7. Scollan K, Bulmer BJ, Heaney AM. Electrocardiographic and echocardiographic evidence of atrial dissociation. Journal of veterinary cardiology: the official journal of the European Society of Veterinary Cardiology. 2008; 10:53-55.

8. Zipes DP, Dejoseph RL. Dissimilar atrial rhythms in man and dog. The American journal of cardiology. 1973; 32:618-628.

ACVIM 2014 Equine abstracts update

Liz Finding
The Royal Veterinary College, London

Equine research abstracts

Cardiovascular effects of oral and intravenous pimobendan in healthy adult horses. T Afonso Six healthy horses were administered 0.25mg/kg pimobendan IV or IG or placebo IG in a latin square design. No adverse effects were seen. Heart rate increased significantly in both pimobendan groups but measures of contractility only increased significantly in the IV group, possibly due to variable bioavailability (not measured).

Correlates between postmortem and echocardiographic measurements of the right ventricle in horses. G Hallowell. Seven horses had right ventricular measurements taken during echocardiographic examination prior to slaughter at an abattoir. Post mortem measurements were then taken. Repeatability of all echocardiographic measurements was moderate to excellent, reproducibility was better for M-mode parameters than 2-D parameters, except for moderator band length which was excellent. Moderator band length and RVIDd were most highly correlated with post-mortem measurements and these echocardiographic measurements were significantly greater in horses with known right sided enlargement. These measurements can be used for evaluating right ventricular enlargement in clinical cases.

Consensus statement discussion - Exercise induced pulmonary haemorrhage
The panel's review of the available evidence only allowed three recommendations to be made.

1. EIPH should be considered a disease (strong evidence)
2. EIPH should be considered a progressive disease (weak evidence)
3. Furosemide should be used in the management of EIPH in racehorses (weak evidence). NB use of furosemide banned in competition horses in UK.

Equine scientific talks

Equine atrial fibrillation: triggers, remodelling and recurrence. G Van Loon
Prognosis: Transvenous electrical cardioversion is more successful in acute cases of AF than chronic cases, and more successful in racehorses than others. Quinidine sulphate and TVEC both have a success rate of about 80%.

Reversibility: Acute (1 week) experimentally induced AF rapidly returns to normal function (hours-days), chronic (4 months) experimentally induced AF returns to normal function more slowly (~6 weeks). Follow up of naturally occurring disease over 6 weeks showed gradual but not complete improvement in LA contractile function.

Recurrence: Monitor 24hr ECG after conversion, if atrial premature depolarisations or atrial tachycardia present then start anti-arrhythmic therapy. Prior to conversion can measure AF cycle length by intracardiac catheter or tissue Doppler (good correlation between measurements). Tissue Doppler allows measurement at different sites but is only possible at slow heart rates. Risk of recurrence after conversion varies with AF cycle length and atrial size.

Risk factors for recurrence (4 month follow up of 133 horses) – previous unsuccessful treatment, mild-moderate mitral regurgitation, low LA contractility at 24 hours post conversion.

The horse with a large heart. C Navas

Studies reviewed to describe echocardiographic changes to different situations which may cause appearance of cardiac enlargement. Relative wall thickness (RWT) used as an estimate of eccentric vs concentric hypertrophy.

RWT = (LVFWd + IVSd)/LVIDd

	Endoxaemia[1]	**Hypohydration[2]**	**Athlete[3, 4]**	**Hypertension[5]**
LVID	↓	↓	↑	↓
FS%	↓	N	N(↓)	N(↑)
MWT	-	↑	N(↑)	↑
RWT	-	↑	N	↑↑
LVM	-	N	N(↑)	↑

Factors which can be used to differentiate these conditions:

- Clinical presentation.
- Normal RWT in athletes.
- Increase left ventricular mass (LVM) with increased RWT and increased thickness interventricular septum in systole in hypertension.
- Decresae in left ventricular free wall thickness in systole or decreased fractional shortening (FS%) in endotoxaemia compared with an increase or normal free wall in hypertension and hypohydration.
- Normal to increased FS% in hypertension, normal in hypohydration, decreased in endotoxaemia.

Equine cardiology SIG. Colin Schwarzvald and Jo Ann Slack. Results of survey on the use of echocardiography – great variability in which measurements taken, consensus needed on standard imaging guidelines to allow comparisons between individual clinicians and for research studies. Interpretation of exercising ECGs – lengthy discussion on how to differentiate APCs from VPCs since morphology not useful

Some ideas:

- VPCs don't disturb underlying rhythm
- Can still see regular P waves with VPCs

Presence of compensatory or non-compensatory pause is less useful in presence of couplets or runs.

References:

1. Slack, J., R. Nolen-Walston, and B. Shaer. ECHOCARDIOGRAPHIC AND ECG FINDINGS IN HORSES WITH EXPERIMENTALLY INDUCED ENDOTOXEMIA. in ACVIM Forum. 2013. Journal of Veterinary Internal Medicine.

2. Underwood, C., et al., Echocardiographic Changes in Heart Size in Hypohydrated Horses. Journal of Veterinary Internal Medicine, 2011. 25(3): p. 563-569.

3. Buhl, R., et al., Changes over time in echocardiographic measurements in young Standardbred racehorses undergoing training and racing and association with racing performance. J Am Vet Med Assoc, 2005. 226(11): p. 1881-1887.

4. Young, L.E., K. Rogers, and J.L.N. Wood, Left ventricular size and systolic function in Thoroughbred racehorses and their relationships to race performance. Journal of Applied Physiology, 2005. 99(4): p. 1278-1285.

5. de Solis, C.N., et al., Hypertensive cardiomyopathy in horses: 5 cases (1995–2011). J Am Vet Med Assoc, 2013. 243(1): p. 126-130.

Ventricular arrhythmias: what worries me in small animals?

John Bonagura
Ohio State University, Columbus, USA

INTRODUCTION

Arrhythmias arising within the ventricles can pose hemodynamic risks of hypotension and hypoperfusion, as well as hold the potential for progression to ventricular fibrillation (VF). These potential outcomes frame the clinical issues assigned by this lecture title, namely those of *risk stratification* and the *priority for antiarrhythmic therapy* in dogs and cats with ventricular ectopy. Certainly most cardiologists have a sense about the relative risks associated with certain ventricular arrhythmias. For example, most would treat a sustained monomorphic right ventricular outflow tract (RVOT) tachycardia of 240/minute in an English bulldog. No doubt even a single episode of torsade de pointes would have most of us scurrying for some antiarrhythmic drug or a magnesium solution. I suspect we would all consider lidocaine administration for an anesthetized dog with cardiomyopathy whose blood pressure (BP) suddenly drops during a bout of ventricular tachycardia (VT). But these examples represent the low-hanging fruits when it comes to assessing risks of ventricular ectopy and appropriateness of treatment. Far more problematic are these situations: 1) is the dog with a breed-risk for cardiomyopathy experiencing frequent premature ventricular complexes (PVCs); 2) the older mixed-breed dog with single PVCs that are punctuated by the occasional couplet and triplet; 3) the young bull mastiff with severe hemorrhagic gastroenteritis manifesting an accelerated idioventricular rhythm of 170/minute; and 4) the cat with asymptomatic hypertrophic cardiomyopathy (HCM) whose Holter report shows 2,800 PVCs in 24h. These cases create uncertainty because it is difficult to predict which patient will experience morbidity or death from their rhythm disturbance. It is equally challenging to know if these type of patients will benefit or be harmed after administration of an antiarrhythmic drug. This presentation offers some suggestions to the risk stratification and therapy of ventricular arrhythmias in small animals. In the void of definitive studies, these recommendations are based on the literature and opinion shaped by respected colleagues and personal experiences.

We largely practice without prospective studies that would delineate the risks of ventricular ectopy or the risk/benefits of antiarrhythmic therapies in dogs and cats. Compared to our medical colleagues,[1,2] we have only rare studies on the likelihood for sudden cardiac death

(SCD); one example is the recent report by Wess and colleagues in Doberman pinschers (summarized below). As I advance some ideas on this subject, I doubt my mileage as a cardiologist can supplant the absence of prospective clinical trials. We actually share problems of assessing ventricular ectopy across the veterinary space, and I suspect Dr. Schwarzwald will advance some of the same limitations and concerns when he discusses the situation in horses. Fortunately few dogs and even less cats can crush their owners during a faint or fall. Nor are we very concerned about canine drivers suddenly losing control of their automobile during a run of VT (an issue our medical colleagues must face). As Dr. Schwarzwald will describe, there is some guidance for equine arrhythmias in the form of an expert-opinion consensus statement; however, similar guidelines are unavailable for small animals. No doubt Dr. Lowe will touch on some studies conducted in human patients, and I hope he can offer us some advice about assessing our small animals. Until then, you will be relegated to listen to the current speaker speculate and advance largely unsubstantiated "recommendations".

To carry on, the program Chair asked: What makes me (or perhaps more importantly, you) worry when presented with a ventricular arrhythmia? To start I worry that I am not confident about defining the patients who can be managed by simply "watching and waiting". In other words, is the performance of the occasional physical examination, in-hospital or at-home ECG, and 24h Holter recording sufficient to alert me when treatment is needed while there is still time? Anyone who has sent a dog home with a Holter monitor to obtain the "baseline recording" and then had the patient die while waiting for the device to return from FedEx might identify with this (fortunately rare) concern. More commonly I am often uncertain what to recommend even after reviewing the full disclosure Holter file. Like most veterinary cardiologists, I can state the clinical situations and the (modified Lown/Wolff[3]) criteria I use to guide antiarrhythmic therapy. But aside from the straightforward examples advanced at the onset of this lecture, few of us can defend our treatment criteria with much conviction. Nevertheless, if you regularly evaluate dogs and cats for ventricular ectopy, a decision to treat or observe must be rendered. Accordingly, this presentation will consider: 1) a brief overview ventricular arrhythmias with some limitations of this classification; 2) a general approach to the clinical evaluation of the patient with ventricular ectopy; 3) potential variables to consider when assessing the risk of PVCs and VT; and 4) some management options for these patients (i.e. what I usually do in the absence of evidence).

CLASSIFICATION OF VENTRICULAR ARRHYTHMIAS

A general classification of ventricular rhythms is listed in Table 1. It states the obvious that an accurate rhythm diagnosis is critical to management. As such, supraventricular tachycardia with aberrancy should be ruled out when evaluating a wide-QRS tachycardia.

Table 1. Simple Classification of Ventricular Arrhythmias	
Rhythm	**Comments**
Ventricular escapes Idioventricular (escape) rhythm	Secondary to sinus bradycardia, sinus arrest, or AV block; idioventricular rhythms can also be a terminal rhythm from "downward displacement" of the pacemaker.
Premature ventricular complexes (PVCs, VPCs)	Timing and coupling interval of PVCs: "R on T" and late-diastolic PVCs (distinguish from escape complexes); variable coupling with parasystole (seemingly rare in dogs and cats) Distributional patterns: isolated or haphazard, bigeminy, trigeminy (two variants), couplets, triplets, and "salvos" (four) Morphology includes uniform ("unifocal") & multiform QRS
Ventricular tachycardia (VT)	Run of VT: four or more consecutive PVCs Various categorizations based on ventricular rate, duration of ectopic rhythm, and QRS complex morphology Nonsustained (paroxysmal) or sustained (>30 s) Accelerated Idioventricular rhythms (AIVR) VT – further characterized as monomorphic, bidirectional (rare), multiform, and polymorphic (including torsades de pointes) Subtypes of VT based on putative mechanisms – limited
Ventricular flutter	Sign-wave like; cannot distinguish QRS from T-wave
Ventricular fibrillation (VF)	No consistently formed waveforms; coarse or fine VF Fine VF can be confused with asystole
Asystole (ventricular standstill)	Absent ventricular rhythm Rule out fine ventricular fibrillation

In terms of electrophysiologic (EP) alterations responsible for ventricular ectopy, there are many hundreds of published studies involving arrhythmogenesis in canine and feline models of cardiac disease. Most of these focus on vulnerability to ventricular tachycardia (VT) and ventricular fibrillation (VF) or the effectiveness of antiarrhythmic drugs or defibrillation devices in the settings of myocardial ischemia or infarction and pacing-induced heart failure. It is difficult to know the relevance of these models to spontaneous cardiac diseases of small animals. With the exception of some data from a few laboratories in located in Italy, the UK, and the USA, we have no EP studies of naturally-occurring arrhythmias in dogs and none (that I am aware of) in cats. Moreover, most veterinary EP labs have focused on accessory pathways and atrial rhythm disturbances. This paucity of EP data prevents us from refining our rhythm diagnoses. I am also unaware of any veterinary studies using programmed electrical stimulation to assess the risk of sudden cardiac death (SCD) in veterinary patients.

Most of us base our risk assessment and therapeutic decisions on a single or multiple lead surface ECG within the context of the species, signalment, and medical history supported by clinical laboratory findings and cardiac imaging. With the exception of some breed-related arrhythmias, the etiology, origin, and EP mechanisms characterizing most ventricular arrhythmias are unclear. Even in breeds well-known to be affected by genetically-predisposed cardiomyopathies, the underlying abnormality is rarely revealed. These gaps lead us to lump most cases of VT together diminishing our ability to stratify risk and develop

cogent treatment plans. Most of the author's patients are treated with a trial and error approach using standard drugs that are selected from a collective clinical experience.

GENERAL EVALUATION OF SMALL ANIMALS WITH VENTRICULAR ARRHYTHMIAS

The clinical association and the electrophysiologic (EP) mechanism for ventricular ectopy should be relevant to prognosis and to therapy. Extensive laboratory studies have indicated that heart of dogs and cats can develop the anticipated EP changes responsible for arrhythmogenesis. These mechanisms include abnormal automaticity, triggered activity (afterdepolarizations), and various forms of micro- and macro-reentry including reflection, flutter, and fibrillation. As in other species, certain drugs that delay conduction (sodium channel blockers) or prolong repolarization (potassium channel blockers) can predispose to VT and VF. However, in just a few disorders, notably the inherited ventricular ectopy of young German shepherds[4-7] and the RVOT tachycardia affecting Boxers[8] and English bulldogs,[9] have the mechanisms for VT been investigated in the EP lab. Certainly educated guesses can be advanced – as with AIVR, arrhythmias due to digitalis intoxication, or when torsades de pointes is identified – but we largely just speculate about the responsible mechanisms.

Understanding the likely *clinical association of an arrhythmia* can direct specific treatments to the underlying cause, guide the type and duration of any therapy, and inform the prognosis. A simple etiologic grouping includes these:

- *Primary cardiac diseases* (structural or electrical diseases; often genetically predisposed). The typical examples are the cardiomyopathies of dogs (boxers, English bulldogs, Doberman pinschers, great Danes, and Irish wolfhounds). Additionally cats with ventricular arrhythmias very often have structural cardiac disease, typically a form of cardiomyopathy.[10]
- *Metabolic & Endocrine disorders* (including hyperthyroidism[11])
- *Autonomic* nervous system-triggered arrhythmias[12,13]
- *Drugs & Cardiotoxic* agents (including digoxin and doxorubicin)
- *"Usual Suspects"* that includes a number of noncardiac disorders capable of inducing arrhythmias through likely causes of ischemia-reperfusion, release of inflammatory cytokines, altered autonomic traffic, or other mechanisms. Examples in dogs include gastric dilatation, sepsis, anemia, severe gastroenteritis, and splenic disease.

In contrast to people, *coronary artery disease* is not currently recognized as a major cause of spontaneous ectopy in dogs or cats. However, intramural arteriosclerosis is often observed in young dogs with aortic stenosis, in older dogs with myxomatous valvular disease,[14,15] and in cats with hypertrophic and restrictive cardiomyopathies[16]. Thus far the clinical significance of these lesions relative to arrhythmogenesis is uncertain. Occasionally clear cut myocardial infarctions are observed, especially in cats with end-stage cardiomyopathies. Undoubtedly ischemia (± reperfusion) also contributes to the development of VT in the critical care unit,[17] but most of these dogs have multisystemic or a primary noncardiac diagnosis.

The typical *clinical evaluation* begins by considering epidemiologic risk of species, age, sex, and breed and proceeds to include the medical history, physical examination, resting ECG, diagnostic imaging (echocardiography ± thoracic radiography), and selected clinical laboratory tests (especially serum sodium, potassium and calcium, and if indicated, a serum magnesium). In the setting of structural congenital and acquired heart diseases, the workup can focus on auscultation, echocardiography and thoracic radiography. When cardiomyopathy, ischemia, myocarditis, heart failure, or another insult is suspected as the cause of ventricular ectopy, cardiac troponins (typically cTnI) are measured, accepting that severe arrhythmias can probably induce secondary elevations in this biomarker. Extreme elevations are suggestive of an acute myocardial insult such as myocarditis or a recent infarction. When there is a possibility of myocarditis (markedly elevated cTnI; myocardial edema; regional epidemiologic risk) or a likelihood of a systemic infection, a CBC along with specialized diagnostic tests for regional infectious diseases should be considered (see "Myocarditis" below). Blood cultures are indicated in suspected cases of infective endocarditis. An endomyocardial biopsy also could be discussed and is not technically difficult to obtain; however, this is an uncommon procedure in dogs. Abdominal ultrasound – often focused on the spleen – is another useful study, especially in older dogs at risk for splenic tumors.

Ambulatory ECG recorders – Holter monitors,[6,8,18-26] event monitors,[21,27] and implantable loop recorders[28-31] – all have their place in diagnosis, assessment and management of ventricular arrhythmias and clinical signs of exertional collapse and syncope. In general a standard 5- or 10-minute ECG is relatively insensitive for predicting the results of a 24h ambulatory monitor, but a hospital (or Echo) ECG that shows ectopy is often predictive of an "abnormal" Holter ECG.[32] Mobile phone ECG apps can be handy for providing a quick check on the prevailing rhythm in the home setting (where identification of abnormalities is more useful than finding a normal rhythm because the recordings are so short). For certain complex heart rhythm disturbances, multipolar intracardiac electrode catheters are needed for definitive diagnosis; this requires a cardiac electrophysiologist and specialized equipment and training; rarities in veterinary medicine. Advanced analyses including signal averaged ECG and heart rate variability (HRV) are considered research tools but might prove useful in risk stratification.

ASSESSMENT OF RISK IN VENTRICULAR ECTOPY

A number of variables can be considered when addressing the risk of a ventricular rhythm disturbance. Despite a lack of study data, these factors often inform our clinical decision-making. A partial listing follows.

Genetic predisposition to arrhythmias – this is most often considered in terms of canine breeds. The rapid "left ventricular" VT in Doberman pinschers,[19,33] bradycardia-induced VT in German shepherds with inherited ectopy,6 and DCM in Great Danes with heart failure and PVCs[34] are each associated with a risk for SCD (although the risks have not been optimally-quantified). The likelihood of SCD in Doberman pinschers with occult or symptomatic DCM is reportedly as high at 50% with Wess' recent review at ECVC placing

the figure at “about one-third”. Despite a report to the contrary,[35] the author still considers boxers with VT from arrhythmogenic right ventricular cardiomyopathy (ARVC) as a risk factor for SCD in that breed. At the recent ESVC congress, Vollmar reported her observations in Irish wolfhounds indicating that SCD occurred in nearly 25% of Irish wolfhounds diagnosed with lone AF with a similar number dying suddenly after the development of overt DCM and CHF (ECVIM-CA Proceedings, p. 25). An uncommon example of genetic risk for ventricular ectopy and SCD is the Duchenne cardiomyopathy in golden retrievers.[36] Other genetic risks for ventricular ectopy might become evident with advances in genetic profiling. For example, it is likely that drugs that interact with ion channels and prolong ventricular repolarization will be identified in dogs and cats (as with the hERG1 gene in people). Mutations predisposing to prolonged Q-T have already been reported in dogs (see following).

Preexisting disorders of ventricular conduction or repolarization – conduction disorders can predispose to both supraventricular and ventricular arrhythmias. Accessory pathways occur in dogs and cats but their role in SCD is unknown.[38] These might permit antidromic conduction or rapid transmission of atrial arrhythmias and be a potential risk factor for VF. The potential contribution of intraventricular conduction disturbances or fascicular blocks has not been sufficiently addressed in dogs and cats, especially in the setting of cardiomyopathies. In addition to drug-induced lengthening of repolarization, a long Q-T interval in a family of English Springer spaniels with KCNQ1 gene mutation has been reported associated with SCD.[37] These mutations are well described in human families but mostly undiscovered in dogs and cats.

Evidence of structural heart disease – this is usually based on auscultation and echocardiographic assessment. For example, we know there is a risk of sudden cardiac death in dogs with moderate to severe subaortic stenosis, in cats with HCM,[10] and in dogs with dilated cardiomyopathy (DCM). Left ventricular dilatation characterized by an end-diastolic volume of >91.3 ml/m^2 (Simpson’s method) was reported as the most important predictor placing Doberman Pinschers at risk for SCD with “the probability increasing 9.9-fold (CI 3.5, 37.0) for each 50 mL/m^2 increment of LVEDV/BSA” (Wess, et al., Proceedings ECVIM-CA 2015, pp. 268-269). Perhaps the type of cardiac disease and patient size are also relevant factors, considering small breed dogs with chronic valvular disease often show isolated PVCs on Holter recordings, but VT seems quite uncommon.[39] Ambulatory electrocardiography often identifies ventricular ectopy in cats with HCM as compared to normal cats[26,40-42] but documented VT as the cause of SCD has been difficult to substantiate. Right ventricular cardiomyopathy in cats has been associated with a variety of rhythm disturbances including complex ventricular ectopy.[43,44]

Myocarditis – inflammation of the myocardium is occasionally documented in dogs and cats with sudden death. In the author’s experience nonsuppurative endomyocarditis is an important postmortem finding in young cats suffering anesthetic-related deaths. Over the years a number of dogs have been seen with clinical features of myocarditis (reversible myocardial thickening from infiltration and edema, severely elevated cardiac troponin)

accompanied by difficult to control ventricular arrhythmias. Parvovirus from in utero infection can linger as a smoldering myocarditis in young dogs. A recent histopathologic study of dogs with myocarditis showed evidence of Borrelia infection in some.[45] In Latin America and the southern USA, Trypanosomiasis is a cause of myocarditis.[46,47] Neospora canis infection,[48] babesiosis,[49,50] and infection with Leismania51 and Bartonella spp. have been associated with histopathologically-proven myocarditis in dogs. A recent presentation (ESVC 2015) by Santilli indicated a number of dogs undergoing EP studies had biopsy proven myocarditis.

Ventricular systolic function – some human studies indicate a higher mortality when PVCs occur in the setting of reduced LV ejection fraction. This should logically apply to dogs and cats as well and impaired systolic function is a diagnostic feature of established canine DCM as well as a number of feline myocardial diseases. However, this has not been proven by multivariate analysis.

Age and Sex – the development of a disease linked to ventricular ectopy or SCD would logically increase with age, but insofar as the author can determine, this has not been specifically studied in veterinary patients. The exception is a recent study in Doberman pinschers showing an increase prevalence of ventricular ectopy with age.[52] Older reports in Doberman pinschers and Irish wolfhounds showed a higher mortality at a younger age[53] but most of these dogs suffered from CHF so SCD was not the only cause of mortality. Female Doberman pinschers are reportedly more prone to developing PVCs as opposed to LV dysfunction (Wess, et al., in ECVIM-CA Proceedings, p 268-9).

Predisposing non-cardiac disorders – many ventricular rhythm disturbances are short-lived, developing secondary to a noncardiac disorder. Some clinical associations include hypokalemia/hypomagnesaemia, pheochromocytoma, splenic diseases, gastric torsion-dilatation, trauma, sepsis, metastatic neoplasia (including hemangiosarcoma and carcinomas), and heat stroke. Careful monitoring or delivery of short-term antiarrhythmic therapy might be all that is needed for these patients, assuming the primary disorder can be managed.

Ischemia and hypoxia – myocardial ischemia and infarction place human patients at higher risk for acute and recurrent ventricular arrhythmias. In models of canine and feline ischemic myocardial injury, cellular EP and myocardial conduction are affected predisposing to reentrant, automatic, and triggered ventricular activity. Demand ischemia can also develop in hearts with pathological hypertrophy, especially in the setting of tachycardia or exercise, and might alter ventricular repolarization and refractoriness. ST-segment deviation is evident in some dogs with aortic or pulmonary stenosis during exercise ECG and has is probably overlooked in cats with HCM and sinus tachycardia. Tissue hypoxia from any cause, including pulmonary disease, anemia, or ischemia is another potentially treatable factor in some seriously ill dogs and cats with ventricular ectopy.

Exercise/Activity induced collapse – many clinicians consider a history of exertional collapse or syncope in a dog with documented PVCs as evidence to support a higher risk

categorization, to limit vigorous exercise, and institute antiarrhythmic therapy. There is probably some difference of opinion about these points, in part due to the overemphasis on ventricular ectopy as a cause of syncope. There is a corresponding lack of appreciation about excitement-triggered, reflex-mediated syncope. For example, both VT and reflex-mediated (vasovagal) syncope are relatively common in dogs, including boxers[54,55] and without an event monitor or fortuitous Holter ECG recording, the precise cause of exertional collapse might be uncertain (even in a dog with frequent PVCs). Of course there is reason for concern when ectopy and exercise induced collapse are observed because these can lead to SCD in dogs with congenital subaortic stenosis, pulmonary stenosis, and occult or manifest DCM. Sudden death is also an important cause of mortality in cats with HCM, but the impact of exercise on this outcome is not reported. This is perhaps due to the nature and duration of their play habits, small-sized heart, (or a sensible reaction to effort-induced angina such as stopping?).

Hypotension – the potential for VT to lead to hypotension in anesthetized and critically ill dogs and cats is relevant to the decision to manage a ventricular arrhythmia, if just for the short-term.

Drugs – both cardiac drugs and treatments for other conditions can play a role in the development of ventricular arrhythmias. Drugs such as digoxin and catecholamines are obvious culprits in the pathogenesis of PVCs. Diuretics can deplete magnesium and potassium potentially increasing risk for PVCs/VT. Additionally, there is at least a risk of proarrhythmia with many of the Class I and Class III antiarrhythmic drugs. Noncardiac drugs such as cisapride and some tricyclic antidepressants (and a host of other agents) can prolong Q-T interval in humans as a class or idiosyncratic effect; these seem to be safe in dogs but we probably miss many of these drug-induced arrhythmias in dogs and cats. Doxorubicin is often used in therapy of canine neoplasia, and cardiotoxicity is identified both in biomedical studies and in our patients, especially when the cumulative dosage exceeds ~160 mg/m^2. In the author's experience conduction delays and ventricular ectopy are not uncommon with doxorubicin therapy, but these are often ignored in light of the primary disease.

Heart rate/Cycle length – whether due to autonomic influences, drugs, or other premature beats, changes in cardiac cycle length can influence the development of ventricular arrhythmias. The well-known example involves the negative impact of beta blockers (or of sleeping) in German shepherd dogs with inherited ectopy wherein long cycle lengths can trigger VT/VF. Older literature refers to "primary" and "secondary" PVCs – a situation where a single PVC (or APC or change in sinus rate) can trigger recurrent ectopy or bigeminy of a different morphology. The author has observed this on a number of occasions. Varying cycle lengths (typically short – long – short) result in dynamic changes in repolarization in the His-Purkinje network and can trigger runs of VT including torsades de pointe. The VT associated with complete AV block In terms often resolves once pacing commences. Some class I antiarrhythmic drugs function more effectively at higher heart rates (a form of use-

dependence). Thus changes in cardiac cycle length can exert proarrhythmic or antiarrhythmic effectives.

Autonomic/Sympathetic Activity – in addition to affecting cardiac cycle length, sudden changes in sympathetic or vagal efferent traffic can influence cardiac EP inducing ventricular rhythm disturbances. For example, catecholaminergic polymorphic VT in children is triggered by sympathomimetic stimuli or catecholamines.[31] Pheochromocytoma can be associated with myocardial injury and ventricular tachycardia in dogs. Vagotonia has some influence on pacemaker activity and also can facilitate AIVR by slowing the sinus node rate.

Clinical Laboratory Tests – the risk of PVCs and VT should logically increase in settings where serum potassium is reduced. Although serum magnesium is measured less frequently in our patients, it can track total body potassium. Unlike the human situation, dogs and cats are not treated with diuretics for systemic hypertension, so we have been less focused on the role of potassium and magnesium in SCD. However, hypokalemia and hypomagnesemia are relatively common in critical care settings and can also occur during chronic CHF therapy with furosemide. In terms of markers of cardiac injury, cardiac troponins have been evaluated in a number of canine and feline studies and have been reported as predictors of mortality in univariate and multivariate analyses; however, prediction of SCD has not been addressed insofar as the author can determine. In the aforementioned oral presentation at ESVC, Wess indicated that cTNI was a potential predictor of SCD in Doberman pinchers. As mentioned previously, dramatic elevations of cTNI are should prompt consideration of myocarditis or an acute myocardial insult such as an infarction.

Electrocardiographic variables – a number of ECG findings can be used to qualify and quantify a ventricular rhythm disturbance. This approach was taken in the PVC risk stratification originally proposed by Lown and Wolff. Although that system has been challenged for a long time,[3] it is still widely quoted and used. We scrutinize Holter recordings for these so-called "warning arrhythmias" that might portend a risk of sudden cardiac death. Some of the variables considered include:

- *Number of PVCs per minute/hour/day* – these are readily determined from a Holter ECG and incorrectly classified by an in-hospital ECG.[12] Although a number of studies use somewhat arbitrary cut-offs of 50 or 100 PVCs in 24h to define "normal", many healthy dogs and most healthy cats have far less than 50 premature ventricular complexes per day (and some have zero in 24h). Additionally, some Holter services indicate the total number of ventricular ectopic complexes and then characterize these as premature based on an algorithm or visual categorization. In many cases late-diastolic "PVCs" would more reasonably be considered escapes associated with sinus bradycardia and sinus pauses but are still totaled in the "ventricular ectopics" count. When deciding how many PVC's are "too much" from a Holter ECG, the first step is to remember there are 1440 minutes in a day so 1000 ventricular complexes represent on average <1/minute.
- *Coupling intervals/Prematurity of the PVCs* – these relate to the risk classification and also the hemodynamic impact of an extrasystole. Certainly late-diastolic PVCs are well tolerated hemodynamically. However, a long coupling interval is not always safe and cases

of torsades de pointes in dogs are sometimes triggered by late-diastolic PVCs (as opposed to long-short cycles). Accepting that short-coupled PVCs are often ineffective mechanically, the potential for "R on T" PVCs to induce VF is probably overemphasized.[56] Additionally, some Holter analysis algorithms seem to base the label or "R on T" from a "prematurity index" relating the onset of the ectopic complex to the dominant R–R interval; this can lead to inaccurate categorization of these complexes, particularly in dogs with pronounced sinus arrhythmia.

- *Repetitive ventricular ectopy* – couplets, triplets, "salvos", and runs of non-sustained VT are logically thought to represent a higher "grade" of ectopy, but there is no compelling evidence for this categorization in dogs except for the recent report by Wess and colleagues who indicated "other variables were not statistically significant in the (multiple) regression analysis, but …..having triplets are further prognostic markers for SCD risk assessment". Additionally, when evaluating couplets and triplets, the closeness of the coupling intervals, a multiform morphology of PVCs, and the triggering of secondary arrhythmias might be relevant in terms of hemodynamic compromise and potential risk for VT or VF.
- *Rate* – the rate of a VT is highly relevant in terms of hemodynamic consequences, myocardial oxygen demand, diastolic time, development of ischemia, and potential for tachycardia-induced cardiomyopathy. "Slow VT" of the AIVR type usually occurs at a rate close to that of the SA nodal discharge and tends to alternate with sinus rhythm. It is usually well-tolerated. The rate at which a monomorphic VT becomes clinically important depends on additional factors including the presence of underlying cardiac disease or ventricular dysfunction, plasma volume status, level of activity, and the ventricular site of origin of the tachycardia. Logically, the rate of the repetitive ventricular activity is also clinically relevant to risk and initiation of therapy. In the Wess oral presentation a maximal rate >260/minute was a potential predictor of SCD in Doberman pinschers.
- *Morphology review* – PVCs are characterized in a number of ways based on their appearance. One common descriptor relates to the "bundle branch block" (BBB) morphology. For example, a typical RVOT tachycardia in a boxer will have a left BBB morphology; whereas, many PVCs with a right BBB morphology are thought to arise from the left ventricle. As shown in human patients, origin of a VT it is certainly more complicated than this simple description, but these do offer some utility. Ventricular ectopics are also classified as monomorphic or uniform ('unifocal') versus multiform ('multifocal'), while monomorphic and polymorphic are used to characterize VT. The latter group includes tachycardias with changing QRS axis typical of torsades de pointes. It should be noted that positional changes on a Holter ECG can lead to reclassification of some ectopics as multiform based on automated analysis; additionally, fusion complexes can be mislabeled as ectopics of different morphology. As one might expect, multiform and polymorphic ventricular rhythms are considered more serious and "warning" arrhythmias.
- *ST-segment* – It is reasonable to inspect the ST segment and T-wave in patients with ventricular ectopy as changes from baseline might suggest an issue related to ischemia or tissue hypoxia. This is especially relevant during anesthesia or in critically ill patients. The normal T-waves of the dog and cat are quite labile and difficult to interpret, but if a baseline recording is available, and the leads and calibrations are static >.15 to .2 mm deviation

should be evaluated further in terms of BP, heart rate, oxygen demand, electrolyte status, the influence of drugs such as catecholamines, and respiratory function. Secondary ST-T changes due to abnormal QRS complexes cannot be interpreted; the analysis is generally confined to sinus complexes.

- *Advanced ECG analysis* – the detection of early afterdepolarizations and altered autonomic traffic have been used to assess risk of SCD in people. Both the signal averaged ECG (for detecting late potentials) and measurements of heart rate variability (and autonomic tone) have been reported in dogs[57-61] but the technique has not yet been sufficiently evaluated to play a clinical role in risk stratification of ventricular ectopy. It would be interesting to know if microvolt T-wave alternans could be clinically applicable to our veterinary patients. This examination has been used to stratify risk for SCD in people and also studied in animal models of repolarization instability. The commercial test is actually a criterion for selecting patients eligible for implantable defibrillator reimbursement by some insurance companies (in the USA….of course).

Advanced imaging of substrate – CRMI, SPECT, PET, and Echo have all been used in human patients in an attempt to identify scar or other substrates for ventricular arrhythmias.[62] Some newer echocardiographic system applications propose to image activation of the ventricles using anatomic templates populated by deformation (strain) imaging. The image outputs purportedly provide a map of mechanical activation that offers insight to the preceding path of electrical activity. (Parenthetically, sometimes less sophisticated Echo methods such as tissue Doppler, 2D and M-mode imaging, and speckle-based strain can provide insight regarding the origin of a wide-QRS tachycardia.)

Electrophysiologic studies – invasive EP studies are a standard of diagnosis and guide catheter based therapies of people. Currently only performed in a handful of veterinary referral centers, this situation has limited our development as a specialty and our understanding of ventricular arrhythmias and potential for therapy.

MANAGEMENT APPROACHES TO VENTRICULAR ARRHYTHMIAS

The decision to treat ventricular ectopy in dogs or cats rarely hinges on a single risk factor, but instead requires a comprehensive consideration of the aforementioned variables along with some practical considerations. In the absence of “symptoms” or objective predictors of SCD, the perception of the client to the risks of their pet dying suddenly is very important. The underlying disorder, the presence of life-limiting comorbidities, the duration and cost of therapy, effectiveness of current drugs, adverse medication effects, ability to treat (especially cats), and opportunities for future follow-up to gauge the effectiveness of treatment are practical concerns. One of the major differences between human and veterinary antiarrhythmic therapy is the absence of implantable pacemakers/ cardioverter/ defibrillation devices in our patients. Thus we are relegated to drug therapy, management of underlying conditions, including heart failure, or simply watchful waiting. The author’s approach to managing ventricular rhythm disturbances in small animals is summarized below.

Idioventricular Rhythms

The *idioventricular rhythm* and the *accelerated idioventricular rhythm* (AIVR) are ventricular arrhythmias that discharge at relatively slow rates. Idioventricular rhythms (escapes) are rescue mechanisms for sinus bradycardia, sinus arrest and high grades of AV block and are not suppressed. The typical idioventricular (escape) rhythm in the dog discharges at 20 to 40/minute and in the setting of sick sinus syndrome or advanced AV blocks the rhythm is managed through single or dual-chamber pacing. One notable exception is the dog with complete AV block that experiences runs of nonsustained VT leading to syncope from suppression of the ventricular escape focus. In our hospital these dogs are urgently paced with a temporary lead and if VT continues a lidocaine or (preservative-free) amiodarone infusion is started. This is followed by permanent transvenous pacing after which most dogs do not seem to redevelop VT. Nevertheless, a Holter ECG should be recorded and if necessary antiarrhythmic drug therapy initiated (see later for drug recommendations).

In most cats with third-degree AV block the idioventricular rate is remarkably faster (110 to 130/minute).[63] For this reason it is sometimes confused with an AIVR. Most cats with a stable escape rhythm tolerate the relative bradycardia so long as there is no comorbidity such as HCM, excessive demand for cardiac output (anemia, thyrotoxicosis), or a sodium-retentive state compromised by fluid therapy (as often done for chronic kidney disease). A thoracic radiograph or ultrasound of the thorax is suggested – along with careful inspection of jugular venous pressure – to assess volume status. If identified pleural effusions can be controlled with an angiotensin converting enzyme inhibitor and a judicious dose of furosemide given once daily or every other day. The cat with intermittent ventricular asystole brought on by failure of ventricular escape activity is difficult to manage. These cats can experience remarkable lapses (>20 seconds) without any ventricular beats and are candidates for a pacemaker. Most often cardiologists recommend a transdiaphragmatic epicardial lead placement with positioning of the pulse generator in the peritoneal space. This approach does prevent obstruction of the systemic venous system; however, these systems are also prone to electrode dislodgement, exit block from myocardial fibrosis, and phrenic nerve stimulation, especially if reprogrammed to a unipolar mode. Low profile transvenous pacing leads can be successfully used in some cats (carefully cut off any tines and do not fully extrude any active fixation lead). Although the concerns about chylothorax are legitimate, in the author's experience, these are probably overemphasized.

Many cases of *accelerated idioventricular rhythm* (AIVR) are thought to derive from normal pacemaker cells stimulated by an injury that has either altered normal pacemaker currents or induced afterdepolarizations. These rhythms are quite common in dogs after ischemia-reperfusion injuries or following prolonged general anesthesia. In most cases the heart is structurally normal. The AIVR manifests at a faster rate than an escape rhythm and tends to initiate in late diastole, "warm-up" for a few beats, then discharge regularly (typically at 60 to 180 per minute). This type of "slow monomorphic VT" often competes with sinus rhythm such that fusion complexes are common. In general these rhythms are well-tolerated,

short-lived, and left untreated in favor of addressing any underlying medical issues. Ventricular preload should be optimized with fluids or colloids (a quick cardiac ultrasound or transmitral Doppler recording can be helpful to assess chamber filling) and most of our patients receive potassium supplementation (10 to 20 mEq/L of fluids) and occasionally magnesium chloride or sulfate (be sure to check on rate guidelines and fluid compatibilities). If the ventricular rate accelerates or encroaches on 200/minute, or if there is evidence of hemodynamic compromise or hypotension, intravenous or oral antiarrhythmic therapy is initiated (see below).

Premature Ventricular Complexes & Ventricular Tachycardia

While it is simple to outline factors worth considering when assessing a ventricular arrhythmia, the related issues of "when do I worry" and "when do I treat" are more controversial. Considering the multiple factors that play into any therapeutic decision, it is challenging to simplify this process to a few rules; nevertheless, this is what I'll try to do and discuss how I typically manage a patient with PVCs or VT.

Initial Assessment

- *Consider the hemodynamic consequences and any clinical signs associated with the arrhythmia*. Do not assume that collapse or syncope accompanying exertion or excitement is invariably caused by VT, especially if the clinic or hospital ECG is unconvincing. Record a 24h ECG or preferably apply a client-activated event monitor if the spells are frequent.
- *If the arrhythmia is evident in the hospital* palpate the arterial pulses and measure the BP during the arrhythmia to assess hemodynamic impact. Consider that dogs and cats with advanced forms of cardiomyopathy might be less tolerant of a ventricular rhythm disturbance than those with structurally normal hearts.
- *Consider the potential variables* outlined under "Assessment of Risk in Ventricular Ectopy", and carefully review the ECG considering the "Electrocardiographic Variables" mentioned in that section.
- *Work up the patient* as described previously. Attempt to identify the underlying cause of the ventricular ectopy, and consider any risks for SCD associated with the breed (especially Doberman pinschers) or underlying heart disease (DCM, HCM, or myocarditis).
- *Obtain an echocardiogram*. Except in cases of AIVR due to known initiators (e.g. gastric dilatation-volvulus, trauma, sepsis), I generally recommend an echocardiogram regardless of the suspicion for primary cardiac disease. In ICU cases that are developing worsening ventricular arrhythmias, I also recommend an Echo.
- *Have blood drawn* for a PCV/TP, serum electrolytes, and cTNI. If the troponin value is dramatically elevated, consider acute myocarditis or infarct and pending the Echo results submit a CBC and laboratory tests for infectious diseases (in my area a "tick-panel" and tests for Bartonella spp. would be done with serologic tests for Chagas disease if the dog has traveled from the south). Depending on the geographic region, different infectious diseases are important.
- *Decide if ambulatory monitoring will be possible*. Holter ECG can provide valuable information about the seriousness of a rhythm disturbance and a "baseline" for a patient

prior to any therapy. Inasmuch as day-to-day variability is common in terms of overall number of PVCs/24h, the often quoted figure of >80-85% reduction in ectopy is one standard for drug effectiveness. Of course reduction of ectopy with antiarrhythmic therapy has never been shown to equate to a decrease in mortality, and our clients and colleagues should be so advised.

Although we encourage regular follow-up ambulatory ECG recordings, many clients do not comply due to costs or the lack of any observable symptoms in their pet. As a less quantitative alternative, clients can purchase an AliveCor® phone ECG attachment (current cost is US $75 for the human device, which works fine in animals) and they can email home recordings to the clinic. (These can be instructive for identifying insufficient therapy, but dealing with these recordings in terms of technical quality, medical records storage, and reimbursement for one's time can be challenging).

Small Animals I would **always** treat for Ventricular Ectopy:

- Any patient with VT >240/minute, even if the VT is nonsustained and well-tolerated
- Any patient with polymorphic VT typical of torsades de pointes
- Any patient with complete AV block complicated by rapid VT (see above)
- Any patient with collapse or syncope proven by ambulatory ECG monitor to be due to VT
- Any anesthetized patient with a sudden fall in BP >20 mm Hg at the onset of VT
- Any patient with frequent single or repetitive multiform PVCs (>10/minute)
- Any patient with R on T ectopy wherein the premature complex falls near the apex (uncommon) or ascending limb (very rare) of the T-wave

Hospitalized Patients with Ventricular Ectopy

- If the arrhythmia is considered clinically significant, the hospitalized patient is managed with intravenous therapies or a combination of intravenous and oral medications.
- In *anesthetized patients*, I err on the side of therapy, especially if there is progressive ST-segment or T-wave changes or an obvious hemodynamic effect of the arrhythmia on BP, strength of the audible Doppler flow signal, or measurements of end-tidal CO2.
- In *critical care patients* I consider the BP, ST-T, rate of any repetitive rhythm and the complexity of the PVCs. I treat patients experiencing a drop in BP of 10 to 20 mm Hg (depending on their starting point), accelerating AIVR or VTs of 180 to 200/min or more in dogs; and PVCs of sufficient complexity to "make me worry" (see below for "suggestions).
- In those *patients with primary cardiac disease and ventricular ectopy requiring hospitalization*, my general approach is similar to other critical care patients, while accepting that long-term treatment will be needed. Therefore early transitioning to oral therapy is attempted.
- Our usual *in-hospital treatment approach* for ventricular ectopy is as follows: 1) lidocaine bolus (es) followed by a constant rate infusion (CRI); remember lidocaine is more neurotoxic in cats!; 2) if lidocaine is ineffective, in dogs, administer preservative-free amiodarone (Nexterone®); 3) begin KCl supplementation in critically ill patients, and if the rhythm is not sufficiently responsive measure serum magnesium and begin a magnesium

infusion. Magnesium salts are also used for the rare cases of torsades de pointes. Procainamide can be used in cats (as well as dogs) if lidocaine fails, and the importance of serum potassium as a promoter or VT in this species should not be overlooked. An oral alternative is sotalol, which often works within 2-3h of administration.

- Supportive care directed to the underlying disorder is important as is support of plasma volume; desaturated patients should be given supplemental oxygen.

Dogs **without** a history of exertional collapse or syncope

- For dogs (and the occasional cat) with *isolated PVCs and no clinical signs* I recommend a 24h ambulatory ECG. No therapy is administered until the results return. If the client declines a Holter ECG, I recommend no therapy but a three-month follow up where a long (10 minute) digital ECG is performed. They are urged to return should clinical signs occur. Considering beta-blockers often make dogs with reflex-mediated syncope worse, I do not like prescribing sotalol to fainting/collapsing dogs (even boxers) when VT has not been established as the certain or likely cause. My clinical prejudice is that a substantial number of boxers have both reflex-mediated syncope and "Type I" boxer cardiomyopathy characterized by sporadic PVCs; I suspect many of these boxers are treated unnecessarily.
- *For dogs with isolated PVCs that occur frequently* (on average, >10/minute) on a Holter ECG, I discuss pros/cons of therapy with the owner and also consider how these are modified during exercise. If present during higher heart rates, I usually prescribe sotalol or atenolol and reevaluate the Holter.
- *Young German shepherds* with ventricular ectopy are assumed to have inherited disease and treated with mexiletine or mexiletine with sotalol until they are 1-1/2 to 2 years old and then re-evaluated by Holter ECG. Beta-blockers slow rate and response to potassium channel blockers is abnormal64 so these drugs are not used as monotherapy in this disease.

In the young dog with mostly bradycardia-associated PVCs and a negative workup, I consider whether a German shepherd might have appeared somewhere in their lineage and either do nothing or give a trial course of mexiletine after discussing pros/cons with the owner.

- *For Doberman pinschers* with frequent PVCs, even if isolated, I generally recommend therapy with sotalol or sotalol-mexiletine (if needed) due to the high risk of SCD in this breed. This recommendation is even stronger if echocardiography shows LV dysfunction, a Holter ECG (or the Echo ECG) shows any repetitive activity (couplets/triplets), or cTnI is elevated.
- *For other breeds with isolated PVCs complicated by couplets or triplets*, the decision is more difficult and these "suggestions" are as likely to sound like conversational dribble as convincing recommendations. For dogs with isolated PVCs and occasional couplets, my tendency is to discuss the pros/cons of therapy with the owner and just re-evaluate the Holter ECG in 3 to 6 months. Frequent couplets (for example more than one per minute), couplets that are truly R on T, or couplets with multiform ("multifocal") PVCs are usually treated in our practice, although as previously indicated I think we over-emphasize R on T

and probably the significance of couplets. Dogs with ventricular ectopy and triplets or short salvos or runs of VT are treated, especially if the instantaneous ventricular rate is high. When repetitive ectopy is monomorphic and relatively "slow" (<160/minute), more resembling an AIVR, the priority for therapy is lower. However, some of these dogs have varying coupling intervals during their AIVR and suddenly accelerate with closely-coupled PVCs at the end of the run; I treat these dogs. Recommendations for therapy are stronger if an Echo shows LV dysfunction or the cTnI is clearly elevated. The priority to treat is also higher in breeds at risk for genetic ARVC or DCM, such as English bulldogs, boxers, and some of the giant breeds.

Dogs **with** a history of exertional **collapse or syncope**

- For *the otherwise healthy dog* with a history of exertional collapse or syncope, I perform a long (10-minute) in-hospital ECG. *If only PVCs are evident* in the clinic, I recommend an ambulatory ECG and once it is removed I have the client begin sotalol while awaiting the results of the Holter ECG. If one is willing to back off from the "pure" 24h analysis (or if cost considerations will prevent subsequent ambulatory ECGs), the first dose of sotalol can be given 4-6h prior to the end Holter recording and noted in the diary; the results are sometimes instructive. The drug will either be continued or not depending on the Holter analysis.
- *If VT is evident on the hospital ECG* in a dog with this history, I begin medical therapy immediately, foregoing a "baseline" Holter ECG and either hospitalize the patient overnight or at the least administer sotalol while monitoring the dog in Cardiology for some hours to evaluate any immediate (positive or negative) effects of the first dose. If the rhythm is complex, hospitalization is recommended and supplemental intravenous therapy with lidocaine is initiated while sotalol is continued. If the rhythm is stable after 24-36h, lidocaine is weaned and the dog is released on sotalol. If the rhythm control is unsatisfactory, both sotalol and mexiletine can be prescribed.
- In the patient who fails sotalol or sotalol-mexiletine, the options are less clear. Amiodarone can be effective but after months of therapy hepatotoxicity can be severe resulting in anorexia, vomiting, and a need of hospitalization. Simple elevation of liver enzymes is not a reason to stop this drug unless the bilirubin is also elevated. Flecainide can be considered in non-ischemic heart disease and preferably in dogs with normal LV systolic function. Propafenone is another drug for which there is limited clinical experience but might be effective in some cases.
- Some degree of exercise restriction is prudent if this is a clear trigger for malignant VT. This must be balanced against quality of life issues for the dog.

Cats with ventricular ectopy

- These patients often have structural heart disease[10] and the same approaches taken in dogs can be used in this species for assessing "risk" of the arrhythmia and the imperative to treat.
- Cats do pose some challenges for ambulatory monitoring and often spend most of their time sitting in one place fuming about the monitor (so I suspect). Some activity should

be encouraged, even if just involves carrying the cat to the litter pan (with the time entered in the diary). Alternatively, a telemetry recording can be made for some hours (e.g. using a Televet 100®) while the cat stays in hospital.

- I use similar criteria for therapy as stated for dogs, but the treatment options are more limited. In any cat with a history of "seizures" or collapse and ventricular ectopy of any sort, my tendency is to treat.
- Most cats tolerate sotalol or atenolol well (unless there is heart failure).

Ventricular Ectopy in the **Heart Failure** Patient

- When ventricular ectopy is identified in the setting of heart failure it is worth having a reasoned discussion with the clients. Many clients opt for no antiarrhythmic therapy even in dogs with runs of VT. This is not unreasonable considering the lack of efficacy data, the potential for drug side effects including negative inotropy, and the simple fact that many pet owners would prefer a "sudden death" to making a "decision for euthanasia". Additionally, many clients are already giving 4 or 5 medications two or three times a day. For these reasons, in dogs with CHF, I usually ignore PVCs and short runs of VT, especially if these runs are not inducing clinical signs.
- When therapy is needed based on "complexity" criteria or clinical signs, and if the client can treat their dog t.i.d., mexiletine is prescribed. If this is not possible, ineffective, or causes adverse effects then pimobendan is increased to t.i.d. and sotalol is administered. If ineffective amiodarone is discussed (ideally an IV infusion to gauge effect followed by oral therapy). The risk of hepatotoxicity might well be acceptable in a dog with shortened life span due to CHF.
- In cats with "serious" ectopy (as described above for dogs), or with signs of collapse, sotalol is initiated in addition to CHF therapy.
- Omega-3 fatty acids are used by some clinicians in dogs with ventricular ectopy.

Table 2. Common Dosages of Selected Antiarrhythmic Drugs	
Drug	**Dosage**
Lidocaine	Dog: initial boluses of 2 mg/kg slowly IV (over 2 minutes), up to 8 mg/kg (over 10 min; stop if vomiting or tremors); or rapid IV infusion at 0.8 mg/kg/minute; if effective, then 25-80 µg/kg/minute CRI Cat: initial bolus of 0.25–0.5 (up to 1.0) mg/kg slowly IV; can repeat boluses of 0.15-0.25 mg/kg, up to total of 4 mg/kg; if effective, 10–40 µg/kg/minute CRI (beware neurotoxicity)
Mexiletine	Dog: 4-8 mg/kg q8h PO
Procainamide	Dog: 2mg/kg IV over 2 minutes to a target dose of 10 mg/kg; repeat if necessary, up to cumulative dosage of 20 mg/kg; if effective a 10-50 µg/kg/minute CRI can be given or 8-20 mg/kg q4-6h IM or SQ Cat: 1.0-2.0 mg/kg IV over 2 minutes, repeat if necessary, up to cumulative dose of 10 mg/kg; 10-20 µg/kg/minute CRI; 7.5-20 mg/kg IM q(6-)8h
Flecainide	Dog: 1-2 mg/kg q12h PO (initial dosing; not advised if CHF or impaired LV function present)
Propafenone	Dog: 2-4 (up to 6) mg/kg q8h, PO (start at lower end of dose)
Atenolol	Cat: 1-3 mg/kg q12h, PO
Esmolol	Dog: 0.1-0.5 mg/kg IV over 1 minute (loading dose), followed by infusion of 0.025-0.2 mg/kg/minute Cat: same
Amiodarone	Dog: 6 (up to 10) mg/kg q12h PO for 7 (to 14) days (loading), then 4-6 mg/kg q24h PO; For IV administration use Nexterone (not standard amiodarone): 2-3 mg/kg slow IV infusion over 1-2 hours and monitor BP; (to cumulative dose of 5 to 6 mg/kg, if tolerated).
Sotalol	Dog: 1-2.5 mg/kg q12h PO Cat: 10-20 mg/cat q12h PO (or 2-4 mg/kg q12h)

References:

1. Zipes DP, Wellens HJ. Sudden cardiac death. Circulation 1998;98:2334-51.
2. Priori SG, Aliot E, Blomstrom-Lundqvist C, et al. Task Force on Sudden Cardiac Death of the European Society of Cardiology. Eur Heart J 2001;22:1374-450.
3. Surawicz B. Ventricular Arrhythmias: Why is it so difficult to find a pharmacologic cure? J Am Coll Cardiol 1989;14:1401-16.
4. Moise NS. From cell to cageside: autonomic influences on cardiac rhythms in the dog. J Small Anim Pract 1998;39:460-8.
5. Moise NS, Gilmour RF, Jr., Riccio ML. An animal model of spontaneous arrhythmic death. J Cardiovasc Electrophysiol 1997;8:98-103.
6. Moise NS, Meyers-Wallen V, Flahive WJ, et al. Inherited ventricular arrhythmias and sudden death in German shepherd dogs. J Am Coll Cardiol 1994;24:233-43.
7. Gilmour RF, Jr., Moise NS. Triggered activity as a mechanism for inherited ventricular arrhythmias in German shepherd Dogs. J Am Coll Cardiol 1996;27:1526-33.
8. Meurs KM, Spier AW, Miller MW, Lehmkuhl L, Towbin JA. Familial ventricular arrhythmias in boxers. J Vet Intern Med 1999;13:437-9.
9. Santilli RA, Bontempi LV, Perego M, Fornai L, Basso C. Outflow tract segmental arrhythmogenic right ventricular cardiomyopathy in an English Bulldog. J Vet Cardiol 2009;11:47-51.
10. Cote E, Jaeger R. Ventricular tachyarrhythmias in 106 cats: associated structural cardiac disorders. J Vet Intern Med 2008;22:1444-6.
11. Peterson ME, Keene B, Ferguson DC, Pipers FS. Electrocardiographic findings in 45 cats with hyperthyroidism. J Am Vet Med Assoc 1982;180:934-7.
12. Meurs KM, Spier AW, Wright NA, Hamlin RL. Comparison of in-hospital versus 24-hour ambulatory electrocardiography for detection of ventricular premature complexes in mature Boxers. J Am Vet Med Assoc 2001;218:222-4.
13. Basso C, Fox PR, Meurs KM, et al. Arrhythmogenic right ventricular cardiomyopathy causing sudden cardiac death in boxer dogs: a new animal model of human disease. Circulation 2004;109:1180-5.
14. Falk T, Jonsson L. Ischaemic heart disease in the dog: a review of 65 cases. J Small Anim Pract 2000;41:97-103.
15. Falk T, Jonsson L, Pedersen HD. Intramyocardial arterial narrowing in dogs with subaortic stenosis. J Small Anim Pract 2004;45:448-53.
16. Fox PR. Endomyocardial fibrosis and restrictive cardiomyopathy: pathologic and clinical features. J Vet Cardiol 2004;6:25-31.
17. Driehuys S, Van Winkle TJ, Sammarco CD, Drobatz KJ. Myocardial infarction in dogs and cats: 37 cases (1985-1994). J Am Vet Med Assoc 1998;213:1444-8.
18. Calvert CA, Jacobs G, Pickus CW, Smith DD. Results of ambulatory electrocardiography in overtly healthy Doberman Pinschers with echocardiographic abnormalities. J Am Vet Med Assoc 2000;217:1328-32.
19. Calvert CA, Hall G, Jacobs G, Pickus C. Clinical and pathologic findings in Doberman pinschers with occult cardiomyopathy that died suddenly or developed congestive heart failure: 54 cases (1984-1991). J Am Vet Med Assoc 1997;210:505-11.

20. Hall LW, Dunn JK, Delaney M, Shapiro LM. Ambulatory electrocardiography in dogs. Vet Rec 1991;129:213-6.
21. Goodwin JK. Holter monitoring and cardiac event recording. Vet Clin North Am Small Anim Pract 1998;28:1391-407, viii.
22. Miller RH, Lehmkuhl LB, Bonagura JD, Beall MJ. Retrospective analysis of the clinical utility of ambulatory electrocardiographic (Holter) recordings in syncopal dogs: 44 cases (1991-1995). J Vet Intern Med 1999;13:111-22.
23. Calvert CA, Jacobs GJ, Smith DD, Rathbun SL, Pickus CW. Association between results of ambulatory electrocardiography and development of cardiomyopathy during long-term follow-up of Doberman pinschers. J Am Vet Med Assoc 2000;216:34-9.
24. Meurs KM, Spier AW, Wright NA, Hamlin RL. Use of ambulatory electrocardiography for detection of ventricular premature complexes in healthy dogs. J Am Vet Med Assoc 2001;218:1291-2.
25. Stern JA, Meurs KM, Spier AW, Koplitz SL, Baumwart RD. Ambulatory electrocardiographic evaluation of clinically normal adult Boxers. J Am Vet Med Assoc 2010;236:430-3.
26. Goodwin JK, Lombard CW, Ginex DD. Results of continuous ambulatory electrocardiography in a cat with hypertrophic cardiomyopathy. J Am Vet Med Assoc 1992;200:1352-4.
27. Bright JM, Cali JV. Clinical usefulness of cardiac event recording in dogs and cats examined because of syncope, episodic collapse, or intermittent weakness: 60 cases (1997-1999). J Am Vet Med Assoc 2000;216:1110-4.
28. Santilli RA, Ferasin L, Voghera SG, Perego M. Evaluation of the diagnostic value of an implantable loop recorder in dogs with unexplained syncope. J Am Vet Med Assoc 2010;236:78-82.
29. MacKie BA, Stepien RL, Kellihan HB. Retrospective analysis of an implantable loop recorder for evaluation of syncope, collapse, or intermittent weakness in 23 dogs (2004-2008). J Vet Cardiol 2010;12:25-33.
30. Ferasin L. Recurrent syncope associated with paroxysmal supraventricular tachycardia in a Devon Rex cat diagnosed by implantable loop recorder. J Feline Med Surg 2009;11:149-52.
31. Leenhardt A, Denjoy I, Guicheney P. Catecholaminergic polymorphic ventricular tachycardia. Circ Arrhythm Electrophysiol 2012;5:1044-52.
32. Wess G, Schulze A, Geraghty N, Hartmann K. Ability of a 5-minute electrocardiography (ECG) for predicting arrhythmias in Doberman Pinschers with cardiomyopathy in comparison with a 24-hour ambulatory ECG. J Vet Intern Med 2010;24:367-71.
33. Rush JE, Keene BW. ECG of the month. The sudden death of a dog with dilatative cardiomyopathy. J Am Vet Med Assoc 1989;194:52-3.
34. Martin MW, Stafford Johnson MJ, Strehlau G, King JN. Canine dilated cardiomyopathy: a retrospective study of prognostic findings in 367 clinical cases. J Small Anim Pract 2010;51:428-36.

35. Meurs KM, Stern JA, Reina-Doreste Y, Spier AW, Koplitz SL, Baumwart RD. Natural history of arrhythmogenic right ventricular cardiomyopathy in the boxer dog: a prospective study. J Vet Intern Med 2014;28:1214-20.
36. Valentine BA, Winand NJ, Pradhan D, et al. Canine X-linked muscular dystrophy as an animal model of Duchenne muscular dystrophy: a review. Am J Med Genet 1992;42:352-6.
37. Ware WA, Reina-Doreste Y, Stern JA, Meurs KM. Sudden death associated with QT interval prolongation and KCNQ1 gene mutation in a family of English Springer Spaniels. J Vet Intern Med 2015;29:561-8.
38. Hill BL, Tilley LP. Ventricular preexcitation in seven dogs and nine cats. J Am Vet Med Assoc 1985;187:1026-31.
39. Crosara S, Borgarelli M, Perego M, et al. Holter monitoring in 36 dogs with myxomatous mitral valve disease. Aust Vet J 2010;88:386-92.
40. Jackson BL, Lehmkuhl LB, Adin DB. Heart rate and arrhythmia frequency of normal cats compared to cats with asymptomatic hypertrophic cardiomyopathy. J Vet Cardiol 2014;16:215-25.
41. Hanas S, Tidholm A, Egenvall A, Holst BS. Twenty-four hour Holter monitoring of unsedated healthy cats in the home environment. J Vet Cardiol 2009;11:17-22.
42. Ware WA. Twenty-four-hour ambulatory electrocardiography in normal cats. J Vet Intern Med 1999;13:175-80.
43. Fox PR, Maron BJ, Basso C, Liu SK, Thiene G. Spontaneously occurring arrhythmogenic right ventricular cardiomyopathy in the domestic cat: A new animal model similar to the human disease. Circulation 2000;102:1863-70.
44. Harvey AM, Battersby IA, Faena M, Fews D, Darke PG, Ferasin L. Arrhythmogenic right ventricular cardiomyopathy in two cats. J Small Anim Pract 2005;46:151-6.
45. Janus I, Noszczyk-Nowak A, Nowak M, et al. Myocarditis in dogs: etiology, clinical and histopathological features (11 cases: 2007-2013). Ir Vet J 2014;67:28.
46. Barr SC, Holmes RA, Klei TR. Electrocardiographic and echocardiographic features of trypanosomiasis in dogs inoculated with North American Trypanosoma cruzi isolates. Am J Vet Res 1992;53:521-7.
47. Saunders AB, Gordon SG, Rector MH, et al. Bradyarrhythmias and pacemaker therapy in dogs with Chagas disease. J Vet Intern Med 2013;27:890-4.
48. Odin M, Dubey JP. Sudden death associated with Neospora caninum myocarditis in a dog. J Am Vet Med Assoc 1993;203:831-3.
49. Dvir E, Lobetti RG, Jacobson LS, Pearson J, Becker PJ. Electrocardiographic changes and cardiac pathology in canine babesiosis. J Vet Cardiol 2004;6:15-23.
50. Lobetti RG. Cardiac involvement in canine babesiosis. J S Afr Vet Assoc 2005;76:4-8.
51. Rosa FA, Leite JH, Braga ET, et al. Cardiac lesions in 30 dogs naturally infected with Leishmania infantum chagasi. Vet Pathol 2014;51:603-6.
52. Wess G, Schulze A, Butz V, et al. Prevalence of dilated cardiomyopathy in Doberman Pinschers in various age groups. J Vet Intern Med 2010;24:533-8.
53. O'Grady MR, O'Sullivan ML. Dilated cardiomyopathy: an update. Vet Clin North Am Small Anim Pract 2004;34:1187-207.

54. Thomason JD, Kraus MS, Surdyk KK, Fallaw T, Calvert CA. Bradycardia-associated syncope in 7 Boxers with ventricular tachycardia (2002-2005). J Vet Intern Med 2008;22:931-6.
55. Meurs KM. Boxer dog cardiomyopathy: an update. Vet Clin North Am Small Anim Pract 2004;34:1235-44, viii.
56. Engel TR, Meister SG, Frankl WS. The "R-on-T" phenomenon: an update and critical review. Ann Intern Med 1978;88:221-5.
57. Spier AW, Meurs KM. Use of signal-averaged electrocardiography in the evaluation of arrhythmogenic right ventricular cardiomyopathy in boxers. J Am Vet Med Assoc 2004;225:1050-5.
58. Calvert CA, Kushner LI, Jacobs GJ, Brown J. Spectro-temporal mapping of the surface electrocardiogram in clinically normal dogs. Am J Vet Res 1997;58:211-7.
59. Calvert CA, Kraus M, Jacobs G, Kushner L. Possible late potentials in 4 dogs with sustained ventricular tachycardia. J Vet Intern Med 1998;12:96-102.
60. Calvert CA, Jacobs GJ, Kraus M, Brown J. Signal-averaged electrocardiograms in normal Doberman pinschers. J Vet Intern Med 1998;12:355-64.
61. Calvert CA, Jacobs GJ, Kraus M. Possible ventricular late potentials in Doberman pinschers with occult cardiomyopathy. J Am Vet Med Assoc 1998;213:235-9.
62. de Haan S, Knaapen P, Beek AM, et al. Risk stratification for ventricular arrhythmias in ischaemic cardiomyopathy: the value of non-invasive imaging. Europace 2010;12:468-74.
63. Kellum HB, Stepien RL. Third-degree atrioventricular block in 21 cats (1997-2004). J Vet Intern Med 2006;20:97-103.
64. Merot J, Probst V, Debailleul M, et al. Electropharmacological characterization of cardiac repolarization in German shepherd dogs with an inherited syndrome of sudden death: abnormal response to potassium channel blockers. J Am Coll Cardiol 2000;36:939-47.

Ventricular arrhythmias: what worries me in horses?

Colin Schwarzwald
University of Zurich, Switzerland

Introduction

A wide variety of cardiac arrhythmias have been recognized in horses, some that are physiologic and others that are potentially dangerous. These arrhythmias can develop as isolated electrical disorders or secondary to other etiological factors.

Of principal concern to the equine clinician are the hemodynamic consequences of arrhythmias (hypotension, low cardiac output, poor peripheral perfusion) and the potential for further electrical destabilization (malignant, potentially fatal arrhythmias). Generally, ventricular arrhythmias are of greater concern in regard to performance capacity and safety of horses compared to supraventricular arrhythmias.

Defining safety risks

Defining the safety risks to the horse and to the rider or driver is critical in cases of ventricular ectopy. Generally, premature ventricular complexes (PVCs) are considered abnormal in the horse. However, isolated PVCs may be more common than recognized from routine ECG studies, even in apparently healthy horses. Not all ectopic ventricular rhythms are considered equally dangerous and the complexity of ventricular arrhythmias is presumed to relate to the risk of hypotension, weakness, collapse and sudden cardiac death (SCD) because of ventricular fibrillation. However, risk stratification for ventricular arrhythmias is imperfect, particularly in horses with isolated PVCs at rest and/or during exercise.

In the absence of clear evidence, recommendations should be biased toward safety, as opposed to maintaining athletic activity. Certainly, a history of collapse or co-existence of important structural heart disease (and cardiomegaly) raises great concern in a horse with PVCs. However, in the absence of obvious clinical signs or of serious structural heart disease, the risk of ventricular ectopy is usually defined by electrocardiographic characteristics, accepting the limitations of this analysis. This assessment includes timing, rate and morphology of the ectopic activity.

As a general rule, ventricular arrhythmias should be considered complex or “malignant” and potentially life threatening, if they are characterized by one or more of the following criteria:

- Repetitive or sustained ectopic rhythms
- Very rapid ventricular rate (exceeding 120 beats/min at rest)

- Multiform or polymorphic QRS morphology (including torsades de pointes)
- Short coupling interval with R-on-T phenomenon (i.e., PVCs occurring on the peak of the preceding T wave)

Complex ventricular arrhythmias can induce hemodynamic impairment resulting in clinical evidence of low cardiac output (e.g., weakness, stumbling, pale mucous membranes, prolonged CRT, syncope) and hypotension. Electrical instability is a particular concern in malignant ventricular arrhythmias and can cause ventricular tachycardia to progress into ventricular flutter or ventricular fibrillation. These commonly represent terminal events.

Many cases with ventricular arrhythmia can be managed by treating the underlying disease and rest. Repeated or continuous ECG monitoring (to document progression of disease or resolution of arrhythmia) is recommended. Complex, “malignant” ventricular arrhythmias should be more aggressively managed by additional use of antiarrhythmic drugs.

Ventricular arrhythmias during exercise

A wide range of ventricular arrhythmias has been reported during and immediately following intense exercise in normally performing horses and horses presented for poor performance. However, the clinical relevance of most of these arrhythmias and their relationship to poor performance and sudden cardiac death is not well defined. Generally, occasional monomorphic PVCs overdriven with exercise or only detected in the immediate post-exercise period are not considered a cause for poor performance. Conversely, PVCs occurring during exercise are considered a cause for concern.

Generally, the criteria for complexity and “malignancy” of ventricular arrhythmias listed above also apply during exercise. However, diagnosing ventricular arrhythmias during exercise is often difficult, since telemetric ECG recordings are affected by motion artefacts. Furthermore, prematurity of ectopic beats is difficult to detect at high heart rates, even when RR intervals are measured using ECG calipers. On modern digital ECG systems, this can be achieved by automated RR analyses, but algorithms are imperfect and prone to error and usually require visual validation by the operator. Also, the distinction between (pathologic) prematurity and (physiologic) heart rate variability can be difficult. The current knowledge indicates that sudden shortening of the RR interval by more than 5-7% during trot and canter phases indicates prematurity, whereas variation of less than 4-5% likely indicates normal heart rate variability. However, exact criteria are lacking to date. The traditional criteria to differentiate ventricular from supraventricular arrhythmias (association with P wave, shape and orientation of QRS complex and T wave) are difficult to apply to exercising ECGs and at high heart rates, and often times premature ectopic beats cannot be unambiguously classified as supraventricular and ventricular, respectively. Finally, variability over time of the frequency and “malignancy” of ventricular arrhythmias in horses is currently unknown. Also, the influence of different types of exercise (e.g., lunging vs. treadmill exercise vs. ridden exercise) on ventricular arrhythmias is not well defined.

Ventricular arrhythmias associated with aortic regurgitation

Aortic regurgitation (AR) is a common (and often incidental) finding in older horses. It is often mild and associated with a normal life expectancy and performance capacity. However, sudden cardiac death associated with fatal ventricular arrhythmias has been observed and is a concern in horses with moderate to severe AR and can occur without poor performance or CHF.

Therefore, all horses with a heart murmur consistent with AR should be evaluated carefully. Clinically, bounding or hyperkinetic arterial pulses and a pulse pressure of > 60 mm Hg (measured by non-invasive blood pressure recordings) suggest hemodynamically relevant AR with LV volume overload and increased likelihood of progression. Echocardiography is recommended to identify the most likely etiology and further assess disease severity. A continuous 24h-Holter ECG and an exercising ECG are recommended when moderate to severe AR and/or performance issues are evident. Analyses should be focused on identifying PVCs at rest and during exercise and appropriateness of the exercising heart rate.

Owing to a risk for SCD, horses with moderate to severe AR should not be ridden by a child or used as a lesson horse or in a high-risk sport. Affected horses should initially be re-examined twice yearly (including echocardiography and ECG exercise test) and at least annually thereafter if progression has been minimal. Heart rate and rhythm should be monitored on a regular basis; an increased resting HR or an irregularly irregular rhythm suggesting atrial fibrillation or PVCs indicate progression of disease. The detection of exercise-induced ventricular arrhythmias is considered an important negative prognostic indicator. Horses with AR and PVCs during exercise are considered less safe to ride than their age-matched peers.

Ventricular arrhythmias associated with atrial fibrillation

Atrial fibrillation (AF) is the most common arrhythmia affecting performance. Although uncommon, collapse during exercise has been reported with AF. Safety is a particular concern with persistent AF when the average maximal heart rate (HR) during exercise at an intensity that is at or slightly exceeding the horse's normal activities is greater than 220/minute. Additionally, ventricular ectopy during exercise or during sympathetic stimulation is not unfrequently observed in association with AF and indicates a possible risk for SCD, particularly when short R-R intervals or R-on-T phenomenon are present. AF associated with exercise-induced ventricular arrhythmias resulting in SCD has been documented by telemetric ECG in at least one horse.

Exercise testing with stress ECG should always be conducted when a horse is used for performance. Cardioversion of persistent AF is strongly recommended for all horses used for athletic activities when the exercising HR during sustained maximal exercise exceeds 220 beats /minute or concurrent ventricular arrhythmias are detected during exercise or

with sympathetic stimulation. Ventricular arrhythmias usually resolve after cardioversion.

When cardioversion is not an option or could not be attained, horses with persistent AF should only be used by informed adult riders and limited to an exercise level considered relatively safe based on exercising ECG. The use of a HR monitor might be useful to track heart rate during exercise and modify the rigor of the work performed. Horses with persistent AF and exceedingly high exercising HR or exercise-induce ventricular ectopy with short R-R intervals or R-on-T phenomenon should be retired for safety reasons.

Cardioversion of AF should only be performed in a controlled setting with continuous (ECG) monitoring, regardless of the treatment method, since all treatments can be associated with adverse events, including (but not limited to) ventricular arrhythmias.

Quinidine sulfate is still the mainstay of pharmacological cardioversion of AF. Potential risks of quinidine cardioversion include rapid ventricular response to AF and complex ventricular ectopy owing to the potential for QT prolongation, proarrhythmia and polymorphic ventricular tachycardia. Such events sometimes necessitate discontinuation of therapy or co-administration of other drugs to control the ventricular response rate or treat ventricular arrhythmias.

In horses with AF and elevated resting heart rate or with sustained (supraventricular) tachycardia during quinidine treatment, digoxin is commonly used for ventricular rate control. Due to the variable pharmacokinetics and the narrow therapeutic window, therapeutic drug monitoring, individualized selection of a digoxin dosage regimen, and close monitoring of the clinical response is advisable. Digoxin can result in supraventricular and ventricular arrhythmias (bigeminy). Factors predisposing to digitalis toxicity include advanced heart disease, atrial fibrillation, impaired renal function, hypokalemia, hypomagnesemia, hypercalcemia, and hypoproteinemia. Quinidine decreases renal clearance and increases circulating blood digoxin concentrations, while phenylbutazone competes with protein binding sites and increases the free digoxin fraction.

Other antiarrhythmic drugs, including amiodarone, flecainide and propafenone, have been used in horses with AF but are not currently recommended for treatment because of lack of efficacy and/or high risk of severe tachycardia and potentially fatal ventricular arrhythmias.

Transvenous electrical cardioversion (TVEC) is considered equivalent or superior to quinidine cardioversion in regard to short-term success of cardioversion, although studies directly comparing the two methods are lacking. In some institutions, TVEC is currently the first-line treatment for AF. The procedure should be performed by experienced operators using specialized equipment and involves a timed shock delivery on the R-wave. The risks of TVEC include general anesthesia or rarely development of a fatal ventricular arrhythmia. The latter is of particular concern if the electrical shock is inadvertently delivered to the T wave, representing the vulnerable period for induction of malignant ventricular arrhythmias.

Sotalol may be used for maintenance of sinus rhythm after successful cardioversion of atrial fibrillation and for chronic treatment of supraventricular and ventricular arrhythmias. Although not well described in the current literature, preliminary studies and clinical experience indicate that orally administered sotalol is well tolerated in horses and is not associated with increased risk of ventricular arrhythmias at doses up to 2-3 mg/kg PO q12h. However, since QT prolongation and proarrhythmic effects are a concern, monitoring of QT interval is recommended.

Ventricular arrhythmias associated with systemic disease

Ventricular arrhythmias can be found in horses with a variety of medical and surgical disorders and are particularly common in horses with gastrointestinal disease. Their etiology is often undefined and likely multifactorial. Factors favoring the development of ventricular arrhythmias include electrolyte imbalances (e.g., hypokalemia, hypomagnesemia), acid-base disturbances, hypoxemia; metabolic and endocrine disorders; systemic inflammation, endotoxemia, sepsis, and fever; hypotension, hemorrhage, anemia, and ischemia; autonomic influences (i.e., high sympathetic or parasympathetic tone or autonomic imbalance); toxicosis/envenomation; and a variety of drugs (including antiarrhythmics, catecholamines, alpha-2 agonists, and anesthetics). Assessment of the overall clinical picture is important, since arrhythmias often resolve with correction of the underlying problem.

Ventricular ectopy observed with systemic disease encompasses the entire range from single, innocuous PVCs to malignant ventricular arrhythmias with tachycardia, multiform QRS conformation and R-on-T phenomenon, potentially triggering fatal ventricular events.

Accelerated idioventricular rhythms (AIVR, also termed slow ventricular tachycardias) are common in horses with systemic disease. They are usually well-tolerated, tend to be monomorphic, start with a relatively long coupling interval, and become established at relatively slow ventricular rates that are equal to or slightly above the sinoatrial rate (50-80/min at rest). AIVRs may easily be misdiagnosed as sinus tachycardia on auscultation or palpation of peripheral pulses, since these rhythms are often quite regular. Persistent, unexplained mild to moderate tachycardia should therefore prompt an ECG examination to ascertain a correct rhythm diagnosis. This said, accelerated idioventricular rhythms generally are of little clinical (electrophysiologic and hemodynamic) relevance and usually resolve spontaneously with appropriate treatment of potential underlying conditions. Electrolyte supplementation (potassium, magnesium) and correction of fluid deficits and acid-base disturbances may be beneficial. Lidocaine is sometimes administered as an intraoperative adjunct to general anesthesia or used as an analgesic and prokinetic drug in the management of post-operative ileus; in these situations, its antiarrhythmic effects may provide some additional preventive or therapeutic benefits.

More malignant ventricular arrhythmias may require immediate antiarrhythmic treatment

in addition to management of the underlying disease and potential pro-arrhythmic factors.

Ventricular arrhythmias associated with long QT interval

The upper limits for the QT interval at resting heart rates are approximately 600 ms in adult horses and 350–400 ms in foals. However, the QT interval shortens at higher heart rates and strongly depends on changes in autonomic tone. A variety of population-based or individual-based methods have been used in other species to correct for heart rate-related changes. Although some data are available for horses, correction formulas cannot be uniformly used for different populations or easily applied to individual horses. The diagnosis of QT prolongation in horses is further complicated by the commonly encountered difficulties to accurately detect the end of the T wave.

Congenital (due to ion channel mutations) or acquired (due to drug effects on repolarizing currents) long QT syndrome (LQTS) associated with life-threatening cardiac arrhythmias and sudden death has not been well documented in horses. However, repolarizing currents in horses are similar to those in other species, and it has been suggested that horses may be at risk for acquired LQTS. Many drugs that potentially prolong cardiac repolarization in other species have also been used in horses, including quinidine, procainamide, flecainide, amiodarone, sotalol, cisapride, metoclopramide, erythromycin, clarithromycin, fluconazole, trimethoprim-sulfamethoxazole, sevoflurane, and isoflurane. Quinidine-induced torsades de pointes, potentially related to drug-induced QT prolongation, have been reported in horses. The slow resting heart rate and the hypokalemia commonly associated with gastrointestinal disease in horses theoretically enhance the risk of drug-induced arrhythmias. It therefore seems advisable to consider potential proarrhythmic effects when QT-prolonging drugs are administered to horses at risk.

Prognosis

The prognosis for horses with ventricular arrhythmias is usually favorable for infrequent, single ectopic beats in the absence of other signs of significant cardiac disease, or for arrhythmias which can be attributed to a treatable underlying non-cardiac disease. The prognosis for sustained ventricular tachycardia is usually guarded, particularly if there is evidence of significant structural heart disease or congestive heart failure. The prognosis for multiform ventricular tachycardia or torsades de pointes is usually poor.

Recommendations for PVCs and VT according to the 2014 ACVIM/ECEIM Consensus Statement on Management of Equine Athletes with Cardiovascular Abnormalities

• Underlying causes should be sought and managed if possible. Assessment of the overall clinical picture is important because ventricular arrhythmias (VA) can be associated with medical or surgical disorders and often resolve with correction of the underlying problem.

- A clinical laboratory profile, including cardiac troponin I (cTnI) should be obtained from all horses.
- While an echocardiogram may be valuable in any horse with VA, this test is

specifically recommended for horses with VT or complex VA; when VA is recurrent or persistent; or when VA is identified in the clinical settings of poor performance, a pathologic cardiac murmur, or a significantly elevated cTnI. The echocardiogram should include imaging for abnormal myocardial echo texture, thickness, or scar, and exclusion of dissecting aortic aneurysm or aorto-cardiac fistula. Left ventricular dilation may be secondary to tachycardia-induced cardiomyopathy or ventricular dyssynchrony. In horses with sustained VT the echocardiogram should be repeated once the horse has returned to NSR.

- A continuous 24-hour ECG should also be obtained to more completely evaluate the VA as they are often intermittent.
- Further work-up of a horse with PVCs or AIVR, in the absence of underlying systemic disease, should include an exercising ECG. Horses with severe VA should not be exercise tested.

• Horses with occasional PVCs, with sustained AIVR that is overdriven by exercise or multiple PVCs during exercise may be used with caution by an informed adult rider. Owing to ongoing concerns about underlying myocardial or electrical disease and increased risks of exercise associated collapse and SCD; these horses should not be used by a child rider or as a lesson horse.

• Horses with sustained monomorphic VT should be rested and treated. NSR should be present for at least 4 weeks before re-evaluation is performed. A continuous 24-hour ECG is indicated prior to returning the horse to work. If normal, an exercising ECG should be performed, followed by another exercising ECG once the horse has returned to full work. Horses affected by a single episode generally have a favorable prognosis, but on occasion monomorphic VT can recur.

• Horses with symptomatic or complex VA should be rested and treated. Follow-up examinations are similar as for horses with sustained monomorphic VT although the safety of these horses remains uncertain. These horses should only be ridden by an informed adult rider.

• Rigorous athletic work is not recommended for horses that showed VA in the setting of moderate or severe structural heart disease, including focal myocardial fibrosis and moderate to severe AR. These horses should only be used by an informed adult rider due to the risk of possible recurrence of VT. These horses are not safe for use by a child rider or as a lesson horse.

• For horses with a history of VT that remain in work follow up 24-hour and exercising ECGs should be performed at least annually.

References:

- Reef VB, Bonagura J, Buhl R, McGurrin MKJ, Schwarzwald CC, van Loon G, Young LE. Joint ACVIM/ECEIM Consensus Statement: Recommendations for Management of Equine Athletes with Cardiovascular Abnormalities. Journal of Veterinary Internal Medicine 2014;28(3):749-761.
- Schwarzwald CC et al.: The Cardiovascular System. In: Muir WW, Hubbell JAE (eds): Equine Anesthesia, 2nd ed. Elsevier Saunders, 2009:37-100.

Further reading:

- Bonagura JD, Reef VB, Schwarzwald CC: Cardiovascular Diseases. In: Reed SM et al. (eds): Equine Internal Medicine, 3rd ed. Saunders Elsevier, 2010:372-487.
- Young LE, van Loon G. Diseases of the heart and vessels. In: Hinchcliff KW, Kaneps AJ, Geor RJ (eds): Equine Sports Medicine and Surgery, 2nd ed. Saunders Elsevier, 2014:695-743.
- Bowen IM: Cardiac Dysrhythmias. In: Robinson NE (ed): Current Therapy in Equine Medicine 5. Elsevier Saunders, 2003: 602-613.
- Jesty SA: Cardiovascular System. In: Orsini JA, Divers TJ (eds): Equine Emergencies: Treatment and Procedures, 4th ed. Elsevier Saunders, 2014:124-156.
- Marr CM, Bowen M (eds): Cardiology of the Horse. 2nd ed. Saunders Elsevier, 2010.

Ventricular arrhythmias: what worries me in people?

Martin Lowe
University College of London, UK

Interventional arrhythmia management in people: where next?

Martin Lowe
University College of London, UK

Accessory pathways: the veterinary practitioner's view

Chris Fellows
Lakes Cardiology Service

Accessory pathways (AP's), or Bypass Tracts (BT's), consist of myocardial tissue that cross the electrically insulating annulus fibrosus of the heart allowing electrical communication between the atria and ventricles bypassing the atrioventricular node (AVN). They can be part of a "macro re-entrant" circuit consisting of atrial tissue, AV node, ventricular tissue and accessory pathway facilitating a supra-ventricular tachycardia (SVT) called orthodromic atrioventricular reciprocating tachycardia (OAVRT). It is also possible for the AP's to be involved in several other abnormal heart rhythms, as a bystander or as an integral part of the circuit.

When sustained for a period of time OAVRT (the most common narrow complex tachycardia associated with with AP's in dogs) can result in congestive heart failure due to tachycardia-induced cardiomyopathy (TCM), which may look phenotypically very similar to "idiopathic" dilated cardiomyopathy (DCM).

The lecture will concentrate mainly on the anatomy, electrophysiology and treatment of arrhythmias caused by accessory pathways.

There will be no information given about the genetics of labradors with this condition - please refer to ACVIM 2011 abstract written by Geoff Culshaw and Kim Summers from the R(D)SVS, Edinburgh, copied below. Geoff has indicated to me that there has been no update yet on the genetic analysis (personal communication 20/10/2015)

Pedigree Analysis

We have acquired pedigrees and DNA of Labradors diagnosed with OAVRT at the R(D)SVS or by other veterinary cardiologists within the UK. Common ancestry has been found in all the dogs where we have sufficient pedigree information. This may reflect the narrow gene pool of coloured Labradors within the UK but could indicate a founder effect leading to inheritance of a common mutation for accessory pathways. A small number of lines appear more than once in most affected dogs and on both the sides of the sire and dam. Affected dogs can be classified into 2 closely related groups. No direct link between the 2 groups closer than 5 generations back has been found as yet but some of the pedigrees are incomplete. European and American ancestry is also within these groups. Pedigree analysis suggests either an autosomal recessive or autosomal dominant with reduced penetrance pattern of inheritance. X-linked recessive inheritance is also possible, given the preponderance of male patients.

Determination of Linkage with Coat Colour

The hypothesis that OAVRT is a recessive trait linked to coat colour is being tested. In Labradors there are 2 main genes responsible for coat colour. They are MC1R and TYRP1[12]. MC1R encodes an "on/off"switch for pigment production. Yellow Labradors (and most pale coloured dogs) are homozygous for a recessive mutation in this gene and produce only yellow or red phaeomelanin pigment. Black and chocolate Labradors are either heterozygous or homozygous for the original dominant form of MC1R so produce dark (eumelanin) pigment in their coat. TYRP1 determines the colour and amount of dark pigment produced. It too has dominant and recessive forms. If homozygous or heterozygous for the original dominant form of TYRP1, the dog is black. If homozygous for the recessive form, the dog is chocolate.

If the mutation for accessory pathways is recessive and linked to coat colour, then affected dogs must be homozygous for the gene it is linked to. This means that it cannot be linked to any form of TYRP1 as both black and chocolate dogs are affected. Also, if the trait is linked to MC1R, affected dogs must be homozygous for the dominant form of the gene. Sequencing of the MC1R genes in known affected dogs is currently under way.

The hypothesis that OAVRT is a trait that is autosomal dominant with reduced penetrance (that is, not all animals carrying the mutation show the condition) linked to coat colour is also being tested. In order for this to be valid, the disease mutation must be linked to the recessive allele of TYRP1 so all affected black dogs would be heterozygous for TYRP1. Sequencing of the TYRP1 genes in known affected dogs is also under way.

It is possible that there is only a chance association without linkage between accessory pathways and coat colour in Labradors. Breeders of black and chocolate Labrador retrievers tend not to use yellow Labrador breeding stock and a random mutation within black and chocolate Labrador lines would result in such an association.

Further Investigation

A screening programme for Labrador retrievers within the UK has been established. This will attempt to identify subclinically affected dogs through identification of SVT, pre-excitation or echo beats on 24 hour Holter ECG. The aim is to acquire pedigrees and DNA samples from more known affected dogs and likely unaffected dogs for further pedigree and genetic analysis. If enough samples can be collected, a Genome Wide Association Study (GWAS) will be undertaken to look for common single nucleotide polymorphisms (SNPs) where specific alleles are associated with disease status. Candidate genes closely linked to these SNPs can then be sequenced to determine whether significant mutations are present..

References:

1. Atkins C, et.al. J Vet Intern Med 1995;9:43.
2. Wright K, et.al. J Vet Intern Med 1999;13:361.
3. Santilli R, et.al. J Am Vet Med Assoc 2007;231:393.
4. Santilli R, et.al. J Vet Intern Med 2008;22:915.
5. Johnson M, et.al. J Vet Intern Med 2006;20:272.
6. Wright K, et.al. J Vet Cardiol 2006;8:95.
7. Haissaguerre M, et.al. J Cardiovasc Electrophysiol 1994;5:532.
8. Packer D, et.al. Am J Cardiol 1986;57:563.
9. Ehtisham J, et.al. J Cardiovasc Electrophysiol 2005;16:1258.
10. MacRae C, et. al. J Clin Invest 1995;96:1216.
11. Gollob M, et.al. N Engl J Med 2001;344:1823.
12. Schmutz S, et.al. Mamm Genome 2002;13:380.

Calcium mismanagement in arrhythmogenesis and heart failure

Liz Bode
R(D)SVS, Edinburgh

Introduction

Excitation-contraction (EC) coupling is the mechanism by which the heart converts electrical activity into mechanical force. This is a highly coordinated and regulated physiological process and results in the heart contracting as a syncytium, pumping blood around the systemic and pulmonary circulations. Alterations to this pathway can have serious consequences in terms of cardiac function and sudden death. Derangements in EC coupling have been well documented in heart failure[1] and abnormalities of both systolic and diastolic function result in worsening cardiac performance. Furthermore, many human heart failure patients die from sudden onset cardiac arrhythmias. In the majority of patients these arrhythmias are due to abnormal automaticity or triggered activity i.e. delayed after depolarisations (DADs) or early after depolarisations (EADs). Triggered arrhythmias, particularly DADs and, under certain conditions EADs, are also the result of abnormal Ca2+ handling[1].

Excitation-contraction coupling

In order for cardiac contraction and relaxation to occur intracellular calcium levels must rise and fall. Changes in intracellular calcium are brought about by the physiological process of EC coupling (figure 1). Initially, an action potential depolarises the cell membrane, penetrating deep inside the cell via the membranous invagination known as the transverse tubule. This depolarisation opens the L-type calcium channels causing a small amount of calcium to enter the cytosol from the extracellular milieu. This calcium then results in the release of a larger amount of calcium from the intracellular calcium store, the sarcoplasmic reticulum, in a process known as calcium-induced calcium-release. Movement of calcium from the sarcoplasmic reticulum is a passive process that involves the calcium release channel or ryanodine receptor. Calcium-induced calcium-release gives rise to the systolic calcium transient. This elevation in intracellular calcium results in calcium binding to troponin C. Binding of calcium to troponin C strengthens the interaction of troponin C with troponin I and destabilises the relationship between troponin I and actin. This allows the troponin T–tropomyosin complex to roll deeper into the actin groove. This movement of the troponin T–tropomyosin complex exposes the sites on the actin filaments where myosin interacts, enabling cross-bridge formation and sarcomeric shortening.

The heart then needs to relax and refill before it can contract again. Free intracellular calcium has to be removed from the cytosol after it dissociates from the myofilaments. There are several pathways by which this occurs. The dominant mechanism is the sarco(endo)plasmic reticulum calcium-ATPase (SERCA), which takes calcium back up into the sarcoplasmic reticulum. SERCA removes 70-90% of calcium from the cytosol,[2,3]

replenishing the intracellular calcium store ready for the next contraction. The sarcolemmal sodium/ calcium exchanger accounts for between 10-30% of calcium removal from the cytosol,[2,3] transporting calcium back in to the extracellular space. Two minor mechanisms known to remove calcium from the cytosol include the plasma membrane calcium-ATPase transporter and the mitochondrial calcium uniport. These transport a very small amount of calcium (1-3%) either out of the cell or into the mitochondria respectively.[2,3]

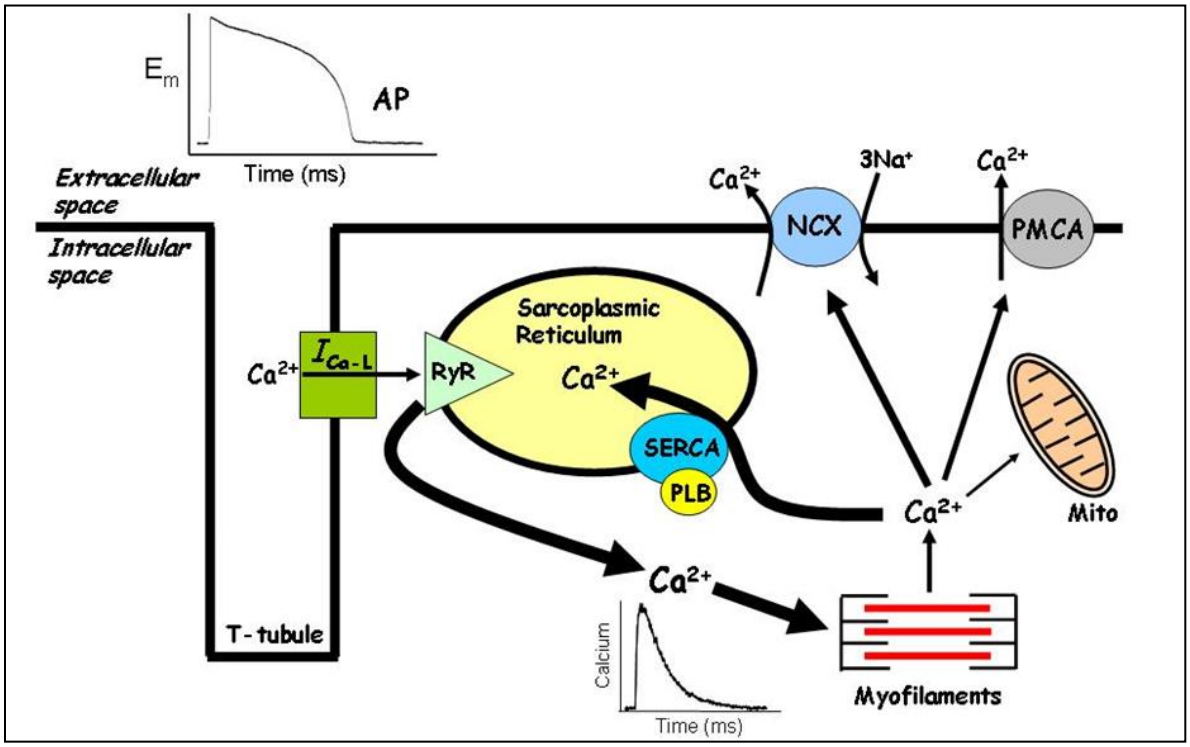

Figure 1. *The excitation-contraction coupling pathway Action potential (AP); ICa-L (L-type calcium current); RyR (Ryanodine receptor); T-tubule (Transverse tubule); SERCA (Sarco(endo)plasmic reticulum calcium ATP-ase pump); PLB (Phospholamban); NCX (Sodium/calcium exchanger); PMCA (Plasma membrane calcium ATP-ase pump); Mito (Mitochondria); Ca2+ (Calcium). Arrows represent the path travelled by calcium, with arrow thickness representing the proportion of calcium taken up by each removal pathway.*

β-adrenergic stimulation

Phosphorylation in response to β-adrenergic receptor (β-AR) stimulation plays a key role in normal EC coupling within the heart. In response to sympathetic stimulation protein kinase A and calcium/calmodulin dependent protein kinase (CAMKII) both phosphorylate multiple targets within the cardiac myocyte, including the L-type calcium channel, phospholamban, ryanodine receptor, troponin-I and possibly the sodium/ calcium exchanger.[4] In most situations β-AR stimulation augments the actions of these cellular targets, resulting in positive inotropy, chronotropy and lusitropy. Perturbations in the β-adrenergic cascade, or in the responsiveness of its receptors, results in a heart that cannot adapt appropriately to sympathetic stimulation.

Excitation-contraction coupling in heart failure

Heart failure is the end result of many disease processes such as hypertension, myocardial ischaemia and cardiac myopathies. Common to these aetiologies are alterations to calcium handling and ionic currents within cardiac myocytes (for general review see[1]). Shifts in the mechanical properties of the myocardium are also observed, largely due to geometric and structural disturbances.[5] These alterations result in systolic and/ or diastolic dysfunction and arrhythmogenesis or a combination of these.

Contractile force and, therefore, systolic function is decreased in heart failure. It is the systolic calcium transient that is crucial for initiating contraction and as such a ubiquitous finding amongst various models of heart failure is one of diminished calcium transient amplitude.[6-8] A reduction in the systolic calcium transient amplitude may be the result of either decreased intracellular calcium stores and/ or altered L-type calcium channel properties. Most studies have found that there is little change to the peak L-type calcium current density in heart failure.[7,9] Therefore, in these studies other factors must cause the diminished calcium transient amplitude. Indeed, in these studies the reduction in the systolic calcium transient amplitude was the result of decreased levels of calcium stored within the sarcoplasmic reticulum.[7,9]

Decreased sarcoplasmic reticulum content may be multifactorial in origin. In heart failure, a general observation is down-regulation of SERCA activity and up-regulation of sodium/ calcium exchanger function.[6,7,9] These alterations work synergistically to lower sarcoplasmic reticulum calcium levels by removing more calcium from the cell than is taken back up into the sarcoplasmic reticulum via SERCA. A lower SERCA activity can also cause diastolic dysfunction due to a slower rate of decline of intracellular calcium. However, up-regulation of the sodium/ calcium exchanger function may help to normalise this by removing a greater quantity of calcium at each beat.[10] Enhanced calcium leak from the sarcoplasmic reticulum in heart failure has also been observed.[11] This leak results in calcium leaving the sarcoplasmic reticulum during diastole. All of these factors will contribute towards a lower sarcoplasmic reticulum calcium content, resulting in less calcium being released at each contraction and a diminished calcium transient amplitude.

Arrhythmogenic mechanisms in heart failure

Disturbances to calcium handling will directly affect contraction and relaxation, but may also lead to arrhythmias.[12] Many heart failure patients die from sudden onset cardiac arrhythmias. In the majority of patients these arrhythmias are caused by either abnormal automaticity or triggered events i.e. DADs and EADs. In a smaller percentage of cases sudden death is due to re-entrant mechanisms. Triggered arrhythmias are caused by abnormal calcium handling whereas re-entrant arrhythmias are generally the result of regional variations in action potential duration.

Triggered arrhythmias due to DADs are the result of spontaneous calcium release from the sarcoplasmic reticulum.[1] This spontaneous release of calcium results in DADs because the calcium that is released from the sarcoplasmic reticulum is removed by the electrogenic sodium/ calcium exchanger. An inward current is then generated, which can depolarise the cell membrane. If this change in membrane potential is sufficient enough to reach threshold an action potential is triggered. Furthermore, there is an up-regulation of sodium/ calcium exchanger function in heart failure.[7,9,10] Enhanced sodium/ calcium exchanger function is thought to generate a larger inward current for a given amount of diastolic calcium release, facilitating a triggered action potential.[10] In contrast, EADs have been classically associated with reactivation of the L-type calcium current.[13] The generation of EADs in this manner relies on a prolonged action potential duration and an L-type calcium channel that has recovered from calcium-dependent inactivation. During the lengthened plateau phase the membrane potential is within the range of the L-type calcium channel's window current (range of membrane potentials where the channel can be both activated and inactivated). This together with a smaller calcium transient makes reactivation of this current more likely. EADs can also be observed during the later phases of repolarisation. These EADs have been linked to a DAD-like origin,[14] where release of calcium from the sarcoplasmic reticulum and resultant sodium/ calcium exchanger activity causes an EAD.

Arrhythmia formation is also associated with gradients in action potential duration that provide the ideal substrate for re-entry.[15] Repolarisation gradients can be caused by action potential duration alternans, which occurs at much slower heart rates in the failing myocardium than in normal hearts.[16] Calcium alternans has been shown to be a possible mechanism for the induction of action potential alternans[16] via slowing of the rate of recovery of sarcoplasmic reticulum calcium release.[17] Other mechanisms of re-entry include regional variation in action potential duration through changes to ionic currents[15] and also structural remodelling e.g. that occurs with myocardial ischaemia.

References

1. Bers DM. (2006) Altered cardiac myocyte calcium regulation in heart failure. Physiology; 21:380-387.

2. Bassani JW, Bassani RA, Bers DM. (1994) Relaxation in rabbit and rat cardiac cells: species-dependent differences in cellular mechanisms. The Journal of Physiology; 476:279-293.

3. Puglisi JL, Bassani RA, Bassani JW, et al. (1996) Temperature and relative contributions of calcium transport systems in cardiac myocyte relaxation. The American Journal of Physiology; 270:H1772-1778.

4. Bers DM. Excitation-contraction coupling and cardiac contractile force, 2nd ed. Dordrecht; Boston: Kluwer Academic Publishers

5. Kass DA, Bronzwaer JG, Paulus WJ. (2004) What mechanisms underlie diastolic dysfunction in heart failure? Circulation Research; 94:1533-1542.

6. Briston SJ, Caldwell JL, Horn MA, et al. (2011) Impaired beta-adrenergic responsiveness accentuates dysfunctional excitation-contraction coupling in an ovine model of tachypacing-induced heart failure. The Journal of Physiology; 589:1367-1382.

7. Piacentino V, 3rd, Weber CR, Chen X, et al. (2003) Cellular basis of abnormal calcium transients of failing human ventricular myocytes. Circulation Research; 92:651-658.

8. Pogwizd SM, Schlotthauer K, Li L, et al. (2001) Arrhythmogenesis and contractile dysfunction in heart failure: Roles of sodium-calcium exchange, inward rectifier potassium current, and residual beta-adrenergic responsiveness. Circulation Research; 88:1159-1167.

9. Diaz ME, Graham HK, Trafford AW. (2004) Enhanced sarcolemmal calcium efflux reduces sarcoplasmic reticulum calcium content and systolic calcium in cardiac hypertrophy. Cardiovascular Research; 62:538-547.

10. Pogwizd SM, Qi M, Yuan W, et al. (1999) Upregulation of Na(+)/Ca(2+) exchanger expression and function in an arrhythmogenic rabbit model of heart failure. Circulation Research; 85:1009-1019.

11. Shannon TR, Pogwizd SM, Bers DM. (2003) Elevated sarcoplasmic reticulum Ca2+ leak in intact ventricular myocytes from rabbits in heart failure. Circulation Research 2003; 93:592-594.

12. Aistrup GL, Balke CW, Wasserstrom JA. (2011) Arrhythmia triggers in heart failure: the smoking gun of intracellular calcium dysregulation. Heart Rhythm; 8:1804-1808.

13. January CT, Riddle JM. (1989) Early afterdepolarizations: mechanism of induction and block. A role for L-type calcium current. Circulation Research; 64:977-990.

14. Volders PG, Kulcsar A, Vos MA, et al. (1997) Similarities between early and delayed afterdepolarizations induced by isoproterenol in canine ventricular myocytes. Cardiovascular Research; 34:348-359.

15. Antzelevitch C. (2005) Cardiac repolarization. The long and short of it. Europace : European pacing, arrhythmias, and cardiac electrophysiology;7 Suppl 2:3-9.

16. Wilson LD, Jeyaraj D, Wan X, et al. (2009) Heart failure enhances susceptibility to arrhythmogenic cardiac alternans. Heart Rhythm; 6:251-259.

17. Wasserstrom JA, Sharma R, Kapur S, et al. (2009) Multiple defects in intracellular calcium cycling in whole failing rat heart. Circulation Heart Failure; 2:223-232.

EP study and radiofrequency ablation: Case presentation

Pedro Oliveira
Davies Veterinary Specialists, UK

Radiocatheter ablation has become the treatment of choice for atrioventricular reciprocating tachycardias mediated by accessory pathways in human medicine. It is a safe procedure that results in definitive treatment in 90-100% of cases. In veterinary medicine this option already exists in a few centres and hopefully will be increasingly available to our patients. In this communication, a case will be presented illustrating the setup of an electrophysiology laboratory and the steps for mapping and ablating an accessory pathway (AP) in a dog with orthodromic atrioventricular reciprocating tachycardia (OAVRT). Briefly, electrophysiology studies in dogs are performed under anaesthesia. Vascular access is normally obtained via the jugular vein, femoral vein or both. A number of catheters are necessary for a study varying from 2-4 depending on the size of the patient and the underlying rhythm disturbance. A 4 catheter study would include: one catheter positioned inside the right atrium (sensing right atrial signals); one catheter placed inside the coronary sinus (sensing signals along the left atrium); one catheter positioned at the level of the bundle of His (sensing His signals); and another catheter positioned inside the right ventricle. Pacing can be performed via any of these catheters and the resulting activation sequence can be studied. In cases with suspicion of an AP the first step is to confirm its presence. This may be achieved by pacing the ventricle and observing the pattern of retrograde atrial activation. In the absence of an AP all impulses should travel up the AV node and result in concentric atrial activation. Alternatively if retrograde conduction through the AV node is not possible ventriculo-atrial dissociation is observed. If an eccentric activation pattern occurs during ventricular pacing an AP must be present (retrograde atrial activation other than by the AV node is termed eccentric and requires an alternative route which is the AP). The impulse is normally delivered when the bundle of His is refractory (His synchronous) to ensure that retrograde activation via the AV node will not occur. Atrial pacing may also disclose the presence of an AP as long as it is capable of antegrade conduction. Normally, the earliest ventricular activation should be sensed by the catheter placed over the His region and subsequently by the right ventricular catheter. If the earliest ventricular activation occurs at a site other than the His region or if the interval between His and right ventricular activation is too short (< 25 ms) antegrade conduction through an AP is suspected (ventricular pre-excitation). Nevertheless, not all AP's are capable of antegrade conduction ("concealed" AP's) and therefore the absence of pre-excitation does not exclude its presence. The second step is to attempt to initiate supraventricular tachycardia and study the activation pattern. If the atrial activation pattern during the tachycardia is the same as the one observed with His-synchronous pacing this is evidence that the AP is involved in the macroreentrant circuit and OAVRT is likely. Additionally, delivering a His-synchronous stimulus during tachycardia may reach the AP when it is also refractory and

will not be conducted to the atrium resulting in termination of the tachycardia. Consistent termination of the tachycardia with His-synchronous extra-stimulus without reaching the atrium is proof that the ventricle and the AP are part of the macro-reentrant circuit confirming OAVRT. After the presence of an AP and its participation in the macro-reentrant circuit is confirmed, its exact location is "mapped". The ablation catheter is positioned in the suspected area (the area in which earliest eccentric atrial activation was observed during ventricular pacing) over the tricuspid or mitral annulus and the electrograms are analysed in search of the exact location of the AP (Activation Mapping). This can be performed during ventricular pacing, during OAVRT, or during sinus rhythm if the AP is capable of antegrade conduction. During ventricular pacing or OAVRT the aim is to find the atrial insertion of the AP by seeking the site of earliest atrial activation. Once this is achieved, radiofrequency energy is deployed to this area to destroy the accessory pathway. Attempts to initiate the AV reciprocating tachycardia and/or document antegrade and retrograde conduction via the accessory pathway are repeated approximately 20-30 minutes after ablation. The aim is to confirm successful ablation (destruction) of the pathway..

References:

1. Wright, K.N., et al., Radiofrequency catheter ablation of atrioventricular accessory pathways in 3 dogs with subsequent resolution of tachycardia-induced cardiomyopathy. J Vet Intern Med, 1999. 13(4): p. 361-71.
2. Murgatroyd, F.D., et al., Accessory Pathways and AV Reentry, in Handbook of Cardiac Electrophysiology. A practical guide to invasive EP studies and Catheter Ablation. 2002, Remedica: London.
3. Murgatroyd, F.D., et al., Mapping and Catheter Ablation, in Handbook of Cardiac Electrophysiology. A practical guide to invasive EP studies and Catheter Ablation. 2002, Remedica: London.

ECVIM 2015 update

Rachel Blake
R(D)SVS, UK
Dave Sewell
Highcroft Veterinary Group, Bristol, UK

TALK SPONSORED BY:

The ECVIM-CA congress 2015 was held in Lisbon, Portugal. 12 veterinary societies were represented. The European Society of Veterinary Cardiology stream included 8 lectures, 23 abstracts and 21 poster presentations covering a variety of topics. Vetoquinol also invited colleagues to a presentation about the launch of Upcard, a formulation of Torsemide, a loop diuretic now licensed for management of congestive heart failure in dogs.

On the subject of Dilated Cardiomyopathy (DCM):

Gerhard Wess presented 2 lectures relating to DCM, some of this was covered at the VCS pre-BSAVA meeting in April 2015, hence I will be brief. The first of his talks was on **Predictors of Sudden Cardiac Death in Doberman Pinschers with DCM:** The prevalence of DCM in Doberman Pinschers in Europe in a recent study was 58%.1 Sudden cardiac death (SCD) during the occult phase occurs in 25 to 30% of affected dogs, however information on prognostic indicators for Dobermans with DCM is limited. Ventricular tachycardia (VT) is suspected to be a risk factor for SCD. Shorter early transmitral flow (TMF) deceleration time (DT) in Dobermans with DCM has been associated with shorter time to CHF or SCD.2 In a longitudinal prospective study, Holter ECG, echo, NT-proBNP and cTnI measurements were performed in 106 Dobermans. 52 dogs died suddenly and were compared to 54 Doberman Pinschers with DCM that were still alive one year after inclusion. An enlarged heart, represented by a normalised LVEDV (indexed to body surface area) > 91.3 ml/m2, was the most important and single statistically significant parameter to identify Dobermans with DCM at risk of SCD. The probability of SCD increased approximately 10-fold for each 50 mL/m2 increment of LVEDV/BSA. Other variables that were not statistically significant, but appeared to be prognostic markers for SCD risk included incidence of VT, an increased cTnI concentration, maximum instantaneous HR of VPC's > 260/min, and having triplets on Holter.

Gerhard Wess went on to present the **ESVC Task Force Committee Report on DCM in the Doberman Pinscher**: The following recommendations are not finalized, adjustments might be made:

Criteria	Details	Notes
Screening recommendations:	○ **From 2 years of age** ○ Repeated **annually** ○ **24-hour Holter + echo**	Males and Females. Emphasis on annual screening in male breeding dogs
Holter criteria:	Exclude systemic diseases that cause VPCs **< 50 single VPCs/24 h considered normal.** Many studies use > 100 VPCs/24 Based on recent work, use of either **> 300 VPCs/24 h on one Holter or** **> 50 VPCs/24 h on two Holter** recordings performed within one year recommended	If VPCs have a short coupling interval (Vmax > 250/min), this could be suspicious of being affected even when <50/24h
Echo criteria:	**EDV/BSA: > 95 ml/m^2** **ESV/BSA: > 55 ml/m^2** M-mode Wess: [4] **LVIDd**: m **> 48 mm***, f **> 46 mm*** **LVIDs:** m & f **> 36 mm*** M-mode O'Grady: [5] **LVIDd: > 0.1749 x (kg) + 40.3 mm or** **LVIDs: > 0.1402 x (kg) + 26.7 mm** EPSS: **> 6.5 mm** [5]	The Simpson method of disc (SMOD) is more sensitive than M-mode to detect early echo changes in Dobermans.[3] (EPSS supportive to M-mode)
Ancillary tests:	○ Clinical Examination; left apical systolic murmur, gallop rhythm, weak pulse, arrhythmia or pulse deficit ○ **NT-proBNP > 500 pmol/l** (especially to predict echo changes) ○ **cTnI > 0.22ng/mL** (sensitivity 79.5%, specificity 84.4%) ○ **1 VPC or atrial fibrillation on ECG.**	Currently not recommended or validated as sole screening tests, however If abnormal, further investigation including Holter and echo is strongly recommended

(VPCs; ventricular premature complexes, m; male, f; female, * any weight.)

1. Wess G, Schulze A, Butz V, et al. Prevalence of dilated cardiomyopathy in Doberman pinschers in various age groups. J Vet Intern Med. 2010;24:533–538.
2. O'Sullivan ML, O'Grady MR, Minors SL. Assessment of diastolic function by Doppler echo in normal Doberman pinschers and Doberman pinschers with dilated cardiomyopathy. J Vet Intern Med. 2007;21:81–91.
3. Wess G, et al. Use of Simpson's method of disc to detect early echo changes in Doberman pinschers with dilated cardiomyopathy. J Vet Intern Med. 2010;24:1069–1076.
4. Wess G, et al. Comparison of new reference values of biplane Simpson rule and new M-mode reference values to detect early echo changes in Doberman pinschers with DCM. In: ACVIM Proceedings, Anaheim 2010.

5. O'Grady MR, et al. Efficacy of benazepril hydrochloride to delay the progression of occult dilated cardiomyopathy in Doberman pinschers. J Vet Intern Med. 2009;23:977–983.
6. Holler PJ & Wess G. Sphericity index and e-point-to-septal-separation (EPSS) to diagnose dilated cardiomyopathy in Doberman pinschers. J Vet Intern Med. 2014;28:123–129.

Sonya G. Gordon presented the abstract **Evaluation of NT-proBNP, High Sensitivity Troponin I and PDK4 for the Detection of Occult DCM: A Prospective Study in 449 Doberman Pinschers:**

449 asymptomatic Doberman Pinschers were evaluated at the American Doberman National Specialty show (median age 5 years, range 1–12). Dobermans were classified as affected (ODCM) if LVIDs was > PROTECT entry criteria with or without VPCs on a 3-minute ECG (n = 22) or normal (NL) if LVIDd and LVIDs < PROTECT entry criteria and they had no VPCs. ROC analysis comparing ODCM and NL was done for NT-proBNP, cTnI, and PDK4.

Test	Selected cut-off	AUC	Percentage correctly classified
NT-proBNP	548pmol/l	0.91	81.8%
cTnI	0.139ng/ml	0.90	80.7%
NT-proBNP + cTnI	As above	0.95	91.3% (0 false negative, 30 false positives)
PDK4	Positive	0.65	56.1% (including 4 false negatives)

Andrea C. Vollmar presented the abstract **Sudden Death in Irish Wolfhounds with Heart Disease:**

Evaluating the incidence of sudden death (SD) in Irish wolfhounds (IW) with DCM and/or AF. 1,552 IW from Western Europe were included. DCM and/or AF were diagnosed in 29%. Long-term follow-up until death was possible in 134 (80 m, 54 f) dogs with DCM and 47 (22 m, 25 f) dogs with lone AF.

Group	n	% affected by SD	Median time to SD	Median age for SD
1. DCM + AF	76	25%	502 (31–2,170) days	6.5 ± 1.9 years
2. DCM + sinus rhythm	29	20.7%	893 (310–1,209) days	7.0 ± 2.5 years
3. DCM, AF + CHF	29	24.1%	232 (2–1,587) days	6.1 ± 2.3 years
4. Lone AF	47	23.4%	956 (482–1,707) days	6.1 ± 2.4 years

SD occurred in 21 to 24% of all groups with DCM or AF. VPCs were recorded in 4/47 IW with AF, and in 6/134 with DCM, while in IWs without heart disease VPCs were seen in 3.7% of 454 males and in 3.7% of 459 females. In conclusion, SD occurs in 23.3% of IW with lone AF before or after development of DCM and CHF, and in 23.9% of IW with DCM.

On the subject of assessment of ventricular function:

John D. Bonagura presented **Ventricular Function in Dogs with Chronic Mitral Regurgitation:**

I found this a useful summary of the subject and would like to include some key points here. There are many echo variables proposed for assessing ventricular function. For each, one should consider the technique, appropriate image acquisition, validity, repeatability, biological variation, sensitivity, patient selection, availability of reference values and the impact on diagnosis, prognosis or therapy.

Systolic function:

Left ventricular (LV) systolic function can be assessed globally or regionally, however these estimates are confounded by the altered loading conditions associated with both acute and

chronic MR. Moderate to severe MR results in a hyperdynamic LV ejection fraction (EF). Among the most studied parameter is the LV end-systolic volume (or diameter) index, which should increase with global ventricular failure. This variable relates with systolic function and diastolic ventricular size. Simple linear measurements for estimating LV volumes are easy to obtain, however estimations for volume and function of the LV can be inaccurate, especially when there is ventricular dilatation, dyssynchrony, or segmental motion abnormalities. Despite this, a number of clinical studies have demonstrated that the end-systolic volume index calculated from M-mode can be a predictor of heart failure or outcome. Area-length-based measurements of the LV can quantify contraction in multiple short-axis segments along with movement across the apical to basilar axis. Incorporation of LV area and length should more accurately predict EDV and ESV (and LV systolic function). The Simpson's method currently seems to be the most favoured technique for assessing LVEF.

Diastolic function:

Potential indices used for estimating diastolic LV function include transmitral flow (E, A and E', deceleration time), isovolumetric relaxation time (IVRT), and various ratios constructed from these measurements. Be cautious when interpreting diastolic function tests in dogs with primary MR, secondary volume overload, and hyperdynamic global systolic function. Diastolic function (and filling pressures) in MR is confounded by enhanced early diastolic filling characterized by larger transmitral E and tissue Doppler E' waves evident in primary MR. Peak E velocity typically exceeds 1.3 m/s with CHF, but the tissue based E' is also augmented, therefore E/E' cut-offs that indicate a high mean left atrial pressure in cardiomyopathy are less sensitive for predicting elevated filling pressures in dogs with primary MR. Other ratios such as E:IVRT might better normalize the E wave to the underlying myocardial relaxation and recoil. An E/A ratio < 1 is useful, being suggestive of mild LV diastolic dysfunction with normal filling pressures.

Right ventricular function was also a popular topic, **Marco Baron Toaldo** presented the abstract **Morphological and Functional Echo Assessment of the Right Ventricle in Normal Beagles Comparing with High-Field Cardiac Magnetic Resonance Imaging**: The goal of the study was to evaluate RV morphology and systolic function using different transthoracic echo (TE) views and compare the results with magnetic resonance imaging (MRI) measurements in ten adult, healthy, anesthetized Beagles. Values of tricuspid annular plane systolic excursion (TAPSE) varied significantly when using different apical views, the same was true for RV fractional area change (FAC). The only TE correlations found were TAPSE with FAC and Tissue Doppler imaging (TDI)-derived tricuspid annulus systolic wave (S'). The only echo variables correlating with the MRI-based stroke volume were FAC and s'. MRI-based EF didn't correlate with any echo variable. In addition to this, **Cecile Damoiseaux** presented the poster **Quantification of Systolic and Diastolic Right Ventricular Function by Conventional Echo and Speckle Tracking Imaging: A Prospective Study in 104 Healthy Dogs with Documented Pulmonary Arterial Pressure and Left Ventricular Function:** A prospective study to assess several indices of systolic and diastolic RV function using conventional echo and speckle tracking echo (STE) in 104 healthy awake dogs of different breeds with documented systolic pulmonary arterial pressure (SPAP) and LV function (LV ejection fraction and global LV systolic strain assessed using the Simpson's derived method of disks and STE, respectively). She found that global RV strain and RV free wall strain were positively correlated with right fractional area change (50.6 ± 10.5%) and negatively correlated with SPAP (17.4 ± 7.0 mmHg [7.0–30.0]). SPAP was also negatively correlated

with the TAPSE:body weight ratio and systolic strain rate. There was no correlation between indices of LV function and STE indices of RV function.

N.J. Pereira presented the abstract **Influence of Feline Diabetes Mellitus on Cardiac Function:**

In human medicine diabetes mellitus (DM) is known to lead to cardiovascular dysfunction and heart failure, characterized by early diastolic and late systolic dysfunction. The aim of the study was to prospectively identify if diastolic dysfunction was present or developed in cats with newly diagnosed DM. Echo was performed at diagnosis and 6 months post-diagnosis. Healthy age-matched control cats were retrospectively enrolled. 32 diabetics (D0) were enrolled in the study (18 f 14 m). Mean age 10.8 y. On March 2015, 15 cats had received a six month echo exam (D6). Ten control cats were enrolled (C) (8 m 2 f). Mean age 9.2 years.

Results:

Group:	**C**	**D0**	**D6**
LA on long axis (mm)	13.2 ± 1.31	14.2 ± 1.42	13.7 ± 1.07
LA/Ao	1.35 ± 0.14	1.36 ± 0.09	1.34 ± 0.11
IVSd (mm)	4.19 ± 0.46	4.06 ± 0.55	4.21 ± 0.67
LVDd (mm)	14.98 ± 1.54	15.72 ± 2.22	15.93 ± 1.47
LVFWd (mm)	4.38 ± 0.49	4.13 ± 0.59	4.19 ± 0.60
E wave (cm/s)	92 ± 26.6	**67.5 ± 20.5**	**62.9 ± 15.4**
E/A	1.24 ± 0.32	1.09 ± 0.38	0.97 ± 0.24
E' wave (cm/s)	90.8 ± 32.6	84.3 ± 28.9	74.1 ± 24.0
E'/A'	1.40 ± 0.61	1.29 ± 0.63	1.30 ± 0.63

D0 ($p = 0.004$) and D6 ($p = 0.03$) had a significantly lower mitral inflow E wave when compared to controls. D6 showed a tendency for lower mitral inflow E:A ratio ($p = 0.08$) and tissue Doppler E` wave ($p = 0.07$) when compared to D0. This study suggests that DM may be capable of influencing diastolic function in cats.

On the subject of measurement of the left atrium:

Mark Rishniw presented the abstract **Interobserver Variability in Two-Dimensional Echo Left Atrial Measurements is Complex:** Highlighting the variability in measurements of the left atrium by cardiologists. 25 images of the right parasternal short-axis view of the left atrium (LA) and aorta (Ao) were examined by 9 cardiologists or cardiology residents. The images depicted an LA of varying size, from both dogs and cats, ranging from normal to markedly enlarged. Each participant was asked to denote the start and finish points of their LA measurements without prior instructions - the first being near the interface with the aorta and the second being along the caudolateral border of the LA. Variability of the origin of the LA measurement (interface with Ao) was small, and scaled with increasing heart size. Variability at the distal measurement point was complex. In only 8/25 images was interobserver variability < 0.3 LA:Ao, and ranged up to 1 LA:Ao (8% to 36% variability). A systematic observer effect was noted. The 2 cases with the greatest variability had severe enlargement and indistinct margins. **The variability did not increase with increasing disease severity or image complexity.** In some instances, the same patient could be classified differently by 2 different observers if relying on LA:Ao thresholds. Thus demonstrating that highly trained individuals vary considerably in their measurement of LA from the right parasternal short-axis view and standardized methods of measurement need to be agreed upon to minimize this variability. So if the most highly trained amongst us vary in how they measure the left atrium, what hope do any of the rest of us have!

Chronic Right Ventricular Pacing: Pros and Cons, Roberto Santilli, Clinica Veterinaria Malpensa.

This talk reviewed the evidence in human medicine that pacing from the right ventricular (RV) apex results in abnormal and dyssynchronous ventricular activation and contraction, leading to adverse haemodynamic effects and possibly a worse long-term outcome. Adverse haemodynamic effects include a decrease in stroke volume and ejection fraction and an increase in left ventricular filling pressures. Up to 50% of humans with atrioventricular block are reported to show ventricular dysfunction following pacemaker implantation, with 10-26% developing post-implantation congestive heart failure (CHF).

In his talk, Dr. Santilli reported a prevalence of 9.7%, 6.7% and 75% new onset CHF following pacemaker implantation in patients with atrioventricular block, sick sinus syndrome and atrial standstill, respectively. During RV pacing, the conduction of the electrical wave propagates through the myocardium instead of the usual conduction system and so activation of the myocardium is slower and more heterogeneous, similar to left bundle branch block. Atrioventricular and interventricular dyssynchrony occur but the considerable dyssynchronous contraction between segments of the LV is probably the most important cause of left ventricular dysfunction. The portion of the LV closest to the pacing site is activated and contracts earlier, at a time of low chamber pressure, and stretches the inactive portion. This stretched portion becomes activated later but the stretching causes a further delay in shortening, an increased force of contraction and higher wall stress, resulting in massive energy wasting and inefficient contraction. The early activated portion thins and the later activated portion hypertrophies due to the changes in mechanical loading and also in sympathetic innervation. LV dilation is seen. Coronary blood flow is redistributed to the later activated segment. Mitral regurgitation also occurs due to increased tethering forces from a remodelled LV and dyssynchronous contraction of the papillary muscles. Pre-existing LV dysfunction can also contribute and is a negative prognostic indicator for patients treated with RV pacing.

Dr. Santilli suggested in his presentation that underlying inflammatory cardiomyopathies and/or viral persistence in the myocardium, or extension of the primary sino-atrial or atrioventricular node disease to the myocardium may significantly contribute to the ventricular dysfunction that occurs. Suggested methods to try and decrease post-implantation dyssynchrony included using alternative stimulation sites and algorithms to promote atrioventricular synchrony and reduce ventricular pacing when not needed.

Arrhythmia-Induced Cardiomyopathy: A Challenging Myocardial Disorder, Roberto Santilli, Clinica Veterinaria Malpensa.

Dr. Santilli's second talk focused on arrhythmia-induced cardiomyopathy (AIC). This term has been modified from tachycardia-induced cardiomyopathy and is defined as an impairment of atrial and/or ventricular function secondary to a tachycardia, an irregular heart rhythm or asynchronous contraction. Correction of the arrhythmia should result in partial or complete resolution of structural changes to the heart and symptoms of congestive heart failure. Pure and impure forms exist, the second being when there is underlying structural cardiac disease already present.

Experimental models show a decrease in cardiac output and systemic arterial pressure within 24 hours of pacing at an increased heart rate. Within a week, increased ventricular filling pressures, pulmonary artery pressures and decreased systemic arterial pressures reach a plateau. Cardiac output and ejection fraction continue to deteriorate over 3-5 weeks by which time end-stage heart failure ensues. An increase in the systolic left

ventricular internal diameter (LVIDs) and less pronounced increase in the diastolic left ventricular internal diameter (LVIDd) is seen as well as a decrease in left ventricular wall thickness and in systolic and diastolic function. Neurohormonal abnormalities similar to those present in dilated cardiomyopathy are seen. Resolution of the arrhythmia results in return of systemic and pulmonary arterial pressure, ejection fraction and cardiac index to normal within 4 weeks, although these parameters begin to approach normal by 48 hours and ejection fraction may be normal by 1-2 weeks. Paradoxical left ventricular hypertrophy is frequently seen by 4 weeks. Increased LVIDd, LVIDs and diastolic dysfunction often persist for longer. Possible mechanisms suggested include myocardial energy depletion, myocardial ischaemia, oxidative stress, abnormal calcium handling, myocyte and extracellular matrix remodelling and β-1 adrenoreceptor downregulation.

AIC can be difficult to differentiate from cardiomyopathies with other aetiologies and can only be confirmed by resolution of ventricular dysfunction following rate and rhythm control. Some authors have suggested criteria for diagnosis of AIC in humans should include dilation of the heart or heart failure, the presence of arrhythmia for at least 10-15% of the day and an atrial rate of > 150% of what would be expected. In humans, LVID is smaller in AIC when compared to dilated cardiomyopathy and rhythm control induces a more pronounced reduction in LVID in AIC. Failure of resolution may indicate an irreversible stage of pure AIC or an impure AIC.

Role of Right Endomyocardial Biopsy to Characterise Unexplained

Myocardial and Rhythm Disorders in the Dog, R.A. Santilli, Clinica Veterinaria Malpensa.

In human medicine, endomyocardial biopsy (EMB) is widely used for the diagnosis of unexplained cardiomyopathies including ventricular dysfunction and arrhythmias. It is associated with a high diagnostic yield and low complication rate.

This study aimed to assess the feasibility of EMB in dogs and to investigate the possible role of viral myocarditis in cases of unexplained dilated cardiomyopathy (DCM), high-grade atrioventricular block (AVB), supraventricular arrhythmias (SVA) and ventricular arrhythmias (VA). Twenty-five dogs were enrolled into the study, 6/25 with DCM, 9/25 for third degree AVB, 6/25 for VA, 2/25 for SVA and 2/25 for VA and SVA. They all underwent percutaneous EMB of the right ventricle via the right jugular vein. The procedure took an average of 42 minutes and 48% of samples were diagnostic. Complications were all self-limiting and included one perforation of the right ventricle and three cases of ventricular tachycardia. Histopathology was carried out in all cases. Samples were non-diagnostic in one case only. 6/25 dogs had normal samples. There were changes consistent with aspecific cardiomyopathy in 7/25 dogs and arrhythmogenic right ventricular cardiomyopathy (ARVC) in 2/25 dogs. Nine of twenty-five dogs had evidence of myocarditis (3 AVB, 5 DCM, and 1 SVA). PCR for enteric and respiratory coronavirus, herpes virus, distemper virus, adenovirus 1 and 2, parvovirus, West Nile virus and Bartonella spp. was also carried out on 16/25 cases. Two dogs with myocarditis were positive for virus involvement (one with enteric coronavirus and one with herpes virus). Two dogs with aspecific cardiomyopathy were positive for virus involvement; one for herpes virus and the other for herpes virus and parvovirus. One dog with aspecific cardiomyopathy was positive for Bartonella. One dog with ARVC was positive for adenovirus 2, herpes virus and Bartonella. No samples were positive with immunohistochemical staining.

This study provides evidence for inflammatory and viral associations with unexplained cardiomyopathies and arrhythmias and shows that EMB is a useful and reasonably safe procedure to facilitate investigation.

Efficacy of Spironolactone (SP) Following Oral Administration of SP in CATS with Heart Failure: Final Results of the SEISICAT Study, R.A. James et al., Nantwich Veterinary Hospital.

This was a prospective, double-blinded, randomized, placebo-controlled study with the aim of evaluating the safety and efficacy of spironolactone (SP) in cats with cardiomyopathy (CM). The study was carried out over 15 months. Twenty cats with CM confirmed by echocardiography and pulmonary oedema confirmed with thoracic radiography were recruited. All cats received an ACE inhibitor and furosemide for congestive heart failure and clopidogrel if necessary but cats were excluded if they received an anti-arrhythmic, pimobendan or aspirin. Hyperthyroid cats and cats with a creatinine over 250 µmol/L were also excluded. There were 9 cats in the SP group and 11 in the placebo group. The only significant difference between the two groups at baseline were a larger aortic diameter in the SP group and a larger LA: Ao ratio in the placebo group. Cats in the SP group received SP at a dose of between 1.7 – 3.3 mg/kg PO once daily and the other group received a placebo.

Results:

15 Month Survival

	Intention to Treat (ITT)	Per Protocol (PP)
Spironolactone Group	78%	71%
Placebo Group	12%	14%

The difference between the two groups was significant (log-rank test: ITT population p=0.011, PP population p=0.033.) The hazard ratio indicates an 84% (ITT) and 80% (PP) reduction in risk of an event occurrence in the SP group. Side-effects were minimal, consisting of two cases of moderate vomiting, one in the SP group and one in the placebo group. This study suggests that spironolactone is safe, well tolerated and appears to be beneficial in the treatment of cats with congestive heart failure due to CM.

Serum and Urine Cardiac Troponin I in Cats with Renal Disease, R. Langhorn et al., University of Copenhagen

The aim of this study was to determine if serum cardiac troponin I (cTnI) is elevated in cats with renal disease but no concurrent cardiac disease and if cTnI is measureable in the urine of both normal cats and cats with renal dysfunction. 13 cats with cardiac disease, 9 cats with renal disease and 8 healthy controls were recruited. Median serum cTnI for the cardiac group was 0.058 ng/ml (range 0.003-3.27 ng/ml), 0.16 ng/ml (range 0.026-0.78) for the renal group and 0.016 ng/ml (range 0.05-0.14 ng/ml) for the control group. The renal group had significantly higher serum cTnI than the control group (p=0.0059) but levels were not significantly different from the cardiac group (p=0.18). Urine cTnI was measurable in 77% of the renal group and 12.5% of the controls but none of the cardiac group. This study indicates that cTnI levels may be increased in cats with renal disease without concurrent cardiac disease and also that cTnI can be detected in the urine of cats with renal dysfunction.

Evaluation of Pimobendan in Healthy Cats: An Echocardiographic Study of Acute

Cardiovascular Effects, M Yata et al., University of Sydney

This study looked at the cardiovascular effects of high and low dose pimobendan on cats over 12 hours after oral administration. 8 healthy cats were recruited into the study. High dose pimobendan [HD] (1.25mg Vetmedin chewable tablet), low dose pimobendan [LD] (0.625 mg Vetmedin chewable tablet) or a placebo were given orally. Oscillometric blood

pressure measurements and standard echocardiography were performed repeatedly for 12 hours following administration. LVIDs showed a 24% reduction from baseline with HD and a 20% reduction from baseline with LD, which were both significant. LVIDs in the HD group remained significantly reduced from baseline for longer than in the LD group (40 mins-10 hours vs. 2-4 hours respectively). The maximal effects were seen at 2 hours post-administration for both HD and LD. Significant effects on aortic velocity and fractional shortening were also seen for both HD and LD.

Effects of Pimobendan on Myocardial Perfusion and Pulmonary Transit Time in Dogs with Myxomatous Mitral Valve Disease: A Pilot Study, G. Menciotti, Virginia-Maryland College of Veterinary Medicine

For this study, 12 dogs with stable, stage C (ACVIM classification) myxomatous mitral valve disease (MMVD) and 6 healthy dogs were enrolled. Standard and contrast echocardiography were performed at the beginning of the study. Dogs were then randomly divided into two groups. One group received pimobendan (0.4-0.6mg/kg) and one group did not. Standard and contrast echocardiography were repeated one week later. Pulmonary transit time was significantly increased in dogs with MMVD at baseline compared to healthy dogs ($p=0.0039$) and decreased significantly with pimobendan treatment ($p=0.0250$). Myocardial perfusion was not significantly different in dogs with MMVD compared to healthy dogs ($p=0.6639$) and did not change significantly with pimobendan treatment ($p=0.8798$). This study demonstrated that contrast echocardiography is a valid tool for analysis of dogs with MMVD. It also showed that pulmonary transit time can be decreased with pimobendan in dogs with MMVD and that myocardial perfusion is not altered in dogs with MMVD or with pimobendan treatment.

Prevalence of Patent Foramen Ovale in Small Animals: A Post-Mortem Study, J. Novo Matos, University of Zurich

This was a prospective study with the primary aim of determining the prevalence of patent foramen ovale (PFO) in dogs and cats. Secondary aims were to investigate the prevalence of atrial septal defects (ASD's) and to establish an association between paradoxical embolism (PE) and PFO, if present. A total of 113 cat hearts and 85 dog hearts were examined. PFO was present in 16% and 29% of cat and dog hearts, respectively. In 84% of dogs and 62% of cats, there was a partially probe patent channel extending from the ostium secundum to the limbus of the foramen ovale, where it was closed by a thin membrane. ASD was not identified in any case. Apart from an aortic thrombus in one dog, there was no evidence of thromboembolic disease. This study demonstrates that PFO in dogs and cats is reasonably common but ASD appears to be rare. There is no evidence that PFO is associated with paradoxical embolism. It was suggested that blunt trans-septal catheterization through the thin, easily rupturable membrane sealing the foramen ovale in a majority of cases may be used to allow access to the left atrium.

Reduction of Fluoroscopic Use with Echoguided Pacemaker Implantation in the Dog,

F. Porciello, University of Perugia

This group investigated the use of transthoracic echocardiography to aid in the placement of bipolar pacemaker leads in 10 dogs. Optimal images of the pacing lead were obtained, first using a right parasternal short-axis view of the right atrium and then changing to a long-axis view of the right ventricle, optimising the ventricular apex. Fluoroscopy was used after placement to confirm appropriate placement. Fluoroscopy was required by the investigators in the first three cases to follow lead progression in the ventricular but the

remaining seven cases used echocardiography alone for placement. This study demonstrated that transthoracic echocardiography provides an image of sufficient quality to guide pacemaker lead implantation, helping to minimize radiation exposure.

We would like to thank the VCS for their generous bursary, which allowed us to attend the 2015 ECVIM congress in Portugal.

Sleeping respiratory rate in dogs and cats with clinically controlled congestive heart failure

F. Porciello,[1] M. Rishniw,[2] I. Ljungvall,[3] L. Ferasin,[4] J. Haggstrom,[3] D.G. Ohad[5]

1) Department of Veterinary Medicine, University of Perugia, Italy

2) Veterinary Information Network, Davis, CA 95616 USA

3) Department of Clinical Sciences, University of Agricultural Science, Uppsala, Sweden

4) CVS Referrals, Lumbry Park Veterinary Specialists, Alton, Hampshire, UK

5) Department of Clinical Sciences, Hebrew University of Jerusalem, Israel

TALK SPONSORED BY:

Introduction

In hospitalised dogs with L-CHF, resting respiratory rate (RRR) proved the most sensitive and specific single test for identifying L-CHF as a cause of respiratory signs and independently predicted L-CHF in multivariable regression analysis. A further study demonstrated that resolution of the L-CHF resulted in respiratory rates returning to pre-CHF ranges. We recently showed that healthy dogs have average sleeping respiratory rates (SRR) <25 breaths/min in the home environment and that dogs with subclinical left-sided heart disease have average SRR that rarely exceed 30 breaths/min. Similarly, we recently showed that most healthy cats and cats with subclinical heart disease have average SRR <30 breaths/min and rarely exceed 40 breaths/min in the home environment.

We hypothesized that dogs and cats with stable, well-controlled L-CHF would have average SRR at home similar to those of dogs and cats with subclinical heart disease. Therefore, we examined the SRR and RRR of dogs and cats in the home environment with previously diagnosed L-CHF that had been satisfactorily controlled with standard medical therapy.

Materials and methods

Animals

The SRR and RRR were measured by owners of 51 dogs and 22 cats with stable, well-controlled CHF. To characterise the disease present, and to ascertain its severity, a comprehensive echocardiographic evaluation of patients was performed by the participating clinicians prior to any SRR or RRR data collection.

Inclusion criteria

Pets were considered to have 'well-controlled CHF' and included if the following criteria were met: (1) A diagnosis of L-CHF at least 6 weeks prior to SRR and RRR data collection; (2) No increase in medications for at least 4 weeks prior to SRR data collection; (3) The client and clinician considered the animal 'as good as could be anticipated or expected', so that no incremental change in medications was contemplated at the time of SRR and RRR data collection; (4) A minimum of either 1.5 mg/kg/day furosemide (cat) or 3.0 mg/kg/day furosemide (dog) to control the CHF was being administered (other medications were permitted at the discretion of the attending clinician). A bioequivalent dose of torsemide (0.3 mg/kg/day) was also permissible.

Measurements

Clinicians were asked to measure and record echocardiographic variables, including left atrial (LA) dimension, aortic (Ao) dimension, LA area, Ao area, left ventricular diastolic and systolic dimensions and wall thicknesses.

Participating clients collected 8-10 SRR measurements from their pets. During data collection, pets were to be in a 'thermoneutral' environment, loosely defined as 'a temperature in which the owner could sit or rest comfortably'; however, temperature ranges that would be acceptable were not specified, and participants did not record ambient room temperatures at the time of collection. Measurements of RRR were performed in a similar fashion, except that pets were awake and recumbent. Participants were requested not to measure RRR if the pet was panting or had recently been exercised.

Statistical analyses

Dog and cat data were analysed separately. First calculated the within-pet average SRR and RRR (SRRmean, RRRmean), within-pet maximum and minimum SRR and RRR (SRRmax, SRRmin, and RRRmax, RRRmin, respectively), and the maximal within-pet difference in SRR and RRR (ΔSRR, ΔRRR) for each pet's set of SRR and RRR measurements, respectively. These within-pet variables were then examined by box-and-whisker or dot plots to describe the data distribution for the SRR and RRR means, maxima, minima and absolute differences in within-pet SRR and RRR for the entire study sample.

To examine whether pulmonary hypertension impacted SRR and RRR, we compared the SRR and RRR of dogs with and without pulmonary hypertension with a rank sum test.

Results

The SRR and RRR were measured by owners of 51 dogs and 22 cats with stable, well-controlled CHF. Median canine SRRmean was 20 breaths/min (7-39 breaths/min); eight dogs had SRRmean ≥25 breaths/min and only one dog had SRRmean ≥30 breaths/min. Canine SRRmean was unrelated to pulmonary hypertension or diuretic dose. Median feline SRRmean was 20 breaths/min (13-31 breaths/min); four cats had SRRmean ≥25 breaths/min and only one cat had SRRmean ≥30 breaths/min. Feline SRRmean was unrelated to diuretic dose. Median canine RRRmean was 24 breaths/min (12-44 breaths/min); 17 dogs had RRRmean ≥25 breaths/min; seven dogs had RRRmean ≥30

breaths/min; two dogs had RRRmean >40 breaths/min. Median feline RRRmean was 24 breaths/min (15-45 breaths/min); five cats had RRRmean ≥25 breaths/min; one cat had RRRmean ≥30 breaths/min; two cats had RRRmean ≥40 breaths/min.

Discussion

Our study suggests that dogs and cats with L-CHF generally achieve SRR similar to those of healthy and subclinically affected dogs and cats, when managed with sufficient diuretics (and adjunct therapies) to stabilize their clinical signs to the satisfaction of the owner and the clinician. Dogs and cats rarely had SRRmean >30 breaths/min when L-CHF was stable and well-controlled. In most cases, SRRmean < RRRmean in both dogs and cats. Thus, if there are no complicating circumstances, clinicians treating animals with L-CHF should consider targeting the SRRmean in dogs and cats to <30 breaths/min in the home environment. Our observations agree with those of previous investigators where dogs successfully treated for L-CHF had RRR ranging from 12-38 breaths/min in a hospital environment.

Dogs with pulmonary hypertension identified at the time of CHF diagnosis did not appear to have a higher SRRmean than those without identifiable pulmonary hypertension. However, in most cases in our study, the pulmonary hypertension would be considered mild or moderate (no tricuspid regurgitation velocity exceeded 4.6 m/s, and most were < 4m/s).

Neither dogs nor cats showed any association between the daily furosemide dose and the SRR. However, due to the variety of adjunct therapies and strategies, we did not examine associations between various strategies and SRR. Nevertheless, furosemide is the most potent drug in routine management of CHF in dogs and cats, and therefore, should have had the greatest impact on SRR and RRR.

Conclusions

Our study demonstrates that most dogs and cats with stable, medically controlled CHF have SRRmean <30 breaths/min and relatively small day-to-day changes in SRR in the home environment. These findings provide reasonable targets for clinicians to strive for when attempting to manage cases of CHF, with the caveat that other factors, such as renal disease, should be considered when managing CHF. In such circumstances, achieving SRR<30 breaths/min might not be feasible or desirable. In animals where the clinician initially achieves SRRmean <30 breaths/min, ongoing SRR measurements could be used to adjust the diuretic to the lowest effective dose, i.e., the dose that maintains SRRmean <30 breaths/min, thereby reducing consequences of excessive diuresis.

Acknowledgements

We would like to acknowledge all veterinary surgeons and their clients who participated in this study, contributing to another small advancement of veterinary cardiology.

Real Time Three–dimensional Echocardiography in Horses – Clinical Application or Research Tool?

John Keen and Karen Blissitt
R(D)SVS, University of Edinburgh

Historically three-dimensional (3D) ultrasound images were created by reconstructing the 3D image from a series of 2D scans. However modern matrix-array probes allow a full volume 3D dataset to be acquired in real time. As with 2D echocardiography (2DE), where increasing the number of scan lines increases the image quality at the expense of frame rate, so increasing the number of voxels increases quality but decreases temporal resolution. To increase image quality and temporal resolution near real time images can be obtained. In this mode, narrow volumes of data are obtained over a number of (usually 4-6) cardiac cycles and these data sets are then 'stitched together' to form a complete pyramid of data to get the final 3D image. This technique is termed multiple-beat 3DE, and whilst this has the advantage of increasing image quality, artefacts can be produced as data sets are stitched together. Human patients are asked to co-operate during the scan by breath holding whilst 3D images are obtained. In cases of AF or other arrhythmias near real time multiple-beat images cannot be achieved and single beat full volumetric images must be recorded.

In human cardiology 3DE has been shown to have advantages over 2DE for the assessment of chamber volumes and LV mass, as geometric assumptions are not made when quantifying the data. Another advantage of 3DE is unlimited viewing planes which are useful when assessing congenital abnormalities and valvular function, especially when using 3D colour flow Doppler echocardiography (CFDE). 3D Speckle tracking is used to determine regional and global LV mechanics with no foreshortening of the LV or angle dependency. Some of the disadvantages of 3DE in human medicine relate to the large mass of data produced and the need to store this, the larger foot print of the transducer, poorer image quality when compared to 2D transducers and the time required for image analysis, although this can be offset by the reduced time required to obtain the necessary images.

In equine cardiology, the major pathophysiology identified is volume overload as a result of valvular regurgitation. Although TR is commonly found in horses, the most clinically significant conditions are mitral and aortic regurgitation where serial measurement of chamber volume is required to monitor progression. Any technique that can improve the reliability of measurement is to be welcomed. The recent ACVIM/ECEIM consensus statement on equine athletes with cardiovascular abnormalities (Reef et al 2014) stated that 'the development of a comprehensive assessment to determine the severity of valvular regurgitation' was crucial. A similar statement could be made for techniques that can improve the assessment of myocardial function. Although myocardial dysfunction in horses is relatively rare compared to dogs, poor athletic performance is common and the association, if any, with myocardial dysfunction is poorly understood.

Satisfactory near real time, multiple-beat 3D images can be recorded from adult horses despite lack of patient co-operation in terms of breath holding. In a study of 40 Thoroughbred horses in training, the main problems in acquiring images occurred in some horses where 4 consecutive images could not be obtained due to AV block and in others where the T wave of the ECG also triggered the 'multibeat' software. Image quality was poor in some cases because of lack of clipping and inexperience in optimising 3D image quality. The majority of the left ventricle could be fitted onto the screen from a right parasternal long-axis 4 chambered view and this could be then manipulated to allow automatic data analysis. Frame rates of 11.4 to 12.6 where obtained at a depth of 30 cm however automatic data analysis could only be used if the frame rate was greater than 12. Higher frame rates were achieved when the harmonic imaging function was turned off. Repeatability of measurements; LV and LA volumes, ejection fraction and sphericity was assessed by one observer measuring 6 horses on 3 occasions.

3DE has allowed better assessment of valve morphology and motion in our clinical cases. For images of the LA, aortic and mitral valve, the reduced depth, narrow angle and zoom function allowed frame rates of over 15 to 30 fps with the harmonics on to improve image quality. Although easy to confirm a suspected diagnosis of MR or AR using 2D CFDE, it can be much more difficult to diagnose the cause of that regurgitation. The ability to evaluate the anatomical structure of the valves from multiple angles including true en face views has allowed more detailed evaluation of subtle lesions, e.g. thickening, ruptured chordae tendinae, and has increased confidence in suspected diagnoses made with 2DE.

3DE has also allowed better assessment of the regurgitant orifice in cases with mitral and aortic regurgitation. Superimposition of 3D colour Doppler on a 3D tissue image maximises alignment with the valve and enhances understanding of the shape and size of the regurgitant orifice and patterns of flow through that orifice. This has allowed us to demonstrate the true shape of many 'large' regurgitant jets and therefore modify our recommendations accordingly. Our limited but growing experience so far has suggested that real time 3D echocardiography, in addition to providing striking ultrasonographic images, may offer great potential for assessing valvular regurgitation in horses. While there are some problems associated with acquiring reliable datasets as noted above, with patience and practice these problems can generally be overcome to provide reliable real time 3D datasets.

Currently it is our practice still to obtain a standardised scan with the 2D probe and then a focused 3D scan with the matrix probe. The matrix probe however can obtain long and short axis 2D images simultaneously and then full volume good quality data sets which would reduce scanning time. Although the 2D images are not as good quality with the matrix probe the measurements appear to be comparable and there is a considerable time saving when recording these images. The challenge in the future will be to have the confidence not to spend time recording multiple 2D images but to spend more time recording and analysing good quality 3D images.

Tissue Doppler and speckle tracking in horses: scientific tool or real-world technique?

Annelies Decloetd
University of Ghent, Belgium

1. Feasibility and reliability of tissue Doppler imaging and two-dimensional speckle tracking in horses

In human and small animal medicine, tissue Doppler imaging (TDI) and two-dimensional speckle tracking (2DST) are frequently used as an objective and more extensive quantification of myocardial function compared to conventional two-dimensional (2D) and M-mode echocardiographic measurements. Over the past years, these techniques have been adopted in equine cardiology, although some hurdles had to be overcome.

The main problem in equine ultrasonography is the cardiac size. In adult horses, an image depth of 26-30 cm is required for imaging the entire heart from a right parasternal view. As a result, the frame rate of conventional 2D echocardiographic images with an image width of 90° is only 16 frames per second (fps) in horses, while the optimal frame rate for 2DST is about 40-80 fps (Mor-Avi et al., 2011) and for color TDI strain rate calculations >180 fps (Sutherland et al., 2006). In order to apply 2DST in horses, the image width has to be reduced in order to increase the 2D grayscale frame rate (Decloedt et al., 2011). The frame rate can be further enhanced by reducing the number of ultrasound beams for building up the sector. However, reduced line density should not be applied for 2DST as it results in decreased lateral resolution. For TDI, the frame rate can be increased to >180 fps by decreasing the image width, narrowing the TDI sector maximally and reducing line density. The decreased image width is no limitation for TDI as accurate measurements can only be performed in a narrow sector with optimal alignment of the ultrasound beam and myocardial wall motion. A low lateral resolution is also no real drawback using parasternal images. Even in the far field, only myocardial tissue is included within the beam width.

The second important limitation for the use of TDI and 2DST in horses is that apical images are impossible to acquire due to anatomical constraints. In human and small animal medicine, longitudinal velocity and deformation assessed from apical images are the most commonly used TDI and 2DST measurements because the thin LV walls cause difficulty for measuring radial strain from parasternal images. In contrast, radial strain measurements in horses are feasible both by TDI and 2DST (Schwarzwald et al. 2009a; Schwarzwald et al. 2009b; Decloedt et al., 2013a; Decloedt et al., 2013b). Radial measurements are facilitated by the large equine myocardial wall thickness, which is about 2.5 cm at end-diastole and 4 cm at end-systole (Patteson et al., 1995). Furthermore, image quality is generally better in horses compared to humans.

As for any diagnostic technique, the evaluation of repeatability and reproducibility is of major importance before the use can be assessed in clinical studies. Both acquisition and measurement variability of TDI and 2DST have been evaluated. For TDI measurements in horses, peak values generally show a higher variability than timing measurements (Decloedt et al., 2011; Decloedt et al. 2013a; Schwarzwald et al., 2009b). The higher variability of peak values can be explained by the angle-dependency of TDI and the influence of manual positioning of the ROI, which both affect peak velocity and deformation measurements but not timing. As expected, the acquisition variability was higher than the measurement variability. In addition to biological variability, TDI image acquisition under a slightly different angle might result in variation of the peak values (D'hooge et al., 2006). In general, 2DST peak strain measurements showed a better repeatability and reproducibility than TDI measurements (Schwarzwald et al., 2009a; Decloedt et al. 2011; Decloedt et al. 2013b). The semi-automated off-line analysis reduces observer variability and the curves are smoothed more extensively than TDI curves.

2. Application of tissue Doppler imaging and two-dimensional speckle tracking in horses

2.1. Left and right ventricular function

The traditional quantification of equine left ventricular (LV) function is most often limited to the calculation of fractional shortening, which is a one-dimensional, focal and load-dependent measurement. In adult horses, the evaluation of longitudinal LV function is not possible from conventional 2D and M-mode parasternal images and optimal alignment with transmitral flow for evaluation of diastolic function is difficult to achieve. TDI and 2DST measurements can overcome some of these limitations and provide additional insights in equine LV function.

Because of the high temporal resolution, TDI is well suited for measurements of time intervals. An increased myocardial performance index (MPI) and increased ratio of pre-ejection period over ejection time (PEP/ET) could be detected by TDI in a mare with nutritional masseter myodegeneration. This indicated systolic myocardial dysfunction (Schefer et al., 2011). In horses with atypical myopathy showing long QT, prolonged isovolumic relaxation time (IVRT) and contraction duration by TDI reflected abnormal ventricular repolarization (Verheyen et al., 2012). In horses with systemic inflammatory response syndrome, LV systolic dysfunction as measured by an increased ratio of PEP/ET could be used to predict mortality (Borde et al., 2014).

Because of the high temporal resolution, TDI can also be used to evaluate diastolic function in horses. In human medicine, the E/E' ratio of early diastolic PW Doppler mitral inflow velocity (E) to early diastolic TDI mitral annular velocity (E') is used to estimate LV filling pressure. Although this ratio has been used in horses, it is rather unreliable because of the lack of accurate transmitral flow measurements (Schwarzwald et al., 2009b). Other possible measurements of diastolic function include the isovolumic relaxation time (IVRT), the peak E velocity and the ratio of early to late diastolic velocity (E/A). Horses with atypical myopathy showed a prolonged IVRT, lower peak E velocities and decreased E/A-ratio by TDI, indicating LV diastolic dysfunction (Verheyen et al., 2012). Similar changes were found

in a mare with nutritional masseter myodegeneration. In that horse, TDI findings were consistent with measurements of transmitral flow (Schefer et al., 2011). TDI measurements in horses with atrial fibrillation showed absence of the A wave and an increased E wave in comparison to a control group (Gehlen et al., 2009).

When evaluating LV systolic function, TDI velocity, strain rate and strain measurements should be interpret with caution. Although the repeatability and reproducibility of timing measurements is good, peak values show a larger variability. As 2DST is a semi-automated technique, the time for off-line analysis is significantly shorter and the measurements are more robust. Because the entire LV cross-section is used for calculating the deformation indices, 2DST is more suited for evaluation of global LV function than TDI. By 2DST, longitudinal myocardial velocity, strain rate and strain could be measured. Horses with severe myocardial damage caused by ionophore intoxication demonstrated decreased longitudinal strain values as well as alterations of FS (Decloedt et al., 2012). Remarkably, 4/15 horses with mild myocardial damage had decreased longitudinal strain values whereas FS was below reference range in only 1/15 horses. Similarly, in horses with atypical myopathy, global longitudinal strain was decreased whereas FS, circumferential strain and radial strain were not significantly different from the control group (Verheyen et al., 2012).

Regional LV function can be evaluated by comparing segmental measurements, both by TDI and 2DST. In human medicine, this is mainly important for diagnosis of coronary artery disease and myocardial ischemia and for detection of mechanical dyssynchrony in patients undergoing cardiac resynchronization therapy (Nesser and Winter, 2009). Changes in preload and afterload in valvular disease or hypertension can also result in regional changes of myocardial function. Due to the asymmetrical LV geometry, some segments develop increased local wall stress as a response to altered loading while others are less affected. Pressure overload causes increased wall stress in the basal septal segment because this segment is less curved than the LV free wall. As a result, decreased deformation and localized hypertrophy can be observed in this segment before other segments are involved (Bijnens et al., 2009). Regional changes have not yet been described in horses with valvular disease. TDI and 2DST could detect local myocardial dysfunction in a horse with severe myocardial fibrosis (Decloedt et al., 2012). Lower longitudinal and radial strain values were found in the interventricular septum compared to the LV free wall. Autopsy confirmed that the fibrosis was predominantly located in the septum.

Finally, TDI and 2DST might be used to assess right ventricular function, for example in horses with pulmonary hypertension caused by recurrent airway obstruction (Gehlen et al., 2013).

2.2. Atrial function

TDI can be reliably used for the assessment of atrial myocardial function in horses, allowing follow-up of atrial contractile dysfunction after conversion of atrial fibrillation (Decloedt et al., 2013; Schwarzwald et al., 2007a; b). Both atrial myocardial peak velocity as well as time to onset of atrial contraction improved from 24 hours to 6 weeks after cardioversion. However, impaired atrial function at 24 hours after cardioversion did not demonstrate

prognostic value for recurrence of atrial fibrillation in a multifactorial study (Decloedt et al., 2015).

During atrial fibrillation, the fibrillation rate can be assessed non-invasively by measuring the atrial fibrillation cycle length using TDI (Decloedt et al., 2014a). Administration of detomidine caused a small but significant prolongation of the atrial fibrillation cycle length (Decloedt et al., 2014). The effect of anti-arrhythmic drugs on atrial fibrillation cycle length measured by TDI remains to be determined.

3. Future prospects

TDI and 2DST allow an objective and more extensive quantification of myocardial function in horses. Currently, both techniques are mainly used as research tools which can provide additional insights into the physiology and pathophysiology of the equine heart. Several clinical studies have been published over the past years. However, the clinical value of TDI and 2DST remains unknown in the most common cardiac disease in horses, subclinical valvular disease.

In the future, TDI and 2DST are likely to become available in an increasing number of equine referral practices. The fast evolution of ultrasound technology and postprocessing software will probably solve many of the current disadvantages. For example, higher frame rates might be achieved without loss of lateral resolution, resulting in improved quality of the TDI and 2DST curves and lower measurement variability. This will also facilitate the use of both techniques at high heart rates during stress echocardiography (Schefer et al., 2010). In addition, new technology such as 3D echocardiography and 3D strain analysis is becoming available in equine cardiology. At present, the off-line analysis of TDI and 2DST is time-consuming and produces a large number of measurements, of which the clinical significance is often unknown. More research is needed to identify those measurements which could reveal subclinical myocardial dysfunction in horses. These measurements might become part of the clinical routine for evaluating horses with cardiac disease or poor performance.

In conclusion, TDI and 2DST offer many opportunities for a more comprehensive quantification of equine myocardial function. However, no single measurement is perfect. Ideally, the quantification of LV function should be based on a complete echocardiographic examination with conventional, TDI and 2DST measurements.

References

Bijnens BH, Cikes M, Claus P, Sutherland GR (2009). Velocity and deformation imaging for the assessment of myocardial dysfunction. Eur J Echocardiogr 10, 216-226

Borde, L., Amory, H., Grulke, S., Leroux, A.A., Houben, R.M., Detilleux, J. and Sandersen, C.C. (2014) Prognostic value of echocardiographic and Doppler parameters in horses admitted for colic complicated by systemic inflammatory response syndrome. J Vet Emerg Crit Care 24, 302-310.

D'hooge J, Bijnens B (2006). The principles of ultrasound based motion and deformation estimation. In: Sutherland GR, Hatle L, Claus P, D'hooge J, Bijnens B, editors. Doppler myocardial imaging: A textbook, BSWK Scientific Consulting and Publishing, 23-48

Decloedt, A., Verheyen, T., Sys, S., De Clercq, D. and van Loon, G. (2011) Quantification of left ventricular longitudinal strain, strain rate, velocity, and displacement in healthy horses by 2-dimensional speckle tracking. J Vet Intern Med 25, 330-338.

Decloedt, A., Verheyen, T., Sys, S., De Clercq, D. and van Loon, G. (2012) Tissue Doppler imaging and 2-dimensional speckle tracking of left ventricular function in horses exposed to lasalocid. J Vet Intern Med 26, 1209-1216.

Decloedt, A., Verheyen, T., Sys, S., De Clercq, D. and van Loon, G. (2013) Two-dimensional speckle tracking for quantification of left ventricular circumferential and radial wall motion in horses. Eq Vet J 45, 47-55.

Decloedt, A., Verheyen, T., Sys, S., De Clercq, D. and van Loon, G. (2013) Evaluation of tissue Doppler imaging for regional quantification of radial left ventricular wall motion in healthy horses. Am J Vet Res 74, 53-61.

Decloedt, A., Verheyen, T., Van Der Vekens, N., Sys, S., De Clercq, D. and van Loon, G. (2013) Long-term follow-up of atrial function after cardioversion of atrial fibrillation in horses. Vet J 197, 583-588.

Decloedt, A., de Clercq, D., van der Vekens, N., Verheyen, T. and van Loon, G. (2014) Noninvasive determination of atrial fibrillation cycle length by atrial colour tissue Doppler imaging in horses. Eq Vet J 46, 174-179.

Decloedt, A., de Clercq, D., van der Vekens, N., Verheyen, T., Ven, S. and van Loon, G. (2014) Influence of detomidine on atrial fibrillation cycle length measured by intracardiac electrogram recording and by colour tissue Doppler imaging in horses. Eq Vet J 2014, DOI: 10.1111/evj.12366

Decloedt, A., Schwarzwald, C.C., De Clercq, D., Van Der Vekens, N., Pardon, B., Reef, V.B. and van Loon, G. (2015) Risk factors for recurrence of atrial fibrillation in horses after cardioversion to sinus rhythm. J Vet Intern Med 29, 946-953.

Gehlen H, Iversen C, Stadler P (2009). Tissue Doppler echocardiographic examinations at rest and after exercise in horses with atrial fibrillation. Pferdeheilkunde 25, 11-16.

Gehlen H, Neukirch S (2013). Tissue Doppler Imaging and Two-dimensional Speckle Tracking of Left Ventricular Function in Horses Affected with Recurrent Airway Obstruction before and after Clenbuterol Treatment. J Eq Vet Sci 34, 471–478.

Mor-Avi V, Lang RM, Badano LP, Belohlavek M, Cardim NM, Derumeaux G, Galderisi M, Marwick T, Nagueh SF, Sengupta PP, Sicari R, Smiseth OA, Smulevitz B, Takeuchi M, Thomas JD, Vannan M, Voigt JU, Zamorano JL (2011). Current and evolving echocardiographic

techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the japanese society of echocardiography. Eur J Echocardiogr 12, 167-205
Nesser HJ, Winter S (2009). Speckle tracking in the evaluation of left ventricular dyssynchrony. Echocardiography 26, 324-336
Patteson MW, Gibbs C, Wotton PR, Cripps PJ (1995). Echocardiographic measurements of cardiac dimensions and indices of cardiac function in normal adult Thoroughbred horses. Equine Vet J Suppl 19, 18-27
Schefer KD, Bitschnau C, Weishaupt MA, Schwarzwald CC (2010). Quantitative analysis of stress echocardiograms in healthy horses with 2-dimensional (2D) echocardiography, anatomical M-mode, tissue Doppler imaging, and 2D speckle tracking. J Vet Intern Med 24, 918-931
Schefer KD, Hagen R, Ringer SK, Schwarzwald CC (2011). Laboratory, electrocardiographic, and echocardiographic detection of myocardial damage and dysfunction in an Arabian mare with nutritional masseter myodegeneration. J Vet Intern Med 25, 1171-1180
Schwarzwald CC, Schober KE, Bonagura JD (2007). Echocardiographic evidence of left atrial mechanical dysfunction after conversion of atrial fibrillation to sinus rhythm in 5 horses. J Vet Intern Med 21, 820-827
Schwarzwald CC, Schober KE, Bonagura JD (2007). Methods and reliability of echocardiographic assessment of left atrial size and mechanical function in horses. Am J Vet Res 68, 735-747
Schwarzwald CC, Schober KE, Bonagura JD (2009). Methods and reliability of tissue Doppler imaging for assessment of left ventricular radial wall motion in horses. J Vet Intern Med 23, 643-652
Schwarzwald CC, Schober KE, Berli AS, Bonagura JD (2009). Left ventricular radial and circumferential wall motion analysis in horses using strain, strain rate, and displacement by 2D speckle tracking. J Vet Intern Med 23, 890-900
Sutherland GR, Hatle L, Claus P, Herbots L, Separovic J (2006). Normal data. In: Sutherland GR, Hatle L, Claus P, D'hooge J, Bijnens B, editors. Doppler myocardial imaging: A textbook, BSWK Scientific Consulting and Publishing, 49-102
Verheyen, T., Decloedt, A., De Clercq, D. and van Loon, G. (2012) Cardiac Changes in Horses with Atypical Myopathy. J Vet Intern Med 26, 1019-1026.

ACVIM 2015 update

Brigite Pedro
University of Liverpool, UK
Jorge Prieto-Ramos
University of Glasgow, UK

TALK SPONSORED BY:

NT-proBNP and TROPONIN I (cTnI) LEVELS AS SCREENING BIOMARKERS IN IRISH WOLFHOUNDS. *William Tyrrell, Steven Rosenthal, Jesse Buch, Melissa Beall, Jancy Hanscom, Frances Abrams, Mariellen Dentino.* In this study, Tyrrell wanted to assess the use of NT-proBNP and cTnI as biomarkers in Irish Wolfhounds (IWH). Ninety IWH were included in the study. Complete history (including history of cardiac disease in the family) was taken. Physical examination, ECG and echocardiography were performed in all the dogs. Bloods were taken for full biochemistry, NT-proBNP and high sensitivity cTnI. Most of these 90 dogs were females (58 females vs 32 males), mean age was 4.61 years (1.2-11.1 years) and mean body weight was 66.4 kg (49.4-103.9 kg). The dogs were divided into seven groups according to the final diagnosis:

		NTproBNP, pmol/L		***High Sensitivity cTnI, ng/ml***	
Diagnosis	**n**	**Median**	**IQR**	**Median**	**IQR**
Normal	35	685	519-1079	0.03	0.02-0.04
Inconsequential Valve insufficiency	28	898	680-1262	0.05	0.038-0.128
Equiv. LVOT	7	471	387-559	0.02	0.0
IWH DCM/AF	10	5090	3863-5668	0.12	0.058-0.218
EquivDCM w/AF	1	3676	-	0.14	-
VPCs	7	976	867-1223	0.06	0.035-0.120
Lone AF	1	4562	-	0.13	-
Chemodectoma	1	1329	-	0.08	-

Considering the 35 normal dogs, reference interval upper limits for NT-proBNP and cTnI were calculated at 2937pmol/L and 0.99ng/mL, respectively. Both correlated well to cardiac

disease and significant differences between groups were evident (P<0.0001 and P=0.0007, respectively). NT-proBNP shows promise as a screening tool for differentiating the presence of equivocal or overt DCM/AF from the absence of DCM/AF in the IWH but this is also likely to be increased in dogs with lone AF without DCM.

IRISH WOLFHOUNDS WITH DILATED CARDIOMYOPATHY: CAUSES OF DEATH. *Claudia Vollmar, Bruce Keene, Barbara Kohn, Andrea Vollmar.* In this study, Claudia Vollmar wanted to compare the survival time of IWH with preclinical DCM and AF or sinus rhythm with the survival time of dogs with DCM and CHF. In this study, 1552 IWH from Western Europe were screened - physical examination, standard echocardiography and ECG were performed in all of the dogs between 1990 and 2014. They were longitudinally followed, and owners instructed to report date and circumstances of death. DCM with AF or sinus rhythm was diagnosed in 29% of the dogs. Long-term follow-up until death was possible in 134 dogs (80 males and 54 females).

	DCM+AF+CHF **(n=29)**	***DCM+AF*** **(n= 76)**	***DCM+ Sinus*** **(n= 29)**
SD (n=)	7	19	6
CHF (n=)	19	18	4
Non-cardiac death (n=) *(Osteosarcoma, pneumonia, soft tissue sarcoma and paraparesis)*	3	39	19
Mean age at diagnosis (years±SD)	5.5±2.6yrs	4.7±1.8yrs	5.0±2.2yrs
Median survival (months)	8	48	49

Survival in dogs with CHF was significantly shorter than dogs without CHF, regardless of their underlying rhythm at diagnosis. In dogs without CHF, there was no difference in survival between dogs with AF and those with sinus rhythm.

LONG TERM OUTCOME OF IRISH WOLFHOUNDS WITH LONE ATRIAL FIBRILLATION. *Claudia Vollmar, Bruce Keene, Barbara Kohn, Andrea Vollmar.* In this study Claudia Vollmar described the long-term outcome of IWH with lone AF and compared it to an age and gender matched control cohort. In this study, 1552 IWH from Western Europe were screened - physical examination, standard echocardiography and ECG were performed in all of the dogs between 1990 and 2014. They were longitudinally followed, and owners instructed to report date and circumstances of death. Of the examined dogs, 52 were diagnosed with lone AF and 55% of these developed DCM after a median of 2.5±1.5 yrs. Forty-seven of the 52 dogs were dead at the end of the study: cardiac deaths occurred in 45% (20% died suddenly and 25% died due to CHF), while 53% died from non-cardiac reasons. A matched control group without lone AF survived significantly longer than dogs with lone AF (P = 0.01, median of 1349 vs 1014 days). Lone AF is associated with increased mortality and represents a strong predictor of cardiac death.

THE URINE ALDOSTERONE TO CREATININE RATIO (UALDO:C) DETERMINED BY RADIOIMMUNOASSAY (RIA) IN NORMAL DOGS GREATER THAN 5 YEARS OF AGE. *Marisa Ames, Clarke Atkins, Kyle Webb.* Aldosterone is one of the many molecules produced when the renin-angiotensin-aldosterone system (RAAS) is activated in cases of CHF. Urine

aldosterone to creatinine ratio (UAldo:C) can be used to assess the status of a patient's RAAS and hopefully help guiding the treatment planning in the future. UAldo:C in 34 normal dogs, between 1 and 6 years old, has been previously reported as 0.40 ± 0.21 µg/g. Only one dog had a UAldo:C greater than 1.0. In this prospective study, UAldo:C in normal dogs older than 5 years of age (age match with dogs with DCM or MDVD) was assessed. Twenty-six dogs were evaluated: complete history, physical examination, brief chemistry panel (BUN, creatinine, ALP, ALT), PCV/TS, and UA were performed. Only 21 were included in the study. There were 14 spayed females and 7 castrated males, mean age was 9.2 ± 2.9 (range, 5.4 to 14.6) years and mean body weight was 25.6 ± 11.1kg. The mean UAldo:C was 0.49 µg/g ± 0.27 and no dog had a UAldo:C greater than 1.0. The difference between the UAldo:C in this group of older dogs was not different from the younger, laboratory dogs previously reported (P=0.2). The reference interval for UAldo:C was calculated to be (0.05 to 0.92 µg/g). In summary, UAldo:C rarely exceeds 1.0 µg/g in normal dogs and the UAldo:C does not appear to change significantly with age in normal dogs. Some preliminary results were also briefly presented: some cardiac patients were also assessed and in 38% of these a breakthrough of aldosterone was noted (despite ACEi administration) when using a cut-off value of 1.0 µg/g. The breakthrough also appeared to be more significant in cases of DCM when compared to MDVD. It is also important to mention that aldosterone and proteins in the urine follow the same pattern and therefore increased UPC will also be associated with increased urinary concentrations of aldosterone.

TIMOLOL OPHTHALMIC SOLUTION FOR DIASTOLIC FUNCTION TESTING IN CATS: A PILOT STUDY OF HEART RATE AND ECHOCARDIOGRAPHIC EFFECTS. *Catherine Gunther-Harrington, Eric Ontiveros, Timothy Hodge, Joshua Stern.* Diastolic function assessment in cats can be challenging due to increased heart rate and transmitral flow pattern fusion (E and A fusion), however this remains extremely important as identification of diastolic dysfunction can aid in the early detection of cardiomyopathies. In this study, Timolol (an ophthalmic, non-selective beta-blocker used in cats with glaucoma) was used with the attempt to reduce the heart rate and allow transmitral flow assessment. Twenty cats were included in the study (14 healthy, 5HOCM, 1 Dynamic RVOTO). ECG and echocardiography were performed before and 20 minutes after one drop of timolol 0.5% ophthalmic solution was administered to the right eye. Cats with respiratory disease, ophthalmic disease, and cardiac arrhythmias were excluded. A significant reduction in heart rate (29bpm – from 188 to 159bpm, with more significant effect in the more tachycardic cats) was noted after timolol (P=0.0005). Of 13 cats with E and A fusion, 8 separated after timolol and 5 remained unchanged (P=0.01). Seven cats without initial E and A fusion remained separated after timolol and E:A ratio was not significantly different (P=0.23). Resolution of obstruction was noted in 6/6 cats (1 dynamic RVOTO and 5 HOCM). No bradyarrhythmias were noted after administration. Described changes after ocular timolol administration were mildly increased LA dimensions, slightly reduced systolic function, ptialism and anisocoria. Ocular timolol safely and reliably reduces heart rate in cats, generates reproducible changes in echocardiographic parameters, may facilitate diastolic assessment, and may rapidly elucidate a cat's response to beta blockade.

FAMILIAL VENTRICULAR ARRHYTHMIAS AND SUDDEN CARDIAC DEATH IN THE YOUNG RHODESIAN RIDGEBACK. *Kathyn Meurs, Jess Weidman, Steve Rosenthal, Keven Lahmers, Steve Friedenberg.* In this presentation, a familial form of ventricular ectopy and sudden cardiac death in young Rhodesian Ridgebacks was described for the first time, after being already described in German Shepherds and English Springer Spaniels. Four related young Rhodesian Ridgebacks died suddenly between 7 and 12 months of age: 2 died while sleeping and 2 died after short exercise or excitement. In one family, two male dogs died suddenly at 9 and 12 months of age. Fourteen surviving dogs including the parents and littermates were evaluated with Holter monitoring. Three additional dogs (all female) were determined to be affected based on increased ventricular ectopy (656, 792 and 3,912 VPCs per 24 hours, respectively). Both parents of all affected dogs had zero VPCs on Holter monitoring. Echocardiography on one affected dog, and post-mortem evaluation on the two dogs that died of sudden death did not identify any structural lesions. A single female with zero VPCs was either the mother (two dogs) or grandmother (three dogs) to all of the sudden death and affected dogs. Additionally, four of the five affected shared a single father with zero VPCs. In the other family, two littermates (1 male, 1 female) died suddenly within 11 days of each other at 7 months of age. Three littermates were found to have frequent ventricular ectopy by Holter monitoring (1,200-8,700 VPCs) and four littermates were normal (0 VPCs). The mother had 90 VPCs. The mother, one affected and one unaffected littermate were available for echocardiography and no structural lesions were observed. Post mortem evaluation was performed on one of the sudden death dogs and no structural lesions were observed. The father of this family was unavailable for evaluation. Overall, eleven dogs (6 female, 5 male) were determined to be affected based on increased ventricular ectopy or sudden death. All four dogs were from two families and both families were distantly related through several dogs. The pattern of inheritance appears to be consistent with an autosomal recessive pattern based on the presence of a fairly equal gender distribution and at least in the first family, the presence of affected dogs with unaffected parents. However, an autosomal dominant mode with incomplete penetrance cannot be completely ruled out. Inbreeding should therefore be strongly discouraged.

DIFFERENTIATING CARDIAC VS NON-CARDIAC CAUSES OF PLEURAL EFFUSION IN CATS USING PLASMA AND PLEURAL FLUID WITH A POINT-OF-CARE NT-PROBNP TEST. *M. Hezzell, J. Rush, E. Rozanski, S. Cunningham, M. Oyama.* NT-proBNP has been shown to be useful differentiating cardiac and non-cardiac pleural effusion in cats by quantitative ELISA measured in plasma and pleural fluid. The aim of this study was to determine if the point-of-care NT-proBNP test would have similar results. Thirty-eight cats with pleural effusion were included in the study from two university teaching hospitals. Blood and pleural effusion were collected as well as a history, physical examination and echocardiography. The diagnosis was determined by a cardiologist that was blinded to all results of NT-proBNP. This was measured both on blood and pleural effusion by a second generation quantitative test and the point-of-care test. Twenty-one cats had cardiac pleural effusion vs 17 non-cardiac. There were no significant differences in weight, age, heart rate or respiratory rate between groups. Plasma (1500 [790–1500] vs 58 [31– 174.5], $P < 0.001$) and pleural fluid (1500 [918–1500] vs 108 [56– 324.5], $P < 0.001$) NT-proBNP by the

quantitative method, left atrial to aortic root ratio (LA/Ao) (2.59 [2.25–2.82] vs 1.3 [1.2–1.4], P < 0.001) and the proportions of male cats (80% vs 35%, P = 0.008) and cats with murmurs (71% vs 29%, P = 0.021) and gallop rhythms (62% vs 6%, P = 0.001) were higher in the cardiac vs non-cardiac group. A cut-off of 452 pmol/L for plasma NT-proBNP by the quantitative method yielded a sensitivity of 90.5% and a specificity of 88.2% with a positive likelihood ratio of 7.29 and a negative likelihood ratio of 0.11 . A cut-off of 537 pmol/L for pleural fluid BNP-quant yielded a sensitivity of 81.0% and a specificity of 88.2% with a positive likelihood ratio of 6.88 and a negative likelihood ratio of 0.22. Plasma NT-proBNP by the point-of-care method yielded a sensitivity of 95.2% and a specificity of 87.5% with a positive likelihood ratio of 7.62 and a negative likelihood ratio of 0.05. Pleural fluid NT-proBNP measured by the point-of –care test yielded a sensitivity of 100% and a specificity of 64.7% with a positive likelihood ratio of 2.83. This study showed that plasma NT-proBNP measured by the point-of-care test differentiates cardiac and non-cardiac pleural effusion similarly than the traditional quantitative test. NT-proBNP measured on pleural fluid by this test is of limited utility.

BIOLOGICAL VARIABILITY OF N-TERMINAL PRO- BRAIN NATRIURETIC PEPTIDE IN ADULT HEALTHY CATS. *Harris, A. Estrada, A. Gallagher, B. Mincey, K. Lamb, M. Bohannon, J. Hanscom, C. Mainville*. The objective of this study was to determine the biological variability of NT-proBNP in healthy adult cats. Thirteen adult healthy cats were evaluated to exclude systemic and cardiac disease by CBC, biochemistry, T4, echocardiography, ECG and blood pressure. Blood samples were obtained at 0, 2, 4, 6, 8 and 10 hours and at 2, 3, 4, 5 and 6 weeks. Intra- and inter- individual biological variation and reference change values were calculated. The median daily and weekly NT-proBNP concentrations for the population were 36.9 pmol/L (range, 23–257) and 24.5 pmol/ L (range, 23–113). The median daily and weekly intra-individual variation for the population were 11.2% (range, 0–40.4) and 21.5% (range, 0–68.4). The median daily and weekly reference change values for the population were 39.6% (range, 17.3- 112) and 69.6% (range, 17.3–188). The study concluded that a change in individual NT-proBNP concentration greater than 70% would be needed in healthy cats to denote a true change and not biological or assay variation.

PLASMA L-CITRULLINE CONCENTRATIONS IN L-ARGININE-TREATED DOGS: A PILOT STUDY FOR THE TREATMENT OF PULMONARY HYPERTENSION. *K. Flynn, H. Kellihan, L. Trepanier.* L-citrulline has been shown to have beneficial hemodynamic effects in humans with pulmonary hypertension. The study aimed to assess if oral supplementation with L-arginine in dogs could increase plasma concentrations of L-citrulline. On the first part of the study, three healthy dogs received 50 mg/kg q 8 h of L-arginine PO for a week. Plasma samples for L- citrulline and L-arginine were obtained at pre-treatment baseline, at steady state trough and 0.5, 1, 1.5, 2, 4, 6 and 8 hours after dosing. Peak concentrations of both substances were consistently seen at 4 hours post dosing. On the second part of the study, eleven healthy dogs received 100 mg/kg q 8 h of L-arginine PO for a week. L-arginine increased from a median (range) of 160.1 uM (100.2–231.4) at baseline to 412.7 uM (206.5–807.3) at 4 hrs post administration and L-citrulline increased from a median (range) of 82.1 uM (59.1–117.1) at baseline to 102.2 uM (47.4–188.3) at 4 hrs post administration. Only 2/11 dogs

showed a > 33% increase in plasma L-citrulline concentrations (target in humans). All dogs had L-citrulline concentrations greater than those (mean 44 uM) associated with pulmonary vascular hemodynamic improvement in people. Blood pressure, heart rate and chemistry profile did not differ after L-arginine administration. They conclude that L-citrulline concentrations are higher in dogs compared to humans. L-arginine dosage of 100 mg/kg PO q8 hrs exceeded peak human target concentrations in all dogs treated but showed more than 33% increase in only 2/11 dogs.

MULTI-DOSE PHARMACOKINETICS AND PHARMACODYNAMICS OF THE COMMERCIALLY AVAILABLE FORMULATION OF ORAL APIXABAN IN CATS: A PILOT STUDY. *C. Weder, C. Olver, L. Wittenburg, P. Trifonova, J. Quimby, J. Bright.* Apixaban is a factor Xa inhibitor that has been shown to be effective in the prevention of thromboembolic events in people.The proposes of this pilot study were to obtain pharmacokinetic and pharmacodynamic data in cats after multi-dose oral administration of apixaban and to establish appropriate oral dose and dosing intervals for this formulation. Three healthy cats received 0.625 mg of apixaban PO q 12 h. Blood samples for plasma concentrations and factor Xa activity were collected on days 1, 2, 3 and 4. Apixaban had a predictable inhibitory effect on factor Xa activity in all cats resulting in factor Xa activity within the therapeutic range (11–42% compared to baseline) used in human patients. Pharmacodynamic data showed cyclical inhibition of factor Xa activity that is typical of novel oral anticoagulant drugs. Pharmacokinetic data showed a lack of drug accumulation and a consistent elimination half-life between the first and last oral doses at approximately 2.5 hours. One cat was removed from the study as it became lethargic and vomited once on day 3. Trough concentrations on this cat were on average 3-fold higher. The signs resolved after discontinuing the drug. Bleeding was not noted in any cat. The conclusion of the study is that apixaban is a safe and effective anticoagulant in cats and should be considered for use in the treatment and prevention of feline ATE.

STENT ANGIOPLASTY FOR TREATMENT OF BALLOON RESISTANT CANINE VALVULAR PULMONIC STENOSIS. *S. Swift, I. Sosa, A. Estrada, A. Jones, C. Fudge*. This presentation reported the use of stents for the treatment of pulmonic valve stenosis in dogs in which balloon valvuloplasty was not successful. Three dogs with severe dysplastic pulmonary valve stenosis were treated with bare metal stents. The initial response to all of them was good with significant reduction in the pressure gradient. Two out of the three dogs remained stable long term. One dog needed reintervention due to stent fracture and embolization. That dog had four additional stents placed in the right ventricular outflow tract to treat severe, dynamic subvalvular pulmonic stenosis. All dogs continue to receive atenolol and clopidogrel. It was conclude that in selected patients, stenting of severe dysplastic pulmonary valve stenosis is a viable option and can provide long term relief of the obstruction.

PACEMAKER IMPLANTATION: ROUND TABLE REVIEW AND UPDATE. *J. Bonagura, M. Oyama, H. Green, A. Batra.* The table discussed different points regarding pacemaker implantation.

- Temporary pacing (transvenous vs transcutaneous vs no pacing): Different people had different approaches. It was suggested that the need to activate the temporary pacing should depend on the evidence of poor cardiac output for example based on the Doppler signal. Transoesophageal pacing was suggested as another alternative in cases of Sick Sinus Syndrome.

- Location of the pulse generator (neck vs thorax; subcutaneous vs under the musculature): Some presenters were of the opinion that placing the pulse generator under the musculature there is less seroma formation. Others opted for the application of a soft bandage for 3-5 days.

- Location of the lead: Epicardial pacemakers were discussed bearing in mind that virtually all patients have endocardial leads. It was discussed that despite some reports, not all cats develop chylothorax with transvenous lead placement and therefore it can be considered an option. There are 4 French transvenous leads available at the moment that could be used for cats or small dogs.

- Complications: Green reported that in his last 50 cases he had 9 major complications including 4 deaths, 1 atrial perforation, 2 thrombus, 2 lead dislodgement; and 4 minor complications including 3 phrenic stimulation and 1 tricuspid regurgitation. It was discussed if some cases of delayed sudden death could have been related with the pacemaker implantation. There is some evidence on this in humans.

- Pacing mode: Disparity of opinions. Some use only VVI/VVIR. Others consider that DDD is more physiological and are in favor of its use when possible. It was commented that a pacing atrial lead could be a good option for West Highland White Terriers with Sick Sinus Syndrome but should be avoided in Cocker Spaniels due to the risk of developing AV block. Batra (human cardiologist) was of the opinion that dual chamber pacing does not give significant benefit and he usually uses ventricular pacing. He also remarked the importance of the concept “minimal effective intervention”.

- Questions of the audience:

o Active vs passive fixation: It was remarked that active fixation does not prevent risk of dislodgement.

o Infection prevention: Disparity of opinions with different protocols.

o Use of MRI safe mode: It was mentioned that the programming gives problems.

Newer (and future) Modalities in Echo: What's Worth Doing?

John Bonagura
Ohio State University, USA

Introduction

Echocardiography has yielded the greatest impact on veterinary cardiologic diagnosis that I have witnessed during my career. First applied to our patients in the 1970's, I had the opportunity (as a new graduate starting practice in 1974) to watch colleagues around the world apply and refine echocardiographic imaging methods to small animals, large animals, and those of sizes in between. The advances in technology since the days of the dedicated M-mode probe have been remarkable! Even using early technology we could finally identify pericardial effusion and the larger valvular vegetations; distinguish the hypokinetic ventricle of dilated cardiomyopathy from primary mitral valve disease; diagnose hypertrophic cardiomyopathy ante mortem; and quantify ventricular size (so we no longer needed a 10-lead ECG and a good imagination). Even some right-to-left shunts could be verified using saline contrast imaging. The boom for large animal diagnosis was similar if not greater considering both ECG and radiography were limited in horses and cattle.

With the advent of mechanical sector scanning, 2D imaging further advanced both cardiac and abdominal imaging. Valves, septal defects, and cardiac mass lesions could now be visualized, even if the picture was a bit fuzzy at first. Doppler instruments were developed independently; for example, the landmark textbook of Hatle and Angelsen[1] was written based on studies that used non-imaging Pedof probes. But with the production of annular and then phased array transducers, PW and color Doppler imaging emerged within the framework of the 2D image, later to be joined by guided CW Doppler. With the onset of digital signal processing at the "front end", frame rates dramatically increased for both grayscale and color 2D imaging. These digital imaging systems, higher frequency and higher element imaging transducers, and harmonic (octave) imaging improved temporal resolution and 2D imaging, facilitating studies in smaller dogs and cats. Transducers were attached to transesophageal echo probes to gain access to better or more unique cardiac and vascular imaging windows. Pulsed wave Doppler techniques advanced to record tissue velocities alongside transvenous and transvalvular flows patterns, and diastology emerged. At that point in time, things seemed pretty well settled and many of us were quite content with the available modalities. After all, we could image most clinically-important cardiac lesions, quantify chamber sizes, identify patterns of normal and abnormal blood flow, assess systolic and diastolic ventricular function, record variables of left atrial function, and estimate hemodynamics to noninvasively learn about pressures, flow, and resistances in our patients. Accepting that some of these techniques presented technical challenges and significant variability, practically speaking, we had all the tools needed to diagnose and assess nearly all of the congenital and acquired diseases affecting the animal heart.[2]

But then vendors started to develop what might be called the "black box" technologies: those proprietary analyses systems that used multiple ultrasound beams, digital reconstruction, automated edge detection, specialized grayscale signal analysis, colorized tissue Doppler imaging, and speckle tracking technologies. These fostered the measurement of real-time volumes, 3D and 4D imaging, and a host of regional and segmental myocardial motion and function indices. Cardiologists of all sorts embraced these new – and expensive – technologies hoping to find more sensitive, more specific, or more quantitative tools that would improve diagnosis and disease staging, while potentially saving the examiner time. And let's be honest: this stuff is colorful and fun (especially if some large institution was buying it).

Which brings us to the question posed by the Program Chair: "Which of these newer technologies and modalities are worth doing?" That is a difficult issue for a person who is probably better at giving history lessons than foreseeing the future and suggesting where we are all heading with echocardiography. Nevertheless during this presentation I will advance some ideas about where we have been and mostly what newer Echo methods I think are ready for prime time – or not – in veterinary medicine. At the end of this short cruise, I will invite some of our colleagues to join into this brainstorming session so we can hear some alternative and better views on this subject.

What are the goals of the Echocardiography Study?

I indicated above some of the outcomes from a complete Echo study and could easily advance the argument that "I do not need 3D, TEE, deformation imaging, twist and torsion, or segmental wall analyses to do my day-to-day clinical work". Personally I agree with that statement, especially in light of the significant costs of these newer imaging processes. But that view can also be somewhat short-sighted in light of the potential information offered by some of these newer echocardiographic modalities and image analyses. The goals of a busy clinical practice might differ from those of a clinical investigator or researcher in pharmacology. Here is a short list of some possible outcomes newer technologies might hold for veterinary patients:

- Identify diseases that have not yet been recognized by ultrasound imaging.
- Provide more accurate estimates of chamber volumes and myocardial mass. We all appreciate the tremendous prognostic implications of left atrial enlargement, ventricular dilatation, and reduced ventricular ejection fraction. The potential to more accurately and rapidly quantify these variables using 4D imaging (with automated measurements and calculations) has already been realized in many human Echo labs. These methods have also been described by some of our leaders in veterinary echocardiography.
- Detect preclinical (occult) myocardial diseases – such detection could potentially guide follow up imaging or other diagnostic evaluations in companion animals as well as provide additional useful information regarding breeding animals
- Characterize abnormal myocardium – systems have previously been developed for analyzing the raw backscatter for myocardial tissue characterization. Most of these earlier

systems were abandoned by vendors, but undoubtedly will re-emerge. Knowing about tissue pathology noninvasively could provide tremendous value for stratifying risk and assessing treatments designed to delay or reverse cardiac remodeling. Systems that provide estimates of deformation under different degrees of compression or following an acoustic "shock" might also offer information regarding stiffness. Such systems are commercially available for abdominal organs.

- Measure coronary artery perfusion – we know that certain congenital and acquired heart disease are associated with intramural coronary artery disease, but do not have good ways to functionally measure the impact. Although deformation imaging (strain) can be used to identify segmental and regional alterations caused by ischemia, the potential for myocardial perfusion imaging should offer even better opportunities to study the coronary circulation in cardiomyopathies, outflow tract obstruction, chronic valvular disease, and hypertension.

- Provide higher resolution imaging and tissue characterization to better evaluate chronic valvular heart diseases. There are already specialized "mitral valve analysis" packages available from different ultrasound and stand-alone vendors. Most of these are related to 4D imaging methods. These will certainly become more important as methods develop to repair valves or improve their function using catheter-based or hybrid techniques.

- Apply echocardiography to pharmacologic studies – Echo is attractive because of the noninvasive nature of the disease and ability to perform repeated measures. New techniques are especially sensitive for quantifying ventricular function. The major issue is accounting for effects of any sedation or anesthesia (which have profound effects) and dealing with all of the variabilities that can affect repeated measures designs (operator, subject, measurement, learning curves, interactions of interventions and treatments).

- Guide interventional therapies including catheter based interventions and hybrid procedures – TEE and trans-cardiac echo (applied to the heart walls) have already been used to guide device closure of PDA, VSD, and ASD; these methods will undoubtedly be used in methods for assessing mitral valve repair or device replacement.

- Study natural history and outcomes from interventions – the use of echocardiography over the course of a natural history study or clinical trial can provide valuable insight about disease progression, natural history, 3 and effects of intervention on clinical outcomes. These measurements are subject to the same variabilities mentioned for pharmacologic studies.

Traditional 2D Imaging

Despite the great advances in transducer design, signal processing, and 2D imaging, we still have problems with current equipment and methods. The following are some of my "pet peeves".

Transthoracic imaging needs better transducers for our varying-sized patients. In some ultrasound systems the transducers jump from about 12 MHz to 6 MHz. Even with

harmonic imaging, this is too wide of a gap and leads to marginal images in big cats or small-breed dogs. We also still have problems with endocardial border resolution that relates to both the imaging technology and our own limitations in finding optimal acoustic imaging windows. Accurate border resolution is critical to obtaining believable chamber volumes using 2D or 3D methods, and can even influence some of our diagnoses. For example, in the cat imaged at a depth of 4 to 5 cm, a two or three pixel of difference in linear measurement can change the value by 0.4 or 0.5 cm, changing the diagnosis from "normal" to "hypertrophic cardiomyopathy" and all of the implications that follow that label.

Similarly, as transducers do more and more things, frame rates have actually fallen from the early days of digital Echo systems. With certain transducer or image settings in some systems, the frame rate can be too low for accurate temporal resolution of the myocardial walls in cats. This leads to variability and to errors in 2D measurements. Consider that at an acquisition rate of 30 frames per second there are 30 x 60 = 1800 image frames/minute. That sounds pretty good until you image a cat with a heart rate of 240/minute. Now there are 1800 frames characterizing 240 cardiac cycles each minute. This equates to 1800 frames per minute / 240 cycles per minute = 7.5 frames per cardiac cycle. In that situation, systole might be captured by only three or four 2D images frames. It is no wonder that the frozen image often seems to "jump" during frame-by-frame playback, and if end diastole is not faithfully captured, the 2D image measurement will be in error. Most digital systems can acquire images at faster rates than this but this assumes sufficient attention is paid to temporal processing and the "fps" monitor. The situation is much worse for 2D color Doppler imaging because slower frame rates common lead to misinterpretation of backflow signals in the left atrium as "mitral regurgitation" when in fact many end during or just after inscription of the QRS complex. Applying the old technology of M-mode echocardiography is still valuable in these situations[4] and the examiner can obtain precise temporal resolution related to the high acquisition rate.

Transesophageal Echocardiography

The technique of transesophageal echocardiography (TEE) uses transducer crystals mounted near the tip of a flexible endoscope. Although this is a relatively old modality, experience indicates that most cardiologists do not own or routinely use TEE in their veterinary practices. General anesthesia is required and this seriously limits the practicality of this procedure, except to guide interventions or image the heart base in special cases. In contrast to the human experience, the improvement in imaging over standard transthoracic windows is less impressive in dogs and cats. The technique of TEE has been applied to cardiac and vascular imaging of healthy animals.[5-10] A number of longitudinal and transverse images can be obtained, including good views of the cardiac valves, atrial and ventricular septa, pulmonary veins, and great arteries. Image planes have been categorized as cranial, middle or caudal (relative to the base of the heart) as well as transgastric. Initial reports suggest transgastric images are inferior for imaging the canine heart but more acceptable in cats.

Although TEE can be used for diagnosis of cardiac diseases TEE studies are mainly used for guidance of interventional catheterization procedures that include device closure of persistently patent ductus arteriosus (PDA) or defects in the cardiac septa.[11-15] Other potential uses include identification of small heart base tumors, atrial thrombi, and vascular defects. TEE has been used for guidance of heartworm extraction.[16] The instrumentation is costly and impractical for all but subspecialty practices. The sizes of the endoscopes can become an issue owing to the different weights of veterinary patients. Both adult and pediatric transducers are available. The endoscopes can integrate single- or multi-plane crystal arrays with the most advanced TEE probes capable of performing real-time, 3D reconstruction with CDI.

Contrast Echocardiography

Contrast echocardiography can be performed to identify abnormal patterns of blood flow, delineate endocardial borders, assess myocardial perfusion, enhance Doppler flow signals, and outline lesions such as an atrial thrombus, cardiac mass, or LV non-compaction.[17-21] The contrast echocardiogram is produced by altering the sonographic characteristics of part of the blood pool with the injection of a fluid that generates microbubbles. The agent is injected in a peripheral vein and followed into the heart using 2DE, often with specified harmonic imaging.[22] These solutions or suspensions alter the acoustic impedance of the blood through the creation of microcavitations or the release of gases that act as powerful US reflectors. A variety of agents have been injected for contrast echocardiography with agitated saline most often used in veterinary medicine. Most non-commercial agents are filtered within the pulmonary circulation and are therefore confined to the right side of the heart unless there is a right-to-left shunt. Contrast agents developed to outline the LA and LV or demonstrate coronary perfusion must first survive transpulmonary passage. A number of proprietary microsphere suspensions are available for this use in human patients. These contain perfluorocarbon gas, which is released when the outer shell of the microsphere is disrupted by US.

Although human contrast agents have been tried in dogs,[20] there has been little movement to adapt microspheres for veterinary patients despite the potential to study myocardial perfusion. We do not perform these studies but if risk stratification can be proven with these methods and the contrast agents are safe (and affordable) when more widely used I'm confident we would offer these studies. Pulmonary artery transit times, a general estimate of cardiac output, also can be determined using commercial contrast agents.[21] The risk of anaphylactoid reactions with commercial contrast agents should be noted,[23] and that human patients have died suddenly following injection of these products.

Saline contrast echocardiography is simple to perform and has demonstrated utility in demonstrating right-to-left shunts. Injection of three to 6 ml of agitated saline is usually sufficient to produce a good quality contrast study. Adding ¼ ml of the patient's own blood can improve the contrast effect, but this is rarely needed. Saline contrast does not endure the pulmonary capillaries; therefore, finding echodense contrast within the left side of the heart suggests a right-to-left shunt. An exception is observed in healthy anesthetized

patients in whom pulmonary arteriovenous shunts have opened. However, in these cases, the arrival of contrast is delayed and enters the LA through a pulmonary vein. In the case of patent foramen ovale (PFO) or right-to-left ASD, contrast moves from right to LA. With the tetralogy of Fallot, contrast can be traced along a path from the RV to the LVOT. Additional diagnostic uses are verification of persistent left cranial vena cava and reversed PDA with imaging over the abdominal aorta to detect the passage of contrast agent through the descending aorta.

Although Doppler studies have largely replaced contrast echocardiography, the technique is relatively sensitive for right-to-left cardiac shunts and results are often less ambiguous than CDI when identifying an ASD or PFO. We routinely perform saline contrast echocardiography in our dogs with PS or severe tricuspid valve malformation. At times negative contrast effects are visualized when blood derived from the left heart crosses a shunt and dilutes the positive saline contrast in the right heart. However, normal streaming of systemic venous return into the RA and RV inlet can create false positives.

Doppler Imaging

In terms of conventional Doppler flow imaging, the biggest problems I see (and create myself) are operator-related. These include selecting inappropriate transducers and gain settings for color Doppler imaging and creating a host of problems related to spectral Doppler imaging. These include: sample volumes that are too large; failure to obtain optimal alignment with blood flow; and using too much transmit power and gain during spectral Doppler imaging, leading to "blooming" or to "channel crosstalk" and a mirror image formation in the spectral envelope. Mirror image artifacts are relatively easy to ignore, but blooming of the spectral edge is ubiquitous and has significant implications with respect to overestimating pressure gradients using the simplified Bernoulli equation. Presetting the transducer for a mid-range or even high-range crystal activation (for example not using the lowest Doppler transmit frequency) or moving to a higher transducer frequency should be considered if the spectral signal strength is too high.

Tissue Doppler imaging can be performed with the standard single sample volume method or with colorized TDI in a "black box" processing system or workstation. We routinely measure single sample volume tissue velocities in the lateral LV wall and dorsal septum in our patients as well as in the dorsal RV free wall; all are obtained from the apical or modified apical planes. The measurements are used as measures of longitudinal systolic function of the LV and RV and for assessing diastolic dysfunction of both ventricles. Challenges in using TDI are the beat to beat variations seen in many TDI velocities (changing from normal to relaxation abnormality), translational movements that affect the image quality (such that larger sample volumes are used), and poor alignment with wall movements. Additionally the TDI systolic velocities are partially related to body size and in the setting of exuberant motion observed in advanced primary mitral valve disease the E' velocities are misleading and "traditional" E/E' ratios for estimating filling pressures in cardiomyopathies cannot be used in mitral valve disease.

Colorized Tissue Doppler Imaging is vendor specific and generally involves storing a colorized image with Doppler information from a standard image plane. These mean values obtained from a limited number of scan lines (you can even record "velocities" in the lung that are derived from the heart), and typically are slightly lower in magnitude than single sample volume TDI measurements. Velocity "gradients" can be calculated to display differences between endocardial and epicardial segments. There are a number of papers identifying abnormalities in colorized tissue Doppler in dogs, cats and horses. The specific applications include estimates of systolic function, diastolic function, and timing of mechanical events. Owing to the impact of angle on velocity measurements, these methods have been somewhat supplanted by deformation imaging based on speckle tracking technology (see below). The method is still clinically useful when good quality TDI cannot be obtained and can also provide some insight about the timing of wall movements relative to the ECG.

Three-dimensional Echocardiography

With the advent of 3D echocardiography (3DE) there has been an explosion in imaging technology, mostly designed for imaging human adults. These systems have been applied to dogs and cats with varying degrees of success. The fully sampled matrix array transducers used for 3D imaging contain thousands of piezoelectric elements and are connected to powerful processing systems offering even real-time (4D) imaging.

Imaging modalities include narrow sector real-time imaging; focused wide sector enlargement of regions of interest; and full volume, ECG-gated, acquisition of the LV and LA useful for calculating ejection fraction and atrial volumes. Images can be manipulated by cropping to highlight specific structures and lesions. Various displays are available including specialized viewing glasses to create a more 3D experience for the reviewer. Surface rendering can create contours or models of the LV and LA[24,25] and these methods have been applied to dogs and cats on a limited basis.[26-30] Additionally, CDI can be superimposed on the 3D image to better assess abnormal blood flow patterns along with the severity of shunts and regurgitant lesions. The mitral valve is a particular focus of interest and a number of vendors have created specific 3D programs to analyze mitral valve anatomy and function. These are mainly used for human patients needed surgical repair, but will likely have future applicability to dogs.

As indicated above, some potential veterinary uses for 3DE include: quantitation of chamber volumes for detection of cardiac dilatation and estimation of ventricular and atrial function; delineation of congenital shunts and guidance for interventional treatments; and improved visualization of valvular lesions and regurgitant jets for to provide more accurate prognostication and guide future catheter-based or open-heart treatments. Some venders have developed technologies to measure myocardial strain in three dimensions. TEE probes with 4D imaging are used in interventional suites. Automated border detection provides outputs for ventricular volumes and ejection fraction using endocardial border detection, speckle tracking or other proprietary technologies.

We have a 4D transducer in our practice, but I find it cumbersome and of little impact in changing how I practice. Occasionally some nice images are obtained of congenital valve defects and the images of a stenotic pulmonary valve can be instructive. I believe there are differences among vendors in the quality of usefulness of their 3D/4D systems in animals. The image must also be available for off line analysis and here the workstation and software analysis systems must be compatible with species other than humans. Currently, the major issues impeding wider 3DE application to veterinary patients include the processing speed of the systems related to the faster heart rates of animals; the requirement for stitching multiple cardiac cycles (ideally with breath holding!) to obtain optimal 3D images; and the large footprint of 3D transducers that limit full transthoracic contact. Nevertheless if future advances include pediatric transducer designs, we can expect 3D technologies to take wider hold in veterinary medicine regardless of the cost.

Critical issues involve the increment in clinical information and the imaging detail provided beyond our current levels of routine transthoracic examinations. Obstacles include quality of images obtainable from cats and smaller dogs as well as the cost-effectiveness of the technologies within the veterinary space. Slow frame rates further hamper the application of this technology to our patients.

Myocardial Strain

Calculation of regional myocardial deformation – strain and strain rate – is a recent application of TDI and of 2D speckle tracking technologies. Longitudinal strain is calculated as a negative value because segments shorten during systole, while radial strain is positive (as the wall thickens). Circumferential strain and segmental rotation are also available from a number of vendors. Global 3D strain can be calculated from 3D images of the LV. Most vendors offer Strain recorded by speckle tracking and this methodology is purported to overcome the TDI limitations of angle and tethering. Limited veterinary publications have described strain imaging for the ventricles.[31-54] Standardization and reference values are needed before widespread veterinary application can be recommended beyond the research setting. Unfortunately, deformation imaging does not appear to be any more sensitive than conventional methods for detecting myocardial dysfunction in dogs with MR and thus far has not been evaluated sufficiently in longitudinal studies of dogs with preclinical DCM that eventually develop overt myocardial failure.

Speckle tracking can also measure the rotation of the heart at the base and apex to allow estimation of ventricular torsion or twist. The apex and base rotate in opposite directions in normal hearts and their calculated differences can be used to assess ventricular systolic function (twisting) and diastolic function (untwisting). It should be noted that the values obtained for ventricular twist are calculated from disparate segments that reach their maximal rotations at different points of time.[39,55,56] There are even off-line analyses systems that outline the pathway of electrical activation based on deformation imaging; this might be useful in the diagnosis or therapy of arrhythmias.

A number of methods are used to measure ventricular dyssynchrony and some of the more advanced include multi-segment TDI or deformation (strain) analyses. Variables such as

time to peak strain across different myocardial wall segments or the standard deviation of differences to peak time can be used to quantify the delays in ventricular activation associated with prolonged QRS complexes, cardiomyopathy, or ventricular pacing. Dyssynchrony is believed to further impair LV function.[37-39,42,46,48,57-60]

References:

1. Hatle L, Angelsen B. Doppler Ultrasound in Cardiology: Physical Principles and Clnical Applications. 2nd ed. Philadelphia: Lea & Febiger; 1985.

2. Bonagura JD, Luis Fuentes V. Echocardiography. In: Mattoon JS, Nyland TG, eds. Small Animal Diagnostic Ultrasound 3rd ed. St. Louis: Elsevier/Saunders; 2015.

3. Hezzell MJ, Boswood A, Moonarmart W, Elliott J. Selected echocardiographic variables change more rapidly in dogs that die from myxomatous mitral valve disease. J Vet Cardiol 2012;14:269-79.

4. Feigenbaum H. Role of M-mode technique in today's echocardiography. J Am Soc Echocardiogr 2010;23:240-57; 335-7.

5. Loyer CG, Thomas WP. Biplane transesophageal echocardiography in the dog: Technique, anatomy and imaging planes. Vet Radiol Ultrasound 1995;36:212-26.

6. Kienle RD, Thomas WP, Rishniw M. Biplane transesophageal echocardiography in the normal cat. Vet Radiol Ultrasound 1997;38:288-98.

7. St-Vincent RS, Pharr JW. Transesophageal ultrasonography of the normal canine mediastinum. Vet Radiol Ultrasound 1998;39:197-205.

8. Chetboul V, Pouchelon JL. [Transesophageal echocardiography: principles, technique and potential indications in veterinary medicine]. SchweizArchTierheilkd 2004;146:321-6.

9. Quintavalla C, Pradelli D, Domenech O, Bussadori C. Transesophageal echocardiography of the left ventricular outflow tract, aortic valve and ascending aorta in Boxer dogs with heart murmurs. Vet Radiol Ultrasound 2006;47:307-12.

10. Domenech O, Oliveira P. Transoesophageal echocardiography in the dog. Vet J 2013;198:329-38.

11. Pariaut R, Sydney MN, Kraus MS, et al. Use of transesophageal echocardiography for visualization of the patent ductus arteriosus during transcatheter coil embolization. J Vet Cardiol 2004;6:32-9.

12. Saunders AB, Miller MW, Gordon SG, Bahr A. Echocardiographic and angiographic comparison of ductal dimensions in dogs with patent ductus arteriosus. J Vet Intern Med 2007;21:68-75.

13. Saunders AB, Achen SE, Gordon SG, Miller MW. Utility of transesophageal echocardiography for transcatheter occlusion of patent ductus arteriosus in dogs: influence on the decision-making process. J Vet Intern Med 2010;24:1407-13.

14. Saunders AB, Carlson JA, Nelson DA, Gordon SG, Miller MW. Hybrid technique for ventricular septal defect closure in a dog using an Amplatzer(R) Duct Occluder II. J Vet Cardiol 2013;15:217-24.

15. Stern JA, Tou SP, Barker PC, et al. Hybrid cutting balloon dilatation for treatment of cor triatriatum sinister in a cat. J Vet Cardiol 2013;15:205-10.

16. Arita N, Yamane I, Takemura N. Comparison of canine heartworm removal rates using flexible alligator forceps guided by transesophageal echocardiography and fluoroscopy. J Vet Med Sci 2003;65:259-61.

17. Bonagura JD, Pipers FS. Diagnosis of cardiac lesions by contrast echocardiography. J Am Vet Med Assoc 1983;182:396-402.

18. Ziegler L, O'Brien RT. Harmonic ultrasound: a review. Vet Radiol Ultrasound 2002;43:501-9.
19. Hoglund K, Bussadori C, Domenech O, Haggstrom J, Pradelli D, Kvart C. Contrast echocardiography in Boxer dogs with and without aortic stenosis. J Vet Cardiol 2007;9:15-24.
20. Crosara S, Ljungvall I, Margiocco ML, Haggstrom J, Tarducci A, Borgarelli M. Use of contrast echocardiography for quantitative and qualitative evaluation of myocardial perfusion and pulmonary transit time in healthy dogs. Am J Vet Res 2012;73:194-201.
21. Streitberger A, Hocke V, Modler P. Measurement of pulmonary transit time in healthy cats by use of ultrasound contrast media "Sonovue(R)": feasibility, reproducibility, and values in 42 cats. J Vet Cardiol 2013;15:181-7.
22. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification. Eur J Echocardiogr 2006;7:79-108.
23. Yamaya Y, Niizeki K, Kim J, Entin P, Wagner H, Wagner PD. Anaphylactoid response to Optison(R) and its effects on pulmonary function in two dogs. J Vet Med Sci 2004;66:1429-32.
24. Yang HS, Bansal RC, Mookadam F, et al. Practical guide for three-dimensional transthoracic echocardiography using a fully sampled matrix array transducer. J Am Soc Echocardiogr 2008;21:979-89; quiz 1081-2.
25. Lang RM, Badano LP, Tsang W, et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. J Am Soc Echocardiogr 2012;25:3-46.
26. Tidholm A, Bodegard-Westling A, Hoglund K, Ljungvall I, Haggstrom J. Comparisons of 2- and 3-dimensional echocardiographic methods for estimation of left atrial size in dogs with and without myxomatous mitral valve disease. J Vet Intern Med 2011;25:1320-7.
27. Tidholm A, Hoglund K, Haggstrom J, Bodegard-Westling A, Ljungvall I. Left atrial ejection fraction assessed by real-time 3-dimensional echocardiography in normal dogs and dogs with myxomatous mitral valve disease. J Vet Intern Med 2013;27:884-9.
28. Jung S, Orvalho J, Griffiths LG. Aortopulmonary window characterized with two- and three-dimensional echocardiogram in a dog. J Vet Cardiol 2012;14:371-5.
29. Meyer J, Wefstaedt P, Dziallas P, Beyerbach M, Nolte I, Hungerbuhler SO. Assessment of left ventricular volumes by use of one-, two-, and three-dimensional echocardiography versus magnetic resonance imaging in healthy dogs. Am J Vet Res 2013;74:1223-30.
30. Young AA, Orr R, Smaill BH, Dell'Italia LJ. Three-dimensional changes in left and right ventricular geometry in chronic mitral regurgitation. The American journal of physiology 1996;271:H2689-700.
31. Chetboul V, Sampedrano CC, Gouni V, Nicolle AP, Pouchelon JL, Tissier R. Ultrasonographic assessment of regional radial and longitudinal systolic function in healthy awake dogs. J Vet Intern Med 2006;20:885-93.
32. Marwick TH. Measurement of strain and strain rate by echocardiography: ready for prime time? J Am Coll Cardiol 2006;47:1313-27.

33. Chetboul V, Gouni V, Sampedrano CC, Tissier R, Serres F, Pouchelon JL. Assessment of regional systolic and diastolic myocardial function using tissue Doppler and strain imaging in dogs with dilated cardiomyopathy. J Vet Intern Med 2007;21:719-30.
34. Chetboul V, Serres F, Gouni V, Tissier R, Pouchelon JL. Radial strain and strain rate by two-dimensional speckle tracking echocardiography and the tissue velocity based technique in the dog. J Vet Cardiol 2007;9:69-81.
35. Margiocco ML, Bulmer BJ, Sisson DD. Doppler-derived deformation imaging in unsedated healthy adult dogs. J Vet Cardiol 2009;11:89-102.
36. Marwick TH, Leano RL, Brown J, et al. Myocardial strain measurement with 2-dimensional speckle-tracking echocardiography: definition of normal range. JACC Cardiovascular imaging 2009;2:80-4.
37. Tidholm A, Ljungvall I, Hoglund K, Westling AB, Haggstrom J. Tissue Doppler and strain imaging in dogs with myxomatous mitral valve disease in different stages of congestive heart failure. J Vet Intern Med 2009;23:1197-207.
38. Chetboul V. Advanced techniques in echocardiography in small animals. Vet Clin North Am Small Anim Pract 2010;40:529-43.
39. Takano H, Fujii Y, Ishikawa R, Aoki T, Wakao Y. Comparison of left ventricular contraction profiles among small, medium, and large dogs by use of two-dimensional speckle-tracking echocardiography. Am J Vet Res 2010;71:421-7.
40. Wess G, Sarkar R, Hartmann K. Assessment of left ventricular systolic function by strain imaging echocardiography in various stages of feline hypertrophic cardiomyopathy. J Vet Intern Med 2010;24:1375-82.
41. Culwell NM, Bonagura JD, Schober KE. Comparison of echocardiographic indices of myocardial strain with invasive measurements of left ventricular systolic function in anesthetized healthy dogs. Am J Vet Res 2011;72:650-60.
42. Griffiths LG, Fransioli JR, Chigerwe M. Echocardiographic assessment of interventricular and intraventricular mechanical synchrony in normal dogs. J Vet Cardiol 2011;13:115-26.
43. Simak J, Keller L, Killich M, Hartmann K, Wess G. Color-coded longitudinal interventricular septal tissue velocity imaging, strain and strain rate in healthy Doberman Pinschers. J Vet Cardiol 2011;13:1-11.
44. Takano H, Fujii Y, Yugeta N, Takeda S, Wakao Y. Assessment of left ventricular regional function in affected and carrier dogs with Duchenne muscular dystrophy using speckle tracking echocardiography. BMC cardiovascular disorders 2011;11:23.
45. Wess G, Keller LJ, Klausnitzer M, Killich M, Hartmann K. Comparison of longitudinal myocardial tissue velocity, strain, and strain rate measured by two-dimensional speckle tracking and by color tissue Doppler imaging in healthy dogs. J Vet Cardiol 2011;13:31-43.
46. Chetboul V, Tissier R. Echocardiographic assessment of canine degenerative mitral valve disease. J Vet Cardiol 2012;14:127-48.
47. Smith DN, Bonagura JD, Culwell NM, Schober KE. Left ventricular function quantified by myocardial strain imaging in small-breed dogs with chronic mitral regurgitation. J Vet Cardiol 2012;14:231-42.

48. Zois NE, Tidholm A, Nagga KM, et al. Radial and longitudinal strain and strain rate assessed by speckle-tracking echocardiography in dogs with myxomatous mitral valve disease. J Vet Intern Med 2012;26:1309-19.
49. Silva AC, Muzzi RA, Oberlender G, et al. Longitudinal strain and strain rate by two-dimensional speckle tracking in non-sedated healthy cats. Res Vet Sci 2013;95:1175-80.
50. Suzuki R, Matsumoto H, Teshima T, Koyama H. Effect of age on myocardial function assessed by two-dimensional speckle-tracking echocardiography in healthy beagle dogs. J Vet Cardiol 2013;15:243-52.
51. Suzuki R, Matsumoto H, Teshima T, Koyama H. Clinical assessment of systolic myocardial deformations in dogs with chronic mitral valve insufficiency using two-dimensional speckle-tracking echocardiography. J Vet Cardiol 2013;15:41-9.
52. Westrup U, McEvoy FJ. Speckle tracking echocardiography in mature Irish Wolfhound dogs: technical feasibility, measurement error and reference intervals. Acta Vet Scand 2013;55:41.
53. Zois NE, Olsen NT, Moesgaard SG, et al. Left ventricular twist and circumferential strain in dogs with myxomatous mitral valve disease. J Vet Intern Med 2013;27:875-83.
54. Motoki H, Borowski AG, Shrestha K, et al. Right ventricular global longitudinal strain provides prognostic value incremental to left ventricular ejection fraction in patients with heart failure. J Am Soc Echocardiogr 2014;27:726-32.
55. Chetboul V, Serres F, Gouni V, Tissier R, Pouchelon JL. Noninvasive assessment of systolic left ventricular torsion by 2-dimensional speckle tracking imaging in the awake dog: repeatability, reproducibility, and comparison with tissue Doppler imaging variables. J Vet Intern Med 2008;22:342-50.
56. Suzuki R, Matsumoto H, Teshima T, Koyama H. Noninvasive clinical assessment of systolic torsional motions by two-dimensional speckle-tracking echocardiography in dogs with myxomatous mitral valve disease. J Vet Intern Med 2013;27:69-75.
57. Estrada A, Chetboul V. Tissue Doppler evaluation of ventricular synchrony. J Vet Cardiol 2006;8:129-37.
58. Lopez-Alvarez J, Fonfara S, Pedro B, Stephenson H, Cripps PJ, Dukes-McEwan J. Assessment of mechanical ventricular synchrony in Doberman Pinschers with dilated cardiomyopathy. J Vet Cardiol 2011;13:183-95.
59. Bank AJ, Gage RM, Burns KV. Right ventricular pacing, mechanical dyssynchrony, and heart failure. Journal of cardiovascular translational research 2012;5:219-31.
60. Baron Toaldo M, Guglielmini C, Diana A, Sarcinella F, Cipone M. Feasibility and reproducibility of echocardiographic assessment of regional left atrial deformation and synchrony by tissue Doppler ultrasonographic imaging in healthy dogs. Am J Vet Res 2014;75:59-66.