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Joint meeting with the Small Animal Medicine Society

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Programme Veterinary Cardiovascular Society meeting

Burleigh Court, Loughborough, UK
Friday 2nd November 2018, Autumn meeting

08:30-09:00	**REGISTRATION**
09:00-09:40	Balloon dilation of pulmonic stenosis, with a closer look at morphology ***Mike Martin,*** *Veterinary Interventional Cardiology Training Consultancy, Kenilworth*
09:45-10:15	Managing cardiovascular disease in the older human patient ***Dr Ruth Copeland****, Queens Medical Centre, University of Nottingham*
10:20-10:35	ECVIM-CA Congress 2018 Update ***Claire Watson****,* Langford Vets, University of Bristol ***Mattia Basilli***, Animed Veterinary Hospital, Shedfield
10:40-11:10	**COFFEE BREAK & SPONSORS' EXHIBITION**
11:10-11:50	Getting to the heart of the matter: an investigation into Great Ape cardiovascular disease ***Victoria Strong****, Nottingham Trent University*
11:55-12:25	Remote platelet function testing: an update ***Mark Dunning****, Willows Veterinary Referrals, Solihull*
12:30-13:10	Echocardiography and ECG protocols for the Great Ape Heart Project ***Mike Martin,*** *Veterinary Interventional Cardiology Training Consultancy, Kenilworth*
13:10-14:10	**LUNCH BREAK & SPONSORS' EXHIBITION**
14:10-14:25	Can an approach be taught that improves diagnostic accuracy in electrocardiographic interpretation? ***Melanie Hezzell,*** *Langford Vets, University of Bristol*
14:30-15:20	Atrial fibrillation: when less is more ***Brigite Pedro,*** *Willows Veterinary Referrals, Solihull*
15:25-15:40	ACVIM Forum 2018 update ***Omri Belachsen****, Southern Counties Veterinary Specialists, Ringwood* ***Jenny Brown,*** *University of Edinburgh*
15:40-16:10	**COFFEE BREAK & SPONSORS' EXHIBITION**
16:10-16:40	So what becomes of the broken (ape) hearted? ***Victoria Strong****, Nottingham Trent University*
16:45-17:00	Case report: advanced unclassified cardiomyopathy in a cat **Oliver Duprey,** *Medivet Southend*

17:00-17:30	AGM: VCS members only
17:30-18:00	Breed-related conditions sub-committee meeting
19:00-19:30	Pre-dinner drinks, joint with Small Animal Medicine Society
1945 onwards	Dinner, joint with Small Animal Medicine Society

Programme Veterinary Cardiovascular Society meeting; joint with the Small Animal Medicine Society (SAMSoc)

Burleigh Court, Loughborough, UK
Saturday 3rd November 2018, Autumn meeting

08:30-09:00	**REGISTRATION**
08:45-09:15	Clinical importance of cardio-renal syndrome in human patients ***Dr Rohin Francis**, University College London*
09:45-10:35	Clinical importance of cardio-renal syndrome in veterinary patients: the story so far, and a summary of current research ***Melanie Hezzell and Natalie Finch,** University of Bristol* *Followed by a panel discussion with Q&A*
10:35-11:00	**COFFEE BREAK & SPONSORS' EXHIBITION**
11:00-11:45	Pulmonary hypertension: non-cardiac causes ***Anne-Christine Merveille,** University of Liege, Belgium*
11:50-12:35	Pulmonary hypertension: cardiac causes ***Domingo Casamian**, Southfields Veterinary Specialists, Southend* *Followed by a panel discussion with Q&A*
13:00-14:00	**LUNCH BREAK & SPONSORS' EXHIBITION**
14:00-14:50	Nutritional considerations for cardiac patients ***Marge Chandler**, VetsNow Referrals, Glasgow*
15:00-15:30	**COFFEE BREAK & SPONSORS' EXHIBITION**
15:30-16:10	An update on hyperthyroidism and acromegaly ***Sophie Keyte,** Langford Vets, University of Bristol*
16:15-16:55	The cardiac effects of systemic diseases ***David Connolly,** Royal Veterinary College, London*
16:55-17:15	Q&A: Cardiac – endocrine interactions **Sophie Keyte and David Connolly**
17:15	Close

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Mike Martin MVB DVC MRCVS

Mike qualified from University College Dublin, Ireland in 1986. He gained the RCVS Diploma in Veterinary Cardiology and Specialist status in 1995 and has successfully been re-validated every five years ever since. Between 1992 and 2015, he ran his own private referral practice (The Veterinary Cardiorespiratory Centre, Kenilworth). In October 2015, he moved his Cardiology Service into Willows Referral Centre, Solihull, UK. Since the beginning of 2018 he has again become self-employed, providing consultancy work, training in cardiac interventions at specialist centres around Europe, lecturing and education at CPD events around the world.

Mike has published over 40 scientific peer reviewed papers. He is author of two small textbooks: Small Animal ECGs: An Introductory Guide (3rd edition) and Cardiorespiratory Diseases of the Dog and Cat (2nd edition) published by Wiley-Blackwell. He is author of the chapter on 'Syncope' in the Textbook of Veterinary Internal Medicine (Ettinger, Feldman & Cote, 2016).

In addition, Mike is the proud recipient of some BSAVA awards: in 1993 the Dunkin Award, in 2000 the Melton Award, in 2006 the Petsavers Award, in 2010 the Dunkin & Blaine Awards and in 2017 the JSAP Achievement Award. He has been examiner for Diploma in Veterinary Cardiology for the Royal College of Veterinary Surgeons. He has been both Honorary Secretary and Chairman of the Veterinary Cardiovascular Society (UK).

Dr Ruth Copeland BMedSci BMBS MRCP

Ruth Copeland is a specialty registrar doctor dual accrediting in geriatric medicine and general internal medicine. Having graduated from Nottingham University Medical School in 2010, she developed an interest in the unique challenges that accompany the care of older patients and has a passion for providing quality health care for this patient group. She has worked in hospitals across the East Midlands and hopes to develop a specialist interest in palliative care for older patients.

Claire Watson BVMS MRCVS

Claire Watson graduated from the University of Glasgow in 2016 with a strong interest in cardiology. She went on to complete a 1-year small animal rotating internship in private referral practice, before working in first opinion practice. In July 2018, Claire joined Langford Vets, University of Bristol, as the Cardiology Clinical Assistant (intern) and hopes to undertake a Residency programme in the coming years. Her current research interest relates to cardiac biomarkers.

Mattia Basilli DVM MRCVS

Mattia graduate from the University of Perugia in 2015, after which time he undertook an externship in cardiology at the University of Liverpool, followed by a rotating internship in private referral practice. He currently works in first opinion practice in England and is undertaking the RCVS CertAVP in Cardiology.

Victoria Strong BSc (Hons) BVSc DVetMet AFHEA MRCVS

Dr Victoria Strong qualified as a Veterinary Surgeon from the University of Liverpool in 2010 after having been awarded a First-Class BSc (Hons) in Veterinary Pathology from the Royal Veterinary College, London in 2008. After 3 years in full time general (mixed farm and small animal) veterinary practice she embarked upon a four-year doctoral training programme at The University of Nottingham and Twycross Zoo, and in 2017 graduated with the Degree of Veterinary Medicine (DVetMed). The DVetMed involved a combination of doctoral research alongside specialist clinical training in zoological medicine. Her doctoral thesis entitled *'Getting to the heart of the matter: an investigation into great ape mortality and cardiovascular disease'* and aimed to confront significant gaps in knowledge about these two key areas of interest.

Mark Dunning MA VetMB PhD CertSAM MRCVS DipECVIM-CA

Mark is an ECVIM Diplomate in Internal Medicine. He has recently moved to Willows Referrals in Solihull from the University of Nottingham. His research interests currently include platelet function testing in dogs and cats.

Melanie Hezzell MA VetMB PhD CertVDI CertVC FHEA MRCVS DipACVIM

Following graduation from the University of Cambridge in 1997, Melanie worked in general practice in the UK, Australia and New Zealand for ten years. During this time, she undertook the RCVS Certificates in Veterinary Diagnostic Imaging and Veterinary Cardiology.
Melanie then completed a small animal rotating internship at the Royal Veterinary College and was awarded a PhD by the same institution in 2012 for her research into mitral valve disease in dogs. She became a Diplomate of the American College of Veterinary Internal Medicine (Cardiology) in 2016 following a four-year Residency in Veterinary Cardiology at the University of Pennsylvania. Her research interests centre on the use of biomarkers in clinical practice and the investigation of cardiac remodelling in response to heart disease.

Brigite Pedro DVM MSc MRCVS DipECVIM-CA

Brigite graduated in 2008 from the University of Porto. She first moved to the UK in 2009 and completed an Internship in private referral practice. In 2010, she was awarded the Leonardo da Vinci scholarship from the University of Porto, which allowed her to undertake an internship in Cardiology at the University of Liverpool Small Animal Teaching Hospital. In 2012, she started a Residency programme in Veterinary Cardiology at the same institution. In 2014, Brigite was awarded a Masters degree in cardiovascular pathophysiology. In 2015, having completed her Residency, Brigite became Lecturer in Cardiology at the University of Liverpool. She achieved the European Diploma in Cardiology in 2016. Since then, she has been working at Willows Referrals in Solihull. One year ago, she started a clinical PhD through the University of Porto, looking at atrial fibrillation in dogs.

Omri Belachsen DVM CertAVP MRCVS

Omri graduated from the university of Kosice, Slovakia in 2011. Shortly after graduation, he moved to the UK to take up a position in first opinion practice, where he worked for two years. He then spent one year undertaking a rotating Internship at Willows Referrals before joining Southern Counties Veterinary Specialists as a Cardiology intern in 2016. During this time, he completed the CertAVP. In March 2017, he began a Cardiology Residency, also at Southern Counties Veterinary Specialists.

Jenny Brown BVM&S MRCVS DipACVIM

Jenny graduated from the Royal (Dick) School of Veterinary Studies in 2011, and subsequently completed an internship at B&W Equine Vets in Gloucestershire, followed by a few months in ambulatory equine practice. She completed a 3-year residency in Large Animal Internal Medicine at the University of Minnesota in 2017 and returned to the Royal (Dick) School of Veterinary Studies where she is currently undertaking a PhD in Veterinary Medicine, studying the effects of exercise on cardiac structure and function.

Oliver Duprey BSc BVetMed CertAVP MRCVS

Oliver originally trained in Zoology at University College London and worked at London Zoo as a keeper, caring for sloth bears, hippos and camels. Desiring a new challenge, Oliver studied veterinary medicine at the Royal Veterinary College and developed an interest in Internal Medicine. He graduated in 2013 with honours and worked in first opinion practice. He completed the CertAVP (Small Animal Medicine) and gained experience with both abdominal ultrasonography and echocardiography. Since then, Oliver has enrolled in the CertAVP in Cardiology, with support from Specialists in the field.

Dr Rohin Francis MBBS BSc MRCP

Rohin Francis is a final year Registrar in interventional cardiology and a clinical research fellow at University College London, undertaking a PhD in advanced cardiac imaging based at Royal Free and University College Hospitals in London. He received his training in London and Cambridge and has taught at St George's, Imperial College and Cambridge Universities. He likes to waste time making YouTube videos about medical science, some even feature animals but he promises he isn't trying to muscle in on veterinary territory. He can be found at medlifecrisis.co.uk or on Twitter @medcrisis.

Natalie Finch BVSc PhD MRCVS DipECVIM-CA

Following graduation from the University of Liverpool in 2005, Natalie worked in small animal practice in Cheshire. Natalie completed her PhD at the Royal Veterinary College in 2011 researching feline CKD. She subsequently undertook a residency in feline medicine at the University of Bristol sponsored by International Cat Care. Natalie is a European Veterinary Specialist in Small Animal Internal Medicine and RCVS Specialist in Feline Medicine. She is currently a Wellcome Trust funded clinical postdoctoral fellow at the University of Bristol. Natalie was awarded the 2013 IRIS award in recognition of her research into feline CKD.

Anne-Christine Merveille DVM PhD DipECVIM-CA

Anne-Christine graduated in 2005 and performed an internship at the university of Liège. She worked during 1 year at the National Veterinary school of Lyon as assistant in small animal internal medicine department. In 2008, she started her PhD on primary ciliary dyskinesia and was involved in a European research project, the "LUPA project". At the same time, she started an alternate training program in Small animal Cardiology between the University of Liège and the Royal Veterinary College in London. In 2015, she defended her PhD and in 2016, she obtained her Diploma of the European College of Veterinary Internal Medicine – Companion Animals, in the subspecialty of Cardiology. Since 2014, she works as a cardiologist in the University of Liège and remains involved in the internship and residency training program in internal medicine. Her area of interest are the use of ultrasonography in an emergency context and pulmonary arterial hypertension due to respiratory or systemic disease.

Domingo Casamian DVM CertSAM CertVC DVC MRCVS DipECVIM-CA

After qualifying from the University of Zaragoza in Spain, Domingo completed an Internship at the Animal Medical Centre (Manchester) and worked in two large hospitals within the UK, where he obtained the RCVS Certificates in Small Animal Medicine and Veterinary Cardiology. He then joined the University of Bristol as a Resident in 2006 where he first completed the ECVIM Diploma in Small Animal Internal Medicine, then the RCVS Diploma in Veterinary Cardiology. He stayed at the University of Bristol Small Animal Hospital until 2016 as a clinician, and later the head of the cardiology service. After 18-months working at Dick White Referrals, he joined Southfields Veterinary Specialists in February 2018. Domingo has published many scientific papers and has written book chapters in both Cardiology and Respiratory Medicine. He has also spoken widely at national and international conferences. He is a visiting lecturer in Cardiology and Respiratory Medicine at the Catholic University of Valencia and is completing a part time PhD at this institution, studying the cardiovascular and arrhythmogenic effects of a protozoal organism.

Marge Chandler DVM MS MANZCVS MRCVS DipACVN DipACVIM

Marge Chandler is a Clinical Nutritionist at Vets Now Referrals (Glasgow) and a private consultant in small animal medicine and nutrition. She has an MS (Animal Nutrition) and a DVM from Colorado State University (CSU). She undertook Residency training in small animal internal medicine and veterinary clinical nutrition at CSU and Massey University (NZ) and is a Diplomate of the American College of Veterinary Nutrition and of the American College of Veterinary Internal Medicine (Small Animal Medicine). She is Co-Chair of the WSAVA Global Nutrition Committee, WSAVA Liaison to the American Academy of Veterinary Nutrition, charter member of the European Veterinary Nutrition Educators Group and a member of the Scientific Advisory Committee for FEDIAF.

Sophie Keyte BVMS (Hons) MVetMed (Dist) FHEA MRCVS DipACVIM

Sophie qualified from Glasgow University in 2008, after which time she spent a few years in first opinion practice. She then completed a Small Animal Medicine and Critical Care Internship and a three-year Residency and masters in Small Animal Internal Medicine at the Royal Veterinary College, London. She became a Diplomate of the American College of Small Animal Internal Medicine (ACVIM) in 2016. Sophie enjoys all aspects of Internal Medicine, but her main areas of interest are endocrinology and infectious disease. During her Residency, Sophie was a member of the Feline Acromegaly Team at the Royal Veterinary College, becoming involved in research projects and both medical and surgical treatment of this syndrome. She is currently leading the hypophysectomy service for canine pituitary-dependent hyperadrenocorticism, alongside the Neurology and Emergency and Critical Care team, at Langford Veterinary Services (University of Bristol).

David Connolly BSc BVetMed PhD CertVC CertSAM MRCVS DipECVIM-CA

After qualifying from the Royal Veterinary College, David pursued a career in research with the Medical Research Council. Having obtained a PhD in molecular genetics, he continued research for three further years, investigating the molecular mechanism underlying early embryonic development. Following a period working for the PDSA in the Midlands, he returned to the RVC and completed a Residency in the Internal Medicine Service. During this time, David obtained the RCVS Certificates in Small Animal Medicine and Cardiology, and subsequently the ECVIM Diploma in Cardiology in 2003. He has published widely in various areas of cardiology, but recently has developed an interest in cardiac stem cells.

Balloon Dilation of Pulmonary Valve Stenosis, and a Closer Look at the Morphology

Mike Martin
Veterinary Interventional Cardiology Training Consultancy, Kenilworth

Pulmonic stenosis (PS) is a common congenital disorder in dogs. PS can be divided into subvalvular (infundibular), valvular and supravalvular; with valvular PS being by far the most common in both dogs and people. In valvular PS in dogs there are three different morphologies, 1) commissural fusion, 2) dysplastic and thickened valve leaflets +/- hypoplastic valve leaflets and 3) narrowing of the pulmonary annulus (pulmonary hypoplasia). These three morphologies are often present in most dogs to a variable degree. However some publications have used only two classifications for the purposes of their study.

PS presents more commonly in certain breeds: an analysis of recent veterinary publications with a total of 338 dogs studied found that the top five reported breeds are Boxer (14%), English Bulldog (9%), West Highland White Terrier (6%), French Bulldog (5%) and Cocker Spaniel (5%).

Dogs with PS present with a variety of clinical signs; the same analysis found the most common presenting signs were syncope (16%), exercise intolerance (15%) and ascites (7%). More than half of dogs studied (57%) were asymptomatic when presented to the cardiologist for examination.[1, 2, 3, 4, 5] PS also occurs in cats, although it is much rarer.

Several different guidelines exist for grading the severity of PS. The most frequently cited in the veterinary literature uses Doppler-derived right ventricle to pulmonary artery pressure gradient (PG). A PG of >10mmHg to 49mmHg is described as mild PS, 50-80mmHg is moderate, >80mmHg is severe and >140mmHg as very severe.

Balloon valvuloplasty (BV) was first performed in a dog in 1980 [6]. The procedure had been developed at Johns Hopkins Hospital, Baltimore, but before permission was given to perform BV in a child, it needed to be tested on a dog. Jim Buchanan took a Bulldog with severe PS to Johns Hopkins for BV. The dog survived the procedure and permission was granted for a trial in children; the first BV was performed in a child in 1982.

Nowadays, following recommendations from human literature, most authorities report a balloon to annulus ratio (BAR) of 1.2-1.5 and found improved post-BV PG with a BAR of 1.2-1.4 [7]; this has since been refined to an optimal BAR in "*typical (i.e. non-dysplastic) PS*" of 1.2-1.25 [8]. A prospective study in veterinary medicine failed to demonstrate a difference between BAR groups of 1.2-1.3 and 1.3-1.5 [9]; this study also found significant interobserver variability in measurement of BAR.

A successful outcome in BV is defined variously in the veterinary literature as, a 50% reduction in pre-BV PG or a final PG < 80mmHg [10]; immediate post-BV PG <50mmHg and no clinical signs [11]; 1y post-BV PG<75mmHg [1]. In human medicine, similar variations in outcome description exist with "optimal" post-BV PG values cited between 25- 50mmHg however two recent articles cite an immediate post-BV PG of <30mmHg as optimal. Other authors require that patients are symptom- and medication-free one year following intervention.

Several authors have identified negative survival predictors for severe PS: the presence of RCHF; clinical signs at presention (lethargy, syncope and exercise intolerance in particular); younger age at diagnosis; severity of PG; presence of tricuspid regurgitation (TR); right atrial and ventricular hypertrophy [2, 3, 4, 10]. One research group have identified worse outcomes in dogs with "type B" PS (dysplastic valve with hypoplastic PV annulus) [1, 2]. However research by the same group [11] reported that type B PS did not affect long-term BV results.

In the human literature *"pulmonary valve dysplasia has been considered … as a relative contraindication for balloon dilatation*" [8]. The author goes on to say, however, that *"based on our own experience and that of others, BV is the initial treatment of choice".* They suggest that a BAR of 1.4–1.5 should probably be used in patients with dysplastic valves. The most important determinant of a favourable result is the presence of commissural fusion; highlighting the need for careful scrutiny of the valve prior to ballooning and supporting the use of BV as the initial treatment of choice for all types of PS.

Both the human and veterinary literature agree that mild PS does not usually require treatment and that both people and animals are expected to live normal lives with the condition. In people with moderate PS, although some controversy exists, authors recommend performing BV if the PG is >60mmgHg, or >50mmHg if the patient is symptomatic [8] or if the PG >64mmHg[12]. A recent veterinary study examined outcomes in dogs with moderate and severe PS: the authors concluded that BV did not significantly increase survival in moderate PS [2]. However, the authors also found that dogs with moderate PS and clinical signs had an increased risk of cardiac death (HR 9.9). Another recent study [4] suggested that animals with PG >60mmHg may benefit from BV, although the statistical significance of this paper has been questioned [13]. More research is needed before we can safely decide on the optimal treatment of moderate PS in dogs.

For dogs with severe PS, several papers demonstrate improved survival and improvement in clinical signs in dogs that underwent BV. One study [3] concluded that BV improves clinical outcome in severe PS and found that it eliminated symptoms in 24 out of 30 (80 percent) of the dogs in which long-term follow-up was available (mean 2.7 years). When adjusted for PG, age and presence of clinical signs, BV was associated with a 53% reduction in the hazard rate in severe PS. Other studies have found a similar protective effect of BV [1, 2].
In the human literature, one study [14] reported that follow-up data of ten years duration suggests BV has equivalent outcomes to surgical valvuloplasty. BV is now the preferred treatment for typical valvular PS (PG>60mmHg in asymptomatic patients, >50 in symptomatic patients). They also stated that beta-blockers (BBs) are not usually necessary and are only indicated if significant infundibular hypertrophy and dynamic stenosis exist post-procedure. In dogs, post-procedure dynamic stenosis seems to be very common and betablockers are often used, though no prospective data showing improvement in clinical signs or outcomes have been published to date.

When contemplating BV one must be familiar with the risks, in order that cases can be selected appropriately and owners able to make informed consent. Intraoperative fatality rates vary between 2.4 and 7.5% in dogs with more recent publications reporting lower rates [1, 3, 11, 15]. Coronary artery abnormalities are a common cause of intraoperative death and should be excluded on echocardiography or angiography prior to BV [10]. One group initially reported

successful BV in four English Bulldogs using conservative BARs (0.6-1) [16]. However, follow-up in these dogs showed poor long-term outcomes with 50% mortality within 7 months and the remaining two dogs demonstrating signs of restenosis and/or right ventricular failure in less than three years post-BV [17].

Other intra-operative complications include development of benign and malignant ventricular arrhythmia, transient bradycardia, hypotension and right ventricular perforation; clinicians performing BV should be prepared to manage these complications in order to minimise procedural risk. A review reported similar complications in BV in human patients: transient bradycardia and hypotension during balloon inflation; transient or permanent right bundle branch block (RBBB) or AV block; balloon rupture, tricuspid papillary muscle rupture and PA tears[11]. These complications are rare and can be avoided by meticulous attention to detail [8]. Dynamic right ventricular outflow tract obstruction occurs in nearly 30% patients; older patients and those with higher PG are more likely to have significant obstruction. When the residual infundibular gradient is >50mmHg, BBs are recommended. Restenosis following BV occurs in 8-10% of human cases; similar data is reported in the veterinary literature. There was no incidence of significant post-BV arrhythmia in large human studies. One study [8] states "*in experienced hands, risk of death or major complications is very low*" (0.24%, 0.35% respectively in 822 procedures).

A recent study [15] describes 39 cases of severe PS undergoing BV from an anaesthesia viewpoint. Complications are described including cardiac arrest in one dog, ventricular fibrillation in another (successfully converted with DC cardioversion) and balloon rupture in two cases; no long-term complications were reported from balloon rupture. Four cases developed significant bradycardia during BV, presumably from the Bramham reflex, whilst twenty-one had intraoperative VPCs. Half the cases developed intraoperative hypotension; nine during balloon inflation and ten before; the authors suggest this was due to anaesthetic effects rather than outflow obstruction during balloon inflation.

The same paper reported their mean general anaesthesia and procedural times as 268 minutes (4.5hrs) and 193 minutes (3h 13 minutes) respectively; this is the only published veterinary data on procedure times in a large cohort found for this review. Unpublished data from clinical audit at the Vet Cardiorespiratory Centre, Kenilworth UK gave GA and procedure times as 73 minutes and 43 minutes respectively (2014).

In human medicine, a study [12] suggests that patients with moderate PS or PR should be assessed annually and undergo echocardiographic examination every two years.

A double-ballooning technique was developed in human medicine for when the pulmonary annulus was very large and/ or femoral vein access small. One study [18] describes the procedure in dogs; the article contains a detailed description of technique and describes potential advantages of the method including reducing the risk for hypotension during balloon inflation and preservation of the jugular vein. In human medicine, a study [19] reported that results of double BV, though excellent, are comparable to, but not superior to, those observed with single BV. The availability of large diameter balloons has made the double BV technique redundant in most centres and theoretical benefits such as reduction of hypotension during balloon inflation do not appear to significantly affect outcome. Importantly, double ballooning

takes more time and involves more clinicians and equipment with (as yet) unproven benefit in veterinary medicine.

There are no scientific publications on the medical management of PS in dogs, other than a paper which reviewed outcome in dogs with PS that did not undergo BV, however only 5 of the dogs in this study were given medical treatment [4]. Dogs with moderate/severe PS, especially if they have dynamic right ventricular outflow tract obstruction, are often prescribed a BB in an attempt to reduce the PG. If a dog is in RCHF then medications for heart failure are indicated.

Recently, human medicine has begun using percutaneous valve replacement for patients with PS who are refractory to BV or surgical therapy [20]. Various systems are available; one uses harvested bovine jugular valve with a segment of vein, mounted upon a wire stent. The device is placed across the native outflow tract and inflated using a "balloon within balloon" technique; early results are promising and this technology may become available to veterinary medicine in the future.

A potential future therapy for dogs may be intravascular stent placement. A brief communication on 2 dogs with supravalular stenosis that underwent successful transcatheter intravascular stent placement [21]. One dog had an extraluminal mass compressing the pulmonary artery and the other had developed a supravalvular stenosis following a patch-graft repair for congenital valvular PS.

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Managing Cardiovascular Disease in the Older, Human Patient

Dr Ruth Copeland
Queens Medical Centre, Nottingham

For people in the UK, living in to old age is the expectation rather than the exception. Life expectancy is increasing and one third of all children born today will live to see their 100th birthday. As the population ages we are faced with an emerging conundrum of how best to treat this ever-enlarging demographic. The oldest old, those more likely to suffer from multimorbidity, frailty and cognitive impairment, are frequently excluded from research trials and there is a paucity of evidence for this patient group. Is it really possible to treat old patients equally to their younger counterparts – and should we?

Hypertension is a key preventable cause of cardiovascular disease in older adults and it has been shown that hypertensive patients aged over 60 will benefit from antihypertensives. However, the benefit is less clear for very old patients (those aged over 80 or 85) and there is evidence that a lower systolic blood pressure, in particular low blood pressure augmented by antihypertensive therapy, is associated with a higher all-cause mortality and accelerated cognitive decline in these patients. Orthostatic and vasovagal syncope are augmented by antihypertensive treatment and are strongly associated with falls. Falls in older adults are a leading cause of morbidity and the resulting loss of confidence, functional deterioration and hospital attendances lead to an increasingly institutionalised and dependent population.

Aortic stenosis is the most common valvular heart disease in Europe and its prevalence increases with age, affecting 10% of people over 80. There is a high mortality rate for symptomatic aortic stenosis unless treated with surgical replacement. Operative mortality for those patients aged over 80 stands at roughly 10% and trials have shown a strong link between operative mortality and frailty as well as other comorbidities which are frequently present in the older patient with aortic stenosis. Consequently, many older patients are deemed to be surgically inoperable. In these patients, transcatheter aortic valve implantation (TAVI) can be undertaken and this has been shown to be non-inferior to traditional surgical aortic valve replacement in those deemed to be at high surgical risk and to reduce mortality by 20% when compared to conservative management. TAVI therefore represents an option for older patients who are not surgical candidates and advanced age need no longer be a barrier to intervention. Older patients who receive a TAVI have been shown to derive the same benefits as younger patients with regards physical activity and quality of life measures.

In humans, the majority of deaths in older adults are due to ischaemic heart disease. The European Society of Cardiology guidance states that early (<12hr) reperfusion therapy (angioplasty or pharmacological) should be provided to patients with ST elevation myocardial infarction (STEMI) but the evidence base is limited in older patients. Providing invasive coronary angioplasty in Non-ST elevation myocardial infarction (NSTEMI) depends on the patient's perceived risk, comorbidities, cognitive status and life expectancy. Decision making

can be difficult for older patients presenting acutely, when clinicians need to provide therapy quickly but may not have a clear understanding of the patient's functional baseline. Clinicians therefore may adopt a more conservative approach in older people. The After Eighty Study supported an invasive strategy in patients over 80, with significantly reduced risk of further myocardial infarction, need for urgent revascularisation, stroke and death (from MI). In a subgroup of patients aged over 90, no significant difference was seen in these primary outcomes and the evidence here remains unclear.

The focus of this presentation is to provide an overview of management in common cardiovascular diseases in older people and to highlight some of the clinical and ethical challenges that can arise when treating the geriatric patient, in particular those with multimorbidity or a limited life expectancy.

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ECVIM Congress 2018 Update

Claire Watson, *Langford Vets, University of Bristol*
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Comparison of ECG-gated Multi-detector Computed Tomography and Two-Dimensional Echocardiographic methods in the Assessment of Left Atrial Size using Left atrial-to-Aortic Root Short-Axis Ratio in Dogs

Presented by Jonathan Bouvard of Edinburgh University

The team at the Edinburgh compared traditional 2D echo measurements of the left atrial-to-aortic root ratio in the right parasternal short axis to the same view obtained on ECG-gated CT. The hypothesis was that were would be a poor correlation between measurements obtained via echo and CT, largely due to cut plane variability and difficulty ascertaining the left atrial border in light of pulmonary vein position on echocardiography. The study involved twenty dogs with no evidence of cardiovascular disease. The dogs had been referred for CT under general anaesthesia with the following echo performed promptly.

In systole the results indicated a good correlation between CT and echo with Pearson's Correlation Coefficient reaching 0.53. A bland Altmans plot was used to compare the two tests and it was found that echo seemingly under-estimates La:Ao, compared to CT, by 0.22. The results in diastole proved to have no correlation.

The under-estimation of La:Ao on echo is interesting, however there were some outliers in the results which is not unsurprising based on the small number of animals in the study.

Of note, both methods of measurement had clinically acceptable inter and intra-observer repeatability. It is possible that our assessment of left atrial size based on La:Ao ratio on echo may be underestimating true size. However, our reference intervals and following treatment recommendations are based on echocardiographically obtained values and so this potential discrepancy unveiled by computed tomography is unlikely to change our approach to left atrial measurement in the future.

LA:Ao – are the old reference intervals valid?

Presented by Mark Rishniw of VIN / Cornell

Our reference intervals for left atrial-to-aortic root ratio measurements originate from Mark's original paper in 2000, which examined a population of 36 Cavalier King Charles Spaniels and established 1.6 as being the La:Ao maximum in healthy dogs (of this breed). He looked again at this measurement but this time in a much broader sense.

The abstract was from a large, multi-centre study of 223 healthy dogs of mixed breeds and weights, each of which had complete clinical history, clinical exam and echocardiographic assessment documented. Any dogs which did not meet these criteria (or had cardiac disease) were excluded. 56 different breeds were examined, with a weight range of 5-65kg.

Results indicated a La:Aomax upper limit of 1.73. There was no correlation to weight, which is in agreement with previous studies. 6% of the dogs measured above 1.6 with three breeds in particular appearing to measure larger: beagles, boxers and English setters. These animals

did not develop any cardiac disease when followed up in the long term, and so the measurements cannot be brushed off as occult disease. Even when these three breeds were excluded from the statistical analysis, the La:Aomax upper limit remained "elevated" at 1.66. From this abstract it would seem that an La:Ao short axis measurement of 1.6 may be a conservative upper limit and particular breeds may be more prone to measure higher than others.

Effect of pimobendan on left atrial function in dogs with stage B2 myxomatous mitral valve disease (F. Sarcinella, et al.)

The abstract shows the results of a retrospective study conducted at the University of Liverpool on pimobendan effects on the left atrial function in dogs affected by stage B2 mitral valve disease (MVD). The authors hypothesized that atrial function would improve after initiation of pimobendan therapy.

Electronic patient records of dogs referred at the Small Animal Teaching Hospital between 2015 and 2017 were reviewed. 20 dogs of different breeds with stage B2 MVD were included in the study. They were all under 30 kg of body weight. Cavalier King Charles Spaniels were overrepresented. An echocardiographic examination was performed that included 2D Doppler echocardiographic images obtained from the right parasternal and left apical views. MVD Stage B2 was defined as a left atrium to aorta ratio of more than 1.6 and a normalized left ventricle internal diameter dimension of more than 1.7. Dogs with other concurrent disease or on any other medical treatment were excluded. Left atrial diameter and volumes were recorded. Pulsed wave tissue Doppler imaging (PW-TDI) of the left ventricular longitudinal myocardial velocity associated with atrial contraction (A'), was also considered indicator of LA function and was measured at the level of the interventricular septum and the left ventricle free wall.

The A' measured with PW-TDI, both at the level of the interventricular septum and at the left ventricle free wall, was increased after pimobendan therapy. The left atrium complete ejection fraction, described as [(LAvol max - LAvol min) /LAvol max], was decreased after pimobendan; the mitral valve regurgitation velocity increased after pimobendan whereas there were no changes in LA diameter and LA volume.

Limitations of this study are largely related to the retrospective nature of the study. There was a small number of dogs included. They did not have a control group that did not receive the pimobendan therapy although this might be difficult to achieve due to ethical issues. The second echocardiography was performed at different times (between 1 and 6 months), which could affect results.

In conclusion, the use of pimobendan in dogs with MVD stage B2 improves the atrial function measured with PW-TDI A'.

Evaluation of NT-proBNP Levels in Sport Dogs After Immediate Physical Activity and After an Intense Two Months Training Session (F. Ivasovic et al.)

This abstract shows the results of a study conducted at the University of Zurich evaluating the changes of NT-proBNP concentrations before and after exercise in two breeds of dogs.

The aim of the study was to compare NT-proBNP levels before and after different type of physical activity in two different breeds of dogs. This was a prospective study with 14 dogs included. 7 were German Shepherd dogs (GSD) that were entering the military service, and 7 were Scandinavian hounds (SH) used in sledge competitions. The SH were rested for 3 weeks before entering the study.

All dogs underwent an echocardiographic scan when entering the study to rule-out any other concurrent cardiac disease. NT-proBNP concentrations were measured at day 0, both at rest and after 10 minutes of exercise, and they were evaluated again 2 months after intense scheduled training, both at rest and after 10 minutes of exercise. The difference between the NT-proBNP concentrations at rest and after 10 minutes was defined as ΔNT-proBNP. The type of exercise differed from GSD to SH. GSD underwent high intensity interval activity whereas the SH were running on a treadmill/sledge exercise.

At baseline, the results showed that SH had a higher NT-proBNP, at rest, and a higher normalized left ventricle diameter in diastole (LVIDDN). The ΔNT-proBNP was positive in both breeds but there was no significant difference in this value between the two breeds. Two months after, at baseline both breeds had similar NT-proBNP values, with the SH having higher concentrations. The ΔNT-proBNP was higher in SH but not significantly.

The results showed the NT-proBNP levels were higher in SH compared to GSD, the exercise affected the concentration of NT-proBNP and SH had larger hearts at baseline. The study has some limitations. Only 14 dogs were included in the study. Moreover, SH were reported to be very excited when manipulated and this could have altered the natriuretic peptide values. The SH were trained dogs before entering the study and, although they had a 3-week break from exercise, their higher LVIDDN could be related to this. The age of the dogs was not reported in the abstract and it is known that in humans age causes an increase in NT-proBNP. Increase in NT-proBNP it has been reported to be increased secondary to multiple factors, for example, kidney disease. Blood tests were not run as far as reported in the abstract, therefore, although unlikely, it is impossible to rule renal disease; though, it was not the aim of the study to detect a normal value of NT-proBNP whereas the authors wanted to emphasize the change in NT-proBNP levels before and after exercise.

Getting to the heart of the matter: an investigation into Great Ape cardiovascular disease

Victoria Strong
Nottingham Trent University

Due to growing threats posed mostly by habitat loss, hunting, the illegal pet trade, climate change and disease, wild populations of great apes are all classified as endangered (bonobos and chimpanzees) or critically endangered (Eastern and Western gorillas; Bornean and Sumatran orangutans) (IUCN 2016). Zoo-housed great apes therefore serve not only as ambassadors for their species in helping to raise funds and public awareness of conservation issues but as a potential source for repopulation, thereby providing insurance against extinction. Great apes housed in zoos across the world are currently carefully managed as part of endangered species breeding programmes, the ultimate success of which depends not only on the occurrence of births, but also the rearing of animals to sexual maturity and the maintenance of a population of healthy adults of sound reproductive status (Munson & Montali 1990). Any disease threat to zoo-housed great apes is therefore of great concern not only for the individual or zoological collection affected but more widely, for the future breeding and conservation of these endangered animals.

A comprehensive and retrospective review of mortality among European (and North American) zoo-housed great apes was carried out, and the main causes of death between 2004-2014 for each genera were identified (Strong et al. 2017; Strong 2017). Cardiovascular disease was found to be associated with significant proportional overall mortality among bonobos (34%), chimpanzees (18%) and gorillas (15%). Cardiovascular diseases only accounted for 10% of orangutan deaths during the period under study. Further analysis of data collected from these animals (n=71) identified advancing age and male sex as factors associated with increased risk of death due to cardiovascular disease (Strong et al. 2018). It also demonstrated the most common clinical presentation (42%) to be sudden and unexpected death, therefore suggesting a need for zoos to undertake proactive ante-mortem screening to identify sub-clinically affected individuals. A variety of conditions including cerebrovascular infarctions and haemorrhages, aortic dissections and cardiomyopathies such as HCM, DCM and ARVC were identified as the cause of death in these animals. The most commonly diagnosed lesion (45%; n=32/71), however, was idiopathic cardiac fibrosis. This lesion is also referred to as fibrosing cardiomyopathy and interstitial myocardial fibrosis and, despite significant literature coverage and research over recent years (Strong et al. 2016), understanding about its aetiopathogenesis remains poor.

Various reasons for current gaps in our understanding have been identified. There exists great variation in the approach to both the ante-mortem and post-mortem investigation of great ape cardiovascular disease between zoological collections. This has until recently

resulted in a paucity of good quality, comparable or consistent data and samples available for research in this field. However, in 2013, a European taskforce entitled the Ape Heart Project (based at Twycross Zoo, UK) was brought together to try to tackle this and other key issues which were limiting progression of understanding in this area. One of the project's outputs to date, has been to develop and disseminate guidelines to improve and standardise the clinical assessment of great ape cardiac health across Europe. Despite great progress to date, further work is required to understand what is normal for these species (especially under anaesthesia), and to better explain how techniques used to diagnose cardiac disease in domestic species and humans can be extrapolated and applied to great apes.

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Remote platelet activity testing: an update

Mark Dunning
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Echocardiography and ECG protocols for the Great Ape heart project

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Heart disease is often reported as a significant cause of death among captive great apes (chimpanzees, bonobos, gorillas and orangutans). However, our understanding about the condition and consequently our abilities to treat and prevent it are limited. In particular, very little work has been done looking at the European population of apes. This project is part of an EAZA Great Ape TAG endorsed initiative striving to develop a collaborative and co-operative approach to the investigation of cardiovascular disease among the European captive great ape population.

There is a need for more suitably trained people to become involved and volunteer their services. These include vets with cardiology training and skills to perform echo in a primate, human cardiologist or sonographers. Most zoos do not have a suitable portable cardiac ultrasound machine, so anyone offers their services needs to bring this along.

The echo protocol has been designed to follow the British Society of Echocardiography protocol for humans, thus being familiar with this is recommended.

Links to the current protocols are given below:

A Guide to Performing a Complete Standardised Echocardiographic Examination

https://twycrosszoo.org/wp-content/uploads/2018/05/C2-Standardised-echo-protocol.pdf

A Guide to Performing a Standard Electrocardiogram (ECG) in Great Apes

https://twycrosszoo.org/wp-content/uploads/2018/05/C4-Protocol-for-Performing-a-Standard-Electrocardiogram.pdf

Can an approach be taught that improves diagnostic accuracy in electrocardiographic interpretation?

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Introduction: Identifying more effective methods to teach ECG interpretation could improve veterinarians' diagnostic accuracy. The research questions were i) does an analytic approach to ECG interpretation improve accuracy and ii) are there "threshold concepts" inherent to learning how to interpret ECGs?

Subjects: Sixteen final year veterinary students and 65 veterinarians (21 with no post-graduate cardiology qualifications, 30 cardiology certificate holders and 14 cardiology diploma holders).

Methods: A questionnaire including an ECG interpretation task that incorporated an arrhythmia and a conduction disturbance was distributed.

Results: Level of experience was not associated with the proportions of respondents adopting an analytic (P=0.091), pattern recognition (P=0.844), or a combined approach (P=0.108), level of difficulty reported in learning to interpret ECGs (P=0.240) or reporting a moment of sudden clarity when learning to interpret ECGs (P=0.669). Most respondents using an analytic approach combined this with pattern recognition (30/34). Students were significantly less likely to correctly identify the arrhythmia (P=0.005), but there was no effect of level of experience on conduction disturbance identification (P=0.103). An analytic approach was significantly more likely to identify the conduction disturbance (P<0.001, likelihood ratio=20.29 (95% confidence interval=2.82 to 146.27). There was no effect of approach on correct identification of the arrhythmia (P=0.414). No "threshold concepts" were definitively identified.

Conclusions: an analytic approach is effective, independent of experience, enhancing recognition of subtle, unusual changes. Pattern recognition is effective for recognition of commonly-encountered arrhythmias, but accuracy improves with experience. Threshold concepts might exist in ECG interpretation but could not be definitively identified.

Atrial fibrillation: when less is more

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Introduction

Atrial fibrillation (AF) is the most common non-physiological arrhythmia in humans and dogs.

The typical chaotic rhythm is easily identifiable on auscultation, however an ECG is always required to confirm the diagnosis. An irregularly irregular rhythm (variable R-R intervals) with no obvious P waves are pathognomonic; the ventricular rate may be variable – most commonly this is fast but occasionally the heart rate can be within normal limits for the breed (the so called “lone AF”).

Lone AF can occur in young, asymptomatic and apparently healthy individuals where cardiac remodelling is often echocardiographically absent (at least in early stages). Lone AF tends to affect giant to large breed dogs, where the atrial area is also large, allowing the development and co-existence of several fibrillatory wavelets that lead to sustained AF.

AF with canine cardiac disease

Most cases of AF have a fast ventricular response rate. With most cases of fast AF, there is significant structural heart disease. Dilated cardiomyopathy (DCM) accounts for most of the cases (45% of dogs with DCM have AF), however myxomatous degenerative valvular disease and congenital diseases associated with marked atrial remodeling can also lead to the development of this arrhythmia. In a recent study, 58% of dogs with AF were affected by DCM, followed by 17% affected by mitral valve disease. Not surprisingly, DCM is the most common underlying cardiac condition as it is most frequently observed in large to giant breed dogs where the increased atrial mass/area can predispose to the development of AF. Most of these dogs present already in congestive heart failure (CHF) at the time of diagnosis of AF and therefore clinical signs are easily perceived – tachypnoea, dyspnea, cough, etc.

Irrespective of underlying heart disease, the prognosis worsens with the development of AF. It is common to see either worsening of the clinical signs associated with a previously well controlled CHF or even episodes of syncope, sudden onset of lethargy or exercise intolerance. By losing active atrial contraction (which contributes to approximately 25-30% of LV filling and cardiac output), dogs with an underlying cardiac disease and a very low cardiac reserve will lose their fragile balance and become symptomatic.

The clinical management of an AF case is not always easy, also because there is still much to learn about this arrhythmia in our canine patients. Several factors should be considered

when deciding the best treatment for the patient: the presence/absence of heart disease, an underlying cause for the arrhythmia, the duration of the arrhythmia, the ventricular rate throughout the day and the animal's lifestyle.

Treating the underlying cardiac disease is always mandatory – most dogs with fast AF will also have CHF and therefore appropriate CHF management is always recommended (diuretics, pimobendan, ACE inhibitors and spironolactone). This is important from the clinical signs point of view, but also because controlling the CHF will reduce the sympathetic tone, which will have a beneficial effect on the AF ventricular response rate.

The treatment of the AF itself can be more challenging and case dependent. It can be divided into rhythm or rate control.

As previously discussed, dogs with lone AF, where structural cardiac disease is excluded, tend to be healthy and have a higher vagal tone, therefore the ventricular rate is usually normal (or near normal), except during exercise. In these cases, withholding treatment is a reasonable option. However, a rhythm control strategy may be also an alternative to consider, in particular if we keep in mind that over time structural remodeling may develop purely as a consequence of AF, rather than due to an occult heart disease. Rhythm control can include DC electrical cardioversion, medical strategies or a combination of the two. Irrespective of method, recurrence of AF post-cardioversion is frequent, and this should also be accounted for when deciding what strategy to pursue.

Rate or rhythm control?

Dogs with fast AF usually require rate rather than rhythm control. Rhythm control would be more physiological, but in the presence of cardiac remodeling the rate of AF recurrence is high and therefore most of the times this strategy will be ineffective at maintaining sinus rhythm. This is also supported by studies performed in humans. The AFFIRM study showed that there was no clear survival advantage of rhythm over rate control in humans with chronic AF and that the latter may be associated with fewer drug-related side effects. Furthermore, the RACE II study investigated the rate control strategy in further detail, comparing strict rate control (<80 bpm rest, < 110 bpm exercise) to more lenient rate control (<110 bpm rest). From the results of this study, the current recommendation in humans is to aim for a lenient rate control (with a target heart rate similar to a ''situation-appropriate'' sinus rate), as there was no clear benefit of achieving a stricter rate control. Strict rate control is now only recommended if the patient continues to be symptomatic despite of a good lenient rate control.

Unfortunately, studies are lacking and information about the best strategy to use in dogs is sparse. Until recently, a mean heart rate (HR) on a 24-hours Holter of less than 140 bpm was considered acceptable by most clinicians.

A recent study from Jung et al reported that in dogs with degenerative valvular disease and AF, a ventricular rate of less than 160 bpm obtained from an in-clinic ECG was associated with a longer survival time than faster heart rates (171 days vs 61 days). These are

promising findings, clearly supporting the importance of rate control in these patients. However, it is widely accepted that the HR in the clinic is falsely increased, as it is affected by a high sympathetic drive and does not reflect the HR in the home environment, where dogs spend most of their time. This was later confirmed by Gelzer et al, who showed that the in-clinic ECG over-estimated the 24-hour Holter mean HR and therefore is not reliable to predict the HR of these dogs at home. It can however be useful to identify dogs with a fast HR at home. This study concluded that an in-clinic ECG HR > 155 bpm suggests poor AF rate control at home, therefore these dogs would benefit from being started on anti-arrhythmic treatment at the time of initial admission.

More recently, the author's group showed that a 24-hour Holter mean HR < 125 bpm is associated with a longer survival time than faster mean HR (1037 days vs 105 days). Furthermore, we showed that for every 10 bpm increase in mean HR, the risk of all-cause mortality increased by 35%. These findings further support a more aggressive rate control strategy, but obviously prospective studies are required to confirm these findings.

Based on the above mentioned findings, the current strategy is based on rate control. The most widely used drugs are diltiazem and digoxin: the combination of these two anti-arrhythmics is more effective than any of them independently. In humans, the use of diltiazem (calcium channel blocker) is controversial in cases of heart failure with reduced ejection fraction (which account for most of our cases), but dogs seem to tolerate its use. When these first-line medications are ineffective, other options may be considered (for example amiodarone, sotalol or even atenolol, depending on the specific case). Atrio-ventricular node ablation and pacemaker implantation is another possibility, however this is reserved for only a few rare cases that do not respond to medical management.

Summary

- AF affects more commonly large/giant breed dogs with underlying cardiac disease
- Congestive heart failure at the time of AF diagnosis is common
- Fast AF requires aggressive rate control treatment
- Combination of digoxin and diltiazem is the best combination for the management of this arrhythmia.

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ACVIM Forum 2018 Update

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So, what becomes of the broken (ape) hearted?

Victoria Strong

Nottingham Trent University

As has already been outlined (see Getting to the heart of the matter: an investigation into great ape cardiovascular disease, page 21), cardiovascular disease and specifically idiopathic cardiac fibrosis have been identified as significant causes of mortality in zoo-housed great apes. In a review of data relating to the death of >680 great apes that died in European and North American zoological collections during the period 2004– 2014, it was found that macroscopic and/or histopathologic examination of the heart is not performed in every case of great ape death (Strong 2017). It was also shown that, when conducted, there were inconsistencies between collections in the expertise of the individual carrying out the examination, the approach followed, samples collected and examined, and the terminology used in subsequent post-mortem reports (Strong et al. 2018a). These factors limit not only the diagnostic power of the examinations performed but also the potential for meaningful comparison between the findings for multiple animals and, therefore, the scope for large-scale multi-centre and longitudinal research studies. Additionally, the resulting paucity of comparable, good quality biological samples available for research leads to competition for resources and further limits the potential for progressive research into great ape cardiovascular disease aetiopathogenesis.

Guidelines for the cardiac autopsy and investigation of sudden cardiac death in people have been published. Based upon two papers outlining such guidelines from the medical literature (Basso et al. 2008; Sheppard 2012), a protocol for post-mortem examination and sampling of the great ape heart was developed (Strong et al. 2018b). It was used to carry out comprehensive, systematic and consistent examinations on formalin fixed hearts from 35 chimpanzees, 8 bonobos, 12 gorillas and 6 orangutans as part of a large-scale prospective study investigating great ape cardiovascular disease pathogenesis.

Details regarding the examination protocol followed and preliminary results from this study will be provided as part of this talk on the topic of great ape cardiovascular disease.

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Case report: Advanced unclassified cardiomyopathy in a cat

Oliver Duprey

Medivet Southend

A 12-year-old cat presented with acute onset dyspnoea to an out of hours emergency veterinary hospital. Not an uncommon clinical presentation by any stretch but certainly not a common underlying cause.

Initial diagnostics identified a pleural effusion, ascites and a significant arrhythmia. After a period of emergency therapeutic stabilisation, an echocardiogram was performed alongside specialist guidance. This revealed a very unusual unclassified cardiomyopathy with both left and right sided chamber dilation, tricuspid regurgitation and atrial fibrillation.

After a challenging period of hypokalaemia, the cat was discharged and remains clinically stable 4-months later. This was a very interesting and unusual cardiomyopathy and reveals the significant benefits of being able to offer in house collaboration between specialist and general practitioners.

Clinical importance of cardiorenal syndrome in human patients

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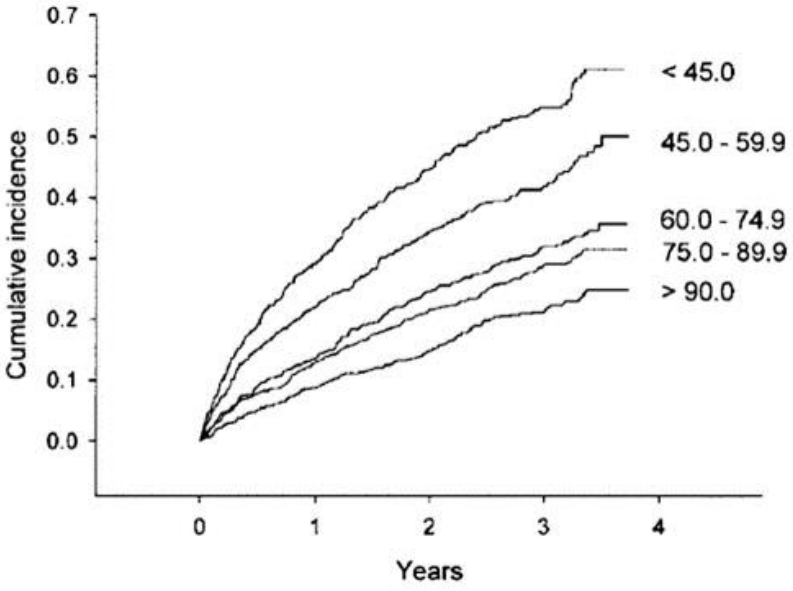
Background

Cardiac and renal disease exhibit a strong and bidirectional effect on one another, both acutely and chronically. Patients with chronic heart failure (HF) frequently develop chronic kidney disease (CKD), with 30-60% developing moderately impaired glomerular filtration rate (less than 60 mL/min per 1.73 m2). A drop in eGFR is an independent marker of increased mortality. Conversely, ischaemic heart disease is a common cause of morbidity and mortality in CKD, accounting for approximately 50% of deaths.

The interplay between cardiac and renal function is multifactorial. It can be subdivided:
* Reduced renal perfusion due to poor cardiac output – (indeed the original definition of cardiorenal syndrome (CRS) was a condition whereby treatment given for HF causes a decline in renal function), although this is probably less important than previously thought
* Neurohumoral changes – HF causes renin-angiotensin-aldosterone system activation and increased antidiuretic hormone and endothelin-1 which promote water and salt resorption. Vasoconstriction occurs in the renal beds.
* Elevated venous pressures – both central venous pressures and renal venous pressure elevation can reduce transrenal perfusion and eGFR.

Risk factors for a patient with HF developing CRS include impaired renal function at baseline, type 2 diabetes, uncontrolled hypertension and atherosclerotic vascular disease. Older, sicker patients will have lower muscle mass so creatinine alone can be inaccurate as a method to estimate GFR. It can be challenging to differentiate between an elevated creatinine due to underlying renal disease, and impaired kidney function due to CRS. A number of techniques exist but none are consistently reliable.



Kaplan-Meier analysis of cumulative incidence of cardiovascular death or unplanned admission to hospital for the management of worsening heart failure stratified by approximate quintiles of estimated glomerular filtration rate in mL/min/1.73m^2 (Hillege et al, Circ 2006).

Management

Pharmacological management can be extremely challenging as conventional therapies for heart failure and renal impairment can be in direct opposition. Drugs to alleviate HF are often nephrotoxic, diuretic use and volume depletion can cause acute kidney injury (AKI); whereas giving intravenous fluid and salt is desirable for renal impairment but likely to exacerbate HF haemodynamics. Clinical judgement is required.

Diuretic resistance is often encountered, particularly to loop diuretics, and can be countered with combination therapy with agents like thiazides, at the cost of significant salt loss. Vasodilators like nitrates/sodium nitroprusside are less nephrotoxic than diuretics and ACE-inhibitors and may improve renal perfusion. Recombinant brain natriuretic peptide and vasopressin antagonists are costly drugs with no demonstrable benefit.

Ultrafiltration is a mechanical process that directly removes plasma water across a semipermeable membrane that maintains the same osmolality as the plasma. Contrast to haemodialysis, which removes solutes from blood across the membrane down a concentration gradient, allowing adjustment of electrolyte and solute concentrations. Recent improvements in ultrafiltration devices allow flexible low-flow catheters to be inserted in the antecubital vein for venous-venous filtration. This is a relatively simple procedure and obviates the need for intensive care admissions and monitoring. It may be of benefit in hospitalised HF patients who are unresponsive to diuretics, exhibit impaired renal function and remain fluid-overloaded.

Clinical importance of cardiorenal syndrome in veterinary patients

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Definitions

The term "cardiorenal syndrome" is an umbrella term that covers a large number of potential pathophysiological mechanisms that may play a role in development of cardiac disease in patients with kidney disease and development of kidney disease in patients with cardiac disease. Patients with cardiorenal syndrome might therefore benefit from a variety of different therapeutic interventions (see notes for the following talk). It is important to remember that the term does not describe a single disease process. However, before the various aspects of cardiorenal syndrome can be investigated they need to be accurately categorized to ensure that clinicians and researchers are standardised in their definitions.

A veterinary consensus statement[1] has modified the previous-published definitions from human medicine[2] from cardiorenal syndrome to cardiovascular-renal disorders (CvRD) as follows (Adapted from: Orvalho *et al* 2017):[3]

Human and veterinary classification of cardiorenal syndrome			
Human classification	Veterinary classification	Brief description	Conditions
Type 1: Acute cardiorenal syndrome	$CvRD_H$ (unstable)	Acute impairment of cardiac function leading to acute kidney injury (AKI)	Acute heart failure Cardiogenic shock
Type 1: Chronic cardiorenal syndrome	$CvRD_H$ (stable)	Chronic cardiovascular disease causing progressive chronic kidney disease (CKD)	Chronic heart failure "Congestive nephropathy"
Type 3: Acute renocardiac syndrome	$CvRD_K$ (unstable)	Acute primary worsening of kidney function that leads to cardiac dysfunction	AKI Hyperkalaemia Uraemia
Type 4: Chronic renocardiac syndrome	$CvRD_K$ (stable)	Primary CKD that contributes to cardiac dysfunction	Chronic glomerular disease Anaemia Systemic hypertension
Type 5: Secondary cardiorenal syndrome	$CvRD_O$	Cardiac and renal dysfunction secondary to an acute or chronic systemic condition	Diabetes mellitus Sepsis

An important difference to note is that the veterinary definition highlights the importance of cardiovascular disorders, which helps to emphasise the importance of secondary effects on the vasculature, as well as the heart, of renal dysfunction in particular in human and veterinary patients.

Evidence for the existence of cardiorenal syndrome

1. $CvRD_H$

   Suggested clinical scenarios that are likely to fall under this category include acute kidney injury secondary to low cardiac output, systemic hypertension causing proteinuria, and cardiovascular thrombus leading to renal infarction.

   Most studies to date have investigated the relationship between congestive heart failure and azotaemia, which is mostly related to the effects of therapy e.g. with diuretics and ACE inhibitors. The prevalence of azotaemia increases with severity of heart disease and heart failure in dogs with myxomatous mitral valve disease.[4,5] Dogs and cats with acute congestive heart failure develop azotaemia during hospitalisation, although this was generally mild and resolved following stabilisation, with no effect on survival shown.[6]

2. $CvRD_K$

   The best characterised effect of renal dysfunction on the cardiovascular system is that of secondary systemic hypertension in dogs and cats with CKD. Evidence of left ventricular remodelling has been shown in several studies, typically with a concentric hypertrophy pattern consistent with pressure overload (although some degree of volume overload is also suspected to occur).[7,8] Evidence of systolic and diastolic dysfunction and aortic insufficiency has also been demonstrated in cats and dogs with systemic hypertension.

   Anaemia is a known complication of CKD and can lead to a high output state as a greater cardiac output is required to supply the tissues due to the decreased oxygen carrying capacity of the blood. To date no conclusive evidence exists in veterinary patients that anaemia secondary to CKD causes worsening cardiac function. However, a retrospective study showed a negative association between anaemia and survival in dogs with myxomatous mitral valve disease, and that anaemia was associated with azotaemia, although this study was not designed to demonstrate causal relationships.[9]

3. $CvRD_O$

   Professor David Connolly will discuss this aspect of cardiorenal syndrome in a later lecture.

Conclusions

Our understanding of the cardiorenal syndrome in veterinary patients, both pathophysiologically and clinically, is very much in its infancy. Extrapolation from physiology, research in animal models of disease and the human medical literature can suggest a variety of areas that are likely to be important (see next lecture). However, until research is undertaken the fascinating interactions between kidney and heart will remain incompletely understood.

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Current veterinary research into cardio-renal syndrome

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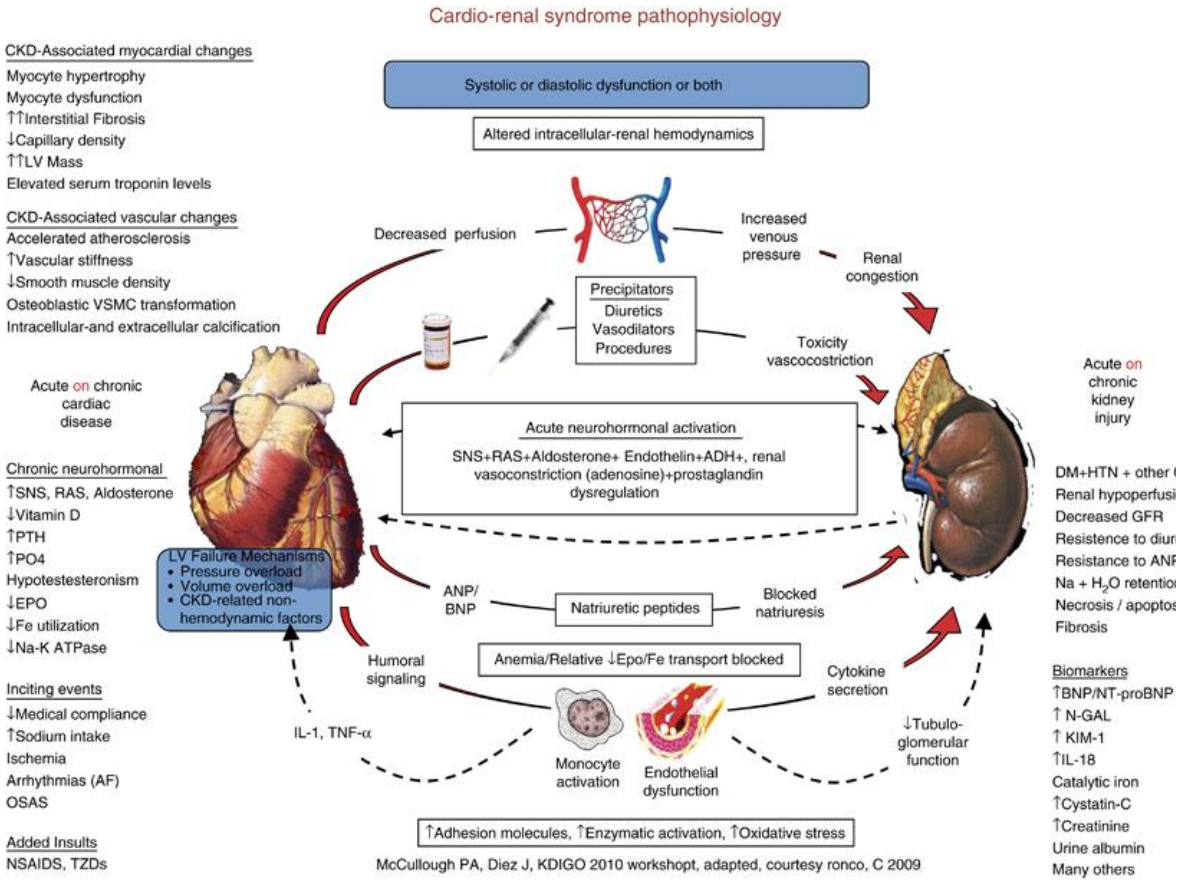
Proposed mechanisms of cardiorenal interactions

By virtue of its role in fluid balance, tissue perfusion, and blood pressure, the physiology of the heart and kidney are inextricably intertwined.[1] As can be seen from the diagram below, a large number of mechanisms for cardiorenal interactions have been proposed in human patients, including decreased renal perfusion, acute neurohormonal activation, the effects of drugs (e.g. diuretics), anaemia, inflammation and endothelial dysfunction. Given the current paucity of data in veterinary patients this is clearly an area ripe for research.



From: Herzog et al 2011[2]

Areas of active research

1. Biomarkers

   A study investigating the clinical utility of novel biomarkers of renal tubular injury, including urinary clusterin, serum and urinary cystatin B, serum inosine and urinary neutrophil gelatinase-associated lipocalin (NGAL) is currently underway at the

University of California.[3] It should be noted that clusterin, cystatin B and inosine are specific to the renal tubules, whereas NGAL is expressed by a variety of epithelia and so lacks specificity for kidney injury. This group have demonstrated significant changes in biomarker concentrations in response to acute congestive heart failure secondary to naturally occurring chordae tendineae rupture in a dog, consistent with an acute kidney injury due to decreased renal perfusion.

2. Cardiovascular-renal disorders due to primary kidney disease ($CvRD_K$)

A study of dogs with stable chronic kidney disease (CKD; IRIS stages 2 and 3) and no evidence of primary heart disease investigated the effect of CKD on cardiac structure and function (Hezzell et al, manuscript in review). Dogs with CKD has significantly lower glomerular filtration rate and higher N-terminal pro-B-type natriuretic peptide, urinary cystatin B, clusterin and NGAL compared to controls. Echocardiographic indices of left heart size and function were similar between dogs with CKD and controls. Median follow-up time was 666 days, during which 6 CKD dogs died. Risk of death increased with increasing age and normalized left ventricular posterior wall thickness (LVPWDN). Presence of $CvRD_K$ was suggested by the association between LVPWDN and survival.

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Pulmonary hypertension: non-cardiac causes

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Pulmonary hypertension (PHT) is a complex and underdiagnosed syndrome in dogs. PHT is defined as a sustained elevated estimated systemic pulmonary arterial pressure (PAP) of > 30 mmHg. PAP is influenced by 3 factors :

- Pulmonary blood flow
- Pulmonary vascular resistance (PVR)
- Pulmonary venous pressure

According to these factors, PHT is subsequently divided as precapillary PHT also known as pulmonary arterial hypertension and post-capillary PHT also known as pulmonary venous hypertension. In precapillary PHT, an increase in PAP results from an increase in pulmonary vascular resistance and a normal pulmonary capillary wedge pressure. Whereas, post-capillary PHT is characterized by an increase in PAP resulting from an increase in pulmonary capillary wedge pressure and a normal pulmonary vascular resistance. Overlaps between these conditions exists.

PHT can also be classified based on the underlying disease process with the most common aetiologies being left-sided heart disease (+/- 40%) and pulmonary disease (+/- 40%).

The normal pulmonary circulation is a low-pressure high-capacitance system with a resistance of approximately one tenth compared to systemic circulation. Any disease processes which increase PVR will cause increases in PAP. Acute PHT is reversible but chronic PHT leads to permanent and progressive vascular remodelling characterized by intimal proliferation, medial hypertrophy and pulmonary arteriolar occlusion. The primary endothelial mediators responsible for the abnormal vascular proliferation and vasoconstriction are endothelin, nitric oxide, and prostacyclin. Pulmonary vasodilating drugs currently in use target these different mediators.

Patients with PHT can present with a variety of clinical signs, some resulting from the primary aetiology or directly from the PHT. These signs include cough, respiratory distress, low output signs, syncope and exercise intolerance. Right-sided congestive heart failure signs might also be present in severe cases. The goals of diagnostic testing in the syndrome of PHT are to identify the underlying aetiology, to quantify the severity of PHT, to assess evidence of hemodynamic impairment and to precise the prognosis.

The goals of treatment are to treat the underlying disease, promote pulmonary artery vasodilation, suppress cellular proliferation, improve cardiac output by decreasing PVR and improving right ventricular inotropy.

Precapillary PHT	Class I Congenital systemic-to-pulmonary shunts (⍰blood flow) Idiopathic Necrotising vasculitis/arteritis	• Patent ductus arteriosus • Ventricular septal defect • Atrial septal defect • Arteriovenous malformation
	Class III (⍰PVR) Pulmonary disease Hypoxia	• Idiopathic pulmonary fibrosis • Chronic obstructive pulmonary disease • Neoplasia • Reactive pulmonary artery vasoconstriction • High altitude disease
	Class IV (⍰PVR) Thrombotic and/or embolic disease	• Thrombo-embolism • Heartworm disease • Angiostrongylosis
	Class V (⍰PVR) Miscellaneous	• Compressive mass lesions
Post-capillary PHT	Class II (⍰Pulmonary venous pressure) Left-sided heart disease	• Mitral valve disease • Myocardial disease • …

Adapted from Kellihan & Stepien, Vet Clin Small Anim 40 (2010)

Right heart catheterization is the most accurate method to diagnose PHT but is often unavailable for routine clinical use and is not without risk in severely affected dogs. Thoracic radiographs can be useful to determine the underlying aetiology. In severe pulmonary hypertension, thoracic radiographs are helpful to support a diagnosis of PHT with the presence of right heart enlargement and pulmonary artery enlargement. Echocardiography remains the non-invasive gold standard to diagnose PHT. Direct estimates of systolic and diastolic pulmonary pressure can be obtained using the peak systolic tricuspid regurgitation (TR) velocity and the pulmonary insufficiency velocity. Pressure gradient derived from TR is used to classify PHT as mild < 50 mmHg, moderate 50-80 mmHg or severe > 80 mmHg. Accurate measurement of TR might be challenging in some cases and this measurement should be used in conjunction with other indirect echo parameters of PHT. Indirect parameters of interest in the setting of PHT are right ventricular morphology, septal flattening, pulmonary flow profile and systolic time intervals, tricuspid annular plane systolic excursion, tei index of myocardial performance, pulmonary vein to right pulmonary artery ratio, right pulmonary artery distensibility index. When present, TR velocity measurement is more repeatable than other indirect parameters.

Pulmonary hypertension: cardiac causes

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Pulmonary hypertension (PH) is defined as an increase in mean, systolic or diastolic pulmonary arterial pressure (mPAP) over 25 mm Hg, 30 mmHg or 19 mmHg respectively.

Historically the disease was overlooked in veterinary medicine, in particular because of the limitation imposed by the need of catheterisation for its diagnosis. However, the widespread use of advanced echocardiography in the last 20 years has made the diagnosis of this disease by echocardiography common in the clinical setting.

The classification of this disease in dogs is adapted from the human classification.

I. Pulmonary arterial hypertension (PAH) due to pulmonary arteriolar vascular disease
- Pulmonary vascular parasitic disease
  - *Angiostrongylus vasorum* (French heartworm)
  - *Dirofilaria immitis* (heartworm disease)
- Congenital systemic-to-pulmonary shunts
  - Atrial septal defect (ASD)
  - Patent ductus arteriosus (PDA)
  - Ventricular septal defect (VSD)
- Necrotizing vasculitis/arteritis
- Idiopathic

II. Pulmonary hypertension with left heart disease (pulmonary venous hypertension)
- Mitral valve disease
- Myocardial disease
- Miscellaneous left-sided heart disease

III. Pulmonary hypertension with pulmonary disease/hypoxemia
- Chronic obstructive pulmonary disease
- High-altitude disease
- Interstitial pulmonary fibrosis
- Neoplasia
- Reactive pulmonary artery vasoconstriction (from pulmonary edema and hypoxemia)
- Tracheobronchial disease

IV. Pulmonary hypertension due to thrombotic and/or embolic disease
- Thromboembolism
  - Cardiac disease
  - Corticosteroid administration
  - Disseminated intravascular coagulation
  - Endocarditis (pulmonic/tricuspid valve)
  - Hyperadrenocorticism
  - Immune-mediated hemolytic anemia
  - Indwelling venous catheters
  - Neoplasia
  - Pancreatitis
  - Protein-losing disease (nephropathy or enteropathy)
  - Sepsis
  - Surgery
  - Trauma
- *Dirofilaria immitis* (heartworm disease)

V. Miscellaneous
- Compressive mass lesions (neoplasia, granuloma)

(From Williams, J. Pulmonary Hypertension. In Ettinger Textbook of Internal Medicine. pp. 1131-1134. Elsvier. 2018)

Within this classification, two entities are causatively associated with cardiac disease: pulmonary hypertension due to congenital systemic to pulmonary shunts and pulmonary hypertension due to left heart disease.

PH can also be classified in three entities from the pathophysiological point of view. The first PH is caused by increase pulmonary flow. The second PH is due to increase pulmonary venous pressure (post-capillary pulmonary hypertension); and the third is PH due to increase pulmonary vascular resistance. Pulmonary vascular resistance (PVR) is equal to the ratio between a driving pressure defined by the difference between mPpa and left atrial pressure (Pla) and cardiac output (Q). PVR = (mPpa-Pla)/Q and therefore the mPpa=PVR x Q + Pla which leads to the concept that PH can be caused by increases in any of those three factors and the three categories aforementioned.

The gold standard for diagnosis of PH is pulmonary artery catheterisation. In this way right atrial pressures, mean pulmonary artery pressure, pulmonary wedge pressure (equivalent to left atrial pressure) and cardiac output can be calculated. From there and following the formula described above pulmonary vascular resistance (PVR) and pulmonary vascular resistance index (PVRi) can be calculated (it is usually measured in Wood units). Drug responsiveness and PVR at different oxygen levels and with nitrous oxide are often carried out in human medicine.

In most cases in veterinary medicine catheterisation in PH cases is not performed due to the costs and the risks involved and limitation of expertise. It is often perceived that such time and money investment may not provide enough information to change therapy in dogs with a suspected poor prognosis. Echocardiography which is non-invasive and more accessible is the main tool used to diagnose PH in dogs and cats. Indeed, the definition of PH for small animal has been adapted in many textbooks and scientific papers as per the estimated systolic pressures on echocardiography over 30 mmHg or peak tricuspid regurgitation velocities over 2.8 m/sec. Peak pulmonary artery pressures (representing mean pulmonary hypertension) over 2.2m/sec are also considered abnormal. Indirect assessment via the change in the pulmonary profile, the ratio acceleration to ejection time and the distensibility index of the pulmonary artery have also been used. Secondary changes in the pulmonary artery (dilation) are also characteristic of severe PH. Right ventricular and right atrial remodelling, flattening of the interventricular septum and abnormal function of the right ventricle can be observed in advanced cases. PVR is also calculated in humans although the formulas have not been validated in the dog.

Congenital systemic to pulmonary shunts

Following birth a series of events lead to vasodilation of the pulmonary arterial tree and to a marked decrease in PVR. This process is primarily led by oxygen entering the lungs, the ventilation itself and the conformational change which occurs in the pulmonary arterial smooth muscle. Circulating bradykinin increases and there is release of nitric oxide which contribute to pulmonary artery vasodilation. The increase blood flow through the lungs and then entering the left atrium will also help closing the foramen ovale. The ductus arteriosus will also be closed (usually by day 7 from birth) stimulated by a local fall in prostacyclin and by the increase in oxygen tension which inhibit ductal smooth muscle voltage-dependent potassium channels, resulting in an influx of calcium and ductal constriction.

If a congenital systemic to pulmonary (left to right) shunt occurs a pulmonary overcirculation will be present at/from birth. The most common, but not the only ones, are ventricular septal defect (VSD), atrial septal defect (ASD) and patent ductus arteriosus (PDA). They are often divided as pre-tricuspid (ASD) or post-tricuspid (VSD and PDA). If the shunt is of large size pulmonary hypertension associated with increase flow first and later with pulmonary vascular remodelling can occur through a number of mechanisms, leading to reversible ad irreversible vaso-occlusive lesions that result in elevated PVR. Exposure of

the pulmonary vasculature to this high flow and shear stress especially with large diameter shunts, may induce progressive pulmonary microvascular changes, including medial hypertrophy, fibrous intimal proliferation, and arterioral obstruction; which ultimately may be irreversible and more severe changes such as plexiform lesions or necrotising arteritis may develop.

When this PH associated with congenital heart disease is advanced, irreversible and severe the syndrome caused is known as Eisenmenger´s (ES). The name comes from Victor Eisenmenger, a doctor who in 1897 described the first case of a patient who presented with cyanosis and dyspnoea due to a VSD and severe lung disease. Dr Paul Wood in 1958 assigned the first definition (which still stands today) as "pulmonary hypertension due to a high pulmonary vascular resistance with reversed or bidirectional shunt at aortopulmonary, ventricular, or atrial level". In many cases in dogs however, particularly in PDAs, it is suspected that the PVR never decreases totally or partially from birth and that the shunt may have always been (or remain) right to left.

PH in PDA

PDA in dogs are usually left to right and if left untreated lead to left sided congestive heart failure. As mentioned above it is suspected that those who present with right to left shunts do so from birth. However, there is a small (and rare) number of cases who can also initially be left to right and develop pulmonary hypertension over time. Some of these may also be affected by concurrent pulmonary processes which may contribute to raise in PVR.

Dogs presenting with mild PH will present with a similar clinical presentation as any left to right shunt. They typically have a continuous murmur at the left heart base/PDA area and are usually asymptomatic or in left sided congestive heart failure presenting with tachypnoea and tachycardia. However, as the PH becomes more severe the murmur will change (first the diastolic phase will not be audible) and then when pressures are closely to equalise there will not be a murmur and a split S2 sound may be heard. R to L shunts will present as ES which is discussed a bit lower down in the text. A particular characteristic however of PDA with ES would be the presence of differential hypoxemia/hypoxia where the lower part of the body has a PO_2 lower than the front legs, neck and head which may lead to back leg collapse after minimal exercise and cyanosis observed in the vulva or penis. This is caused as the R to L shunt occurs after the branching of the brachyocephalic trunk and left subclavian artery.

On echocardiography of the L to R shunt left sided overload will be observed. When the shunt is R to L shunt and ES is present the changes will be as per described for a dog with PH above with severe pulmonary artery and right ventricular remodelling. The PDA (usually type III) can also often be seen but it may be more difficult to differentiate from the left pulmonary artery as it is large and has a forward flow similar to this vessel. When a bubble study is performed the bubbles will not be seen in the heart but will be seen in the abdominal aorta as per an extracardiac shunt. For those dogs with PH of various degrees the image will vary as per a transition from left side overload to right sided remodelling. This will vary depending on the chronicity and the severity of the PH.

Therapy (occlusion or ligation) for left to right shunts with mild PH is usually straight forward as any left to right shunt. Those with Eisenmenger syndrome are treated medically as described below. In the cases however where the pulmonary hypertension is high-moderate or severe but there is still left to right shunts (or even bidirectional) the decision is more difficult. In those cases catheterisation to established the PVR and its potential reversibility is recommended in human medicine. The general criteria for closing cardiac shunts in PH associated with congenital heart defects (including VSDs and ASDs) following the JACC PH guidelines classifies a shunt as correctable (PVR <2.3 Wood units or PVRi <4 Wood units) or non-correctable (PVR >4.6 Wood units or PVRi >8 Wood units). Cases in between need to be assess individually. For PDA however, partial correction (by placing temporarily the device, occluding it with a balloon catheters or temporarily occluding it during surgery) of the ductus with an observed drop in mean pulmonary pressure of 20% is an alternative to assess whether the PDA can be closed and it is the technique usually carried out in veterinary medicine.

Another interesting strategy to consider in the face of any shunt with PH is the the so-called "treat-and-repair" strategy aimed at reducing PVR thus improving their PVR and operability of cases. In humans, although small studies showing promising data has been reported (in particular for pre-tricuspid shunts) the long-term adaptation of the right ventricle and the pulmonary circulation after correction of the congenital heart defect remains unknown. Within this context sildenafil is often used acutely in dogs with medium to high PH pressures PDA prior to urgent partial occlusion/ligation procedure/surgery. If partial closure confirms the shunt is correctable permanent occlusion/ligation is carried out.

Lastly, lung biopsy prior to shunt closure has been used in the past in human medicine for evaluating the severity and potential reversibility of the arterial lesions. However, this has been questioned as the sample represents a small part of the lung and correlation with haemodynamic studies is often not observed.

PH in VSD ad ASD

The vast majority of dogs with ASD and VSD have left to right shunt with no clinical consequences. Those with high Qp/Qs (higher than 2/2.5) are in theory candidates for closure and left sided heart failure (VSD) or right sided heart failure (ASD) may occur if they are not closed. Closure by percutaneous transcatheter using an Amplatzer, hybrid procedures and surgery with bypass support have all been described for both defects. Right to left shunt in isolated ASD and VSD (without other congenital defect) is very rare. If Eisenmenger has not developed with moderate to severe PH the criteria for when a defect is considered correctable or non-correctable in human medicine by haemodynamic testing follows the same principles as previously described. A recent case report describes the surgical closure with bypass support of a dog with a left to right ASD and moderate PH.

Eisenmenger's Syndrome

Eisenmenger's occurs more frequently when flow is extremely high, and the shunt exposes the pulmonary vasculature to systemic-level-pressure such as in VSD, PDA or truncus arteriosus. However PAH may also occur with low pressure and high flow abnormalities

such as atrial septal defect. If the PH occurs early in life the heart is still able to change phenotypically and present markedly hypertrophied but this is not possible later in life (a more eccentric hypertrophy phenotype). This is one of the main reasons why it is believed that people with ES have much better survival than people with idiopathic pulmonary arterial hypertension.

Dogs with Eisenmenger's will show signs of hypoxemia (generalised for ASD or VSD and initially differential in the case of PDA) with evidence of intolerance to exercise, cyanosis and chronic wasting disease. An appropriate secondary polycythaemia will often ensue and signs of hyperviscosity such as weakness, hemostatic deficiencies, renal dysfunction, metabolic acidosis, cerebrovascular events, thromboembolic events and seizures can occur.

Surgical closure of the shunt is not possible in dogs with Eisenmenger as it will lead to RV failure, circulatory collapse and death. Pulmonary vasodilator therapy with sildenafil is usually employed in dogs and its benefits in these species have been reported. Pimobendan is often used anecdotally in dogs to improve ventricular (both right and left) performance. In people there is established evidence that PAH-specific therapeutic drugs are efficacious. Current therapy is targeted towards the three pathways involved in the vasoactive reponses in the pulmonary vasculature. The NO cascade is targeted via PDE5 inhibitors such as sildenafil, the endothelin receptors are targeted with antagonists such as bosenthan and the prostacyclin pathway is targeted with prostacyclins.

Clear criteria to treat the polycythaemia does not exist. Recommendations vary from maintaining the HCT below 65% to not focusing on the PCV unless signs of polycythaemia ensue. Phlebotomies and therapy with hydroxyurea are used if decreasing the HCT is deemed necessary. If phlebotomies are carried out iron levels should be monitored although this does not seem to be a significant problem in dogs. A diagnosis of Eisenmenger does not lead to imminent death: dogs with Eisenmenger's can be managed for many years with good quality of life.

PH in left heart disease

Pulmonary hypertension associated with left heart disease is initially caused by passive transmission of elevated left-sided filling pressures. With long-standing pulmonary venous hypertension (post-capillary PH) and the associated neurohormonal upregulation some patient will develop pulmonary vasoconstriction (pre-capillar PH) with or without remodelling. The distinction in human medicine has been historically based on the transpulmonary gradient (TPR=mPAP-Pulmonary artery wedge pressure) or the PVR. Patients with high TPG or PVR are diagnosed as having significant pre-capillary disease and have been traditionally referred as out of proportion, reactive or mixed.

Pulmonary hypertension is observed in canine mitral valve disease in 29% of dogs in stage B2 and 71% of dogs in stage C. It has also been shown that dogs with worse PH have worse outcomes and that dogs with estimated systolic PH pressures above 48mmHg are unlikely

to resolve after therapy for congestive heart failure (more likely to also have pre-capillary disease). Although PH has also been reported in DCM dogs in CHF this information is sporadic and there is little information about its impact on prognosis. The possible presence and clinical significance of PH in cats with cardiomyopathies is unknown.

Therapy for PH in cases of MVD or DCM in dogs in heart failure is usually aimed firstly towards treating the CHF. However, if the PH persists following CHF therapy pulmonary arterial vasodilators such as sildenafil are often used. However, although there are reports of improvement in clinical signs with this treatment large studies documenting its efficacy have not been performed. It is important to also bear in mind that many of these patients can have concurrent respiratory disease such as bronchial collapse, tracheal collapse or brachicephalic syndrome which may be a causative contributor for the PH.

Interestingly, although in human medicine patients with left heart disease and concurrent "precapillary" PH are also often treated with PH-specific drugs targeting the NO, endothelin and prostacyclin pathways results from studies are conflicting and there has been a call for larger studies focusing first on more severe cases or cases with higher PVR.

References:
A complete list is available on request.

Nutritional considerations for cardiac patients

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Maintenance of Optimal Weight

Cardiac cachexia is common in dogs with chronic heart failure, involving a loss of lean body mass (LBM) which has direct and deleterious effects on strength, immune function, and survival. Anorexia is present in up to 75% of dogs with heart disease. Inflammatory cytokines, particularly tumour necrosis factor a (TNFα), interleukin-1 beta (IL-1), and interleukin-6 (IL-6), appear to be primary mediators of cachexia by causing anorexia, increasing the LBM loss, and increasing energy requirements. Tumour necrosis factor, IL-1, and IL-6 cause cardiac myocyte hypertrophy and fibrosis and have negative inotropic affects contributing to disease progression

Supplementation with fish oil, high in n-3 fatty acids, can decrease cytokine production, improve cachexia, may improve food intake, and help prolong survival time (Freeman and others 1998).

Sodium

As sodium excretion is reduced even in early cardiac disease sodium restriction has been recommended; however, dietary sodium restriction can further activate the renin-angiotensin-aldosterone (RAA) system. It is not clear if sodium restriction in early heart disease is beneficial or harmful. Sodium restriction plus furosemide in normal dogs resulted in hyperkalaemia (Roudebush and others 1994). A study in dogs with CHF showed that measures of cardiac size decreased significantly on a low-sodium diet, but the effect of low sodium diets on survival or disease progression has not been studied (Rush and others 2000). Further, sodium does not directly affect the blood pressure of dogs or cats. Due to the stimulation of the RAA system, excessive sodium restriction could be detrimental in early cardiac disease. The clinician should discuss the sodium content of treats and human food, especially if these are being used to administer medications. Foods such as lunch meats, sausages, most cheeses and most processed foods are high in sodium.

Potassium

Angiotensin converting enzyme inhibitors and spironolactone can increase serum potassium, potentially causing hyperkalaemia. As some commercial cardiac diets contain increased potassium concentrations, these diets contribute to hyperkalaemia.

Protein

Recommendations for restricting the dietary protein intake of pets with CHF were once common to reduce the "metabolic stress" on kidneys and liver. There is no evidence that protein restriction is necessary; it probably is deleterious since these patients are predisposed to LBM loss. Diets designed for renal disease should not be fed to heart disease patients unless renal dysfunction is present.

Taurine

While current cases of feline DCM are not taurine deficient, it should be ruled out. Cats fed a homemade, vegetarian, poor quality, or otherwise unbalanced diet are at risk for taurine deficiency. Unlike cats, dogs are able to synthesize adequate amounts of taurine and are thought not to require dietary sources. While most dogs with DCM do not have taurine deficiency, low taurine concentrations have been found in some, most commonly in American cocker spaniels, golden retrievers, Labrador retrievers, Newfoundlands, Dalmatians, Portuguese water dogs, and English bulldogs. Taurine deficiency in dogs may be related to dietary factors as it is more common in dogs on high fibre or some lamb and rice-based diets, or low protein, low taurine diets. Increased renal or faecal taurine loss or metabolic defects may be present in some breeds. Some of the potential taurine benefits may be due to its positive inotropic effects or a role in calcium regulation in the myocardium. Current recommendation is 500-1000 mg q 8 to 12 hours for dogs and 250 mg (per cat) PO q12-24h for cats.

Magnesium

Hypomagnesaemia can play an important role in a variety of cardiovascular conditions including hypertension, congestive heart failure, and cardiac arrhythmias. As some cardiac drugs are associated with magnesium depletion there is an increased risk for hypomagnesaemia. Hypomagnesaemia can increase the risk of arrhythmias, decrease cardiac contractility, cause muscle weakness, contribute to renal potassium loss, and can potentiate the adverse effects of certain cardiac medications.

L-Carnitine

A relative carnitine deficiency is associated with primary myocardial disease in some Boxers and American cocker spaniels (Keene and others, 1991; Costa and Labuc, 1995; Kittleson and others 1997). Even if carnitine deficiency is not the cause of DCM, supplementation could be beneficial by improving myocardial energy production.

Commercial Diets Heart Disease

Commercial diets for CHD vary, but they usually are mildly to severely restricted in sodium and may contain increased levels of B vitamins and antioxidants. The choice should consider the level of sodium restriction desired for a specific patient. The majority of people use food to administer medications to their pets. Recommendations on appropriate treats and methods of administering medications is an important part of a successful nutritional program.

Boutique, Grain Free, Limited Ingredient, Exotic Ingredient Diets and DCM

Recently there have been diet related reports of DCM. Diets in cases frequently list potatoes or legumes such as peas, lentils, other pulses, and their protein, starch and fibre derivatives in their ingredient list, as the main ingredients. High levels of legumes or potatoes appear to be more common in diets labelled as 'grain-free,' but it is not yet known how these ingredients are linked to cases of DCM. Diets with exotic ingredients like kangaroo or ostrich have also been implicated. The link between DCM and these diets may or may not be taurine related, as some dogs did and some did not have low taurine concentrations. Dogs who have DCM and are on one of these diets should have a diet change to a more conventional diet by a reputable manufacturer and taurine supplementation.

Reference available upon request

An update on hyperthyroidism and acromegaly

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Feline hyperthyroidism

Aetiology

- 98-99% of cases are caused by benign adenomatous hyperplasia/adenoma of thyroid tissues. ≥ 70% of cases are bilateral; 1-2% of cases are caused by malignant thyroid adenocarcinoma
- 20% hyperthyroid cats have ectopic thyroid tissue (a goitre may not be palpable).

Diagnosis

- **compatible history, clinical and physical findings (especially if a palpable thyroid nodule is present)**
- Total serum T4 concentration (TT4) (increased in 90-95% cases) = screening test of choice
- Occasionally TT4 normal results are obtained in hyperthyroid cats (usually in upper 1/3 of reference interval) – can consider Free T4 (fT4), TSH with TT4 or Thyroid scintigraphy (limited availability).

Treatment options *(varies for each individual case since all treatments carry some disadvantages).*

1. Medical management – Anti-thyroid drugs (use initially to stabilise where possible)
2. Diet – Low iodine (Hills y/d)
3. Surgical management - Thyroidectomy
4. Radioactive iodine

Hyperthyroidism, pre-existing azotaemia and chronic kidney disease (CKD)

- **Treatment of hyperthyroidism results in a significant fall (normalisation) in GFR which may unmask existing CKD**
- CKD can be difficult to diagnose in the hyperthyroid cat
    - Reduced muscle mass – creatinine levels are often lower than expected - SDMA can be helpful (Peterson and others 2018).
    - Cats with USG >1.035 can still have underlying renal dysfunction develop post-treatment (Riensche and others 2008)
    - Cats with pre-existing azotaemia have a less favourable prognosis (MST approx.6 months) (Syme 2007)(Syme, 2007;Peterson, 2013).

- Failing to treat hyperthyroidism or achieve euthyroidism can contribute to progression of renal dysfunction (Van Hoek and others 2009)

Post-treatment development of azotaemia

- Post-medical management
    - Up to 20-25% cases with unknown CKD develop azotaemia following treatment
    - Most cats are unlikely to increase by more than 1 IRIS stage following treatment
    - No major predictive factors for which cats will develop azotaemia post-treatment
    - If treatment and euthyroidism precipitates a significant clinical deterioration (e.g. fragile stage 3 or stage 4 IRIS CKD case), medical treatment can be reduced to levels where the cat remains stable or stopped if necessary.
- Post-radioactive iodine treatment
    - Renal function will stabilise within one month of ^{131}I and therefore should be assessed at this point
    - Development of mild azotaemia does not affect survival

Iatrogenic hypothyroidism and renal function

- Diagnosis = low total and free T4 and increased TSH concentration in azotaemic cats (Peterson and others 2017)
- Iatrogenic hypothyroid cats that developed azotaemia within 6 months post-treatment had significantly shorter survival times (median survival time 456 days, range 231-1589 days) than those that remained non-azotaemic (median survival time 905 days, range 316-1869 days). (Williams and others 2010)
- Cats with iatrogenic hypothyroidism and post-irreversible treatment azotaemia (post-thyroidectomy or ^{131}I) require immediate treatment with thyroxine supplementation
- Normalisation of thyroid hormones should restore GFR and improve renal function/azotaemia (Williams and others 2014).

Feline hypersomatotropism (FeHS; acromegaly)

Aetiology

- excessive growth hormone (GH) production from a benign tumour/hyperplasia of somatotrophs within the pituitary gland
- prevalence of this disease in the UK amongst diabetic cats is reported to be 25%, but not all affected cats are diabetic
- environmental contaminants have been implicated as a cause of pituitary tumours. Levels of organohalogenated chemicals (OHCs) were significantly higher in the

plasma of cats with FeHS-induced diabetes mellitus (DM), compared to cats with non-FeHS DM and age-matched control cats without DM (Dirtu and others 2013)

- a possible association with a single non-conservative single nucleotide polymorphism (SNP) within the AIP gene (AIP:c.9a>T), development of acromegaly in cats and risk of larger tumour development was proposed but further work is required (Scudder and others 2017).

Clinical signs include insulin-resistant uncontrolled diabetes mellitus (usually), weight gain, organomegaly, prognathia inferior (protrusion of the mandible), increased interdental spacing, prominent facial features (e.g. broad head), stertor. Pancreatic pathology (including neoplasia) appears to affect a large percentage of acromegalic cats.

Diagnosis

Requires documentation of an increased serum insulin-like growth factor 1 (IGF-1) concentration (>1000ng/ml; positive predictive value 95%), a marker for GH production, and in most cases confirmation of the presence of a pituitary mass on intracranial imaging (CT or MRI). Definitive diagnosis is achieved through histopathology of the pituitary tumour. Other biomarkers such as serum NT type III procollagen (PIIINP) have also shown promise (Keyte and others 2016).

Treatment

- **Hypophysectomy** (surgical removal of the pituitary gland): results in rapid normalisation of IGF-1 concentrations and reported diabetic remission rates are as high as 85%, even in cats that have been diabetic for several years. Lifelong supplementation with oral levothyroxine and corticosteroids is necessary following surgery. Mortality rates of 14% are reported. Post-operative obesity (occurring in approx. 70% cases) and 12% increase in body weight is reported.
- **Radiation therapy:** variable response to conventional fractionated radiotherapy; some cats have shown improved glycaemic control and reduction in insulin requirement, but positive effect can be slow in onset. Stereotactic radiation has been shown to be both safe and more effective compared to other radiation protocols, thus offering a possible better outcome.
- **Medical management**
    - **Somatostatin analogues** (e.g. pasireotide-up to 25% of cats treated once monthly achieved diabetic remission (Gostelow and others 2017), possibly as it targets SSTR 1 and 5, which are present and more abundant on the pituitary of cats with hypersomatotropism compared to other SSTR types (Scudder and others 2016).
    - **Dopamine receptor agonists** (e.g. cabergoline)
    - **Palliative** i.e. Increasing insulin doses in an attempt to control clinical signs

The cardiac effects of systemic disease

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The theme of the talk will be the cardiovascular manifestations of systemic disease including thyroid dysfunction, hypersomatotropism and diabetes mellitus. It will primarily cover veterinary literature but also draw on human literature where appropriate to outline the pathophysiology underlying the cardiac phenotype.

A major confounder when determining the cardiac effect of systemic disease is the high prevalence of HCM in the feline population (between 17-20%) which can give a cardiac phenotype similar to a number of systemic diseases.

Cardiac manifestation of Hyperthyroidism:

Thyroid hormone receptors are present in myocardium and vascular endothelial tissues and minor alterations in thyroid hormone (TH) concentration can affect cardiovascular (CV) physiology. Mechanisms that link CV disease with altered thyroid function are endothelial dysfunction, myocardial systolic and diastolic dysfunction and changes in blood pressure. In human patients subclinical thyroid dysfunction has been associated with a 20% to 80% increase in vascular morbidity and mortality risk. TH can directly influence the myocardium to altering function and causing hypertrophy and act on the vasculature reducing systemic vascular resistance and increasing circulating volume

Action of TH on Cardiomyocytes:

The effects of TH are mediated by TH receptors located in the nucleus. The protein receptors bind T3 with greater (>10) affinity than T4. The TH receptors bind to TH response elements in the promoter regions of TH responsive genes and activate expression of positively regulated genes in the presence of T3 and repress expression in its absence.

Positive regulation	**Negative regulation**
α-Myosin heavy chain	β-Myosin heavy chain
SERCA2 (SR Ca^{2+}-ATPase)	Phospholamban
β_1-Adrenergic receptors	Adenylyl cyclase
Na^+/K^+-ATPase	TRs α_1
Voltage gated K^+ channels	Na^+/Ca^{2+} exchanger

Myocyte contraction and relaxation are regulated by intracellular free calcium concentration, which is largely determined by the SR Ca^{2+} release via the Ca^{2+}release channels (part of the ryanodine receptor complex) followed by re-uptake into the SR by SERCA2a. Upregulation of the fast α-MHC by T3 will increase the speed of myocardial contraction/relaxation. This is further enhanced by the upregulation of SERCA2 and downregulation of its inhibiting counterpart phospholamban. Other important cardiac genes regulated by TH include the voltage-gated potassium ion channels (Kv1.5 and Kv4.2), and the sodium/calcium ion exchanger (NCX1).

Furthermore, excess T3 also lead to the development of cardiac hypertrophy both in vivo and in vitro models. The mechanism for this is not full understood but is initially considered an adaptive response due to sustained volume overload and increased cardiac work leading to increased protein synthesis in the terminally differentiated cardiac myocytes. Several studies have demonstrated that RAAS is involved in the development of cardiac hypertrophy in chronic hyperthyroidism, since the use of RAAS blocking drugs are able to prevent or to reduce the hypertrophy.

T4 and T3 also exert non-genomic effects on the cardiac myocyte which are usually rapidly acting, receptor-independent and regulate ion transporter activity. At the level of the atrial myocyte they are responsible, in part, for the ability of T3 to increase the heart rate. TH also mediates chronotropy through decrease in vagal tone and enhanced adrenergic tone characteristic of HyperT4. This may lead to sinus tachycardia (AF in humans) and atrial and ventricular arrhythmia and intraventricular conduction abnormalities in cats.

Action of TH on the vasculature:

TH effects on the vasculature include genomic and nongenomic (Na^+, K^+ Ca^{2+} ion channels) mechanisms that occur at both the vascular smooth muscle and endothelial cell levels. TH also signals via PI3K/Akt pathways to generate endothelial NO causing vasodilation through its effects on vascular smooth muscle cells. The pulmonary vasculature is not as responsive to the vasodilatory effects of T3. Increased tissue catabolism will also act as a stimulus for endothelial NO production.

The result of this is decreased SVR due to excess T3 leading to:

- arterial underfilling and upregulation of RAAS

- increased circulating volume

- increased venous return

- increased cardiac output

The net effect of excess T3 on blood pressure is dependent on the balance between increased cardiac output and decreased SVR.

Cardiovascular consequences of hyperthyroidism in humans:

Short-term hyperthyroidism increases LV systolic and diastolic function, however, despite the high cardiac output state, hyperthyroid human patients have impaired cardiopulmonary function during effort, reflecting their reduced CV and respiratory reserve during exercise. Untreated hyperthyroidism is associated with increased CV morbidity and mortality mainly due to higher incidence of CHF. Severe hyperthyroidism may induce high-output HF, even in patients without underlying heart disease. Patients with severe hyperthyroidism may have coronary vasospasm leading to chest pain at rest or myocardial ischemia.

A sample of the Veterinary literature will be briefly discussed:

Jacobs G, Hutson C, Dougherty J, Kirmayer A. **Congestive heart failure associated with hyperthyroidism in cats.** J Am Vet Med Assoc. 1986 Jan 1;188(1):52-6.

Moise NS, Dietze AE, Mezza LE, Strickland D, Erb HN, Edwards NJ. **Echocardiography, electrocardiography, and radiography of cats with dilatation cardiomyopathy, hypertrophic cardiomyopathy, and hyperthyroidism.** Am J Vet Res. 1986 Jul;47(7):1476-86.

Bond BR, Fox PR, Peterson ME, Skavaril RV. **Echocardiographic findings in 103 cats with hyperthyroidism**. J Am Vet Med Assoc. 1988 Jun 1;192(11):1546-9.

Arrhythmias and murmurs associated with hyperthyroidism will be outlined and echocardiographic examples given.

Summary:

My personal experience is that we see a heterogeneous cardiac phenotype in cats with hyperthyroidism comprising:

a) A predominantly volume overload phenotype
b) A LV wall thickening phenotype – confounded by the high incidence of HCM (15-20%) in cats
c) A mixture of both
d) Variable atrial enlargement based on chronicity of disease and HCM status
e) A variety of arrhythmias
f) Murmurs associated with the high output status
g) Stress induced dyspnoea
h) Raised circulating biomarkers

Hypothyroidism

Generally opposite pathophysiology to hyperT4:

a) Reduction in cardiac output
b) Decrease in heart rate
c) Increase in peripheral vascular resistance and diastolic dysfunction
d) Arrhythmia also present

Additionally and more commonly associated with the condition in human patients is an increase in atherosclerotic risk factors, including hypercholesterolemia, diastolic hypertension, increased carotid intimal-media thickness. All these clinical features are reversible with TH replacement.

Veterinary Literature:

Panciera DL. **An echocardiographic and electrocardiographic study of cardiovascular function in hypothyroid dogs**. J Am Vet Med Assoc. 1994 Oct 1;205(7):996-1000.

Tidholm A, Häggström J, Hansson K. **Effects of dilated cardiomyopathy on the renin-angiotensin-aldosterone system, atrial natriuretic peptide activity, and thyroid hormone concentrations in dogs**. Am J Vet Res. 2001 Jun;62(6):961-7.

Phillips DE, Harkin KR. **Hypothyroidism and myocardial failure in two Great Danes**. J Am Anim Hosp Assoc. 2003 Mar-Apr;39(2):133-7.

Chow B, French A. **Conversion of atrial fibrillation after levothyroxine in a dog with hypothyroidism and arterial thromboembolism**. J Small Anim Pract. 2014 May;55(5):278-82. doi: 10.1111/jsap.12184. Epub 2014 Feb 13.

Beier P1, Reese S, Holler PJ, Simak J, Tater G, Wess G. **The role of hypothyroidism in the etiology and progression of dilated cardiomyopathy in Doberman Pinschers**. J Vet Intern Med. 2015 Jan;29(1):141-9

Cardiac manifestation of Hypersomatotropism:

HS is caused by a functional pituitary adenoma or hyperplasia of the pars distalis of the anterior pituitary gland, which results in a syndrome of growth hormone GH excess. In skeletally mature patients, this results in the disease known as acromegaly. In humans with HS, CV disease is a significant contributor to morbidity and mortality with 60% of patients suffering a cardiovascular cause of death. Increased LV mass and echocardiographic measures of LV wall thickness and impaired overall cardiac performance are observed. A DCM phenotype has also been rarely described in human acromegalics. Histopathology changes seen in human patients comprise myocardial fibrosis and myocyte hypertrophy ± cellular infiltrates or small vessel disease.

Cats with HS most frequently present with signs of diabetes mellitus and 25-33% of diabetic cats have HS. As with hyperthyroidism, understanding of the CV manifestation of HS is complicated by high HCM prevalence and the potential confounding effect of diabetes. Although diabetes causes LVH in humans, less is known about the CV effects of diabetes in cats.

Veterinary Literature:

Peterson ME, Taylor RS, Greco DS, Nelson RW, Randolph JF, Foodman MS, Moroff SD, Morrison SA, Lothrop CD. **Acromegaly in 14 cats**. J Vet Intern Med. 1990 Jul-Aug;4(4):192-201

Myers JA, Lunn KF, Bright JM. **Echocardiographic findings in 11 cats with acromegaly**. J Vet Intern Med. 2014 Jul-Aug;28(4):1235-8

Results:

LVH was identified in 7 cats (63.6%). Of these, hypertrophy of both the IVS and LVFW was noted in 4 cats (57.1%), hypertrophy of the IVS alone was noted in 1 cat (14.3%), hypertrophy of the LVFW alone was noted in 1 cat (14.3%), and the papillary muscles alone were subjectively hypertrophied in 1 cat (14.3%). All cats had normal LVIDd and the left atrium was enlarged in 7 cats (63.6%). Abnormal diastolic function was identified in 8 cats (72.3%). Of these, 5 cats had impaired relaxation and 3 had a restrictive left ventricular filling pattern. Impaired systolic function was noted in 1 cat.

Borgeat K, Niessen SJM, Wilkie L, Harrington N, Church DB, Luis Fuentes V, Connolly DJ. **Time spent with cats is never wasted: Lessons learned from feline acromegalic cardiomyopathy, a naturally occurring animal model of the human disease**. PLoS One. 2018 Mar 29;13(3):e0194342

Methods: Prospectively recruited Cats with HS (IGF-1>1000ng/ml and pituitary mass; n = 67) and two control groups: diabetics (IGF-1<800ng/ml; n = 24) and healthy cats without known endocrinopathy or cardiovascular disease (n = 16). Echocardiography was performed in all cases, including following Tx for HS Myocardial samples from cats with HS, HCM and age-matched controls (n = 21 each) were collected and reviewed by histopathology

Results: Echo HS cats > LV wall thickness (6.5mm, 4.1±10.1mm) than diabetic (5.9mm, 4.2±9.1mm p<0.001) or control cats (5.2mm, 4.1±6.5mm p<0.001). LAD was also greater in HS cats with (16.6mm, 13.0±29.5mm) than in diabetic (15.4mm, 11.2±20.3mm p<0.001) and control cats (14.0mm, 12.6±17.4mm p<0.001). After hypophysectomy and normalization of IGF-1 concentration (n = 20), echocardiographic changes proved mostly reversible.

Histopathology Results: Myocyte hypertrophy was present in all 63 cats. Severe hypertrophy was detected in some cats of both the HCM and HS groups but not in the control group. There was no significant difference between the groups for perivascular, subendocardial, or replacement fibrosis or intramural arteriosclerosis. There was no significant difference in interstitial fibrosis between the HS and HCM (p = 0.343) or HCM and control (p = 0.052) groups but it was more frequent in the HS group than the control group (p<0.001). Myofiber disarray was more frequently observed in the HCM group than the HS (p<0.001) or control (p = 0.002) groups, and in the control group than the HS group (p = 0.016). *Therefore as in humans, histopathology of the feline acromegalic heart was dominated by myocyte hypertrophy with interstitial fibrosis and minimal myofiber disarray.*

Acromegaly as an HCM phenocopy: (ECVIM abstract Connolly DJ *et al* 2018)

Up to 50% of acromegalic humans are non-diabetic. A small proportion of cats with confirmed HS do not present with DM. Therefore, do some non diabetic cats with LVH previously diagnosed with HCM have an acromegalic heart? We found a prevalence of 6.7% of cats with HS amongst a cohort of non-diabetic cats with LVH previously diagnosed with HCM. The study had a number of limitations.

Cardiac manifestation of Diabetes mellitus:

In human patients, DM is a significant independent risk for HF. Diabetic cardiomyopathy is defined as diabetes-associated structural and functional myocardial dysfunction not related to other confounding traditional factors such as coronary artery disease, hypertension, congenital or valvular heart diseases. LVH and myocardial fibrosis are the main findings in diabetic cardiomyopathy together with associated diastolic dysfunction (lower transmitral E/A ratios, greater E/E‘) and increased LA volume. Diastolic dysfunction in diabetes indicates worse prognosis for instance E/E‘ >15 in patients with DM is associated with subsequent HF and increased mortality. Multiple vascular effects are also identified and categorised into Macrovascular (e.g., coronary artery disease, stroke, and

peripheral vascular disease) and Microvascular (e.g., retinopathy, nephropathy, and neuropathy) complications.

Cats generally suffer from the Type II diabetes where glucose levels are high because cells in the body do not respond appropriately to insulin (insulin resistance). The prevalence of feline DM in the UK is about 0.6%.

Veterinary Literature:

Sennello KA, Schulman RL, Prosek R, Siegel AM. **Systolic blood pressure in cats with diabetes mellitus**. J Am Vet Med Assoc. 2003 Jul 15;223(2):198-201

Little CJ, Gettinby G. **Heart failure is common in diabetic cats: findings from a retrospective case-controlled study in first-opinion practice**. J Small Anim Pract. 2008 Jan;49(1):17-25

Pereira NJ, Novo Matos J, Baron Toaldo M, Bartoszuk U, Summerfield N, Riederer A, Reusch C, Glaus TM **Cats with diabetes mellitus have diastolic dysfunction in the absence of structural heart disease**. Vet J. 2017 Jul;225:50-55

Conclusions: Diastolic dysfunction is common in diabetic cats at the time of diagnosis, and over the following 6 months an increase in the prevalence of diastolic dysfunction can occur, despite antidiabetic therapy. Feline diabetic cardiomyopathy is similar to that seen in humans.

Diabetes in dogs:

Primary insulin deficiency diabetes (IDD) in dogs is characterised by a progressive loss of pancreatic beta cells. The aetiology of beta cell deficiency/destruction in diabetic dogs is currently unknown, but a number of diseases processes are thought to be involved:

a. Congenital beta cell hypoplasia/atrophy;
b. Beta cell loss associated with exocrine pancreatic disease;
c. Immune-mediated beta cell destruction;
d. Idiopathic disease

Veterinary Literature:

Vichit P, Rungsipipat A, Surachetpong SD. **Changes of cardiac function in diabetic dogs**. J Vet Cardiol. 2018 Sep 11. pii: S1760-2734(17)30157-1.

Conclusions: In a population of naturally occurring diabetic dogs changes in echocardiographic values, suggestive of left ventricular diastolic dysfunction were seen. The duration of DM may affect diastolic function and NT-proBNP concentrations in diabetic dogs.

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