If one were to summarise the status of veterinary medicine compared to ten years ago, then one could do worse than say, “Most things are much better.” This is by no means facetious. Veterinary medicine, like much of modern society, has advanced hugely in concert with technology. However, veterinary cardiology is particularly well-suited to benefit from the ongoing digital revolution. Yet, arguably, the outstanding advance of the last decade has been therapeutic rather than diagnostic.

Enter pimobendan, the positive inotrope that increases myocardial contractility without increasing myocardial oxygen consumption and intracellular calcium concentrations. These almost unique properties lend themselves particularly well to the failing heart. If the decade following its licensing in 1999 consisted of its intuitive use in systolic (pump) failure conditions such as dilated cardiomyopathy (DCM) and its initially counter-intuitive use to combat valvular insufficiency in myxomatous mitral valve disease (MMVD), the past decade has given us an intravenous formulation for emergency use, and firmly established the oral form alongside diuresis atop the hierarchy of therapy for congestive heart failure (CHF) due to MMVD (QUEST) \(^1\). There is also clear, strong evidence, that pimobendan delays CHF or death in stage B2 MMVD \(^2\) (EPIC) and stage B2 Dobermann DCM \(^3\) (PROTECT). These are groundbreaking advances for two reasons. First they demonstrate pre-clinical and clinical pharmacological intervention to significantly prolong life expectancy and quality of life in some of the commonest debilitating diseases encountered in veterinary practice. Second, they are the result of the largest clinical trials ever conducted in veterinary medicine, establishing the benchmark for all future evidence-based medicine. Such large-scale, multi-centre, international, prospective studies represent a happy and productive union of pharma, and academic and private referral specialists, yet a union that is entirely dependent on the general practitioner. For the next decade, which promises to expand further the applications of pimobendan in non-Dobermann DCM and, more significantly, feline cardiomyopathy, the position of general practitioners as stakeholders of clinical research must be nurtured. For example, by continuing to refer pre-clinical MMVD to determine whether dogs meet EPIC criteria and are likely to benefit from pimobendan, referral centres will have access to clinical material that has previously been scant, despite the prevalence of the disease. This will ultimately give further insight into the pathogenesis of the disease and determine whether subpopulations, defined by new or novel biomarkers, might benefit from even earlier pharmacological intervention. Several research groups have already identified key mechanisms that contribute to the dysregulation of matrix deposition, organisation and dissolution that leads to the expansion of the mitral valve’s spongiosa layer. At the R(D)SVS, we have demonstrated the deleterious consequences that MMVD has for the layer of endothelium that coats the valve. Endothelial cells are sheared away, exposing the subendothelial collagen network \(^4\). Valvular interstitial cells (VICs), a form of fibroblast or myofibroblast, multiply and migrate towards the damaged endothelium \(^5\). There is crosstalk between VICs, and endothelial cells and even transition of endothelial cells to VICs \(^6\). These interactions appear to activate key pathways involving transforming growth factor (TGF) \(\beta\) signalling, inducing the VICs to secrete glycosaminoglycans uncontrollably. The next decade will determine which of the
myriad of key pathways downstream of TGFβ are activated and which are suppressed, offering the tantalising possibility of arresting the myxomatous response, or even, remarkable to relate, reversing it.

These research goals may appear unrealistic, yet they complement other recent advances in veterinary cardiology. We now know that the endothelium, one of the biggest organs in the body, and capable of mediating significant and widespread tissue effects, is also dysfunctional in cardiac and metabolic disease. Serum biomarkers such as nitric oxide metabolites, and application of functional vascular studies such as flow-mediated dilation, show progression of endothelial dysfunction with progression of MMVD \(^7\), \(^8\). However, endothelial dysfunction, which is a major risk factor for cardiovascular events in people, can obviously affect organs other than the heart. For example, the kidneys are highly vascularised and have a unique relationship with the heart, exemplified by cardiorenal syndrome, in which acute or chronic dysfunction in one organ leads to acute or chronic dysfunction in the other \(^9\). On a day-to-day level, this might mean elevated serum renal parameters in patients with advanced heart disease, and a challenge to managing diuresis and ACE inhibition. However, earlier identification of the derangement of the interaction between the heart and kidneys could lead to significant prognostic benefits. In people, both the heart and the kidneys are recognised as the main determinants of blood pressure regulation. Blood pressure is intimately linked to cardiovascular risk \(^10\) but, although we recognise the consequences of increased blood pressure on target organ stress and injury, we have yet to maximise its potential as a biomarker. Despite major advances in indirect BP techniques in cats and dogs, where BP measurement is now commonplace in general practice and an important component of any cardiovascular work-up, we have a lot to learn from our medical counterparts.

As well as the success of pimobendan, the more widespread use of spironolactone should be recognised. There are now published clinical data to support its use in canine CHF \(^11\), although whether a beneficial effect in addition to that achieved with pimobendan, is not known. As for ACE inhibitors, despite starting the decade as an established treatment modality in canine CHF \(^12\), that position is now in doubt.

While we celebrate pharmacological achievements, we must not forget the major advances in imaging, many accessible to general practitioners. In the last decade, echocardiography has continued to advance. From tissue Doppler imaging, speckle tracking has now come to the fore as the preferred method of choice for determining strain and strain rate imaging. Conceptually extremely simple, tracking the displacement and deformation of random pairs of “speckles” generated by reflection of ultrasound from the myocardium identifies regional areas of impaired systolic and diastolic function. From diagnosis of microinfarctions to optimisation of pacemaker lead implantation, the potential applications for this modality appear to increase on an almost daily basis. Three dimensional (3D) echocardiography is now performed by many cardiology specialists and optimises calculation of cardiac function from volumetric analysis, as well as providing insight into the dynamic nature of cardiac topographical anatomy. It can also map and measure mitral leaflets, paving the way, hopefully, to developing interventional methods for MMVD \(^13\). The challenge for the next decade will be to channel these new ultrasonographic functions into real practical clinical benefit. For example, we find transoesophageal echocardiography to be particularly useful for aiding device selection, sizing and guiding for Amplatz-closure
of patent ductus arteriosus (PDA) and balloon valvuloplasty of pulmonic stenosis. This means we are less reliant on fluoroscopy, reducing radiation exposure of both operator and patient. But imaging outwith echocardiography has also advanced. Digital radiography has enhanced thoracic imaging making it easier to answer simple but incredibly important questions such as whether coughing or dyspnoea is due to cardiac or respiratory disease. Computed tomography (CT) and magnetic resonance imaging (MRI) modalities are now accessible to many if not most general practices. Traditionally, cardiologists have requested CT to investigate or rule out diseases of the upper and lower respiratory tract, pulmonary interstitium and mediastinum. However, ECG-gated angio-CT is now used to complement colour flow and contrast Doppler echocardiography, and, importantly, sometimes fluoroscopy to determine location and magnitude of intra- and extra-cardiac shunts. A study at the R(D)SVS is using ECG-gated CT to validate left atrial volumes obtained from 3D echocardiography, so that patients at higher risk of CHF can be identified. ECG-gated MRI, increasingly available, is recognised as the gold standard for measurement in vivo of cardiac mass and volume. T1 and T2 weighted studies also identify areas of impaired myocardial perfusion and infarction, which may allow us to identify myocardial ischaemia and coronary vascular dysfunction in canine and feline cardiac disease.

Over the last decade, intracardiac surgery has had more variable success. While mortality associated with valvular implants remains unacceptably high, it is now understood that surgical success is strongly linked with experience, and future hopes will depend on dedicated teams of surgeons, nursing and support staff. This is exemplified by the remarkable successes achieved by Dr Masama Uechi and his colleagues, based in Japan 14, but even these astounding achievements utilise mitral repair rather than replacement. For MMVD, due to cost, risk, prevalence, and surgical expertise and experience, pharmacological management will be the only option available to the vast majority of dog owners. Elsewhere, surgery on the right side of the heart has proved more rewarding. Pericardial patch graft valvulotomy, tricuspid valve dysplasia repair, and surgery for double-chambered right ventricle have now acceptable risk levels, testament to the dedicated work of the only open heart surgery unit in the UK, based at the RVC in London.

Biomarkers continue to provide useful diagnostic and prognostic information. Now that issues of sample stability have been addressed, NT proBNP has been shown to offer exceptionally good sensitivity and specificity for discriminating between coughs of cardiac and respiratory origin in dogs, and determining congestive status in both cats and dogs 15. It is increasingly used as a screening tool for identifying cats and dogs at higher risk of developing cardiomyopathy. Even the major disadvantage of delay before receiving a result from an external laboratory has been partially addressed with the advent of a bedside semi-quantitative snap-test. This has been trialled in dyspnoeic cats and its ability to discriminate different aetiologies of pleural effusion 16 is of particular use in practices where there is no immediate access to point-of-care ultrasonography. Troponin I remains the mainstay of diagnosing myocardial insults. Whilst in referral centres, it is particularly useful for diagnosing active myocarditis (including prior to pacemaker implantation) and before performing additional expensive tests for infectious myocarditis, in general practice, where myocarditis is less frequently presented, its usefulness is slightly more limited. New in-house ultra-sensitive assays give rapid results and identify myocardial injury in primary or secondary myocardial disease, including infarction, considered a reason for acute
deterioration in pets with previously diagnosed cardiac disease. Troponin also has diagnostic value in pericardial effusion due to haemangiosarcoma, may have value in screening for early DCM in Dobermanns, and is a useful prognostic tool in feline hypertrophic cardiomyopathy (HCM).

In general, diagnosis and treatment of feline cardiomyopathy lag behind advances made in canine cardiology. There is some but little evidence-based medicine for therapeutics. We now know that clopidogrel is superior to aspirin for prevention of recurrent thromboembolism and there is now a more owner-friendly formulation. Low molecular weight heparins for long-term management are less in favour, and newer generation anti-platelet therapies such as rivaroxaban may rival clopidogrel in the future. However, treatment of aortic thromboembolism, once it has occurred, remains frustratingly basic, with an over-reliance on luck combined with analgesia, management of congestive failure, and prevention of further thrombus formation.

Polypharmacy for CHF in cats includes a combined formulation of ACE inhibitor and spironolactone, and the potential to replace twice daily furosemide with torasemide. Evidence of clinical benefit from ACE inhibition and beta blockade, such stalwarts of feline cardiomyopathy management 10 years ago, remains elusive, but at least there is now some evidence for a benefit from spironolactone, and without the skin hypersensitivity response that blighted its initial use in the species.

As stated earlier, technological advances lend themselves particularly to veterinary cardiology. In the last 10 years, diagnosis of syncope in both cats and dogs has advanced incredibly. Gone are the days of relying on a serendipitous camcorder, primed by a client to video a syncopal event. Mobile phone technology not only allows events to be readily filmed and e-mailed, but ECGs can now be recorded at home through additional hardware such as LiveCor. This can give the clinician vital information on, for example, rate control of atrial fibrillation in the home environment. In the future, it is likely that mobile phones will act as transceivers to implanted devices such as implantable loop recorders (already dramatically smaller than previous models) or pacemakers, before relaying data to specialist centres. Currently though, 24-hour Holter ECGs remain a mainstay of prolonged rhythm assessment. Units are now much lighter, more tolerant of movement, with the digital capacity to record for longer periods. We have been analysing our data in the form of Poincaré plots, in which heart rate variability (HRV, a measure of autonomic tone) is determined from a visual plot of R-R intervals. These minimise the impact of artefacts on HRV calculation, always useful in panting and exercising dogs, and they afford rapid visual qualitative assessment as well as more detailed quantitative analysis. We believe that they may be of particular use in differentiating vagally-induced from non vagally-induced syncope and for prognosticating on critically ill patients.

Finally, major advances have been made in interventional procedures. Amplatz ductal occluders are firmly established as the treatment of choice for PDA occlusion. However, as imaging has improved, we now appreciate that PDAs come in a range of shapes and sizes, not always amenable to the Amplatz device. For these, the newer generation human vascular plugs offer a viable alternative and have been used with success in cats as well as dogs. Options for balloon valvuloplasty have expanded too. Many cardiologists are now using much higher pressure balloons to treat pulmonic stenosis, and cutting balloon valvuloplasty may offer hope for subaortic stenosis.
Pacemakers have also benefited from technological advances. Single chamber pacemakers have a rate-responsive function that is sensitive to movement and paces the heart at appropriately faster rates with exercise. Dual chamber lead implantation is still an option to optimise physiological pacing and reduce the risk of pacemaker syndrome and CHF. However, new generation single leads with sensory components on the portion of lead passing through the atrium may supercede this.

In summary, our patients have benefited hugely over the last decade from advances in diagnostics, therapeutics and interventional modalities. We may not know what the future will bring, but it is very likely that veterinary cardiology will be in the vanguard of technological development and application.

I have no conflicts of interest.

References


