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Case Reports

TREATMENT REGIMEN TO CONTROL RIGHT HEART FAILURE DUE TO GROUP 2 PULMONARY HYPERTENSION SECONDARY TO MYXOMATOUS MITRAL VALVE DISEASE IN A TOY POODLE

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SUMMARY

A 12-year-old toy Poodle was presented to the hospital to determine the cause of chronic ascites. The complete cardiology work-ups which included radiography, echocardiography, and electrocardiogram revealed that the right heart failure was due to moderate-to-severe pulmonary hypertension secondary to myxomatous mitral valve disease as the cause of the ascites. The consistently lower tricuspid regurgitation velocities measured throughout the observation periods indicating underestimation of pulmonary hypertension severity were worthy of note. During the follow-up periods, the treatment regimens were adjusted in accordance to the clinical signs to control the right heart failure.

Keywords: Myxomatous mitral valve disease, pulmonary hypertension, right heart failure, ascites, canine

INTRODUCTION

Myxamatous mitral valve disease (MMVD) is a common canine heart disease, especially in small breed dogs (Reynolds et. al., 2012). One of the sequela of MMVD is the development of pulmonary hypertension (Kellihan et. al., 2010), which occurs at a rate of 29% and 71% in American College Veterinary Internal Medicine (ACVIM) stage B2 and C dogs (Borgarelli et. al., 2015), respectively.

CASE REPORT

A 12 year-old, female toy Poodle weighing 4 kg was presented in June 2019 for a second opinion to treat the chronic ascites. The dog had up-to-date vaccination, deworming and heartworm prevention. Since 30 October 2018, it had been treated with enalapril (Ranitec 10mg, 0.63 mg/kg, PO, SID), furosemide (Lasix 40mg, 2.5 mg/kg, PO, SID), and pimobendan (Vetmedin 1.25mg, 0.31 mg/kg, PO, SID) without a specific diagnosis. Physical examination showed that the dog was bright and alert, with a body condition score of 2.5/5 and bilateral mature cataracts. It was panting and had a heart rate of 156 bpm. The capillary refill time (CRT) was 2 seconds. Heart auscultation revealed a grade V/VI left apical systolic murmur and a grade IV/VI right apical systolic murmur. The abdomen was very distended and tense, and fluid waves were palpable. Abdominocentesis was carried out and removed 400 mL of semi-transparent brownish fluid. However, blood pressure was not measured due to the unavailability of the machine.

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Right lateral chest radiography (Figure 1) showed generalized cardiomegaly (vertebral heart score: 12.5), an enlarged left atrium (vertebral left atrial score: 3), and dorsally elevated trachea. Engorged pulmonary vessels were also apparent. In addition, a loss of the abdominal serosal details indicating ascites was also observed.

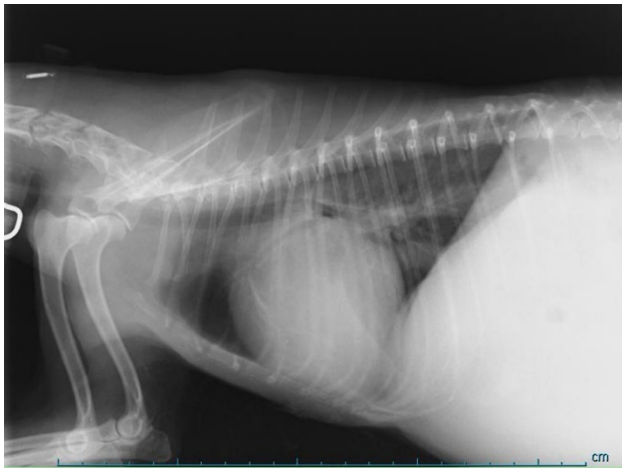

Figure 1. Lateral thoracic radiograph showing an enlarged cardiac silhouette and a loss of abdominal serosal details

The left echocardiogram showed left atrioventricular dilations (left atrium to aorta (LA/AO) ratio: 2.39, left ventricular end-diastolic diameter (LVDD): 3.08 cm), moderately thickened anterior and posterior mitral valves, and severe mitral regurgitation. Prolapsed, flail mitral valve leaflets into the left atrium during systole were also evident (Figure 2). Further, high mitral E and A wave velocities (E: 1.53 m/s, A: 0.89 m/s, E/A: 1.72) suggestive of diastolic dysfunction of the left ventricle were also documented. On the other hand, the right echocardiogram showed tricuspid regurgitation (TR), prolapse of thickened tricuspid valves, right atrium (RA) and ventricular (RV) dilations, and pulmonary artery enlargement (pulmonary artery to aorta (PA/AO) ratio: 1.32).

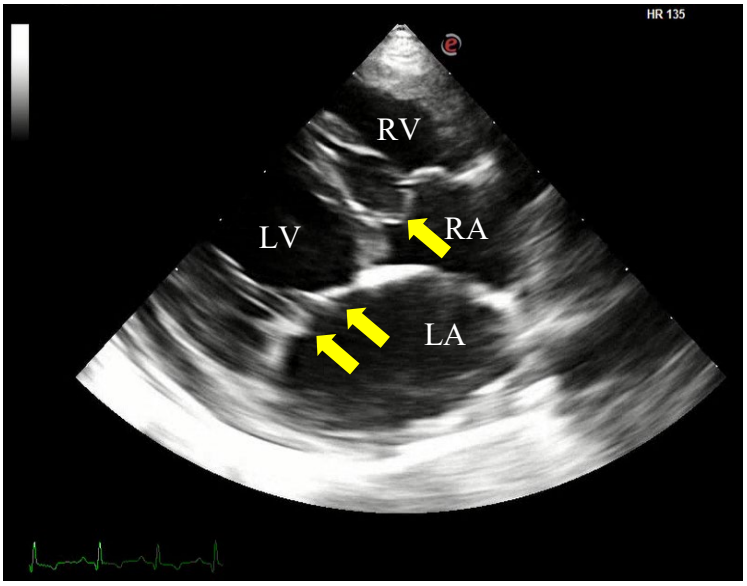

Figure 2. Right parasternal long axis view showing bilateral atrial enlargements and bilateral atrioventricular valve thickening and prolapse. Flail mitral valves and septal tricuspid wave were also observed (arrows).
LA; left atrium, RA; right atrium, LV; left ventricle, RV; right ventricle.

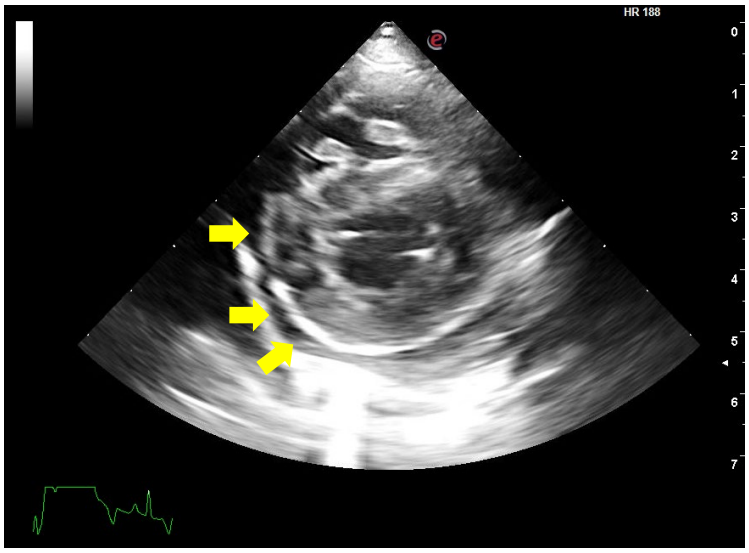

Figure 3 Right parasternal short axis view showing septal flattening of the left ventricle during the systole. Mild collection of pericardial fluid (arrows) was also appreciable.

The maximal TR velocity (TRmax) was 3.21 m/s. Using modified Bernoulli's equation, the estimated systolic pulmonary arterial pressure (SPAP) was 41.2 mmHg. Besides, systolic and diastolic septal flattening and mild pericardial fluid (Figure 3) were also seen.

Thus, a diagnosis of MMVD with right heart failure due to group 2 pulmonary hypertension (PH) was made. The probability of PH was high, based on the ACVIM consensus statement guidelines for the diagnosis, classification, treatment, and monitoring of pulmonary hypertension in dogs (Reinero et. al., 2020). With a focus given to address the right heart failure, the existing treatment protocol was altered. Sildenafil (Viagra 50mg, 1.6 mg/kg, PO, BID) was initiated. The pimobendan (Vetmedin 1.25mg, 0.31 mg/kg, PO, BID) and furosemide (Lasix 40mg, 2.5 mg/kg, PO, TID) dosages were also increased. The owner was instructed to give the sildenafil and pimobendan medications to the dog an hour before food to increase drug bioavailability. Besides, dietary salt restriction was also recommended.

On day 9, the owner informed that the ascites in the dog did not resolve. Therefore, the sildenafil (Viagra 50mg, 1.6 mg/kg, PO, TID) and pimobendan (Vetmedin 1.25mg, 0.31 mg/kg, PO, TID) medications were up-titrated. On day 17, the revisit showed that the dog was bright and alert. According to the owner, there had been no episodes of inappetance, vomit or diarrhea. However, the ascites was still very prominent. Complete blood count and serum biochemistry showed non-regenerative anaemia (RBC: 4.29x10^6/mm^3; normal: 5.5-8.5x10^6/mm^3, haemoglobin: 12.79 g/dL; normal: 15-20 g/dL; PCV: 28.09%; normal: 44-57%), mildly increased alkaline phosphatase (185: U/L; normal: 20-150 U/L), and increased blood urine nitrogen (51 mg/dL; normal: 7-25 mg/dL). The normal albumin (3.1 g/dL; normal: 2.5-4.4 g/dL), globulin (3.8 g/dL; normal: 2.3-5.2 g/dL) levels ruled out hypoproteinaemia as a cause of the ascites. The echocardiogram showed a larger left ventricular chamber (LVDD: 3.43 cm) and a higher TRmax (4.01 m/s) (Figure 4) and a larger pulmonary artery (PA/AO ratio: 1.48) (Figure 5), whereas other parameters remained almost

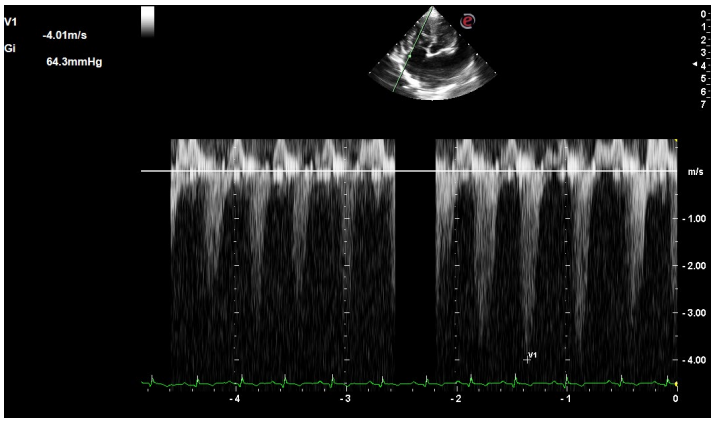

Figure 4. Continuous wave Doppler echocardiogram showing maximal tricuspid regurgitation velocity of 4.01 m/s, equivalent to systolic pulmonary artery pressure of 64.3 mmHg.

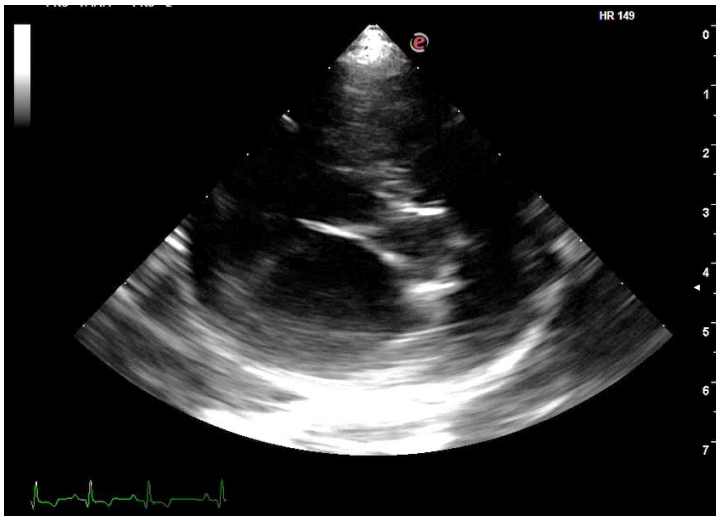

Figure 5 Right parasternal short axis view showing enlarged left atrium and pulmonary artery during end-diastole. LA, left atrium; AO, aorta; PA; pulmonary artery; RVOT: right ventricular outflow tract

unchanged (LA/AO ratio: 2.36, E wave: 1.54 m/s). In addition, the septal mitral annulus tissue Doppler imaging demonstrated decreased myocardial systolic and diastolic functions (S': 0.07 m/s, E': 0.04 m/s, A': 0.05 m/s). The tricuspid annular plane systolic excursion (TAPSE) was less than 8 mm, whereas the liver ultrasonography showed dilated hepatic veins with minimal contractions. To further reduce the left atrial pressure, enalapril (Ranitec 10mg, 0.63 mg/kg, PO, SID) was re-introduced to the therapy. Since then, the dog had been doing well for 3 months without apparent ascites. However, the dog was presented on day 132 as the owner noticed that the abdomen of the dog became very tense (Figure 6). As owner was away for 3 weeks, she was unsure if the dog was properly medicated or not. Nonetheless, the dog was bright and alert, and had a heart rate of 144 bpm. Although abdominal breathing was observed, the respiratory rate was normal at 28 bpm, and the CRT was less than 2 seconds.

A total of 490 mL of protein-rich (specific gravity: 1.028, protein concentration: 3.8 g/dL) brownish fluid was withdrawn via abdominocentesis. The presence of high number of erythrocytes (30-50 /hpf via microscopy; 4+ on dipstick) might contribute to the higher protein concentration. As the fluid continued to drip out from the needle puncture site, a pressure bandage was applied for 2 days. The dog had high serum BUN (44 mg/dL) but normal creatinine levels (1.1 mg/dL; normal: 0.5-1.8 mg/dL), despite the chronic furosemide therapy at a dose of as high as 7.5 mg/kg/day.

In addition, the electrocardiogram (Figure 7) showed decreased QRS complexes (R wave: 0.6 mV) probably due to pericardial effusion which dampened the voltage. Surprisingly, despite the moderate pericardial effusion, electrical alternans was not observed. On the other hand, the echocardiogram showed unremarkable changes in the hemodynamic parameters (TRmax: 3.54 m/s) except a

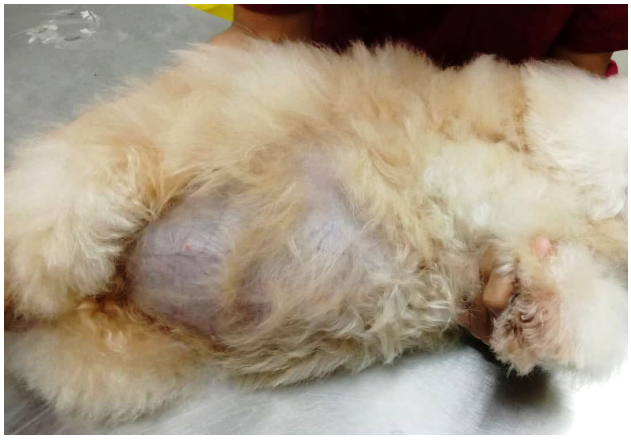

Figure 6. A photograph showing a very distended abdomen with abdominal vessel engorgement.

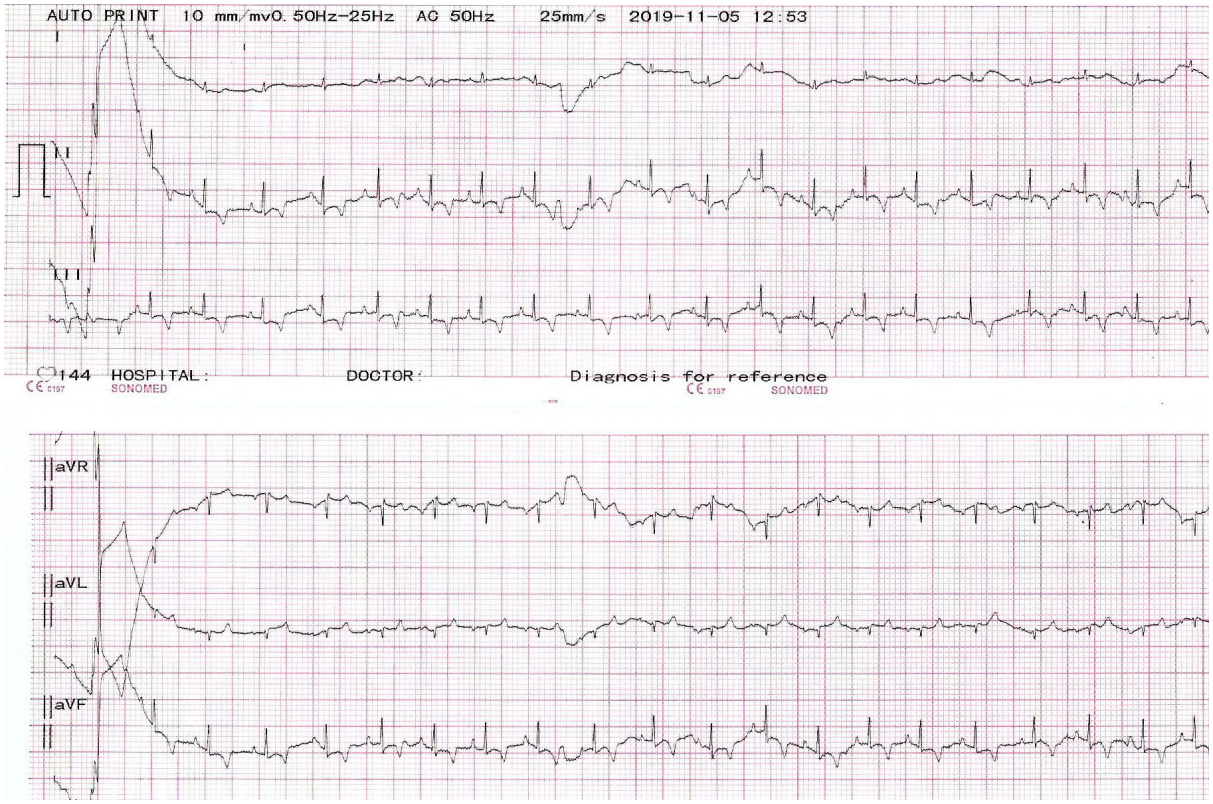

Figure 7. An electrocardiogram showing low QRS complexes

higher collection of pericardial fluid. The sildenafil therapy was raised to 3.1 mg/kg, PO, TID, whilst maintaining dosage of other medications. At present day (day 240), the dog was doing well and the abdominal distension was well controlled.

DISCUSSION

Canine myxomatous mitral valve disease (MMVD) or chronic degenerative mitral valve disease occurs in about 30% of dog population of greater than 10 years of age (Reynolds et. al., 2012), while pulmonary hypertension (PH) due to left heart disease (group 2 PH) is the most prevalent form of PH in human (Rabiller et. al., 2006) and veterinary (Kellihan et. al., 2010) patients.

In the group 2 PH, the increased left ventricular filling pressure exerts passive back transmission to pulmonary capillaries, leading to pulmonary venous congestion. With time, the progress becomes irreversible, resulting in reactive pulmonary hypertension (Guazzi et. al., 2010). Reactive pulmonary hypertension is characterized by proliferation of the smooth muscle cells of pulmonary vein and artery (Guazzi et. al., 2010) through a myriad of signaling pathways, in a process known as cardiopulmonary remodeling (Leong et. al., 2018), which eventually leads to right heart failure and even death.

The dog presented in this report demonstrated marked remodeling of the left heart disease, evidenced by the presence of mitral endocardiosis and severe left atrioventricular dilations on the echocardiogram, although the generalised cardiomegaly on radiograph might be partly due to the pericardial effusion. While cardiac catheterization remains the gold standard to diagnose PH, the Doppler echocardiograms consistently demonstrated TRmax which exceeded 3 m/s, giving rise to SPAP > 36 mmHg. Further, several anatomic sites also supported a high probability of PH in the dog, which include RV hypertrophy, RA dilation, septal flattening, and pulmonary artery enlargement. Most importantly, the occurrence of right-sided heart failure (ascites and pericardial effusion) strongly suggested that the dog had a high right atrial pressure (estimated at 15 mmHg), thus a much higher SPAP value (41.2 to 64.2 mmHg + 15 mmHg = 56.2 to 79.3 mmHg). While grading of PH based on the estimated SPAP is no longer recommended by the ACVIM panel (Reinero et. al., 2020), the combined clinical signs and Doppler and B-mode results equated at least a moderate PH in the dog.

Although a moderate correlation exists between Doppler estimates of pulmonary artery and right arterial pressures and invasively measured values in the dogs, under-diagnosis of PH or misclassification of the severity of PH in many canine patients is not an unusual phenomenon. Besides, there is a higher tendency of underestimation than overestimation (Soydan et. al., 2015). In the present case, the underestimation of the SPAP was believed to be attributable to the RV dilation and systolic dysfunction, which collectively lowered the TRmax. Nevertheless, other factors such as chronic respiratory disease and pulmonary thromboembolism were unlikely to have caused the PH in the dog given the lack of relevant clinical symptoms.

With respect to the management of the right heart failure, the dog was medicated with sildenafil, a

phosphodiesterase-5 inhibitor which dilates the pulmonary vasculature. Despite the treatment, a significant hemodynamic improvement was not seen throughout the observation period, consistent with that reported by Kellum (2007). Not only that, the sildenafil therapy was up-titrated from 1/8 tab, twice daily (3.1 mg/kg/day) to thrice daily (4.7 mg/kg/day), and eventually to 1/4 tab thrice daily (9.4 mg/kg/day) to reach the optimal response, although complete resolution of ascites is often impossible. Taken together, this might imply the disease severity and progression due to the active pulmonary arterial remodeling. Nonetheless, the sudden relapse of severe ascites might also be caused by improper medication during when the owner was away or diuretic resistance (Shah et. al., 2017).

As the MMVD dogs with PH had a shorter survival than those without (Borgarelli et. al., 2015), the owner was informed about the fair prognosis of the dog. Meanwhile, maximising its quality of life with the polypharmacy therapy approaches remains the current goal of treatment.

CONCLUSION

Pulmonary hypertension commonly occurs a complication of MMVD in dogs and may manifest signs of right sided heart failure. Diagnosis and treatment of the PH is indispensable to confer optimal therapeutic efficacy in treating canine MMVD.

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REFERENCES

Borgarelli, M., Abbott, J., Braz-Ruivo, L., Chiavegato, D., Crosara, S., Lamb, K., Ljungvall, I., Poggi, M., Santilli, R.A., Haggstrom, J. (2015). Prevalence and prognostic importance of pulmonary hypertension in dogs with myxomatous mitral valve disease. Journal of Veterinary Internal Medicine 29: 569–574.

Reinero, C., Visser, L.C., Kellihan, H.B., Masseau, I., Rozanski, E., Clercx, C., Williams, K., Abbott, J., Borgarelli, M., Scansen, B.A. (2020). ACVIM consensus statement guidelines for the diagnosis, classification, treatment, and monitoring of pulmonary hypertension in dogs. Journal of Veterinary Internal Medicine. 1–25.

Guazzi, M. and Arena, R. (2010). Pulmonary hypertension with left sided heart disease. Nature Reviews Cardiology 7: 649–659.

Kellihan, H.B. and Stepien, R.L. (2010). Pulmonary hypertension in canine degenerative mitral valve disease. Journal of Veterinary Cardiology 14: 149–164.

Kellum, H.B. and Stepien, R.L. (2007). Sildenafil citrate therapy in 22 dogs with pulmonary hypertension. Journal of Veterinary Internal Medicine 21: 1258–64.

Leong Z.P., Okida, A., Higuchi, M., Yamano, Y. and Hikasa, Y. (2018). Reversal effects of low-dose imatinib compared with sunitinib on monocrotaline-induced pulmonary and right ventricular remodeling in rats. Vascular Pharmacology 100: 41–50.

Rabiller, A., Jaïs, X., Hamid, A., Resten, A., Parent, F., Haque, R., Capron, F., Sitbon, O., Simonneau, G., Humbert, M. (2006). Occult alveolar haemorrhage in pulmonary veno-occlusive disease. European Respiratory Journal 27: 108–113.

Reynolds, C.A., Brown, D.C., Rush, J.E., Fox, P.R., Nguyenba, T.P., Lehmkuhl, L.B., Gordon S.G., Kellihan, H.B., Stepien, R.L., Lefbom, B.K., Meier, C.K., Oyama, M.A. (2012). Prediction of first onset of congestive heart failure in dogs with degenerative mitral valve disease: the PREDICT cohort study. Journal of Veterinary Cardiology 14: 193–202.

Shah, N., Madanieh, R., Alkan, M., Dogar, M.U., Kosmas, C.E. and Vittorio, T.J. (2017). A perspective on diuretic resistance in chronic congestive heart failure. Therapeutic Advances in Cardiovascular Disease 11: 271–278.

Soydan, L.C., Kellihan, H.B., Bates, M.L., Stepien, R.L., Consigny, D.W., Bellofiore, A., Francois, C.J., Chesler, N.C. (2015). Accuracy of Doppler echocardiographic estimates of pulmonary artery pressures in a canine model of pulmonary hypertension. Journal of Veterinary Cardiology. 17; 13–24.