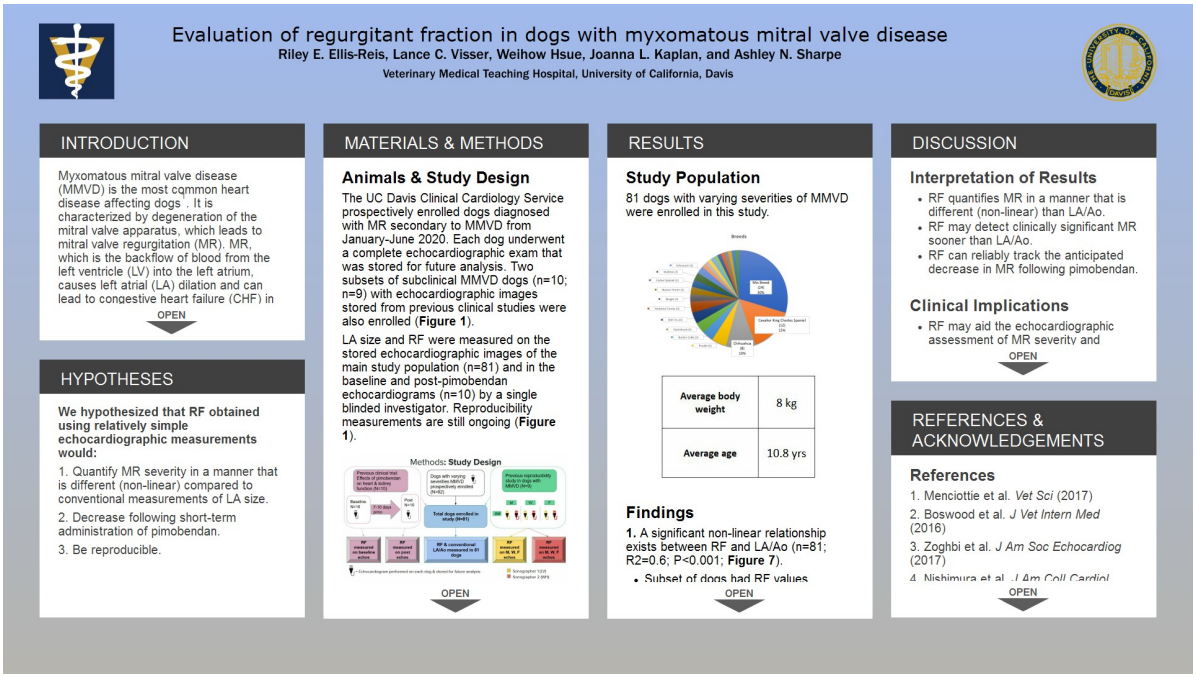
Evaluation of regurgitant fraction in dogs with myxomatous mitral valve disease



Riley E. Ellis-Reis, Lance C. Visser, Weihow Hsue, Joanna L. Kaplan, and Ashley N. Sharpe

Veterinary Medical Teaching Hospital, University of California, Davis

PRESENTED AT:

AAVMC Association of American Veterinary Medical Colleges

VSSS Veterinary Summer Scholars Symposium

INTRODUCTION

Myxomatous mitral valve disease (MMVD) is the most common heart disease affecting dogs[1]. It is characterized by degeneration of the mitral valve apparatus, which leads to mitral valve regurgitation (MR). MR, which is the backflow of blood from the left ventricle (LV) into the left atrium, causes left atrial (LA) dilation and can lead to congestive heart failure (CHF) in some dogs[1]. Pimobendan, an inodilator drug commonly used to treat MR secondary to MMVD, has shown to prolong the onset of CHF in dogs with subclinical MMVD and cardiomegaly[2]. In veterinary medicine, MR severity is traditionally assessed on 2-D echocardiography (2DE) using relatively crude and indirect linear diameter measurements of LA size. In human medicine, MR severity is assessed using additional measurements, such as regurgitant fraction (RF)[3]. RF, a more direct measure of MR, can be obtained from routine 2D and Doppler echocardiography yet studies evaluating the clinical use and reproducibility of RF in dogs with MMVD are limited.

HYPOTHESES

We hypothesized that RF obtained using relatively simple echocardiographic measurements would:

1. Quantify MR severity in a manner that is different (non-linear) compared to conventional measurements of LA size.

2. Decrease following short-term administration of pimobendan.

3. Be reproducible.

MATERIALS & METHODS

Animals & Study Design

The UC Davis Clinical Cardiology Service prospectively enrolled dogs diagnosed with MR secondary to MMVD from January-June 2020. Each dog underwent a complete echocardiographic exam that was stored for future analysis. Two subsets of subclinical MMVD dogs (n=10; n=9) with echocardiographic images stored from previous clinical studies were also enrolled (**Figure 1**).

LA size and RF were measured on the stored echocardiographic images of the main study population (n=81) and in the baseline and post-pimobendan echocardiograms (n=10) by a single blinded investigator. Reproducibility measurements are still ongoing (**Figure 1**).

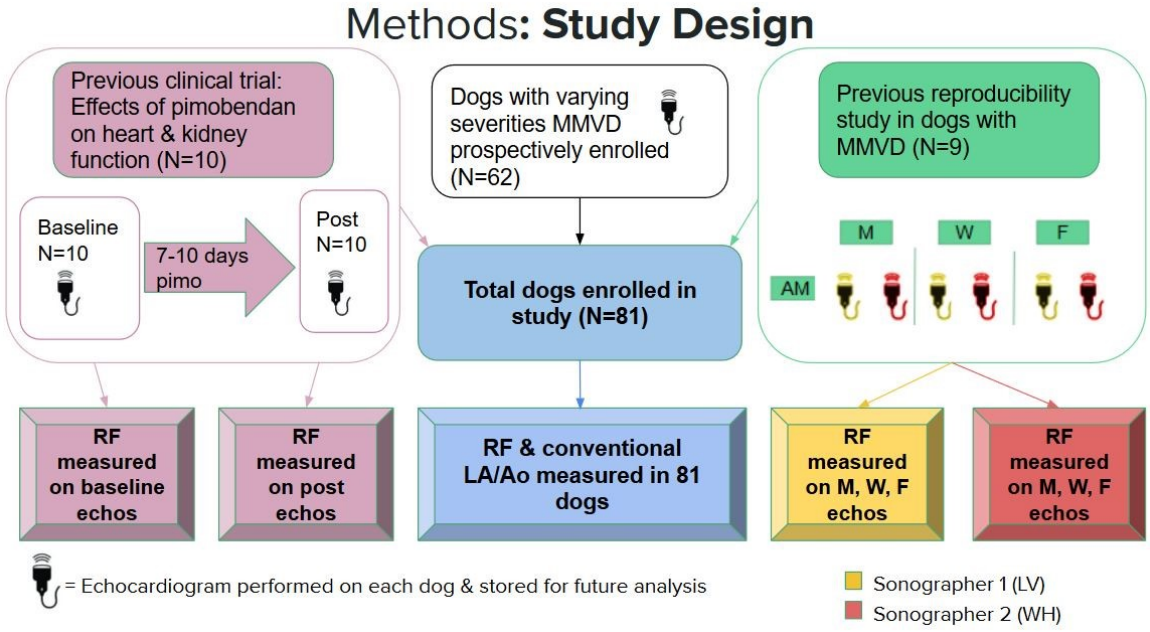


Figure 1. A flowchart describing enrollment and measurements performed.

Echocardiography

Left Atrial Size

LA size was quantified using the conventional left-atrium-to-aortic-root ratio (LA/Ao) where the LA diameter is indexed to the aortic diameter (**Figure 2**).

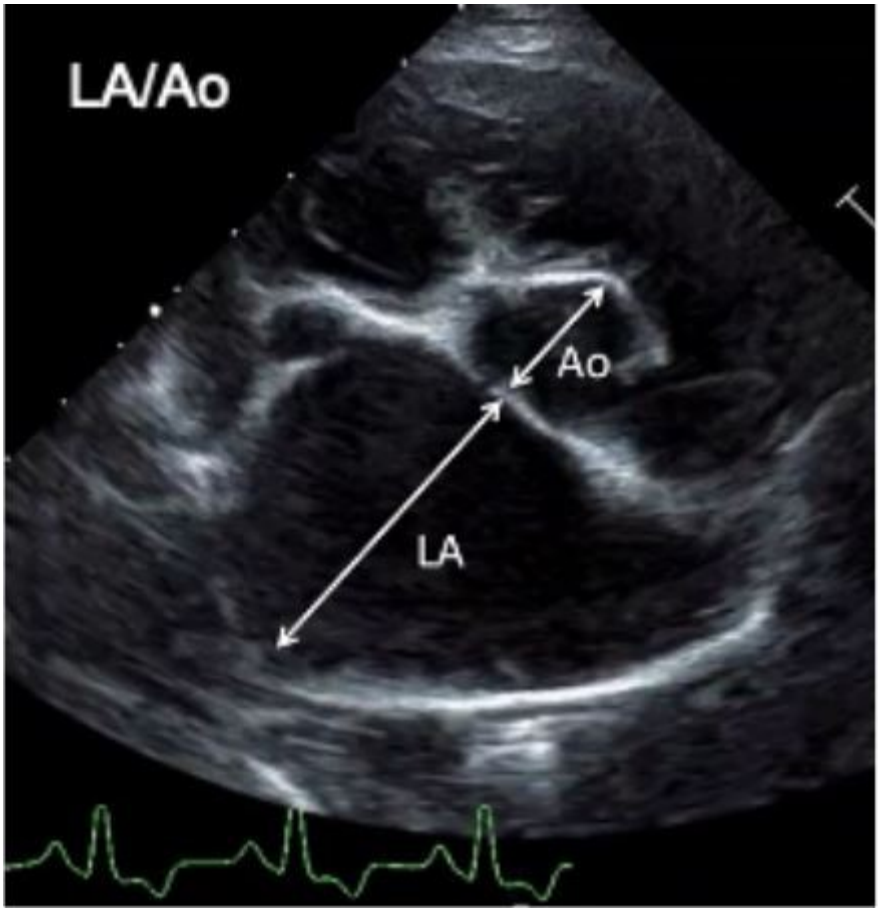


Figure 2. Echocardiogram demonstrating the LA/Ao measurement on a right-sided parasternal short-axis view. LA= Left atrium; Ao=Aorta.

Regurgitant Fraction

RF was obtained by measuring total stroke volume and forward stroke volume on routine echocardiographic images (**Figure 3**).

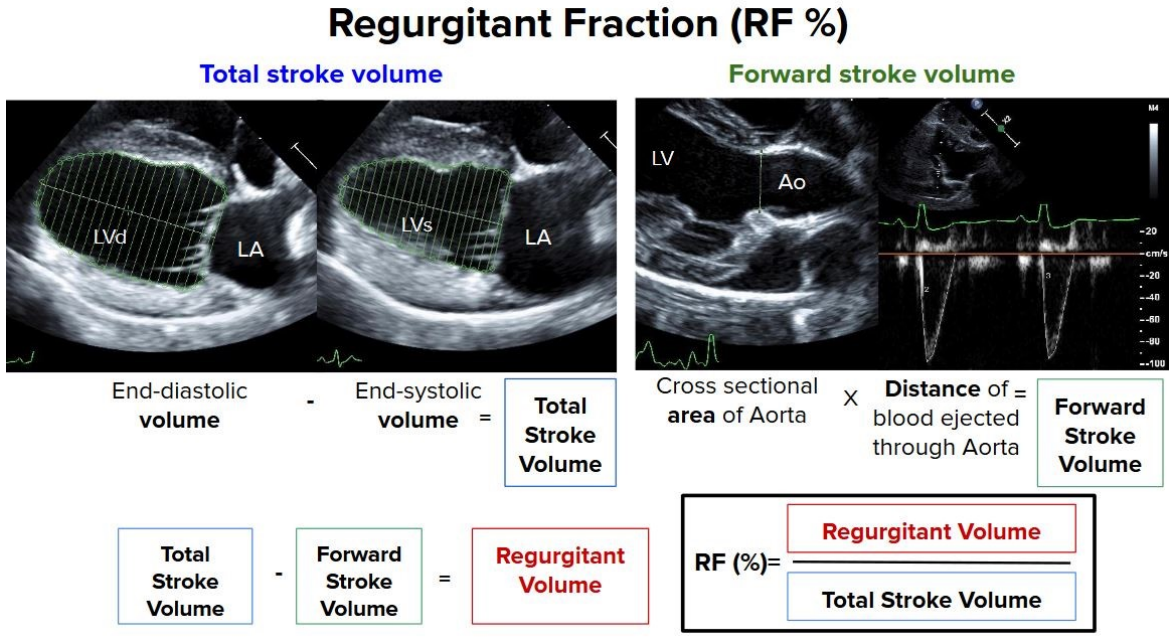


Figure 3. Measurements and calculations performed to obtain RF. LVd= Left ventricle in diastole; LA= Left atrium; LVs= Left ventricle in systole; LV= Left ventricle; Ao= Aorta.

Data Analysis

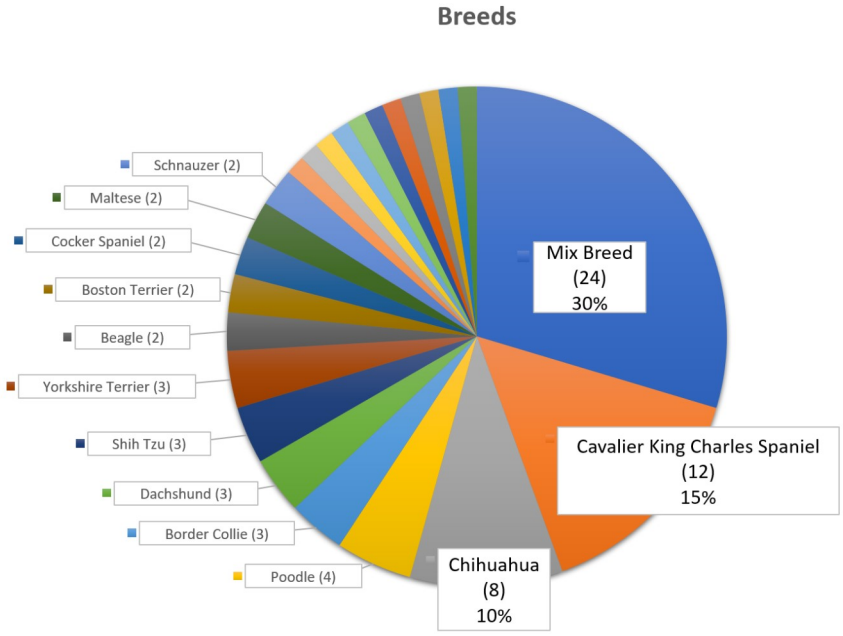
Regression analysis was used to assess the relationship between RF and LA/Ao.

The difference between RF at baseline and post-pimobendan was determined using a paired t-test with statistical significance set at $P<0.05$.

RESULTS

Study Population

81 dogs with varying severities of MMVD were enrolled in this study.



Average body weight	8 kg
Average age	10.8 yrs

Findings

1. A significant non-linear relationship exists between RF and LA/Ao (n=81; R2=0.6; P<0.001; **Figure 7**).

- Subset of dogs had RF values between 30-60% (suggestive of moderate to severe MR) with normal LA/Ao values (LA/Ao<1.6) (**Figure 7**).

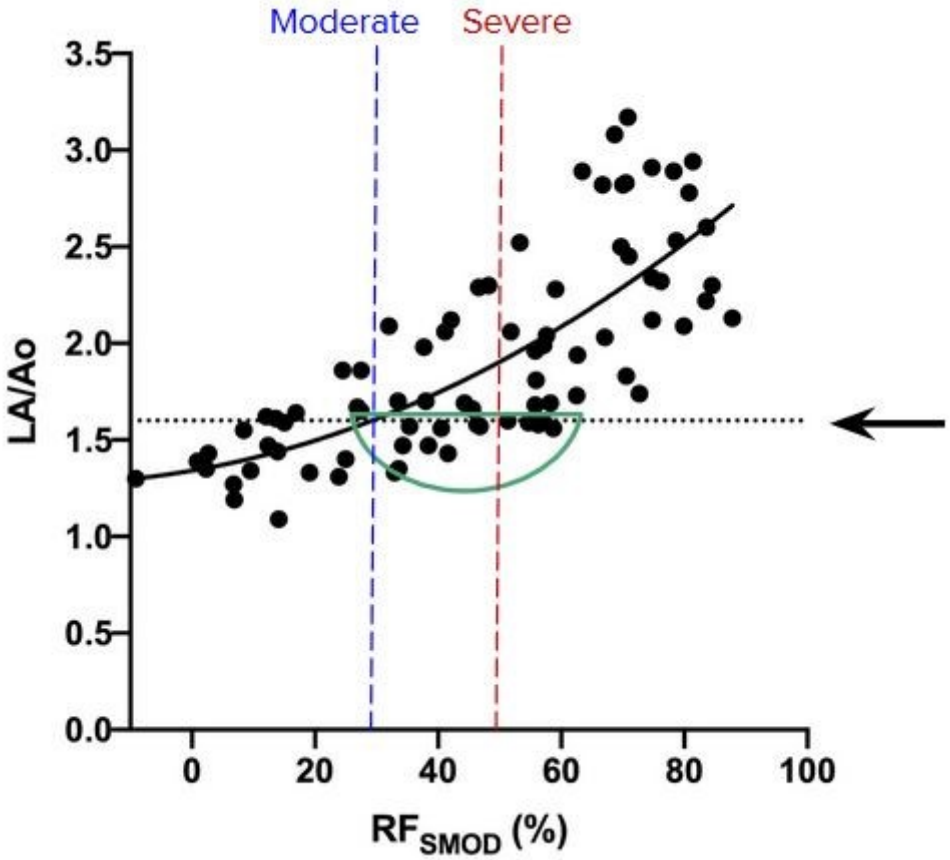


Figure 7. Scatterplot demonstrating the significant non-linear relationship between RF and the conventional LA/Ao (n=81, R2=0.6; P<0.001). Black arrow indicates LA/Ao=1.6, the clinical cut-off used to indicate left atrial enlargement. The blue dotted line represents RF=30%, indicating moderate MR and the red dotted line represents RF=50%, indicating severe MR[4]. Green semi-circle represents the subset of dogs with normal LA/Ao yet moderate-severe MR.

2. Pimobendan significantly (P=0.002) reduced RF in dogs (n=10) with subclinical MMVD (mean percent decrease 32 +/- 23%; **Figure 8**).

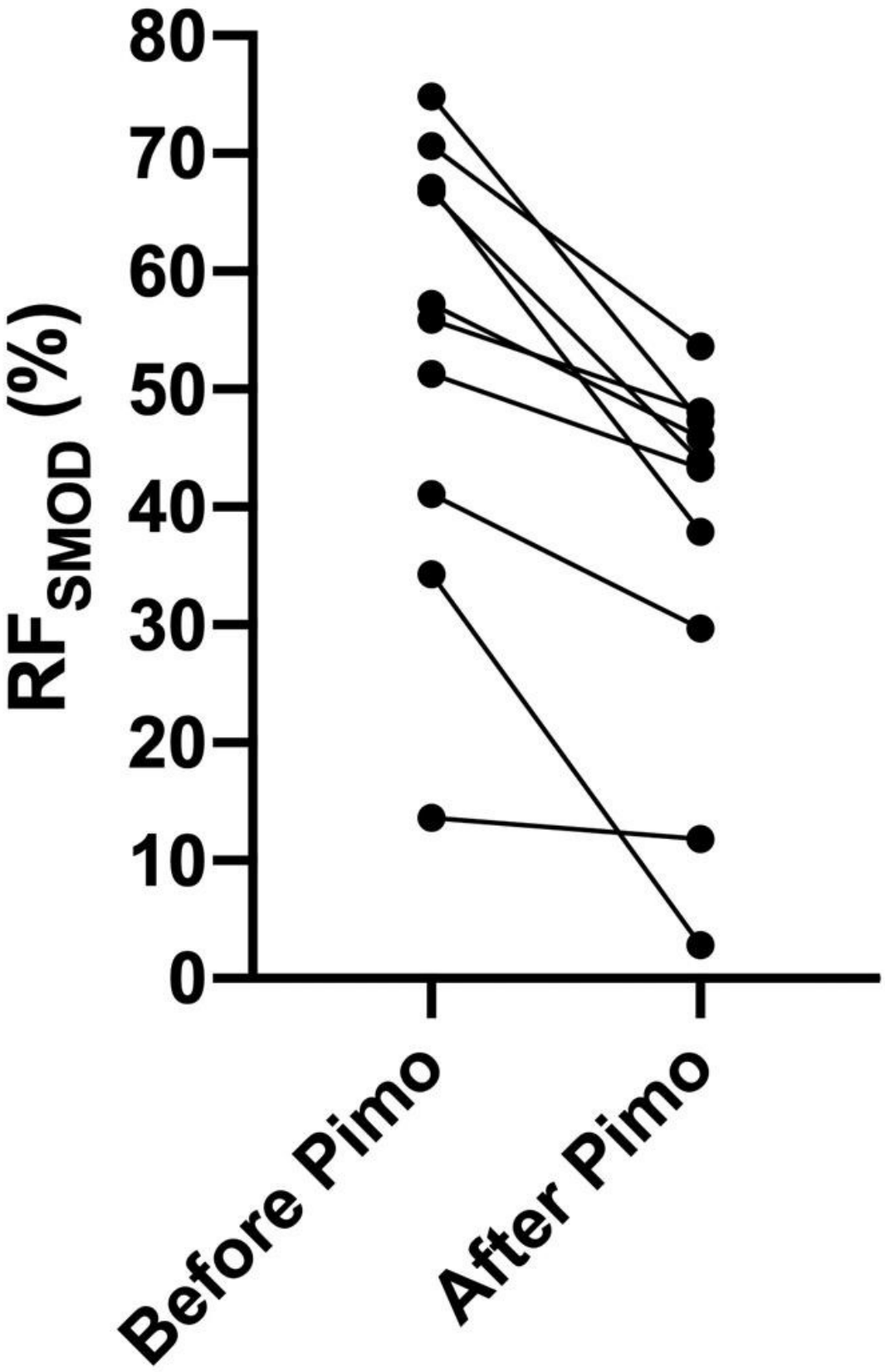


Figure 8. RF at baseline and post-administration of pimobendan in 10 dogs with subclinical MMVD (P=0.002; mean percent decrease 32 +/- 23%).

DISCUSSION

Interpretation of Results

- RF quantifies MR in a manner that is different (non-linear) than LA/Ao.
- RF may detect clinically significant MR sooner than LA/Ao.
- RF can reliably track the anticipated decrease in MR following pimobendan.

Clinical Implications

- RF may aid the echocardiographic assessment of MR severity and clinical management of MMVD.
  - Supplementing traditional measurements of LA size.
  - Track changes in MR to monitor disease progression.
- Future studies are warranted investigating the relationship between changes in RF and the onset of CHF and survival in dogs with MMVD.
  - Determine RF's role in treatment decisions and as a prognostic indicator.

REFERENCES & ACKNOWLEDGEMENTS

References

1. Menciottie et al. *Vet Sci* (2017)

2. Boswood et al. *J Vet Intern Med* (2016)

3. Zoghbi et al. *J Am Soc Echocardiog* (2017)

4. Nishimura et al. *J Am Coll Cardiol* (2017)

Acknowledgements

- Dr. Lance Visser for his mentorship and support
- Dr. Weihow Hsue, Dr. Joanna Kaplan, and Dr. Ashley Sharpe for their contribution
- Students Trained in Advanced Research (STAR) Program for their funding & support
  - Funding provided by Boehringer Ingelheim Animal Health (BI)
- Grant Support:
  - American College of Veterinary Internal Medicine
  - Center for Companion Animal Health at the University of California, Davis, School of Veterinary Medicine