THESIS

FEEDLOT HEART DISEASE: UNDERSTANDING HEART SCORE AND ITS RELATIONSHIPS TO ECONOMICALLY RELEVANT TRAITS

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In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Fall 2022

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ABSTRACT

FEEDLOT HEART DISEASE: UNDERSTANDING HEART SCORE AND RELATIONSHIPS WITH ECONOMICALLY RELEVANT TRAITS

The increasing occurrence of feedlot heart disease caused by pulmonary hypertension has precipitated a growing concern from producers and geneticists alike. Utilization of genetic technology for selection and breeding decisions has made a substantial amount of progress in past decades within economically relevant traits, but the focus on high performing cattle may have had adverse consequences on cardiovascular fitness. Pulmonary hypertension has become a more frequent occurrence in low to moderate elevation feedlots, causing feedlot death and the potential to predispose cattle to co-morbidities. Previously, once considered only a high-altitude issue, pulmonary hypertension appears prevalent in high genetic merit cattle within moderate elevation, high plains feedlots. With no options for treatment, management, and prevention in feedlot cattle may be the only strategy for producers struggling with the balance of desirable, fattening cattle and pulmonary hypertension risk. The objective of this study was to establish the foundation for a new heart grading system known as heart score and discover its genetic and phenotypic relationships with economically relevant traits and differentiate phenotypic differences between healthy and unhealthy scored Angus-influenced cattle.

The third chapter of this thesis included phenotypic differences between cattle with healthy and unhealthy heart scores (n = 1,422). Data were obtained from Cactus Feed Yard LLC in Canyon, Texas over a two-year period (2020-2022). Means were compared between heart score groups (1,2 & 3+) to test for significant differences between the two groups. Linear models

and the ANOVA table displayed significant fixed effects to each model. Systolic, diastolic, PAP, and marbling scores differed among groups (*P < 0.05*), while hot carcass weight displayed a tendency *(P < 0.10*). Unhealthy heart scored cattle tended to be heavier carcasses associating heavier cattle with pulmonary hypertension. Healthy heart scored animals had overall lower (*P < 0.05*) PAP, systolic, and diastolic measurements.

The fourth chapter of this thesis highlighted the differences between repeated PAP measurements at 9 and 14 months of age. The cohort of Angus influenced cattle were housed at a feedlot in Canyon, TX and was a moderate altitude (1,080 m). Repeated PAP measurements exhibited an increase in PAP measurements between 9 months and 14 months of age, which were later grouped by their heart scores. No differences were observed among heart scored cattle at 9 months (mean minimum: 39.61 ± 2.47; mean maximum: 40.36 ± 3.47) but distinct differences were observed among cattle grouped in their 14-month PAP (mean minimum: 45.27 ± 5.69; mean maximum: 79.20 ± 21.09). High heart scores were associated with higher PAP measurements. There was a correlation of 0.20 between the measurements showcasing a positive trend between measurements, but also the inability of PAP measurements taken at 9 months may not be predictive of cattle's scores at 14-month-old. Furthermore, there were no differences between phenotypic traits of the cattle who had greater PAP differences between their measurements.

The third study estimated the heritability of heart score and the phenotypic relationships with economically relevant traits (n = 1,507) in progeny of 88 sires. Phenotypes included heart scores, PAP (14 months), hot carcass weight, marbling, ribeye area, and backfat. Heart score was found to have a moderate heritability estimate 0.28 ± 0.10. Heart score had a very strong genetic correlation with PAP, and strong correlation with hot carcass weight. Positive genetic

correlations were found between heart scores and carcass traits with genetic correlations between 0.07 to 0.63. Overall, these results suggest heart scores to be useful in genetic selection for a healthier cardiopulmonary system. while not drastically influencing carcass traits.

ACKNOWLEDGEMENTS

I would first like to express my sincere gratitude to my advisors Dr. Scott Speidel and Dr. Mark Enns. Their mentorship and guidance have contributed to my success in completing my degree program at Colorado State University and encouraging me to continue my education in Animal Genetics. I would also like to thank my committee members Dr. Milt Thomas and Dr. Timothy Holt, for their assistance and challenges to help guide me in their expertise on the project.

Many thanks to my graduate students in my program including Roderick Gonzalez Murray, Kelley Duggan, Lane Giess, Sydney Baty, Kathryn Heffernan, and Caleb Hurst. Their willingness to help collect data for the project, learn about heart score every seminar, and encouragement has made my Master's program an amazing experience.

I would also like to include our external partners Matt Cleveland and Grant Sardella at ABS Global, who supply their genetics data for this thesis and who are always willing to answer any questions throughout the process. I would also like to thank Ben Holland, Alyssa Word, and Dr. Guy Ellis, and the cattle crew at Cactus Research Feed Yards, who help collect feedlot data and for their assistance in data collection and collaboration.

Lastly, I would like to thank my friends and family for their consistent support through my program, whether they were in Colorado or throughout the United States, their encouragement was impactful to my success in the completion of this thesis.

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CHAPTER 1: INTRODUCTION

Feedlot heart disease (FHD) is a devastating and untreatable disease for beef producers in low to moderate altitudes. The disease is caused by pulmonary hypertension with the pulmonary artery developing lesions and constriction of vascular system such as in cattle suffering from high altitude disease (HAD) but without the hypoxic environment (Moxley et al., 2019). Limited data on the disease hinders the advancements producers can make to prevent FHD. This is a major constraint for feedlots as a large proportion of beef production is found in central United States as shown in Figure 1.1 where, there is no practical option for s moving cattle to a lower altitude as one would with cases of HAD.

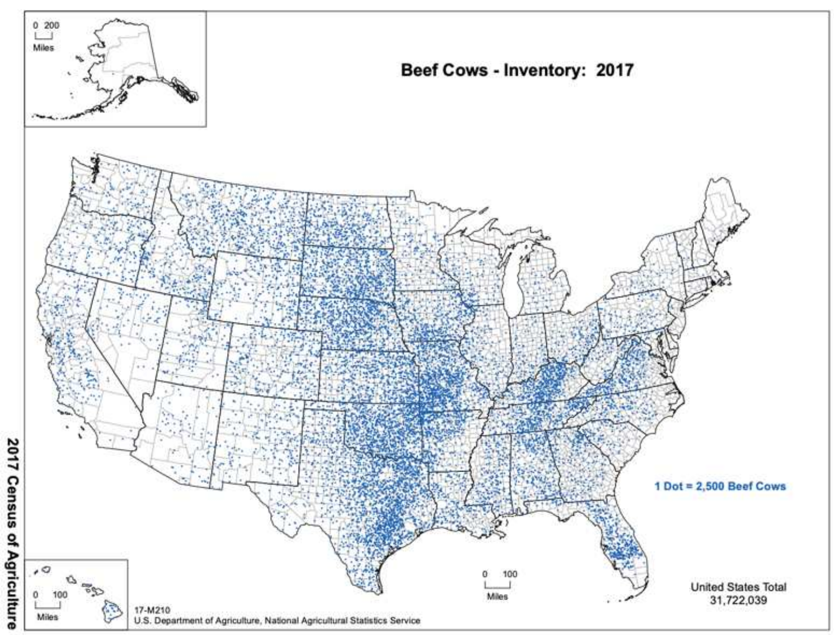

Figure 1.1: Demographic map of beef cattle in United States. Provided by United States Department of Agriculture 2017 Census. https://www.nass.usda.gov/Publications/AgCensus/2017/Online_Resources/Ag_Atlas_Maps/17-M210g.php

The gravity of feedlot heart disease and its effect on the industry is still being determined. A recent three-year study following 28,950 cohorts of feedlot cattle in 22 US commercial feedlots found that out of the 75,963 deaths, 3,282 died from noninfectious heart disease (Johnson et al. 2021). Although, that is only ~5% of the cause of death, that only represents mortalities and not associated complications from heart disease and its affiliation with other diseases. Neary et al. (2015) reported that cattle previously treated for bovine respiratory disease were three times more likely to die of heart failure. Studies capturing heart disease prevalence in the feedlot sector as a total have yet to be completed.

The USDA speculated that a single feedlot operation in the United States could inquire annual losses of $250,000 due to heart failure caused by pulmonary hypertension (BCHF, 2020). Producers and researchers interested in pulmonary hypertension have equated much of the success in HAD with a preventative tool for pulmonary hypertension in the form of pulmonary arterial pressure estimated progeny differences (PAP EPD). Pulmonary arterial pressure, also known as PAP, is an effective way to measure the amount of pulmonary arterial pressure, by inserting a catheter into the jugular vein, and feeding that into the pulmonary artery (Holt and Callan, 2007). PAP was found to have a moderate heritability estimate of 0.26-0.41 as reported by Crawford et al. (2016), Shirley et al. (2008), Speidel et al. (2019) and therefore the creation of PAP EPD was introduced to the American Angus Association in 2019 and updated again in 2020 for commercial use in bull selections (American Angus Association, 2020) and now is updated weekly. Although PAP at lower elevations (< 1500m) has been shown to be an indicator trait for high altitude usage with a genetic relationship of low and high-altitude PAP measurements being 0.83, suggesting strong, positive correlations (Pauling et al. 2017), there still is the unknown to how this translates to the prevention of feedlot heart disease strategies. Through the observations of feedlot heart morphology, a visual grading system was created by Dr. Tim Holt of Colorado State University to provide a record and indication of severity of feedlot heart remodeling (Holt, 2020). The scale encompasses scores 1-5(1, Normal heart structure to 5, severe heart remodeling), where a trained grader can access the hearts being processed at harvest. The potential of a new method of recording pulmonary hypertension could prove to become a preventative and selective tool within the industry but requires additional background as to the degree of genetic influence and other factors necessary for development of a selection tool. Therefore, the objective of this thesis includes:

1. Evaluate the relationship of heart scores and phenotypic differences seen in fattening, Angus-influenced cattle in the United States.
2. Understand the genetic influence on heart score through the estimation of heritability for the trait.
3. Estimate phenotypic correlations between heart score and economically relevant traits of interest in fattening, Angus influenced cattle.

LITERATURE CITED

American Angus Association. 2019. Research PAP EPD launched by Angus Genetics Inc. Available from https://www.angus.org/Pub/Newsroom/Releases/020119-pap-epd-launch.aspx [accessed May 6, 2022].

Blaine T Johnson, David E Amrine, Robert L Larson, Robert L Weaber, Brad J White, Retrospective analysis of cohort risk factors and feeding phase timing associated with noninfectious heart disease deaths in U.S. feedlot cattle, *Translational Animal Science*, Volume 5, Issue 4, October 2021, txab220, https://doi.org/10.1093/tas/txab220

Bovine Congestive Heart Failure (BCHF) in Feedlot Cattle. 2020. BCHF, USDA ARS. Clay Center, NE: U.S. Meat and Research Center.

Crawford N. F., Thomas M. G., Holt T. N., Speidel S. E., and Enns R. M.. 2016. Heritabilities and genetic correlations of pulmonary arterial pressure and performance traits in Angus cattle at high altitude. *J. Anim. Sci*. 94:4483–4490. doi:10.2527/jas.2016-0703.

Holt, T. 2020. Heart visual grading image. Colorado State University.

Holt T., Callan R. 2007. Pulmonary Arterial Pressure Testing for High Mountain Disease in Cattle. Veterinary Clinics of North America: Food Animal Practice. 23(3):575-596. Doi:10.1016/j.cvfa.2007.08.001

Moxley, R. A., Smith, D. R., Grotelueschen, D. M., Edwards, T., & Steffen, D. J. (2019). Investigation of congestive heart failure in beef cattle in a feedyard at a moderate altitude in western Nebraska. *Journal of Veterinary Diagnostic Investigation*, *31*(4), 509–522. https://doi.org/10.1177/1040638719855108

Neary J., Booker C., Wildman B., Morley P. 2016. Right-Sided Congestive Heart Failure in North American Feedlot Cattle. J Vet Intern Med. 30(1):326-34. doi: 10.1111. PMID: 26547263; PMCID: PMC4913666.

Pauling R., Speidel S., Thomas M., Holt T., Enns R. 2018.Evaluation of moderate to high elevation effects on pulmonary arterial pressure measures in Angus cattle, *Journal of Animal Science*. 96(9): 3599-3605.

Shirley K. L. Beckman D. W. Garrick D. J. 2008. Inheritance of pulmonary arterial pressure in Angus cattle and its correlation with growth. J. Anim. Sci.86:815–819. doi:10.2527/jas.2007-0270

Speidel S.E., Thomas M.G., Holt T., and Enns R.M. 2020. Evaluation of sensitivity of pulmonary arterial pressure to elevation using a reaction norm model in Angus Cattle. *J. Anim. Sci*. 98(5).

CHAPTER 2：PULMONARY HYPERTENSION TO HEART SCORES REVIEW OF LITERATURE

SECTION 1: INTRODUCTION TO CATTLE CARDIOVASCULAR HEALTH

The mystery of feedlot death in fattening beef cattle contributes to the misunderstanding of managing cattle in intensive feed regimes especially when considering high altitude environments. The number of cattle not reaching harvest due to unclear causes becomes more apparent as the beef industry continues to investigate genetic components of health traits. The disease known as Bovine Congestive Heart Failure (BCHF) leads for concerns and questions from producers and scientists alike. According to the USDA Meat Animal Research Center (2020), bovine congestive heart failure describes a condition that develops from the constriction of the right ventricle, narrowing of the pulmonary artery, and increased pressure within the heart that ends up constricting blood flow and ultimately ends in fatality for cattle. The hypothesis as to the cause of this phenomenon in high altitude cases is likely due to hypoxia caused by low oxygen levels but the disease at low to moderate altitudes is still undetermined. Severely affected cattle never reach their harvest date and are seen as economic loss to the producer as well as were progeny of sires that will never have early death progeny recorded for performance and growth traits. In 1974, 407,000 head of cattle were surveyed for death and illnesses, within this sample, 1,988 necropsies occurred. Out of those animals necropsied ~6% had signs of high-altitude disease, a popular name for BCHF due to the commonality of it effecting animals at altitude and the distinction of brisket edema (Jensen et al., 1974). This study builds on one of the earliest recorded studies by Glover et al. (1914) on bovine congestive heart failure, showcasing records of the characteristic gross changes within affected animals that continuously remain an area of concern for producers.

Although the physical environment may be a large component to triggering hypoxia in cattle, genetically, it is possible that animals with predisposition or sensitivities may have a gene variant causing them to have a disadvantage in their cardiovascular fitness when exposed to an unidentified catalyst, but this is yet to be determined. The lack of genomic information presents new areas of exploration for recording physical differences and detection methods for understanding all the components factoring into bovine heart failure.

The physical testing and diagnostic tools for BCHF have ranged from the development of pulmonary arterial pressure (PAP) to use of ultrasound examination for means of diagnosis for BCHF. Pulmonary arterial pressure measures the pressure within the pulmonary artery of the cattle similar to blood pressures taken in human medicine. Due to animals experiencing the constricting of vessels due to the lack of oxygen present in blood, the ability to record pulmonary arterial pressure gave way to recording how these animals are affected especially in low altitudes. Pulmonary arterial pressure also allows producers to definitively identify whether an animal is experiencing these cardiovascular challenges, the information in turn, allows veterinarians to look at other specific diseases of concern. A group of male angus calves were followed from suckling until their finishing phase. They received a mean PAP score at 6 months of age and one again at 18 months of age. From these recordings, the animals with higher mean PAP at 6 months, tended to also be the ones who had the higher PAP score at 18 months. The phenotypes at 6 months of age were shown to be indicative of which animals would be more predisposed to BCHF during their finishing phase (Neary et al., 2015). With the prediction abilities of PAP, recording pressure scores helps to understand what changes were happening within the heart structure. Above all, there is limited research on the overall physical changes and trajectory of cardiovascular strain on the rest of the body, especially encompassing economically relevant traits that may not be as well known to all producers. Ultrasound examinations can prove to be useful in diagnostic techniques to concretely diagnosis and differentiate true cases of BCHF rather than looking at other factors that are analogous to well-known symptoms of other diseases. Using ultrasonographic commonalities characteristics such as jugular enlargement, muffled cardiac sounds, edema in the brisket, inflammation of the pericardium, and enlargement of the liver were described as internal signatures of the CHF affected cattle (Rauof et al., 2020). The development of diagnostic techniques for BCHF recently developed in the last decade and aims to bring about new methods of properly categorizing heart failure within cattle disease in the feedlot, while establishing preventative tools to combat the spread of genetically predisposed cattle. This literature review aims to investigate the development of bovine congestive heart failure and awareness to producers to eventually mitigate the prevalence within their operations. This review aims to examine the past and current research on bovine congestive heart failure and emphasis the need of cardiovascular prevention methods through new genetic selection criteria.

SECTION 2: PHYSIOLOGICAL CHANGES

Bovine congestive heart failure displays in cattle in a multitude of ways, most commonly it is known the name of brisket disease. As mentioned, brisket disease became a descriptive title to BCHF because of the noticeable swelling within the brisket area of cattle. Compared to other species of livestock, brisket disease is not seen as commonly as a health concern and is commonly identifiable in cattle. Research suggests the incidence of this disease in cattle is greater than other livestock species due to their disproportionate ratio of body size to lung capacity. For instance, when compared to horses, cattle have increased respiration and an overall smaller lung capacity despite both species occupying roughly similar weights and sizes (Gallivan, 1989). This difference between cattle and horses also manifests itself in the general vital signs of respiration rate and heart rate between both species, where cattle range between 10 to 30 breaths per minute at rest and a heart rate between 40-70 beats per minute. In comparison, horses are much more efficient, taking 8-16 breaths per minute and having an average heart rate of 28-40 beats per minute (Le Viness). These discrepancies between cattle and the similarly sized equine species, notes these physiological differences as a causative factor to why cattle may be more prone to cardiopulmonary distress. Comparatively, no differences are seen between dairy cattle and beef cattle despite the drastic production and stature differences that have been selected for. Beef cattle and dairy cattle have drastic weight differences between life stages but when comparing internal organs, beef cattle and dairy cattle have no significant differences in size and weight (Swett et al., 1939). This lack of similarity of body weight reveals a hypothesis that body weight may put cattle at risk as body weight creates an external pressure that the heart than must work against. Beef cattle grow rapidly due to the previous selection decisions in the industry, but there has been no evidence of organ size growth to handle these more heavily muscled beef cattle. As previous stated in Jensen et al. (1976), causative reasons for risk of brisket disease include rapid growth rate, high altitude grazing, and genetic susceptibility. All of which, beef cattle generally encounter throughout their management system more than dairy cattle. Recognizing this physiological setback for bovines and how it may be weighing into cardiorespiratory distress, bovine congestive heart failure can be further dissected to examine some other setbacks cattle face.

With cattle, their demand for oxygen must be met with more respiratory and cardiovascular work as noted previously. Biologically, when oxygen requirements are not met, cattle begin to experience the first catalyst for bovine congestive heart failure, vasoconstriction. Vasoconstriction, is traditionally known to be caused by hypoxic environment, causing an increase in pressure within the right heart ventricle and the pulmonary artery. There are still other catalysts of vasoconstriction seen in cattle experiencing feedlot heart disease, but currently these causes are undetermined. This pathway transports blood from the heart to the lungs to be reoxygenated. In response, the heart needs to work harder, gaining muscle wall thickness in the process, elasticity in the muscles stretches, and as time progresses, the heart's capacity grows until it no longer can beat (Thomas et al., XXXX). These heart changes are internal to the animal and ultimately this cardiac remodeling is unlikely to be seen until post-harvest. Clinical signs of these heart changes have been recorded in cattle such as mandibular and brisket edema, jugular enlargement and pulsation, increased heart rate, abnormal lung sounds, and abnormal heart sounds (Raouf et al., 2020). The physiological changes that directly impact cattle suffering from this disease have no known treatments and severe cases can lead to early death prior to harvesting date. With irreversible changes, a need for identifying these animals within the feedlot system, especially cattle raised at high altitude, needs to occur through breeding decisions or moving at risk cattle to lower altitudes as this is the current preventative/management tool.

SECTION 3: BOVINE HEART DISEASES IN LITERATURE

High Altitude

High altitude disease (HAD) or high-altitude pulmonary hypertension originally was described as bovine congestive heart failure occurring at elevations greater than 2,500m in altitude. This disease leads to vasoconstriction of the pulmonary artery in response to oxygen deprivation in the atmosphere (Hans, 1962). In more recent times, high altitude disease not only causes death loss in growing cattle at 2,500m but also at lower elevations where high altitude can be experienced 1,500m and above. The degree of severity with the disease's effect on cattle is dependent on breed, age, altitude, genetics, body condition score, and environmental conditions (Holt, 2007). A study evaluating high altitude ranches followed groups of Angus calves that had sires with low PAP scores. Necropsies were used to identify the overall cause of death to look for any signs of pulmonary hypertension. In the group, 59 calves out of 612, roughly 10%, had died between spring branding and fall weaning. Only 28 of these calves were able to have a conclusive necropsy where about half of the calves had signs of pulmonary hypertension and the other half had signs of pneumonia. These causes of early death for calves enlightens the hypothesis that pulmonary hypertension at high altitude cannot be only confined to the utilization of the selection of low PAP bulls (Neary et al., 2013). Signs of pulmonary hypertension follow these at-risk groups (previously sick cattle or growing cattle) despite selective efforts and call for further investigations into different ages of cattle at high altitudes. Even if high altitude calves survive past weaning, there is much concern for their overall genetic ability in their production traits. The concern being that pulmonary hypertension is irreversible and will continuously cause heart stress to cattle. Selection based on genomic information has become a more popular practice amongst producers, there is a desire to use this information in the cases of high-altitude cattle management, although there may not be one answer for every environment. Considering the influence of environmental effects on phenotype, a study by Speidel et al. (2020) investigated whether PAP heritability would stay consistent across altitudes by examining 9,177 PAP observations on angus cattle at varying elevations. Lower heritability estimates was found for PAP at lower altitudes with heritability increasing as elevation increased. Rank correlations between estimated progeny differences for PAP at moderate to high altitudes displayed strong, positive rank correlations, showcasing that lower elevation could be used to rank sires at high elevation uses. This further displayed that elevation needed to be kept in mind as a factor when recording PAP measurements. The use of genotyping technology with single nucleotide polymorphisms, ingenuity analysis pathways, and gene profiling using gene set enrichment analysis of affected cattle can also advance our understanding of predisposed cattle. When comparing affected cattle to unaffected cattle, forty-six genes were overexpressed in cattle experiencing HAD. There were also known cases of downregulation, and a 60-mRNA signatures identified between both groups (Newman et al., 2011). Knowing which genes will transcribe into potential expression compromising cattle for HAD is crucial to understanding what cardiovascular risk will be passed down from sires to offspring.

To further investigate the potential genes involved, researchers investigated a whole-exome sequencing technique to find an association between oxygen degradation and a protein variant known as hypoxia inducible factor 2 alpha (HIF2alpha). Twenty six of the twenty-seven animals showing signs of high pulmonary hypertension had an upregulation of HIF2alpha and 41% of the low altitude cattle showed to be carriers of the gene, although, carriers did not present signs of hypertension. It was then concluded that the phenotype may not be apparent unless the animal was hypoxemic (Newman et al., 2015). Further investigation to this claim was done in 2019 to review the protein variant's presence in moderate altitude feedlots. There was no evidence of HIF2alpha variants being heavily associated with cattle at moderate altitudes, thus further inspection needed to occur to understand the contributors (Heaton et al., 2019).

Pulmonary Arterial Pressure

Pulmonary arterial pressure, PAP, is utilized as a selective tool in identifying animals at moderate to high risk of pulmonary hypertension, a catalyst of progressive BCHF or as an identification for predisposition to high altitude disease. PAP scores have been used for these conditions for several years in order to curb the frequency of BCHF in fattening cattle but the collection of information, also, contributes to a wide variety of research that encompasses an understanding of where the problems arise for fattening cattle. As research shows, calves at high altitude with signs of moderate to high pulmonary pressure younger ages leads to cattle with even higher pulmonary pressure during the finishing phase (Neary et al. 2015). PAP research was taken one step further in 2016, where fattening angus cattle were phenotyped to be either Low or High PAP. Tissue samples were taken from the right ventricle, aorta, and pulmonary artery of these animals to identify any tissue specific variants. Through this analysis 139 SNPs were deemed key regulator genes within the involvement of high-altitude disease, or BCHF (Canovas et al., 2016). Although, it will not be feasible to utilize or expose PAP scores as a selection measurement to every producer, therefore its importance ranking resides within individual animal breeders. When examining PAP measured at different elevations, the phenotype itself may not even have the same genetic interaction either. Recorded PAP measurements at moderate elevations (1,600m or less) were compared to measurements from high elevations (greater than 1,600 m). Using a bivariate animal model, elevation was not seen as a significant factor to PAP variability within the differing elevations. Both heritability estimates were considered moderately heritable at both high and moderate elevations. This study did reveal that PAP scores at different elevations may not be related. There can be the use of PAP measurements at higher moderate elevations to produce an EPD for one elevation, and a separate EPD for another. This would show which animals may be at less risk for pulmonary hypertension at moderate elevations but identify individuals that may not do well if moved to a higher elevation. This separation between elevations within an EPD allows for better management of individual animals in geographical at-risk locations (Pauling et al., 2018) (Speidel et al. 2021).

These findings were further investigated in 2020, through the estimations of correlations between bulls across the elevations and ages. Cattle received multiple PAP scores at different ages and elevations and included breed as a factor of both Hereford and Angus bulls. The interaction between elevation and age as well as the breed had a positive association with the variation within PAP predictability. The yearling PAP measurements collected at moderate altitude were correlated with high altitude PAP measurements for the same individuals (Zimprich et al., 2020). The differences between yearling and weaning weight PAP differed when measuring PAP score at altitude. The study supported the findings that yearling PAP can be indicative of how cattle perform at altitude than the predictability of only using weaning age PAP. This relationship of higher PAP in growing cattle at altitude is shown when following calves born at moderate/high elevations compared to calves born at lower elevations. The calves raised at higher elevations showed a significant increase in their mean PAP scores, comparatively, calves at moderate elevation did not experience this same trending progression. Findings showcased the mean PAP score increasing with age are positively associated with the altitude the claves are raised in (Neary et al., 2015). Calves growing at high altitudes (>2,170m) had their mPAP scores increase as they aged. Adversely calves raised at moderate altitudes (1,470m) did not have an increase in their mean PAP scores as they aged. Based on the results, PAP scores would be associated with the altitude at which the cattle are born and raised at, specifically seen as the cattle increase in age. This would signify those cattle at this higher altitude may experience increases in their PAP score as they grew larger and got older. This also may present itself as one of the risk factors of moving cattle from moderate altitude to high altitude.

PAP as a selection tool for bulls to pass on their low PAP scores to their offspring is a hopeful step in decreasing the incidence of BCHF. There are multiple facets of PAP score that make it inaccessible for many producers to utilize due to time, cost, and accessibility. Collection of phenotypic PAP data is costly, time consuming, and can range from $10 to $17 per test (Gjermundon, 2000). The need for a veterinarian to perform the procedure is one more veterinary visit and one more time cattle need to be brought up to a secure chute area. These issues make finding relationships between PAP and less invasive techniques beneficial. Human cardiovascular research has suggested that increased body fat percentages increase a person's risk to cardiovascular diseases (Littleton et al., 2017). The same idea carries over to bovine research where body fat distribution in cattle would be indicative of their PAP score and the other pressure readings taken in the heart. Pressures were taken in a cohort of crossbreed beef animals in the finishing stage, six days before harvest in a study done by Freeman et al in 2016. The body measures included KPH (Kidney, Pelvic, and Heart Fat) percentages, USDA quality grade, empty body fat, and 12th rib fat thickness. PAP and central venous pressure were significantly, positively associated. Keeping mean PAP scores controlled, central venous pressure of animals with 2% KPH had a higher pressure than animals with a KPH of 1.5 %. These findings were significant ($P < 0.01$) and showed that as fat around the pelvic, kidneys, and heart increased, the higher the pressure. No other body fat measurements including USDA quality grade, empty body fat percentages, and fat thickness over the 12th rib were found to be significant (Freeman et al., 2016). Fat percentages may be beneficial in having a correlation with central venous pressure because central venous pressure has a relationship to PAP. Unfortunately, but with no other strong correlations of other body fat measurements and a small sample size of crossbred animals, more research needs to be done in high altitude and breed specificity. A major takeaway Freeman et al. (2016) reveals is the utilization of the relationship between fat and central venous pressure, which does off an explanation of why higher pressures are prevalent during the finishing period as more fat encases the heart and cardiovascular system.

Predicting PAP and the adaptability of cattle has become the next step in PAP research and development. Cattle have been shown to adapt in a variety of ways. One way specifically to adapt to the high altitude is by increasing respiration rate. Increasing respiration rate allows for a more frequent exchange of oxygen and carbon dioxide in the body in response to the oxygen scarcity in the high-altitude environments. Although oxygen may be entering the body at a more frequent rate due to the animal's attempt to adapt, Gullick et al., (2016) presented that this sign of a physical adaptation does not necessarily aid cattle in obtaining a greater oxygen / carbon exchange as efficiently as the cattle would be in low altitude settings. Their research found that because the hematocrit or red blood cells within the body does not increase, cattle still show signs of hypoxemia and hypocapnia despite the body's active role in attempting at adaptation.

Altitude Adapted Bovine

Hypoxic environment challenges feedlot production because of altitude and prevalence of heart strain and disease. It is also apparent that with high altitude, 1800m or greater (Thomas et al.,2018) comes the introduction of colder temperatures. Cattle living at altitude experience these extreme conditions but not all cattle struggle with these environmental factors to the same degree. To overcome these obstacles adaptations in cattle consistently living in high-altitude environments may hold some answers to genetic differences for improved adaptability. The yak, a native high altitude dwelling ruminant has been used as specie of interest to study high altitude adaptability. The yak displays some key adaptations that give evidence of phenotypic changes due to high altitude environments including grazing mechanics, lack of pulmonary artery dilation, and lack of abnormal heart wall thickening (Friedrich et al., 2020). These aforementioned adaptations illustrate evolutionary effects the yak has experienced due to its environment and with that, there are potentially some genetic adaptions researchers may be able to pinpoint for with further analysis.

Genetically, the yak possesses inherent differences when compared to both the *Bos taurus* and *Bos indicus* breeds. The genetic differences between species is apparent when comparing yaks (*Bos grunniens*) to yak crossbreds, Urangs (*Bos grunniens* x *Bos indicus*) and Dimjos (*Bos grunniens* x *Bos taurus*). These specific crosses were investigated by Barsila et al., (2014) at an altitude of 4,700 m and subsequently moved to a lower elevation (3,050 m) to measure high elevation grazing effects in the Himalayan Mountains. After one week of adaption, the yaks and yak crosses received measurements on body weight, milk yield/composition, blood hemoglobin levels, movement behavior, and metabolic traits. At high altitudes, the Urangs had the highest blood lactate levels while the yaks had the lowest, inversely yaks had the highest amount of blood hemoglobin. Overall, Yaks, when comparing the frequency of movement at different altitudes, were equally as active in the high altitude as compared to moderate altitude (Barsila et al., 2014). The overall ease that yaks have in adaptation to high altitude that is missing in other bovines means that there are some genetic variations that conform to more adaptability to harsh environments. This physical change between *Bos grunniens* and *Bos taurus*/ *Bos indicus* was further investigated evaluate the genetic differences between all species. Zhang et al., (2020) evaluated copy number variants using a high density BovineHD SNP array investigated Chinese indigenous cattle breeds and composite breeds that typically span across diverse environments found in Asia. The breed compositions of the Chinese indigenous cattle compared to high altitude adapted yaks found that roughly 14% of the bovine genome was covered in autosomal copy number variants regions related to hypoxia adaptations. This showcased that copy number variants that had strong signatures for positive high-altitude adaptations may be responsible for the differences between species. (Zhang et al., 2020). Considering the genome of the Yak helps to understand some evolutionary genetic differences that aid in the utilization of this information for gathering further understanding in hypoxia resilience in *Bos taurus* breeds.

Feedlot Heart Disease

It has been reported that pulmonary lesions, a result of BCHF cases, was found in less than a third of the population of beef cattle raised in the Midwest region of the United States (Rezac et al., 2014) which may make BCHF sound of lesser concern, but recent trends argue that BCHF is climbing annually. Neary et al. (2016) looked at ten feedlots in western Canada during the years 2000, 2004, 2008, and 2012, and five feedlots in the US in 2012. The environment of each of these locations varied ranging from 596m to 1,282m. The Neary study concluded that the incidence of BCHF had increased in risk by 91% since 2000 to the data presented in 2012.

Before the 1970s, reports of cattle with BCHF were at altitudes above 2,130 m but in more recent times, have been recorded at altitudes as low as 657m. Right sided heart failure (RHF) occurred throughout the feeding period, specifically the majority occurring after 19 weeks. Even though a greater number of cattle died from digestive disorders, right sided heart failure cases are particularly costly and with the prevalence found in lower altitude may become almost unavoidable. This study by Neary et al. 2016 did not show that RHF increased over time in the feeding period as one may suspect that the risk length would increase. This highlights the increased frequency and prevalence of the disease and indicated that a higher altitude was not the sole contributor to cardiovascular stress in cattle.

The recognition that altitude is not the sole factor affecting the frequency of occurrence of BCHF induces a potential fear within the industry that the incidence of BCHF is not an isolated event only affecting a particular geographical region of the country. To further understand what causes BCHF in cattle, a group of angus cattle in a Nebraska feed yard at 1,369m were examined for the prevalence of BCHF in the study by Moxley et al. (2019). Cattle were observed over a 15-month period. Researchers identified 17 cases of animals with clinical right sided heart failure, edema, and chronic passive congestion of the liver. Gross examination confirmed right ventricular hypertrophy. Microscopic examination of the hearts tissue yielded the fact that all cases had interstitial fibrosis with six showing signs of replacement fibrosis in the right ventricle meaning scarring was present in the lungs and heart Fourteen of the cases had interstitial fibrosis in the left ventricle. Pulmonary arteries and arterioles had lesions comparable with hypoxia induced pulmonary hypertension. Moderate hypobaric conditions significantly contributed to disease in cattle predisposed to hypoxia induced pulmonary hypertension (Moxley et al., 2019). This study further emphasizes the increase in prevalence of cases of BCHF at different altitudes, promoting the idea that simply raising cattle at low altitudes will not be the permanent solution to combating this disease.

Feedlot heart disease is another name presented in literature to describe bovine congestive heart failure in moderate to low altitudes. Since heart failure was first recorded in high altitude environments, the name high altitude disease would not explain its prevalence in these lower elevations. As explained in Jensen et al. (1976), rapid growth rate and genetic susceptibility to deformities or potential intolerances to altitude are causes for heart failure. Low oxygen levels in the body can still be explained by fast, rapid growth rates. As seen in humans, obesity often leads to difficulties in efficiently reoxygenating blood as extra weight compresses on the internal body (Littleton et al., 2017). The same is hypothesized to happen with cattle. As cattle gain weight, their heart and lungs cannot always sustainably keep up with the oxygen demand of the individual, therefore animals begin experiencing cardiac stress in response. As the heart begins to work harder, pulmonary hypertension begins, and the heart's physiological structure begins to change in a similar way seen in high-altitude cattle. Not all high altitude or rapid growing cattle will experience PH, but it does explain how the genetic susceptibility might be the first piece of bovine congestive heart failure. It also explains how our selection decisions can be influencing the overall growing trends described in Neary et al. (2016). A similar result is seen when examining the rapid growth rate in broiler chickens, a specie that also shares this predisposition to right sided heart failure (Olkowski, 2007). Although, poultry and cattle share different anatomical structures and body to weight ratios, the support behind repaid growth and its effect on heart remodeling is deduced from these findings. Feedlot heart disease overall, encompasses causes of pulmonary hypertension without the need of low oxygen levels within high altitude climates.

Bovine Dilated Cardiomyopathy in Dairy

The dairy industry advances in the utilization of genetic technology for fulfilling their production needs while quickly adapting to continuous genetic advancements. Dairies often focus on milk production, birth weights, and other economically dairy relevant traits (lactation persistency, reproduction, calving ease, daughter pregnancy rate, etc.) . Recently, health traits of dairy cattle have arisen to become a popular index selection tool (Miglior et al., 2017). An emerging area of research is the research in dairy cattle heart health. Dairy cattle face fewer extreme challenges in their environment due to their intensive management systems and unlike the beef industry, may not experience as much high elevations due to geographical locations, at least in the United States. A survey collected location decision factors and determined their importance found that the in the western United States dairymen focused on the availability of adequate water supplies, availability of land for waste management, and nutrient load of land were among the top decision factors (Winklet and St-Pierre, 2003). The ease of accessibility to co-ops, grazing, and flat surfaces to build the infrastructure of the parlor, housing, and the rest of the components needed hinder the expansion on mountainous, high elevated terrain.

Despite the limitations on where dairies can be located, research still emerges on cardiovascular challenges identified in dairy cattle. In a small study using feedlot beef cattle and dairy cattle at an elevation of 970 m, all cattle regardless of their cause of death revealed signs of pulmonary physiological remodeling. These animals also had signs of lesions within the pulmonary artery and within the liver, displaying liver disease as a secondary cause of death resulting from vasoconstriction (Gulick et al., 2016). Recognizing dairy cows that are affected by low elevation similar to what is seen in fattening feedlot cow, supports the hypothesizes that more mechanisms in the cardiovascular are in conjunction within our cattle than high-altitude pressures.

Comparable to beef cattle, Holsteins and other dairy breeds raised in the smaller population of dairies in higher altitudes have recorded and echoed similar struggles in regard to heart disease. In the study conducted by Malherbe et al. (2012), two dairies located in Colorado, reported loss of 55 animals over a span of 5 years in their heifer raising facilities This appearance of BCHF came second in ranking when it came to cause of death or early culling. Affected animals showed signs of pulmonary hypertension with jugular enlargement, edema, labored breathing, weight loss, and other similar symptoms of brisket disease in feedlot cattle. Affected animals included heifers born at the altitude and heifers born in a low elevation and then transported from the northern United States to Colorado. Upon the examination of a necropsy, cardiovascular remodeling findings matched to all signs of pulmonary hypertension/ brisket disease in fattening cattle.

These findings of dairy cattle suffering from high altitude diseases resembled a one-year exposure study to test for Holstein adaptation to hypoxia published by Wang et al. (2017). Healthy Holsteins were transported from a lower plain region to an elevation of 3,658m in Lhasa, Tibet. By the end of the year, ten heifers had brisket disease and their plasma samples were analyzed for differenced endothelial nitric oxide synthases, respiratory rate, pulmonary arterial pressure, oxygen saturation, and blood velocity. Endothelial nitric oxide synthase was included because based in human medicine the decrease function of the nitric oxide pathway contributes to cardiovascular diseases (Vallance et. al., 1999). All of which were higher in healthy heifers compared to the heifers with brisket disease. Heifers with brisket disease had ventricle thickening, smaller diameters in their arteries and smooth muscles were proliferated.

Within the plasma sample, the heifers with brisket disease had low endothelial nitric oxide synthase expression in the intima, the inner layer of the pulmonary artery. These findings concluded that there was a possibility that high expression in endothelial nitric oxide synthesis within the vasculature structure may protect against progression of pulmonary hypertension, which was particularly interesting because pulmonary arterial pressure was used as a selective technique to predict for pulmonary hypertension, but in dairy cows the brisket diseased animals all had a lower PAP score in mean PAP, systolic PAP, and diastolic PAP (Wang et al., 2017). The expression of endothelial nitric oxide synthase expression in beef cows is a topic unexamined by the industry, but potentially an adaptation in Holsteins may be more responsive to engaging this high expression to suppress the effects of pulmonary hypertension.

Findings of the similarities within both dairy and beef sectors pertain to the need for approaching the research of BCHF to a broader scope to including more different types of bovine industries within studies. A unique area of research recording the presence of C*oxiella burnetii*, a bacterium that causes infection in the cardiovascular system, by Agerholm et a. (2017). These bacteria have been shown to cause endocarditis, or the inflammation of the lining within the heart vessel lining. The presence *of Coxiella burnetii* has been studied more in depth in humans, but Danish researchers were surprised by the presence of the bacteria within slaughterhouses responsible for the harvesting of Holsteins. The resulting findings of this bacteria in Holsteins were responsible for lesions and inflammation similar to the changes seen in BCHF (Agerholm et al., 2017). This point is especially important because of the similarities to BCHF, and no known research of bacterium infection research in fattening beef cattle, it is noteworthy to suggest potential other external causes of catalysts that begin the increased demanding forces the heart begins to work against. The similar thickening of the heart due to bacterial endocarditis was compared to other non-affected and other cardiorespiratory disorder cows to determine if the valvular thickness was significantly different. If measurements were significantly different, then bacterial endocarditis could be a portion of the affected bovine group that is being mislabeled and ultimately causes a different plan of action. The cows that had bacterial endocarditis were found to have a greater thickness in their pulmonary and aortic valve compared to the uninfected but cardiorespiratory diseased animals (Buczinski et al., 2013). Based on this introduction of bacterial disease found in dairy cows and no known research on whether beef cattle have been affected, it is difficult to narrow the cause of dairy pulmonary hypertension cases caused by hypoxia or bacterial infection when solely measuring valve thickness. The refutable cause of death in these cases make it challenging to correctly classify each case.

A narrow section of dairy bovine research is the topic of bovine dilated cardiomyopathy, a similar condition to BCHF. This disease has been recorded in Holsteins for several decades, with similar symptoms seen in feedlot cattle with brisket, high altitude, or feedlot heart disease. These symptoms include both left sided and right sided heart failure, a distended jugular vein, edema, dilated heart, and vessel chambers (Nart et al., 2004). The inheritance of bovine dilated cardiomyopathy is similar to the beef cattle research, and also lacked much insight to how to manage this disease. Using a pedigree consisting of 75 animals and five different diagnostic cases, a pedigree analysis concluded what allele(s) may be responsible and if there was a genetic transcendence of the disease through generations. The models included a major gene model, environmental model, and a mixed model. These models differed in the degree of which animals were considered infected with bovine dilated cardiomyopathy. All three data sets revealed that there was a biallelic major locus with a recessive allele that would be controlling the diseases prevalence amongst these dairy animals (Dolf et al., 1998). The research within the dairy industry is similar to what is seen in the beef industry. Separate research within Holsteins especially can assist with understanding what may be occurring within our cattle, further research needs to be conducted with more inclusivity especially now, with the expanded use of beef on dairy breeding. It is apparent that despite the differences between dairy and beef similar physiological changes occur within the cardiovascular system of the bovine, causing extreme system distress and the downfall of a once healthy animal.

SECTION 4 RELEVANCE OF BOVINE CONGESTIVE HEART FAILURE

Health Economic Relevance

The economic relevance of bovine cardiovascular disease in literature has yet to be examined in the scientific community but with previously growing trends of BCHF, every animal that does not make it to harvest or begins to struggle due to heart stress will become seen as some loss for producers. Although there is limited research on BCHF impact economically specifically, there are still parallels in research that supports better immunity in our cattle decreasing loss per head. A study, developed by Hine et al. (2021), focused on immune competence in a sample size of 838 finishing phase, angus steers residing in Australia. These animals had an immune competence phenotype recorded based on the cattle's reaction level to an Ultravac 7 in 1 vaccine versus a control saline injection through a 21-day period. The animals were than assigned low, normal, or high immune competency (IC) based on their reactions to the vaccine. Recording the average daily gain of the animals during this period, differences or similarities were examined, finding no effect on average daily gain between groups. The difference between experimental units was related to the mortality rate between the groups, where 6% of low immune competency cattle died before harvest. The resulting conclusions on production costs were determined by the incidence of diseases within each level of IC groups. The monetary health associated, and production costs were determined to be $74/head for low IC, $18 for normal IC, and $2/head for high IC. This study concluded that selecting for high IC was beneficial for the producer's minimization of costs per head (Hine et al., 2021). With animals that are more prone to BCHF, there is some immune compromise due to the inclusion of stress on the internal body (Manteca, 2013).

Another prevalent disease known as Bovine Respiratory Disease, BRD, tends to go hand in hand with animals suffering from BCHF or animals who are immunocompromised. This was shown in results that showcased cattle identify as high risk for BRD were 2 to 3 times more likely to die of heart failure (Neary et al. 2016), Often BCHF is misdiagnosed as BRD due to the similarities in clinical symptoms. Cattle tend to be treated for BRD and often never recover in severe cases because heart failure has already begun. When looking at the performance of animals with BRD cases, there was an average net loss of $1,193 per BRD mortality case. Animals treated with 3 or more times for BRD had carcass weights 87 lbs less than animals who had no BRD treatments. Cattle with lung lesions at harvest were 31 lbs lighter at harvest and returned $66 less than cattle with healthy lungs (Blakebrough-Hall et al., 2020). Complications with the lungs due to BRD is similar to complications of BCHF, and with more research on economic relevancy of BCHF, similar results of economic loss are expected in BCHF cases. In cases of BCHF, individual feedlots are recognizing that finding a solution may be economically relevant within their feedlots. An individual feedlot in Nebraska stated that that over the past 5 years, they have experienced 538 cases of BCHF on their feedlot overall costing them ~$1,000,000 in loss (USDA, 2018). The economic relevance of BCHF is still yet to be concretely analyzed through inferences of individual feedlot loss records while also looking at disease prevalence in the feedlot and how disease effects performance in our fattening feedlot cattle.

SECTION 5: KNOWN RELATIONSHIPS WITH HEART HEALTH

The relationship between the heart and the rest of the body is crucial to any system which makes the irreversible damage to the heart, a hindering factor for fattening cattle. Any animal that receives genetic predictions may not always perform as expected. The irreversible damage to the heart through BCHF, pushes research to measure the effects of pulmonary hypertension and their relationship with other parts of the body. If a relationship is found, this only strengthens the urgency for decreasing heart failure prevalence in cattle and recognizing its economic relevance greater than just cattle death. Even if the cattle reach the harvest date, their performance, carcass quality, and other bodily systems are typically severely affected. This section aims to represent some confounding research of the effects of animals living with stages of bovine congestive heart failure.

Liver

A multitude of outcomes from cardiovascular diseases lies in the presence of liver lesions associated with the disease. These liver lesions are noted in several studies (Moxley et al. 2019, Gulick et al. 2016, Raouf et al 2020.) and liver disease in feedlot cattle has been investigated for known relationships with other conventionally recorded traits. The group in (Gullick et al,. 2016) measured PAP using a catheter to measure pulmonary pressure twice during the duration of the project and taking the average of the scores to assign mean PAP scores. Researchers also included the addition of the mean central venous pressure (CVP) to investigate its relationship to PAP and the CVP's association with liver disease. Central venous pressure has been described in Vesal et al. 2006 as measuring the various interactions between alteration in the vascular bed, blood volume, and cardiac pumping action. All three of these interactions make up an estimate of the right atrial pressure. It has been commonly used to measure heart failure in ruminants and cases of dehydration. This study was done at low altitude with a cohort of fattening crossbred yearling steers It was found that there was a positive association between PAP and CVP six days prior to slaughter but not 54 days prior. All steers in this study showed histological damage within the liver and was highest in the steers with high CVP. This study showcased some connections between the signs of right heart failure and hepatic congestion, liver disease, in the feedlot cattle (Gullick et al,. 2016). These results echoed earlier findings of an association between liver lesions and pulmonary artery lesions as reported by Rezac et al. (2014). In this larger study, 19,229 cattle, collected in Kansas and Texas, were observed for the presence of heart, liver, and rumen lesions at the time of processing. These researchers found that 31.4% of cattle had mild to severe liver lesions. Of those affected, 39% had mild to severe pulmonary lesions, and a higher percentage (51.44%) had ruminal lesions. Severe rumenitis had a significant association with decreases in hot carcass weight and average daily gain. The implications of these studies lead to an area of understanding the management of beef health and the need for improvement since a substantial amount of animal's experience subclinical signs of diseases that cannot be recognized during pre-harvest. These findings interlock the body systems of cattle and showcase the cascading effects of bovine health.

Carcass Characteristics

The relationship between carcass traits and cardiac function is another area of unidentified consequences to beef cattle's fast growing and high-altitude environments. Research conducted at Colorado State University by Heffernan et al. (2020), described heart morphology having a weak to modest association with carcass quality and feed efficiency. As the heart presented more malformities, carcass quality and feed efficiency decreased (Heffernan et al., 2020). Similarly, the heart overloads itself by fighting against pulmonary hypertension that these results support earlier findings and exhibit the consequences of the symptoms of BCHF. A study (Munro et al., 2020) looking at variation within the heart structure as it relates to carcass characteristics, supports these newer findings of cardiovascular health on carcass traits. Right ventricle wall thickness positively correlates with residual feed intake. The greater the heart must work in those identified cattle; the more feed would be left over indicating less feed consumed by those animals. Observationally, through a multiple regression model, heart structure accounted for the largest proportion of differences in residual feed intake, indicating that selecting for low residual intake cattle would suggest a positive indication of better cardiovascular health (Munro et al., 2020). The best hypothesis literature can offer through the importance of carcass and cardiovascular health is the previous research on beef cattle's stress response.

Stress and meat quality are often linked together as increased stress as a negative correlation with meat quality. As shown in the study by Carrasco-Garcia et al. (2020), prior to harvesting animals with higher cortisol levels resulting in higher pH values in muscles, creating dark, dry, and tough meats. This relationship between stress and cardiovascular disease parallels with findings in human medicine research where the relationship between the risk of heart attacks and cortisol level shows that as people who experienced high levels of the stress hormone cortisol had an increased risk of cardiovascular events (Horwich, et al., 2021). Naturally if humans are experiencing higher cortisol levels in response to stress, biologically cortisol levels it would be expected that higher cortisol levels be found in cattle experiencing environmental stress, in addition to their prone risk to cardiovascular disease. Therefore, it is not too far of a stretch to deduce what stress is doing to our carcass quality in beef cattle.

Performance

The performance of beef cattle is largely due to the focus on their genetics passed down from parent to progeny. Systematic diseases such as BCHF add an internal environmental stress to the system often suppressing the cattle's ability to thrive in high altitude. This idea is supported by similar research in bovine respiratory disease, where steers with lung lesions had lower than average daily gains, lower fat percentages (includes marbling), and lighter hot carcass weights (Gardner et al., 1999). Measuring the performance of cattle in response to health compromising diseases directly affects economically relevant traits and challenges genetic prediction outcomes in other difficult to measure traits such as fertility and stayability.

A high-altitude study performed in southern Wyoming by Duggan et al. (2020), looked at the fertility performance between high PAP and low PAP cattle. In other words, cattle experiencing pulmonary hypertension are at greater risk of performing lower than their genetic predictions compared with cattle considered low risk or no signs of pulmonary hypertension. Pulmonary arterial pressure was found to have an inverse relationship with rate of pregnancy ($P < 0.05$) whereas, rate of first conception was not significant within PAP groups ($P > 0.05$). The indication that high PAP animals have a lower pregnancy rate showcases the physiological stress and its overall lasting effect.

Survival of calves to harvest is crucial for any sector of the beef industry. A study evaluated mean, systolic, and diastolic PAP and pulmonary arterial pulse pressures, and systemic oxygen extraction fraction on the survival of calves at 2,730m in CO. The high-altitude environment housed 58 calves, 7 of which died between 3 months to 7 months of age. The deceased calves had previous records of a higher mPAP measurement and greater systolic pressure than the remaining survived calves (Neary et al., 2016). The trait of survivability allows for producers to identify animals who will be struggling at these altitudes but potentially struggle in weight gain in the fattening stage. Moving these animals to lower altitude and culling earlier, prevents less economic loss in the long run when these decisions are taken account for.

SECTION 6: HEART SCORES

Heart score is a relatively new visual grading score system developed by Dr. Tim Holt at Colorado State University the grading system scores heart by the degree of physiological structure change due to the heart's remodeling overtime. The remodeling of the heart due to pulmonary hypertension can be noted during harvest organ examination or through a necropsy. The scale is of 1 to 5, 1 being no remodeling through a gradient of 5 being severe remodeling. Figure provides a visual example of the heart score grading system, Grade 1 (normal anatomical heart) compared the gradual enlargement of right ventricle and pulmonary artery until muscle flaccidity in Grade 5.

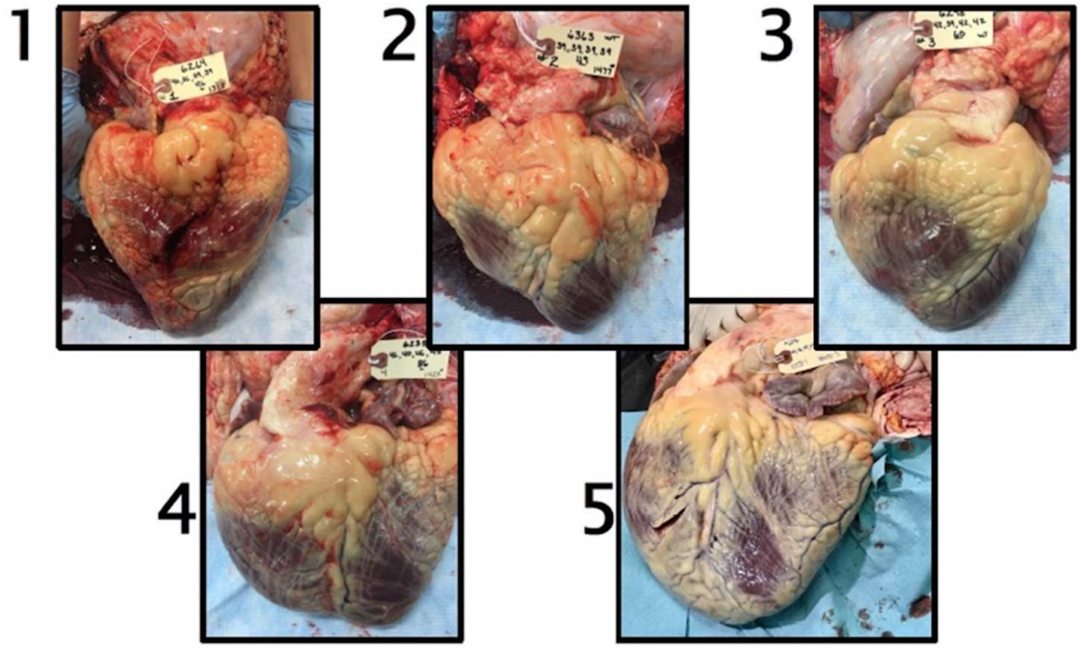

Figure 2.1:Heart score visual grading system provided by Dr. Holt of Colorado State University

Using the heart score grading system records the remodeling changes expected with higher-than-normal PAP scores. Research conducted at Colorado State University by Heffernan et al. (2020), concluded the relationship between PAP to heart score (HS) was positive, meaning as PAP increased the cattle would also have a greater heart score at harvest. This research with heart score was the only current research utilizing a heart visual grading system and therefore with foundational research in animal sciences, many of the answers of the utilization of heart's remodeling is examined in human medicine.

In humans, the advantage of being able to visualize the heart becomes more feasible than compared to cattle. The use of cardiac visualization and monitorization uncovers and supports remodeling's relationship with heart failure. The current implications of recording heart failure in humans highlights the pattern of structural changes, especially in the left ventricle, to cardiovascular disease. Based on these changes, the volume of the left ventricle was the most important area of focus on heart remodeling that correlated with patient's survival (Konstam et al., 2011). By measuring the degree in which heart remodeling occurs, the impact of certain therapies and drugs can be predetermined for overall supporting patient health. Similarly, the hope for utilizing HS and predicting cattle's risk for remodeling by genetic prediction in the form of the creation of an EPD, would be the most beneficial tool in predicting the impact of specific management and environment effects. Similar concepts of understanding the heart's remodeling aids to understand better implication of management and genetic technology.

SECTION 7: CONCLUSION

The adverse effect that heart remodeling has on the success and profitability of the beef industry specifically in genetically superior performance and high-altitude cattle has the potential to be minimized with the use of genetic selection for cardiovascular fitness. Many genetic companies with available sires offer the inclusion of PAP EPD in their sires' information, to further promote the inclusion of health in breeding decisions. In addition, the economic relevancy of diseases affecting the cardiovascular system, spreads between both the beef and dairy industry, making heart remodeling, a global cattle industry health crisis. The further development of heart score with the inclusion of prior knowledge and success with PAP, leads to a potential successful path on combating the issue through genetic mechanisms and overall reduce the risk for our cattle.

Through further analysis, the genetic connection between heart score and heart disease will mitigate the trending concern of diseases such as brisket disease, cases of lesions within the liver/lungs, and overall decrease the frequency of heart failure in feedlot management systems.

The inclusion of health traits in cattle in turn decreases the need in some areas of antibiotic usage, decreases feedlot production losses, and overall lead to further phenotypic expression of effected cattle, who would have previous died due to cardiovascular stress. Advancing our knowledge and research on health traits such as heart score may not absolve all risk of heart remodeling but is expected to minimize its industrial effects on our cattle production.

LITERATURE CITED

Agerholm J., Jensen T., Agger J., Engelsma M., Roest H. 2017. Presence of Coxiella burnetii DNA in inflamed bovine cardiac valves. BMC Veterinary Research. 13(1):69. DOI: 10.1186. PMID: 28274243; PMCID: PMC5343293.

Ahola J., Enns R., Holt T. 2006. Examination of potential methods to predict pulmonary arterial pressure score in yearling beef cattle, *Journal of Animal Science*,84(9):1259–1264, doi:10.2527.

American Heart Association. "Elevated stress hormones linked to higher risk of high blood pressure and heart events." ScienceDaily. ScienceDaily, 13 September 2021.

Barsila S.R., Kreuzer M., Devkota N.R., Ding L., Marquardt S. 2014. Adaptation to Himalayan high altitude pasture sites by yaks and different types of hybrids of yaks with cattle. Livestock Science. 169(1):125-136. doi:10.1016.

Bassett A. 2019. Evaluating the Epidemiology and Management of Bovine Congestive Heart Failure. Dissertations & Theses in Veterinary and Biomedical Science. 27.

Blakebrough-Hall C., McMeniman J., González L. 2020. An evaluation of the economic effects of bovine respiratory disease on animal performance, carcass traits, and economic outcomes in feedlot cattle defined using four BRD diagnosis methods. J Anim Sci. 98(2). doi:10.1093. PMID: 31930299; PMCID: PMC6996507.

Bovine Congestive Heart Failure (BCHF) in Feedlot Cattle. 2020. BCHF: USDA ARS.

Buczinski, S., Francoz, D., Fecteau, G., & Difruscia, R. 2010. A study of heart diseases without clinical signs of heart failure in 47 cattle. *The Canadian veterinary journal = La revue veterinaire canadienne*, *51*(11), 1239–1246. PMID: 21286323.

Buczinski S., Tolouei M., Rezakhani A., Tharwat M. 2013. Echocardiographic measurement of cardiac valvular thickness in healthy cows, cows with bacterial endocarditis, and cows with cardiorespiratory diseases. Journal of Veterinary Cardiology: the Official Journal of the European Society of Veterinary Cardiology.15(4):253-261. DOI: 10.1016. PMID: 24252809.

Cánovas A., Cockrum R., Brown D., Riddle S., Neary J.M., Holt T.N., Medrano J.F., Islas-Trejo A.,Enns R.M., Speidel S.E., Cammack K.,Stenmark K.R., Thomas M.G.,2016 Functional SNP in a polygenic disease induced by high-altitude in fattening Angus steers using systems biology approach, *Journal of Animal Science*, 94(5):124, doi:10.2527/jam2016-0260.

Carrasco-García A., Pardío-Sedas V., León-Banda G., Ahuja-Aguirre C., Paredes-Ramos P., Hernández-Cruz B., Murillo V. 2020. Effect of stress during slaughter on carcass characteristics and meat quality in tropical beef cattle. Asian-Australas J Anim Sci. 33(10):1656-1665. doi: 10.5713/ajas.19.0804. PMID: 32054158; PMCID: PMC7463084.

Dolf G., Stricker C., Tontis A., Martig J., Gaillard C. 1998. Evidence for autosomal recessive inheritance of a major gene for bovine dilated cardiomyopathy, *Journal of Animal Science*, 76(7):1824–1829, doi:10.2527.

Duggan K., Doyle S., Foxworthy H., DeAtley K. 2020. PSI-32 Effect of pulmonary arterial pressure on reproductive performance in Angus heifers located in south central Wyoming, *Journal of Animal Science*. 98 (4): 473. doi:10.1093.

Fernández M., Ferreras M., Giráldez F., Benavides J., Pérez V. 2020. Production Significance of Bovine Respiratory Disease Lesions in Slaughtered Beef Cattle. *Animals: an open access journal from MDPI*, *10*(10):1770. Doi:10.3390/ani10101770

Freeman K., Gulick A., Bernhard B., Rathmann R., Sarturi J., Neary J. 2016. 0212 Body fat distribution was a determinant of pulmonary arterial and central venous pressures in feedlot cattle, *Journal of Animal Science*.94(5):100-101.doi: 10.2527.

Friedrich J., Wiener P. 2020. Selection signatures for high altitude adaptation in ruminants, Animal Genetics. 51(2):157-165. doi:10.1111.

Gallivan G., McDonell W., Forrest J. 1989. Comparative pulmonary mechanics in the horse and the cow. Res Vet Sci. 46(3):322-30. PMID: 2740626.

Gardner B., Dolezal H., Bryant L., Owens F., Smith R. 1999. Health of finishing steers: effects on performance, carcass traits, and meat tenderness, *Journal of Animal Science*, 77(12): 3168-3175.

Gjermundson C. 2000. Danger at 5,000 Feet: High Altitude disease can bring heartache and death. *Angus Journal,* 47-50.

Glover G., Newsom I. 1914. Brisket Disease: Dropsy of high Altitude. The Experiment Station. Book. Fort Collins, Colorado.

Gulick A., Freeman K., Bernhard B., Sarturi J., Neary J., 2016. Subclinical right heart failure may contribute to the development of liver disease in feedlot cattle during the finishing phase, *Journal of Animal Science*. 94(5):82, doi:10.2527.

Gulick A., Garry F., Holt T., Retallick-Trennepohl K., Enns R.,Thomas M., Neary J. 2016. Angus calves born and raised at high altitude adapt to hypobaric hypoxia by increasing alveolar ventilation rate but not hematocrit, *Journal of Animal Science* 94(10):4167–4171, doi:10.2527.

Gulick A., Neary J. 2016. 0171 Evidence of cor pulmonale and liver disease in association with pneumonia in feedlot and dairy cattle at an altitude of 975m, *Journal of Animal Science*, 94(5):83, doi:10.2527.

Heaton M.P., Bassett A.S., Whitman K.J., Krafsur G.M., Lee S.I., Carlson J.M., Clark H.J., Smith H.R., Pelster M.C., Basnayake V., Grotelueschen D.M., Vander Ley B.L.. 2019. Evaluation of *EPAS1* variants for association with bovine congestive heart failure. doi: 10.12688 PMID: 31543958; PMCID: PMC6733380.

Hecht H., Kuida H., Lange R., Thorne J., Brown A. 1962. Brisket Disease: II. Clinical features and hemodynamic observations in altitude-dependent right heart failure of cattle. The American Journal of Medicine. Doi: 10.1016/0002.

Heffernan, K.R., M. G. Thomas, R. M. Enns, T. N. Holt, S. E. Speidel. 2020. Phenotypic relationships between heart score and feed efficiency, carcass, and pulmonary arterial pressure traits, Translational Anim. Sci. 4(1):S103–S107. doi:10.1093 tas/txaa114

Hine B., Bell A., Niemeyer D., Duff C., Butcher N., Dominik S., Porto-Neto L., Li Y., Reverter A., Ingham A., Colditz I. 2021.Associations between immune competence phenotype and feedlot health and productivity in Angus cattle, *Journal of Animal Science*, 99(2). doi:10.1093.

Holt T., Callan R. 2007. Pulmonary Arterial Pressure Testing for High Mountain Disease in Cattle. Veterinary Clinics of North America: Food Animal Practice. 23(3):575-596. Doi:10.1016/j.cvfa.2007.08.001.

Jensen R., R. E. Pierson, P. M. Braddy, D.A. Saari, A. Benitez, D. P. Horton, L. H. Lauerman L, A. E. McChesney, A. F. Alexander, D. H. Will. 1976. Brisket disease in yearling feedlot cattle. J Am Vet Med Assoc. 169(5):515-517. PMID: 956029.

Krafsur G., Neary J., Garry F., Holt T., Gould D., Mason G., Thomas M., Enns R., Tuder R., Heaton M., Brown R., Stenmark K. 2019. Cardiopulmonary remodeling in fattened beef cattle: a naturally occurring large animal model of obesity-associated pulmonary hypertension with left heart disease. Pulm Circ. 9(1):2045894018796804. doi: 10.1177 PMID: 30124135; PMCID: PMC6333945.

Konstam M., Kramer D., Patel A., Maron M., Udelson J. 2011. Left Ventricular Remodeling in Heart Failure: Current Concepts in Clinical Significance and Assessment. JACC: Cardiovascular Imaging. 4(1):98-108. Doi:10.1016.

Kreikemeier K., Unruh J., Eck T. 1998. Factors affecting the occurrence of dark-cutting beef and selected carcass traits in finished beef cattle, *Journal of Animal Science*, 76(2):388–395, doi:10.25271.

Le Viness E. Vital Signs in Animals: What Cattle Producers should know about them. Beef Cattle Handbook. Extension Beef Cattle Resource Committee.

Littleton S., Tulaimat A. 2017. The effects of obesity on lung volumes and oxygenation. Respir Med. 124:15-20. doi: 10.1016/j.rmed.2017.01.004.PMID: 28284316.

Malafaia P., Granato T., Costa R., Carneiro de Souza V., Costa D., Tokarnia C. 2016. Major health problems and their economic impact on beef cattle under two different feedlot systems in Brazil. Sci Flo Brasil. Pesq. Vet. Bras. 36(09). doi:10.1590.

Malherbe C., Marquard J., Legg D., Cammack K., O'Toole D. 2012. Right ventricular hypertrophy with heart failure in Holstein heifers at elevation of 1,600 meters. J Vet Diagn Invest. 24(5):867-77. doi: 10.1177. PMID: 22914818.

Manteca X., Mainau E., Temple D. 2013. Stress in Farm Animals: Concept and Effects on Performance. Farm Animal Welfare Education Centre. Fact Sheet. Issue:6.

Migloir F., Fleming A., Malchiodi F., Brito L.,Martin P., Baes C. 2017. A 100 Year Review: identification and genetic selection of economically important traits in dairy cattle. *Journal of Dairy Science.*100(12):10251-10271.

Moxley, R. A., Smith, D. R., Grotelueschen, D. M., Edwards, T., & Steffen, D. J. (2019). Investigation of congestive heart failure in beef cattle in a feedyard at a moderate altitude in western Nebraska. *Journal of Veterinary Diagnostic Investigation*, *31*(4), 509–522.doi:10.1177.

Munro J., Physick-Sheard P., Pyle W., Schenkel F., Miller S., Montanholi Y. 2019. Cardiac function and feed efficiency: Increased right-heart workload in feed inefficient beef cattle. *Livestock science, 229*, 159-169. doi: 10.1016/j.livsci.2019.09.029.

Nart P., Thompson H., Barrett D., Armstrong S., McPhaden A. 2004. Clinical and pathological features of dilated cardiomyopathy in Holstein-Friesian cattle. Vet Rec.155(12):355-61. doi: 10.1136. PMID: 15493603.

Neary J., Brown R., Holt T., Stenmark K., Enns R., Thomas M., Garry F. Static and dynamic components of right ventricular afterload are negatively associated with calf survival at high altitude, *Journal of Animal Science*, Volume 94, Issue 10, October 2016, Pages 4172–4178. doi:10.2527.

Neary J., Booker C., Wildman B., Morley P. 2016. Right-Sided Congestive Heart Failure in North American Feedlot Cattle. J Vet Intern Med. 30(1):326-34. doi: 10.1111. PMID: 26547263; PMCID: PMC4913666.

Neary J., Church D., Reeves N., Rathmann R. 2018. Successful treatment of suckling Red Angus calves for bovine respiratory diseasewasnot associated with increased mean pulmonary arterial pressures at weaning, *Journal of Animal Science*.96(8):3070–3076.

Neary J., Garry F., Holt T., Brown R., Stenmark K., Enns R., Thomas M. 2015.The altitude at which a calfwasborn and raised influences the rate at which mean pulmonary arterial pressure increases with age, *Journal of Animal Science*, Volume 93:(10):4714–4720, doi:10.2527.

Neary, J., Garry F., Holt T., Krasfur G., Morley P.,Brown R., Stenmark K., Thomas M., Enns R. 2015. High Altitude Disease, PAP, Feedlot hypertension, and Respiratory Issues. The Range Beef Cow Symposium XXIV Proceedings.

Neary, J., Garry F., Holt T., Thomas M., Enns R. 2015. Mean pulmonary arterial pressures in Angus steers increase from cow-calf to feedlot-finishing phases. J. Anim. Sci. 93:3854–3861. doi:10.2527.

Neary J., Gould D., Garry F., Knight A., Dargatz D., Holt T. 2013. An investigation into beef calf mortality on five high-altitude ranches that selected sires with low pulmonary arterial pressures for over 20 years. J Vet Diagn Invest. 1(2):210-8. doi: 10.1177.PMID: 23512918.

Newman J., Holt T., Cogan J., Womack B, Phillips J. 3rd, Li C., Kendall Z., Stenmark K., Thomas M., Brown R., Riddle S., West J., Hamid R. 2015. Increased prevalence of

EPAS1 variant in cattle with high-altitude pulmonary hypertension. Nat Commun. 15;6:6863. doi: 10.1038. PMID: 25873470; PMCID: PMC4399003.

Newman, J., Holt T., Hedges L., Womack B., Memon S., Willers D., Wheeler L., Phillips A. 3rd., Hamid, R. 2011. High-altitude pulmonary hypertension in cattle (brisket disease): Candidate genes and gene expression profiling of peripheral blood mononuclear cells. *Pulmonary circulation*, *1*(4), 462–469. doi:10.4103.

Raouf, M., Elgioushy, M., & Ezzeldein, S. A. (2020). Congestive heart failure in cattle; etiology, clinical, and ultrasonographic findings in 67 cases. *Veterinary world*, *13*(6), 1145–1152. doi:10.14202.

Rezac D., Thomson D., Bartle S., Osterstock J., Prouty F., Reinhardt C. 2014. Prevalence, severity, and relationships of lung lesions, liver abnormalities, and rumen health scores measured at slaughter in beef cattle. J Anim Sci. 92(6):2595-602. doi: 10.2527/jas.2013-7222

Rotta P., Prado I., Prado R., Moletta J., Silva R., Perotto D. 2009 Carcass Characteristics and Chemical Composition of the Longissimus Muscle of Nellore, Caracu and Holstein-friesian Bulls Finished in a FeedlotAnim Biosci. 22(4):598-604. doi:10.5713.

Olkowski A. 2007. Pathophysiology of heart failure in broiler chickens: structural, biochemical, and molecular characteristics. Poult Sci. 86(5):999-1005. doi: 10.1093/ps/86.5.999. PMID: 17435038.

Pauling R., Speidel S., Thomas M., Holt T., Enns R. 2018.Evaluation of moderate to high elevation effects on pulmonary arterial pressure measures in Angus cattle, *Journal of Animal Science*. 96(9): 3599-3605.

Schmidt T., Olson K. 2007. The effects of nutritional management on carcass merit of beef cattle and on sensory properties of beef. Vet Clin North Am Food Anim Pract. 23(1):151-63. doi: 10.1016/j.cvfa.2006.11.004. PMID: 17382845.

Shirley K., Beckman D., Garrick D. 2008. Inheritance of pulmonary arterial pressure in Angus cattle and its correlation with growth, *Journal of Animal Science*,86,(4): 815–819, doi:10.2527.

Swett W., Graves R. 1939. Relation Between Conformation and Anatomy of Cows of Unknown Producing Ability. Jounral of Animal Research. 58 (3): 199-234.

Sydykov A., Maripov A., Kushubakova N,. An Exaggerated Rise in Pulmonary Artery Pressure in a High-Altitude Dweller during the Cold Season. 2021 International Journal of Environmental Research and Public Health.18(8). DOI: 10.3390. PMID: 33920082; PMCID: PMC8069572.

Thomas M. G., Neary J. M., Krafsur G., Holt T. N., Enns R. M., Speidel S. E., Garry B. F., Cánovas A., Medrano J. F., Brown R. D. 2018. *Pulmonary hypertension (PH) in beef cattle: complicated threat to health and productivity in multiple beef industry segments*. CAB White paper.

Vallance P, Hingorani A. 1999. Endothelial nitric oxide in humans in health and disease. *Int J Exp Pathol*. 80(6):291-303. doi:10.1046.

Vesal N., Karimi A. 2006. Evaluation of central venous pressure in ruminants. *Veterinarski Arhiv,* 76(1):85-92.

Wang S., Wang Y., Cao Z., Li S. 2017. 061 Chronic hypobaric hypoxia induces high expression of nitric oxide in Holstein heifers in Tibet, *Journal of Animal Science*, 95(4):30 doi:10.2527

Williams J., Bertrand J., Misztal I., Łukaszewicz M. 2012. Genotype by environment interaction for growth due to altitude in United States Angus cattle, *Journal of Animal Science*, 90 (7):2152–2158, doi:10.2527.

Winkler Stirm J., St-Pierre N. 2003. Identification and Characterization of Location Decision Factors for Relocating Dairy Farms. Journal of Dairy Science. 86(11):3473-3487. doi: 10.3168.

Xing T., Gao F., Tume R., Zhou G., Xu X. 2018. Stress Effects on Meat Quality: A Mechanistic Perspective. Comprehensive Reviews in Food Science and Food Safety. 18(2): 380-401. Doi:10.1111/1541-4337.12417

Zhang Y., Hu Y., Wang X., Jiang Q., Zhao H., Wang J., Ju Z., Yang L., Gao Y., Wei X., Bai J., Zhou Y. and Huang J. 2020. Population Structure, and Selection Signatures Underlying High-Altitude Adaptation Inferred from Genome-Wide Copy Number Variations in Chinese Indigenous Cattle. *Front. Genet.*10:1404. doi:10.3389/fgene.2019.01404.

Zimprich T., Speidel S., Schafer D., LaShell B.,Holt T., Enns R., Cunningham S., Thomas M. 2020. 276 Repeated Measures of PAP at Different Elevations in Beef Bulls in Colorado, *Journal of Animal Science*, 98(4):205–206, doi:10.1093.

CHAPTER 3 STUDY OF PHENOTYPIC RELATIONSHIPS IN CATTLE WITH NORMAL AND REMODELED HEART STRUCTURES IN RESPONSE TO PULMONARY HYPERTENSION

SUMMARY

Pulmonary arterial pressure has been in many decades the indicator trait for identifying cattle at risk for pulmonary hypertension. More commonly seen in high altitude cattle due to the hypoxic environment in which they reside, pulmonary hypertension can severely affect cattle causing irreversible damage to the heart and overall lifetime performance. Further complications of pulmonary hypertension include its association with other respiratory complications and health concerns. Despite its prevalence in high altitude cattle, little is known about why cattle at moderate to low altitudes seem to experience pulmonary hypertension in a similar capacity without experiencing the same hypoxic environment. The disease known as Feedlot Heart Disease (FHD) categorizes these animals experiencing pulmonary hypertension at lower altitudes and includes high PAP measurements. Without the ability of managerial decisions to move cattle to lower elevations, further analysis was needed to understand what the effect of fattening feedlot cattle health was in order to determine at risk cattle. Using a visual grading system that categorizes the extent of heart remodeling due to pulmonary hypertension, the differences in phenotypic performance of Angus-influenced cattle raised in a feedlot system in Canyon, TX (moderate altitude) could inform how cardiovascular health plays a role in the overall performance of beef cattle. The objective of this study was to determine the phenotypic relationship between grouped healthy heart scores (n=1,018; 72%) and unhealthy heart scores

(n=404; 28%) in a cattle feedlot system located at moderate altitude. The study was comprised of 1,422 heifers and steers, who were raised through the feeding period and harvested in a packing plant Amarillo, Texas. Phenotypic information was collected in both feed yard and harvest facilities at varying times depending on the lot of cattle sampled. Results varied with cardiovascular traits such as pulmonary arterial pressure, systolic pressure, and diastolic pressure being vastly different between heart score groups ($P < 0.05$). The unhealthy group displayed higher pressures in all three categories, showing increased risk of early feedlot death. Pressures for unhealthy hearts were systolic pressure 85.88 ± 20.89 mmHg, diastolic pressure 26.21 ± 19.28, and PAP 55.20 ± 18.67. Carcass traits such as marbling also differed between the groups, but these differences were not identified in ribeye area and backfat thickness. Hot carcass weight had a tendency ($P < 0.10$) to be higher in the unhealthy group at 408.45 ± 52.84 kgs, potentially supporting the hypothesis that fast growing, fattening cattle leads to higher risk of pulmonary hypertension. Linear models were used for twelve traits of interest and included heart score and lot in the model. Heart score's linear model included the predictor variables of scorer and lot as the contemporary group effect in the model. Heart scores were an important predictor in late feeding PAP measurements and marbling. ($P < 0.05$). When analyzing heart score, the predictor variables of scorer and lot were found to be significant to the model. However, scorers had differences within their distributions of scoring ($P < 0.05$). Overall, the decision to select for healthier hearts may not yield extreme phenotypic differences directly related to carcass or performance traits. Heart scores were found to have very weak positive relationships with hot carcass weight, weaning weight, and marbling $r < 0.3$. Moderate, positive relationships $0.3 < r < 0.5$ were also found between heart score, PAP, systolic, and diastolic measurements.

INTRODUCTION

Pulmonary hypertension (PH)was associated with heart remodeling in high altitude cattle (1,500 m and above) and growing feedlot cattle (evidence of incidence within cattle raised at altitudes 1,500m below) as Bovine Congestive Heart Failure (BCHF). The response to the heart's difficulties with efficiently transporting blood to the lungs to be reoxygenated was still under investigation relative to the catalysts, predispositions, and effective preventive tools for this disease. Research surrounding heart remodeling severity and phenotypic associations in cattle was unknown. Previously, confirming BCHF cases in cattle has been the first step in quantifying disease prevalence through gross examination (Moxley et al. 2019). Feedlot deaths in production could only be speculated to have resulted from heart failure but due to symptomatic similarities with bovine respiratory disease could be misclassified. Confirmation of death due to heart failure requires necropsy. Pulmonary hypertension research reported by Neary et al. (2013) showed the presence of pulmonary hypertension in 14 out of the 28 necropsies in calf mortality cases (are these in the feedlot or cow/calf?), giving a small glimpse of just how prevalent heart failure was in cattle. Little was known of the relationship to performance and carcass traits during the gradual progression of heart failure malformation and necessitated further investigation on the overall impacts of the disease on the industry.

Pulmonary hypertension in humans typically associates 38% to 48% of patients with primary or secondary pulmonary hypertension cases with obesity based on Body Mass Index scores (Friedman et al., 2013). Obesity has been shown to impair respiratory function by decreasing muscular strength around the rib cage, increasing mechanical complications due to the increase of adipose tissues in turn, causing the production of excess cytokines, and a decrease in lung volume (Mafort et al., 2016). These complications begin as patients experience chest pain, fatigue, shortness of breath, lower extremity edema, and abnormal auditory heart sounds (Friedman and Andrus, 2012). Pulmonary hypertension cases arise in human cases of Interstitial Lung Disease, with 30% to 40% of patients having both lung disease and pulmonary hypertension. Similarly, abnormal lung sounds are commonly associated with animals experiencing pulmonary hypertension with about 58% affected cattle displaying that diagnostic symptom of abnormal lung sounds (Raouf et al., 2020). The relationship between heart and lungs immediately leads to speculation of the overall effects on animal performance.

Parallels could be drawn to fast growing, fattening feedlot cattle, with growth being an excess strain on the animal's heart and lungs, although no research today can pinpoint the true catalysts of FHD cases. Cattle often are genetically selected for higher weight gain performance, to put on weight in a shortened timeframe. In both cases, cattle and classified obese patients are at jeopardy due to the abundance of excess weight on chest and abdomen, difficulties breathing are common and known as obesity hypoventilation syndrome **(Matshela,2015.)** This decrease in lung capacity and decrease in muscle strength leads to the idea that the inefficient heart and lung functions, lower blood oxygen within the cattle themselves and would affect the growth and performance of affected individuals. Correspondingly, the objective of this study was to determine differences among cattle performance between healthy heart scores and unhealthy heart scores. The hypothesis was that we will see phenotypic differences between these two distinct groups based on heart modeling score severity.

MATERIALS AND METHODS

Animal and Data Collection

Data were collected on multiple cohorts of cattle from Cactus Feeder's Wrangler Feed yard in Canyon, Texas during the years 2020-2022. All animals in the study were Angus influenced and consisted of both heifers and steers. All cattle were fed similar diets while in the feedlot with no differences in their nutritional management. For purposes of this study data were included only when animal heart score information was recorded with a total of 1,422 animals. There were 760 steers, and 662 heifers. Each lot had varying phenotypic information available in total including: back fat thickness, marbling, ribeye area, , weaning weights, and heart scores (Further detail is presented in Table 3.3). Lots were of similar sex, harvest date, and under the same environmental management. The lot designation in this study acted as the contemporary group in further analysis. Breakdown of lot details are shown in Table 3.1.

Table 3.1: Description of lot breakdown in data, including amount of cattle in each lot, sex of cattle, and respective harvest dates.

Lot Number	n	Sex	Harvest Date	Scorer
675	57	Steer	February 4, 2020	2
676	60	Steer	February 4, 2020	2
682	59	Heifer	February 4, 2020	2
25447	115	Steer	January 7, 2021	1
25448	119	Steer	January 7, 2021	1
25449	180	Steer	February 9, 2021	1
25450	185	Heifer	February 9, 2021	1
25451	217	Heifer	December 17, 2020	2
26163	111	Steers	February 16, 2022	3
26164	95	Heifers	January 27, 2022	3
26165	109	Steers	February 16, 2022	3
26166	115	Heifers	January 27, 2022	3

Besides being analyzed as a continuous outcome from 1 to 5, heart scores were also grouped with scores of 1 and 2 coded as a 0 (normal) and scores of 3+ as 1 (remodeled). This allowed for the identification of healthy hearts and unhealthy hearts in each comparison for the phenotypic trait (Holt, personal comm). Scores 1 and 2 were considered have either no or mild changes in the heart restructuring model, indicating little to no evidence of pulmonary hypertension. Scores 3 and greater were likely the result of pulmonary hypertension occurring within the heart causing gross changes. There is still little knowledge of how severe heart morphology might influence other traits.

All animals in this study were harvested at the Tyson Processing Plant in Amarillo, Texas and were on average 483d of age at the time of harvest. Carcass data were collected by meat science personnel and collected in conjunction to heart scores. Heart Scores were scored using the heart score visual grading system, highlighted in Figure 1. The breakdown of scoring can be found in Table 3.2.

Table 3.2: Heart score descriptions for the categorization of the visual grading system provided by Dr. Tim Holt DVM (Holt, 2020).

Score	Description
1- No Change (Healthy)	Normal conical shape, right ventricle smaller than left, normal pulmonary artery, no vessel wall thinning
2- Mild Change (Healthy)	Normal conical shape, right ventricle becoming pronounced, enlargement of pulmonary artery, losing apex point, no vessel wall thinning
3- Moderate Change (Unhealthy)	Beginning to lose conical shape, right ventricle larger than left (reverse D shape), thinning of vessel walls, pulmonary artery enlarged, blunting of apex
4- Severe Change (Unhealthy)	No conical shape, no apex due to rounding of right ventricle, dark spots on pulmonary artery, cardiac muscle becoming softer
5- Severe Change (Fatal)	Heart completely flaccid, right ventricle extremely pronounced, very enlarged pulmonary artery, no muscle tone, heart was flat.

Trained heart scorers, who were trained in a course of the visual grading system at the Colorado State University Teaching Hospital, provided the scores. There were three separate heart scorers (Scorer 1, Scorer 2, Scorer 3particpated in this study and were specific to lot and harvest date. Lots never contained more than one scorer. The summary statistics for the cattle data included 88 sires, with 760 steers and 662 heifer progeny. The number of progeny for each sire ranged from 1 to 97 animals. Equal proportions of heifers and steers had healthy heart scores and unhealthy heart scores, ~70% healthy and ~30% unhealthy within each respective group. Phenotypic information (heart score, pulmonary arterial pressure (9 months and 14 months), backfat, marbling, ribeye area, hot carcass weights, and weaning weight) as shown in Table 3.3**.** These were the traits evaluated for relationships with heart score.

Table 3.3: Summary statistics on cleaned data used in analysis. Contains n (number of animals), means, standard deviations, minimums, and maximums for the respective traits.

Trait	n	Mean	Standard Dev	Min	Max
Heart Score	1,422	2.13	0.78	1.00	4.00
Backfat (mm)	1401	17.78	5.33	4.64	41.66
Marbling Score	1401	502.2	97.23	281.00	952.0
Ribeye Area(mm^2)	1401	9116.11	922.58	5374.18	12619.33
Hot Carcass Weight (kg)	1414	404.77	50.31	214.09	561.82
Weaning Weight (kg)	868	208.23	42.09	87.27	349.09

Statistical Analysis

An analysis of these data was conducted using RStudio Team **(2020)**. Heart scores were organized using R studio into heart score groups. To test for the differences in means between healthy heart scores and unhealthy heart scores with their corresponding phenotypic information, a Welch t-test was used, which was useful when the two samples have either unequal variances or numbers for each sample rather than pooled variances. The equation for Welch t-test is below:

$$t = \frac{\mu_A - \mu_B}{\sqrt{\frac{\sigma^2}{n_A} + \frac{\sigma^2}{n_B}}}$$

Where μ_A and μ_B represented the means of their respective sample size, σ_A and σ_B represented the standard deviation for each. The null hypothesis was $\mu_{A=}\mu_B$ and the alternative hypothesis was $\mu_{A\neq}\mu_B$ The p-value displayed the probability that the observed differences among means was insignificant meaning both means fall within the same 95% CI or significant where means were statistically different based on the observed values. Multiple fixed linear regression models were used to regress phenotypic traits of interest (i.e. Marbling, hot carcass weight, backfat thickness, ribeye area, yield grade, marbling, PAP scores, systolic scores, diastolic scores) on the predicter categorical variables of heart score and lot. The heart score model contained scorer and sex. There was a total of 9 linear models run to analyze each trait of interest and heart score. The general form for this model is presented below.

$$y_{ij} = B_0 + B_1x_{ij} + B_2x_{ij} + e_{ij}$$

In the above model equation, y_i= observed phenotypes for trait of interest, B_0 represented the overall mean for the trait of interest, B_1= regression of the effect of heart score on y where x_i = i^{th} observation on j^{th} lot, B_2= the solution of lot on y where x_{ij}= the i^{th} observation in the lot group. Analysis of variance was created with the package *tidyverse* and *dplyr*. Packages such as *reshape 2* were utilized to create comparative boxplots to visualize the summary statistics for areas of interest to display summary statistic differences within categorical data (put R Studio citation here). The package *lsmeans* package was utilized to calculate the different least square means for each phenotype while utilizing the predictions based on the linear model.

Phenotypic correlations between phenotypic traits presented in Table 3.3 were calculated using the *GGally* and *Hmisc packages,* functions ggpairs, ggcorr (heat map), and rcorr. Correlations include both Pearson correlation and Spearman rank correlation coefficients, where a linear relationship was assumed between both traits of interest and a monotonic function (values follow as one either increases or decreases, often causing a curved shape). The equation for the Pearson correlation coefficient is shown below:

$$r = \frac{\sum(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum(x_i - \bar{x})^2 \sum(y_i - \bar{y})^2}}$$

Above, r was the Pearson correlation coefficient, x_i were observations from our sample on X variable, $\bar{x}$ was the mean of X variables, y_i were the observations on the Y variable, and $\bar{y}$ was the mean of the y variable. In our data set, heart score or PAP was included as our X variable and our phenotypes alternate as the y variable. The function rcorr allows for correlations and their respected p values be outputted in matrix form and the addition of "method = "Pearson" specifies the correlation type.

The equation for the Spearman correlation coefficient is shown below:

$$\rho = 1 - \frac{6 \sum d_i^2}{n(n^2 - 1)}$$

where d_i represented the difference between two ranks of each observation, n = number of observations, and ρ represented the spearman's rank correlation coefficient. Ranks were determined by organizing factors by highest to lowest, for example the highest numerical observation will receive the rank of 1, while the lowest observation will receive the rank equal to the number of observations. This statistic accounts for any relationships that would be monotonic, as one factor increased the other increased as well, but not always at the same rate, causing a curve or bend in the trajectory of the line when graphed, unlike linear which would be a straight line through data points.

RESULTS AND DISCUSSION

Phenotypic Differences

Summary statistics for traits utilized in this analysis are displayed in Table 3.4**.** The table includes number of observations, mean, standard deviations, and the range for the observations.

Table 3.4: Summary statistics on cleaned data used in analysis. Contains n (number of animals), means, standard deviations, minimums, and maximums for the respective traits.

Trait	n	Mean	Standard Dev	Min	Max
Heart Score	1422	2.13	0.78	1.00	4.00
Backfat (mm)	1,401	17.78	5.33	4.64	41.66
Marbling Score	1401	502.2	97.23	281.00	952.0
Ribeye Area(mm^2)	1401	9116.11	922.58	5374.18	12619.33
Hot Carcass Weight (kg)	1414	404.77	50.31	214.09	561.82
Weaning Weight (kg)	868	208.23	42.09	87.27	349.09

The traits chosen were selected based on economic interest and present the phenotypic differences between healthy and abnormal heart scores. Heart scores were assigned by trained scorers familiar with the gross visual grading system. To determine the influence of scorer, the cattle within each scorer was further investigated. Utilizing a linear model, scorer and sex were fitted in the model to test for differences between scorer regarding overall heart score. Three separate scorers included Scorer 1, Scorer 2, and Scorer 3 and each scorer graded complete lots. Sex was not found to impact overall heart score, but scorer did have a significant impact on scores ($P < 0.05$). Study of score data, Scorer 1 graded 42.12% (n = 599), Scorer 2 graded 27.64% (n = 393), and Scorer 3 graded 30.24% (n= 430) of the sample size, but interpretation must be made with care, as differences may be due to true difference in heart score and/or differences in score. No matter, inclusion of harvest date in contemporary group definition will likely account for any scorer differences. Although sex of the animal was not an important factor in the model, it was still noted that within the data of each scorer there were differing proportions of heifers and steers scored. Scorer 3 scored an equal number of heifers and steers while Scorer 1 scored 3 times as many steers than heifers and Scorer 2 scored twice as many heifers than steers within each distinguished lot. This was important to note as we evaluate at how similarly individual scorers were to each other. Scorers 1 and Scorers 2 had statistically similar averages in their groups 2.23 ± 0.70 and 2.31 ± 0.74 respectively, despite having differing sample sizes and distribution of cattle sexes. Scorer 3 scored proportionally different than the other scorers by having an overall lower average of 1.80 ± 0.80 than the other two scorers. The proportions of each grade to scorer are highlighted in Table 3.5.

Table 3.5: Scorer proportions for each heart score grade.

	HEART SCORE				
SCORER	1	2	3	4	5
Scorer 1	73	335	168	23	0
Scorer 2	38	221	106	28	0
Scorer 3	179	172	66	13	0

Scorer 3 graded lower on average than the other scorers with most scores being equally 1 or 2, and fewer unhealthy heart scores. More studies on repeatability measures and further analysis of multiple scorers in the same lot could be done to test relationships amongst different scorers.

The phenotypic data collected was presented below in grouped heart score categories in Table 3.6.

Table 3.6: Summary statistics for the comparison of healthy hearts versus unhealthy hear scores resulting in their phenotypic differences. Each trait displays the means, standard deviation, and features the Welsh Two Sample t- test p values for differences in means.

Trait	Healthy Hearts (Scores 1&2)			Unhealthy Hearts (Scores ± 3)			P Value Difference of means
	n	mean	sd	n	mean	sd	
Backfat(mm)	1007	17.78	5.33	399	17.78	5.08	0.998
Marbling	1007	507.03	101.12	399	483.81	100.87	<0.01***
Ribeye Area (mm^2)	1007	9148.37	961.21	399	9129.01	954.84	0.752
Hot Carcass Weight (kg)	1014	403.35	49.24	400	408.45	52.84	0.10*
Yield Grade	1018	3.97	0.87	404	4.02	0.89	0.318

Grouped Heart Score:

Backfat thickness, ribeye area, yield grade, and hot carcass weight were similar (*P < 0.05*) between heart score groups; however, marbling was found to be important (*P < 0.05*) displaying a score of 507 compared to 484 for unhealthy hearts shown in Table 3.6. Marbling scores are defined as the amount of intramuscular fat between muscle fibers, often associated with palatability, quality of meat, tenderness, and juiciness (Lee et al. 2018). There are several sources of variation that influence marbling scores such as genetic relationships, nutrition, management, sex, and slaughter weight (Nguyen et al., 2021), potentially even cardiovascular health. Due to these contributing factors, a linear model was performed to analyze our response variable, marbling, with the effects of heart score group, sex, and harvest date. The Type III ANOVA revealed important sources of variation (P < 0.05) for the predictor variables of heart score group, sex, and harvest date. Heart score group resulted in an estimate of -15.66 (P < 0.01) decrease in marbling score from healthy to unhealthy heart scores. In the linear modeling examining hot carcass weights as our response variables and heart score group, sex, and harvest date as the predictor variables, heart score group was not important to the model while accounting for sex and harvest date. Pauling et al., (2017) reported that higher PAP animals are related to heavier muscled animals, but within the grouped data this is not distinct. Heart scores individually could trend in a similar matter as PAP, prompting the continuation of the investigation.

Individual Heart Scores:

The magnitude of heart morphology changes needed to influence cattle performance and carcass traits was still unknown. Pulmonary hypertension research indicates detrimental effects of high PAP contributing to biological mechanics, productivity loss, and likelihood of further respiratory complications (Thomas, 2018). To gain more perspective the same analysis for group data were examined in individual heart scores. Figure 3.7 displays the summary statistics broken down for each trait by each heart score (Note: there were no heart scores of 5 in this data).

Table 3.7: Heart Score phenotypic summary statistics broken down by heart score from 1 to 4 with mean and standard deviations. Including traits of interest Backfat Thickness, Marbling Score, Ribeye Area, Hot Carcass Weight, Yield Grade.

	Heart Scores			
	1	2	3	4
Trait	Mean	Mean	Mean	Mean
Backfat(mm)	17.78 ± 5.84	17.78 ± 5.80	17.78 ± 4.82	17.27 ± 5.33
Marbling Score	520.06 ± 107.09	502.51 ± 96.49	484.87 ± 102.43	478.17 ± 92.73
Ribeye Area (mm^2)	9290.30 ± 941.93	9206.43 ± 903.22	9174.18 ± 941.93	8896.76 ± 987.09
Hot Carcass Weight (kgs)	390.71 ± 51.49	407.23 ± 47.37.	410.19± 51.51	393.74± 57.28
Yield Grade	2.95 ± 0.90	3.00 ± 0.83	3.06 ± 0.81	3.02 ± 0.96

Backfat thickness showed no significant differences between scores. Higher marbling scores were favorable and attributed to the animal's overall score of being labeled as prime, choice, select, or utility. In terms of ribeye area, the optimal range according to the University of Arkansas Division of Agriculture (Troxel and Gadberry, 2009) was between 11 and 15 in^2 or 7096 to 9677 mm^2. All heart scores fall in optimal range, but there was a gradual decline in ribeye area as heart score increased. Hot carcass weights between score 1 and 4 on average differ by 7 lbs. Investigating the feeding period by heart scores, cattle with weights from after and before feeding period were subtracted to find weight differences (~45 days on feed). Summary statistics were then used to group the weight differences by each specific heart score category (1,2,3,4), and summarized to attain their distinct category weight gain means Table 3.8.

Table 3.8: Weight differences amongst heart score grouping in cattle with recorded feed in weights and feed out weights.

Heart Score	n	Mean of weight gain (kg)	Standard Deviation (kg)
1	290	78.58	20.63
2	728	92.23	21.77
3	340	95.84	23.14
4	64	81.19	45.92

Heart score 1 had the lowest amount of weight gain through the feeding period of 45 days, but this increased as heart scores increased in severity until score 4. Scores of 2 were also considered normal with mild changes to the heart structure. Scores of 3 were where the most gain on average occurred, suggesting heavier, fast-growing cattle tend to suffer with pulmonary hypertension. Once an animal reached a score of 4, these cattle were the second lightest, this could be because as cattle experience pulmonary hypertension at an earlier stage, their hearts have severely remodeled in the fattening stage, where they were no longer efficient and able to maintain weight aligning with previous hypothesis presented by Maddox et al. (2010), Briggs et al. (2019), Thomas et al. (2018), and Heffernan et al. (2020). These results suggest that without knowing the rate of cardiovascular remodeling, cattle with higher pulmonary hypertension may be in a more severe stage of heart remodeling than expected.

Each trait (Backfat Thickness, Marbling Score, Ribeye Area and Hot Carcass Weight) was analyzed to determine the effect of heart score on each response variable. Lot was utilized as our contemporary group and heart score was another categorical predictor variable. The backfat thickness (mm) linear regression model did not show heart score to be a significant contributor to the model, but lot had several levels with significant differences. These lots with differences included lots containing heifers and steers. Marbling linear regression model displayed an intercept 517.85 with heart score being a tendency predictor in the model ($P < 0.10$), the most important difference was found to be in score 4 ($\beta = -26.11$, $P < 0.05$). Lot was an important predictor in the model and was found to have differences of means that included both heifers and steers. The linear model containing ribeye as the predictor variable displayed heart score and lot to be significant to the model. Heart score 4 displayed an important differentiation ($\beta = -0.45$,, $P < 0.05$), meaning the cattle with scores of 4 had significantly different ribeye areas that trend smaller than scores 1,2, and 3. The hot carcass weight model with the same predictor variables as previous models, displayed all predictor variables to be important to the model ($P < 0.0001$). Scores 2 and 3 were the significant levels of difference, score 2 ($\beta = 16.37$, $P < 0.0001$), and score 3 ($\beta = 20.82$, $P < 0.0001$). These differences between scores are displayed utilizing least squared means in Table 3.9.

Least square means further emphasized some main differences between scores 4 compared to scores 1. In many cases heart score of 4 consisted of cattle with less backfat, worse marbling, smaller ribeye areas, and lighter carcass weights. Even though score 3 cattle did not have such massive difference such as having the heaviest carcass weights, differences in marbling scores and ribeye area beginning to trend downward tend to potential show some of the negative effects with worsening cardiac remodeling.

Phenotypic Correlations

To further visualize the relationship between all traits, phenotypic correlations utilizing the Pearson method are presented. Heat maps (ggcorr from GGally package) are indicated by a gradient of blue to red, red being positive correlation and blue being a negative correlation as shown in Figure 3.1. This map visually briefly illustrates the directional relationships and their strengths between each trait and overall shows how typically performance traits, carcass traits, and cardiovascular traits are all related.

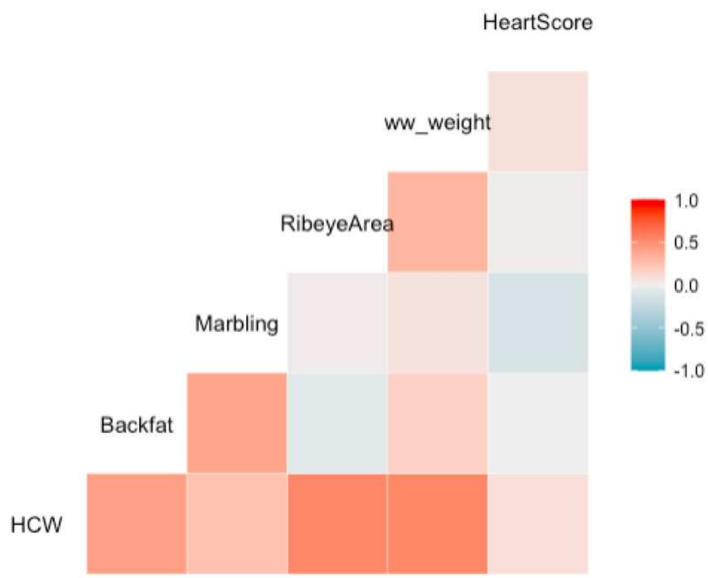

Figure 3.1: Heat map created with ggcorr in GGally package in R studio to display positive and negative correlation relationships with all traits of interest. The scale of color intensity indicates strength of relationship.

The unique aspect that this heat map shows was a glimpse of the differences of relationships between heart scores. Heart score has more positive relationships with traits such as hot carcass weight, meaning that heart morphology at harvest may have a different relationship with performance traits than pulmonary pressure taken later in the feeding period. To investigate these relationships further, phenotypic correlations utilizing Spearman and Pearson methods are shown below in Table 3.9.

Table 3.9: Phenotypic correlations between heart scores and traits of interest. PAP with phenotypic traits. Pearson method above the diagonal and Spearman method below.

	Heart Score	HCW[1]	BF	MARB	REA	WWT
Heart Score	1.00	0.08***	0.00	-0.12***	0.01	0.08***
HCW	0.11***	1.00	0.42***	0.25***	0.54***	0.54***
BF	0.03	0.40***	1.00	0.39***	-0.06**	0.16***
MARB	-0.14***	0.21***	0.39***	1.00	0.03	0.06 .
REA	0.02	0.51***	-0.06**	0.01	1.00	0.31 ***
WWT	0.07**	0.52***	0.17***	0.08**	0.27***	1.00

[1] HCW=Hot Carcass Weight (kg), BF =back fat (mm^2), MARB= Marbling score, WWT= Weaning Weight (kg).

Heart score had very weak, positive correlations with HCW (r= 0.08 and 0.11) and weaning weight (0.08 and 0.07), with a very weak negative correlation with marbling (*P < 0.05*). In summary, heart scores do not have strong phenotypic relational values with the traits in this study but genetic relationships between traits utilizing a multi trait model may yield more solidifying information on the additive genetic effects and relationships. Phenotypically, there was the illusion that in the future through the selection of lower heart scores, PAP measurements at low to moderate elevations could be lower in cattle and potentially through the selection of heart score high PAP scores at moderate to low altitude would be reduced.

CONCLUSIONS AND IMPLICATIONS

Results from this study revealed that there are phenotypic differences between cattle grouped by healthy versus unhealthy heart scores. As cattle begin to fatten in the feedlot system, and as age increases, cattle who are at risk display higher cardiovascular stress which was reflected in the differences of PAP scores between 9 month and 14 months of age. The unhealthy heart group had larger carcass weight, and on average, was considered extremely at risk for bovine congestive heart failure. Furthermore, it was observed that while healthier animals may display better quality marbling scores, a trait heavily desired by consumers, this may lead to slightly leaner cattle, but decreased risk of early feedlot death. It was also observed that heart scores of 3, considered to be in the moderate stage of heart remodeling, may not be severe enough to cause decrease in growth and carcass traits. These findings within heart score individual grades may yield answers to understanding bovine cardiovascular system and how it was affected by fast growing, fattening cattle. The rate of severity of heart score and its impact is not known, but it was apparent that scores of 4 are too severe and cause negative effects on hot carcass weights, marbling, and ribeye area. Further data needs to be collected on cattle with feed performance to truly understand the impact of the cardiovascular distress and performance outcome. Due to heart scores accessibility at harvest, this phenotype is plausible. Scoring data such as repeatability and uniformity, however, is undetermined. Not to mention, if heart failure does not cause severe decline in performance the susceptibility to respiratory disease increases the risk of a plethora of unknown complications. Overall, there may be some tradeoffs when considering cardiovascular health in our cattle, not only was there economic risk with early death but animal health and welfare questions as well. If selecting lower heart scores yields healthier and sustainable cattle without severely harming genetic improvement goals, it may prove to be a feasible option for operations severely affected by bovine congestive heart failure and early feedlot death.

LITERATURE CITED

Briggs, E. A., Enns, R. M., Thomas, M. G., & Speidel, S. E. 2019. Genetic and phenotypic parameter estimates for feed intake and pulmonary arterial pressure. *Translational animal science*, *3*:1, 1655–1657. https://doi.org/10.1093/tas/txz049.

Friedman S.E. and Andrus B.W. 2012. Obesity and Pulmonary Hypertension: A Review of Pathophysiologic Mechanisms. *J. of Obesity.* 2012. Doi: 10.1155/2012/505274

Gilmour A. R., Gogel B. J., Cullis B. R. and Thompson R. 2009. *ASReml user guide. Release 3.0*. VSN Int. Ltd., Hemel Hempstead, UK.

Heffernan, K.R., M. G. Thomas, R. M. Enns, T. N. Holt, S. E. Speidel. 2020. Phenotypic relationships between heart score and feed efficiency, carcass, and pulmonary arterial pressure traits, Translational Anim. Sci. 4(1):S103–S107. doi:10.1093 tas/txaa114

Lee Y., Lee B., Kim H.K., Yun Y.K, Kang S.J., Kim K.T., Kim B.D., Kim E.J., and Choi Y.M. 2018. Sensory quality characteristics with different beef quality grades and surface texture features assessed by dented area and firmness, and the relation to muscle fiber and bundle characteristics. *J. Meat Sci.* 145:195-201. Doi: 10.1016/j.meatsci.2018.06.034.

Maddock T. D., Marquezini G. H. L., Mercadante V. R. G., and Lamb G. C.. . 2010. The relationship of pulmonary arterial pressure with feed efficiency, performance, temperament, and feeding behavior in growing beef cattle. *J. Dairy Sci*. 93 (E-Supplement 1):683–684.

Mafort T.T., Rufino R., Costa C.H., and Lopes A.J. 2016. Obesity: systemic and pulmonary complications, biochemical abnormalities, and impairment of lung function. *Multidiscip Respir Med*. 11:28. Doi: 0.1186/s40248-016-0066-z

Matshela, M. 2015. The association between obesity and pulmonary hypertension: a tale of two diseases. *PVRI Chronicle.* 2:1. ISSN: 2057-5351.

Moxley R.A., Smith D.R., Grotelueschen D.M., Edwards T., and Steffen D.J. 2019. Investigation of congestive heart failure in beef cattle in a feedyard at a moderate altitude in western Nebraska. *J. Vet. Science Diagnositic.* 31:4, 509-522. Doi: 10.1177/1040638719855108.

Neary, J. M. et al. 2013. An investigation into beef calf mortality on five high-altitude ranches that selected sires with low pulmonary arterial pressures for over 20 years. J. Vet. Diagn. Invest. 25: 210-218.

Nguyen D.V., Nguyen O., Malau-Aduli. 2021. Main regulatory factors of marbling level in beef cattle. Veterinary and Animal Science. 14. doi: 10.1016/j.vas.2021.100219.

Pauling R. 2017. Pulmonary arterial pressure in angus cattle: environmental influences and relationship with growth and carcass traits ProQuest. Dissertations Publishing [accessed April, 2022] http://search.proquest.com/docview/1975772534/?pq-origsite=primo.

Raouf, M., Elgioushy, M., and Ezzeldein, S. A. 2020. Congestive heart failure in cattle; etiology, clinical, and ultrasonographic findings in 67 cases. *Veterinary world*, *13*(6), 1145–1152. doi:10.14202.

RStudio Team (2020). RStudio: Integrated Development Environment for R. RStudio, PBC, Boston, MA URL

Thomas M. G., Neary J. M., Krafsur G., Holt T. N., Enns R. M., Speidel S. E., Garry B. F., Cánovas A., Medrano J. F., Brown R. D. 2018. *Pulmonary hypertension (PH) in beef cattle: complicated threat to health and productivity in multiple beef industry segments*. CAB White paper.

Troxel, T.R., Gadberry, S., and Barham, B.L. 2009.. Agriculture and Natural Resources FSA 3089 Understanding Beef Carcass Information. University of Arkansas.

CHAPTER 4 HEART SCORES RELATIONSHIP TO EARLY AND LATE FEEDING PERIOD PULMONARY ARTERIAL PRESSURE

SUMMARY

Growth of cattle raised in feedlot production systems involves intensive feeding. Each animal was expected to supply a nutritious product to consumers and offer availability of quality beef globally. Unfortunately, early feedlot death has become increasingly prevalent in this segment of the industry. Each animal resulting in early death due to feedlot heart disease was detrimental to end profits, and its onset decreases the profitability of cattle affected but able to make it to harvest date. This also could raise welfare concerns to consumers, who may be unwilling to support beef products if cattle production continues to experience increased prevalence of feedlot death. A leading and instrumental tool for understanding pulmonary hypertension was pulmonary arterial pressure (PAP) due to its ability to measure the pressure within the pulmonary artery and categorize cattle for different risk levels of heart failure. Higher pulmonary arterial pressures yield to high risk of heart failure, as the heart begins to pump blood against the increasing pressure, heart muscle begins to thicken in response, ultimately leading to a less efficient heart. Pulmonary arterial pressure has been successful in its implementation as a management tool and genetic improvement tool for high altitude beef production systems but limited research at lower altitudes yields uncertainties in its adaptability to determine and predict feedlot heart disease risk. In a cohort of 178 angus influenced cattle, 67 heifers and 111 steers had two PAP measurements recorded at two distinct times during their feeding period. The first measurement provided an early PAP measurement at 290 days of age at the beginning of the

feeding program. The late PAP measurement was conducted 445 days of age as these individuals exited the feeding program. Pulmonary arterial pressure measurements drastically increased, over time, when the same individuals were measured again at the end of the feeding period. Cattle in this study were of similar ages and weights by the end of the feeding trial period. Pulmonary arterial pressure at 9 months s averaged 39.84 ± 2.82 mmHg and 14 month PAP measurements averaged 49.12 ± 10.40 mmHg. These measurements were further examined by heart score groups using the heart score visual grading system created by Dr. Tim Holt of Colorado State University Veterinary Teaching Hospital. Heart scores were categorized by the heart morphology changes in response to pulmonary hypertension and are scored between 1 and 5. Scores of 1 and 2 are no to mild changes in the hearts structures and scores 3, 4, and 5 range from moderate to severe remodeling, often the score of 5 does not make it to harvest and results in a flaccid heart. All heart score groups were similar in their early PAP measurements, but they were vastly different in late (14 months) PAP measurements. Unhealthy scores (scores 3+) showed greater variability and elevated phenotypic PAP measurements, suggesting unhealthy heart scores to be associated with higher PAP measurements. These were further broken down by individual heart scores. All heart scores were found to be similar in early PAP and significantly different in late PAP measurements. This relationship of PAP scores to heart scores could strengthen the potential utilization of heart scores as a feedlot heart disease indicator trait. Furthermore, it was investigated the relationship between early and late PAP measurements. A linear regression model and phenotypic correlation estimation revealed correlation of 0.20, which can be described as a weak, yet positive relationship. Differences between PAP showed a right skewedness in the data with many cattle increasing by 5-10mmHg, but some extreme cases showed extreme rate of change within the feeding period.

INTRODUCTION

Pulmonary arterial pressure (PAP) an indicator trait for pulmonary hypertension has been utilized since 2007, presented in Holt and Callan (2007), to combat the prevalence of High Mountain Disease. Pulmonary arterial pressure as an indicator trait with estimated progeny difference (EPD) through the American Angus Association (AAA, 2019) are currently available to producers. This allows producers to select for low PAP bulls to potentially decrease the risk of pulmonary hypertension at high altitudes by assessing the amount of pressure found within the pulmonary artery and only utilizing bulls who are unaffected by the hypoxic environment in their breeding decisions. Due to PAP assessing the amount of risk cattle experience at high altitude, PAP can mitigate the prevalence of high mountain disease, or pulmonary hypertension in cattle raised at high elevations. The difficulties in feedlot cattle are the similarities of symptoms between cattle raised at high altitude and feedlot cattle raised at moderate to low altitudes which ever experience high altitude in their lifetime. The high pulmonary hypertension measurements and cattle suffering from pulmonary hypertension resulting in early feedlot death are described as Feedlot Heart Disease (FHD) due to the differentiating altitudes cattle. Pulmonary arterial pressure's success in understanding high mountain disease in cattle, has yielded further investigation of PAP in cases of feedlot heart disease, or heart failure in feedlot cattle below 1,500m.

The remodeling of the pulmonary artery due to pulmonary hypertension has been found to be caused by three potential factors: high altitude housing due to the hypoxic environment, lung diseases such as pneumonia, or noninfectious diseases restricting the ability to breathe (Neary et al. 2015a). Ultimately, these catalysts create an external or internal hypoxic environment decreasing either oxygen available in the bloodstream due to what is available in the environment and health complications decreasing the ability to bring oxygen in and maintain appropriate oxygen levels. The three known catalysts of pulmonary hypertension, high altitude, does not explain pulmonary hypertension cases in feedlot heart disease housed at low to moderate altitude. The second factor, lung diseases such as bovine respiratory disease, BRD, a costly and multifactorial disease that is known to increase the prevalence of heart disease due to blood oxygen complications. Diseases are a probable cause of increasing cardiovascular distress in feedlot cases, but it is difficult to differentiate which disease began first as each could put cattle at risk for the other. Research conducted by Neary et al. (2016), described cattle identified to be high risk cases of BRD and male were two to three times more likely to die of right sided heart failure. Troubled breathing due to infectious diseases could be a catalyst but there also is the factor of noninfectious reasons for difficulties breathing specific to feedlot cattle.

Fast growing feedlot cattle could be comparative to obese human patients, due to the sudden increase of body weight. The increased weight due to obesity is similar to the weight accumulated by fast growing and fattening cattle, which could cause a shift in breathing patterns as seen in obese humans due to excess weight creating excess pressure on the diaphragm and lungs. Obesity typically causes differences in breathing patterns, causing an increase in respiration rate consisting of slow, shallow breaths (Peters and Dixon, 2018). Shallow or obstructions to the breathing pattern as stated earlier by Neary et al. 2016, was found to be a hypothesis for pulmonary hypertension occurring; thus, the cattle creating a low, hypoxic environment at low to moderate altitudes. Investigating the rate of gain for heifers and steers, an average glance at this trait indicate that this could be an average of 3 to 4 lbs per day (Stehle et al. 2018). This rapid growth, could increase the pressure within the heart to receive blood to be reoxygenated, causing pulmonary hypertension to occur. The difficulty of discerning the gravity of fast-growing cattle is identifying when pulmonary hypertension begins to negatively affect or overshadow any performance or carcass traits. As cattle experience high performance in early feedlot period, this could yield to an earlier onset of stress on the heart causing our genetically superior growing cattle to begin to suffer from feedlot heart disease. A study by Heffernan et al. (2020) concluded that animals with high levels of remodeling in the heart utilizing the heart score grading system and high PAP had high feed to gain conversion weights, lower hot carcass weights, lower average daily gain, and lower overall gain. Building from previous studies, the objective of this study was to examine a cohort of Angus-influenced cattle to discover the relationship between pulmonary arterial pressure measurements in early and late feeding periods and its overall influence on heart remodeling to further understand how the feeding/finishing period may influence cattle performance and carcass traits.

MATERIAL AND METHODS

Data were collected from Cactus Feed yards in Canyon, Texas during 2021, 2022 at an elevation of approximately 1,080 m. Cattle (n = 178) were as Angus-influenced and included heifers (n = 67) and steers (n = 111). There were two separate lots in this study, with each lot being separated by sex. Cattle in both lots received a first PAP scores at 291d ± 16d of age, representing a PAP within one week after entering a feeding period, and a second PAP score at 446d ± 16d of age. Management, nutrition, and protocol were similar between lots. Both lots were harvest within 3 weeks of each other, steers harvested 27 days after last PAP score and heifers harvested 7 days after the last PAP measurement. There was a 20-day difference between ages of heifers and steers, steers were harvested at an average of 472 ± 16.94 days of age, while heifers were harvested at an average of 452 ± 15.05 days of age. The difference of both PAP measurements was determined by subtracting late PAP from earlier PAP. Rate of change for PAP was taken from PAP difference divided by the number of days between each PAP measurement. RStudio Team (2020) was used to analyze the data (packages: *tidyverse* and *dplyr*). Pearson correlations were utilized to test the relationship between PAP9 and PAP14. Linear models (package: *car*) were utilized to determine age and sex effect on each measurement of PAP and difference, ANOVA and summary function to analyze results of the model. LSmeans package was used to test for least square means for each group. R Studio *ggplot2* and *reshape* allowed for the construction of the graphs and plots presented. Tukey pairwise comparisons looked for differences in group means.

RESULTS AND DISCUSSION

PAP measurements taken at early feeding period and late feeding period yielded mean are showcased in Table 4.1. The average difference between these two measurements was an increase of 9.28mmHg, furthermore the results of a t.test show PAP at 9 months and PAP at 14 months were significantly different ($P < 0.05$). Figure 4.1 displays the overall distribution of

PAP measurements at 9 months and 14 months with PAP measurement on the x axis and frequency on the y axis.

Table 4.1: Summary statistics for PAP data in repeated PAP measurement study.

Trait	n	Mean	Standard Dev	Min	Max
Heart Score	1422	2.13	0.78	1.00	4.00
PAP (9 months) mmHg	178	39.84	2.83	34.00	48.00
Systolic (9 months) mmHg	178	68.8	8.32	55.00	95.00
Diastolic (9 months) mmHg	178	11.62	6.40	-12.00	26.00
PAP (14 months) mmHg	352	49.36	12.84	32.00	151.00
Systolic (14 months) mmHg	352	80.95	15.93	35.00	193.00
Diastolic (14 months) mmHg	352	20.85	13.90	-30.00	113.00

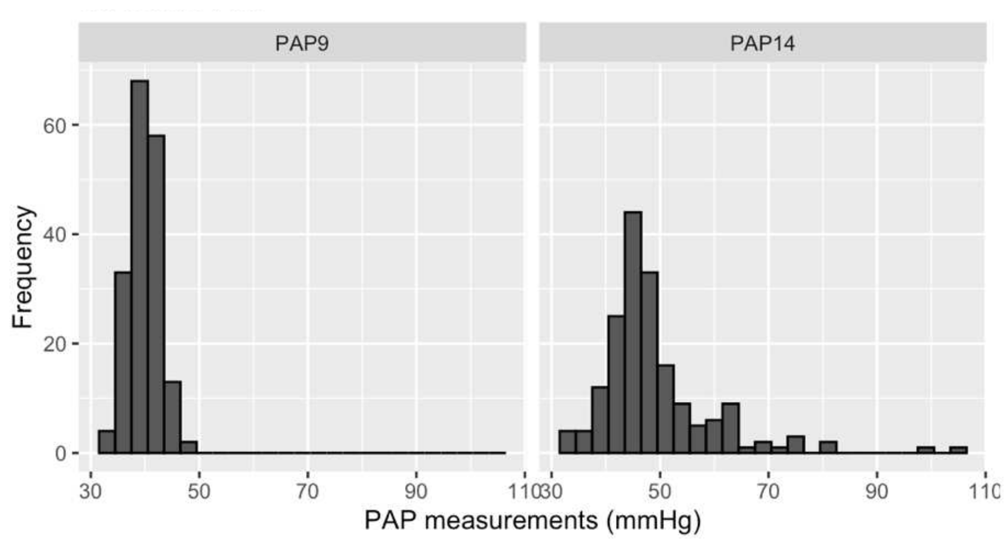

Figure 4.1: Distribution of PAP scores between repeated measured individual at 9 months and 14 months of age.

A measurement of 45mmHg was considered high risk of pulmonary hypertension as highlighted in Holt and Callan (2007) for high mountain disease (elevation greater than 1500m). It was expected that feedlot cattle who have not experienced high altitude would have less risk for pulmonary hypertension, therefore a measurement <50 mmHg, according to BIF guidelines (BIF, 2019) for low altitude <1,220m. At the 9-month measurement of PAP, all cattle were observed below this threshold. At 14 months of age, cattle PAP scores spread out and there were cases of cattle at moderate to high risk. Cattle at this elevation can only be labeled as low, moderate, to high risk, in relation to their risk of pulmonary hypertension at greater altitudes, PAP measurements have only been used for screening cattle for altitude in high altitude beef systems at this time. Late PAP measurements did not reflect this assumption, there was an average of 49 ± 10.4 mmHg in PAP measurements taken at the end of the feeding period. This shows that the sample had a steep increase in PAP, greater than previous measurements.

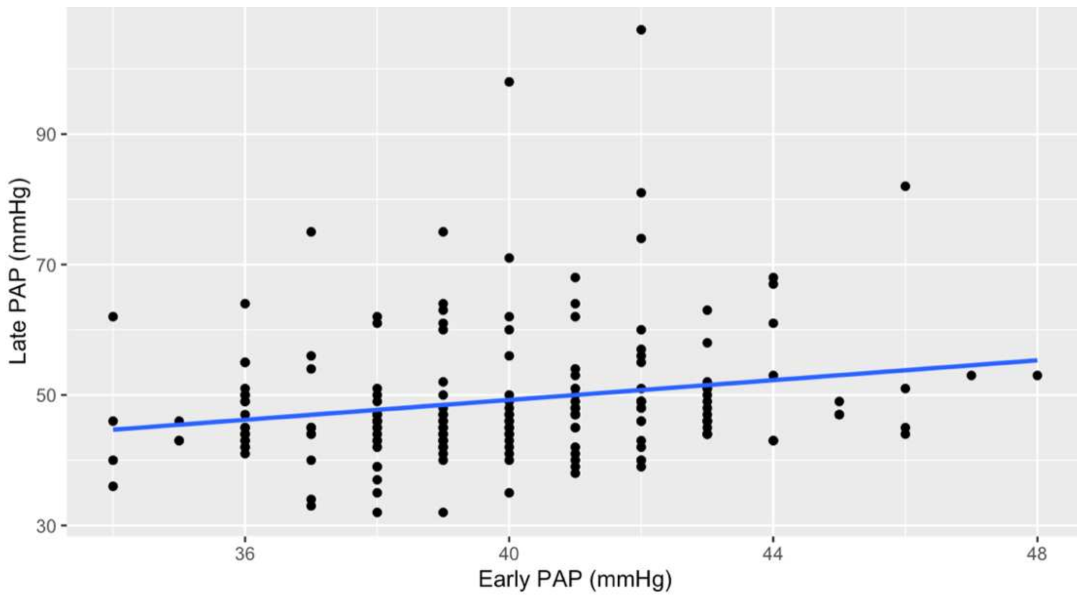

Figure 4.2: Plot of Early PAP (entering feedlot) and Late PAP (exiting feedlot) relationship on repeated measures on cohort of angus cattle at low elevation.

The overall rate of change between 9mo PAP and 14mo PAP was shown in Figure 4.2 which includes a slope of 0.76 between both recordings. Recalling our model and assigning these values, PAP at 14 months = 18.87 + 0.76*9month PAP measurement ± 0.27. The linear regression models overall revealed that there was a 0.76 increase in 14-month PAP for every increase in one unit of early PAP. This begins to display the relationship between the earlier and later measurements but was unlikely make accurate predictions for the cattle who rapidly increased in PAP at an above average rate. The phenotypic Pearson correlation was 0.20 between both traits.

Pulmonary arterial measurements are further indicated in Figure 4.3 by the time they were collected to show summary statistics in a box plot formation.

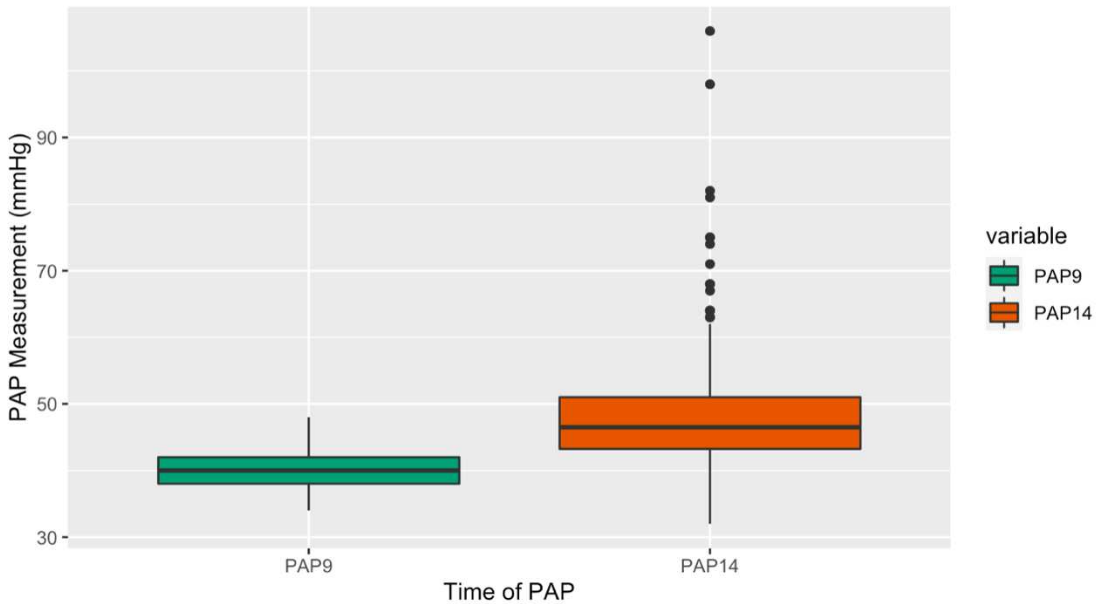

Figure 4.3: Individuals with PAP scores at 9 months and 14 moths represented in boxplot comparison to graph differences in group PAP scores as age increases and intense feeding regime commences.

As cattle continue to grow during the feeding period, PAP scores begin to increase and begin to have a larger interquartile spread showcasing more variability in PAP scored at the end of the feeding period versus the beginning of feeding period. This could be explained as cattle simply aging in this period and displaying higher PAP but a preliminary study analyzing the influence of altitude and age on pulmonary hypertension within cattle at varying altitudes and ages found age to be significant in altitudes greater than 2,500m, but not a factor in altitudes below (Will et al. 1975). These findings were echoed again by Neary et al. (2015) reporting that the altitude at which cattle are managed was positively associated with cattle age, meaning there was little age effect at lower altitudes, and a greater age effect at higher altitudes. Cattle at lower altitudes do not have increases in their PAP scores as they age, while cattle at higher altitudes usually experience significantly higher PAP scores the older the age. The cattle in this study were similar ages and Zeng et al. (2015) study further emphasized that PAP measurements before 10 months of age are found to be less predictable.

The previous Figure 4.3 was then separated by grouping unhealthy and healthy heart scores, scores 1 and 2 (healthy) versus 3+ scores (unhealthy), which cattle received at harvest using a visual grade scoring system. In the sample, 140 animals had a healthy heart score with 38 animals having unhealthy heart scores, leaving 21% of the sample displaying unhealthy heart remodeling at harvest. Examining Figure 4.4, the variation in the later mPAP assessment, unhealthy scores more variation and yields the highest recording of PAP measurement in the study. Overall, both groups had elevated mean PAP at 14 months showing that today's cattle have high risk for pulmonary hypertension and high PAP measurements, unhealthy heart scores just have even more extreme measurements. Heart score was associated with pulmonary arterial pressure, and similar findings were reported by Heffernan et al. (2020). Higher heart scores yielded higher mPAP averages, which was what Figure 4.2 supports. It was important to note that scores 1 and 2 are no to mild changes, and difficult to differentiate, but scores 3 and 4 consist of moderate to severe changes. These scores have more prominent identifiers when visually grading between the categories. These differences between 3 and 4 and their relationship to negative outcomes of heart remodeling are still not very known but reflected another breakdown of scores to be investigated.

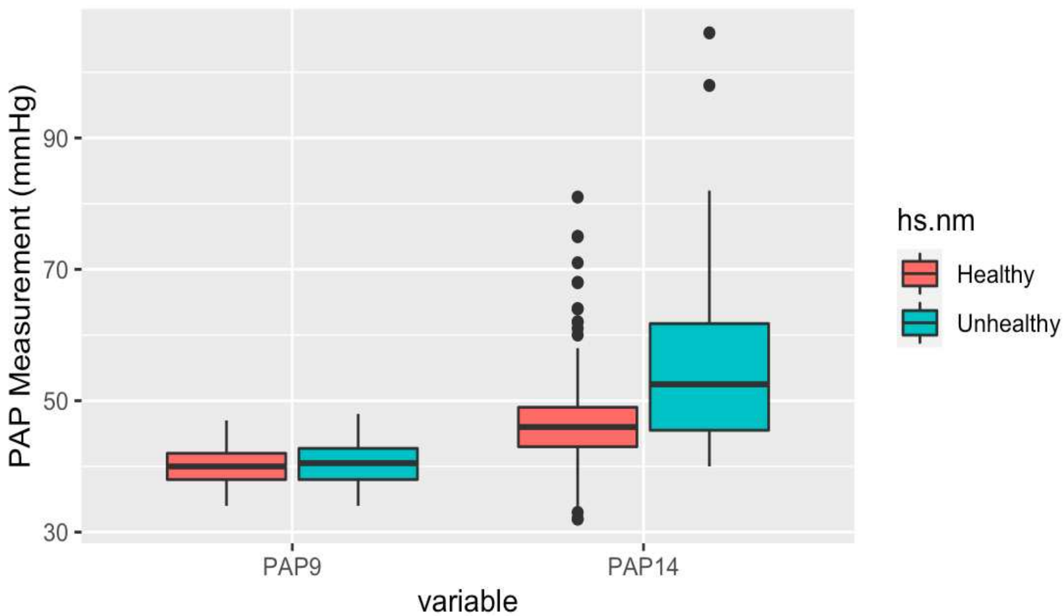

Figure 4.4: The PAP repeated measures on individuals at 9 and 14 months of age. The measurements are separated by healthy (1 and 2) and unhealthy scores (3+).

To examine the difference of variance between the power of individual scores the cattle were examined in Figure 4.5. Looking at individual heart scores, the differences between PAP scores assigned to score 3 animals and 4 had an even greater spread of variability within their data. Leading us to see how there would be a relationship between score and PAP measured at the end of the feeding period.

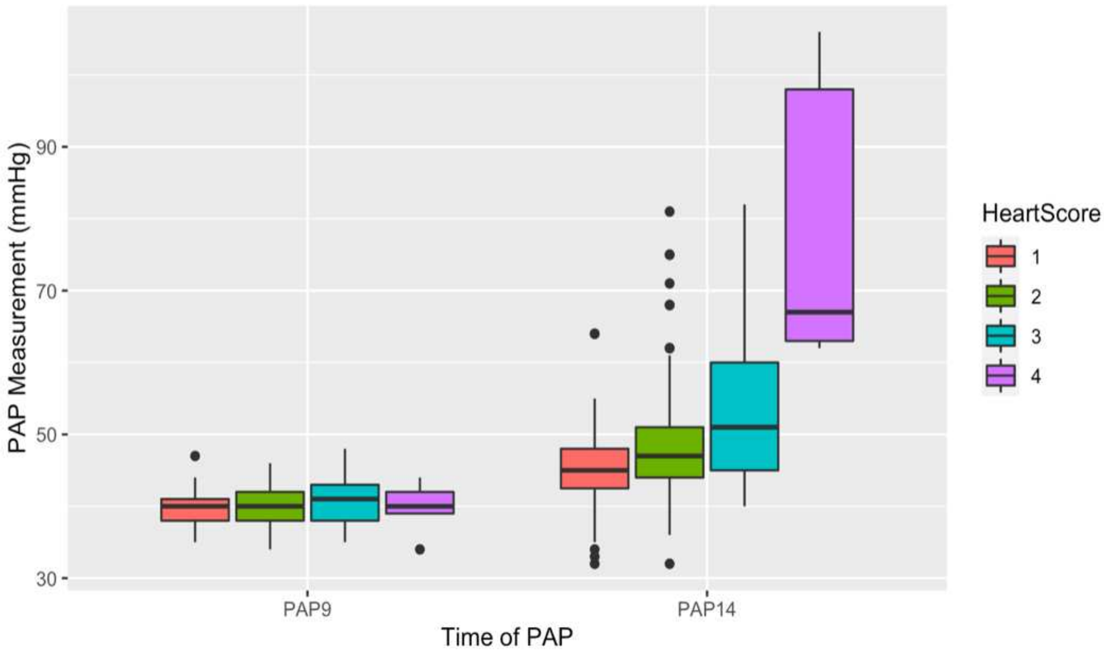

Figure 4.5: Repeated PAP measurements on individuals with 9 month and 14 month aged scores, examined by the individual heart score group at harvest.

Examining the scores, score 1 (n= 67), Score 2 (n = 73), Score 3 (n = 33), Score 4 (n = 5), Score 5 (n= 0). Early PAP measurements are as follows: score 1 mPAP 39.61 ± 2.47 mmHg; score 2, mPAP 39.82 ± 2.78 mmHg; score 3, mPAP 40.36 ± 3.47mmHg, and score 4, 39.89mmHg ± 3.76mmHg. Late PAP measurements scores are as follows: score 1 mPAP 45.27 ± 5.69 mmHg; score 2 mPAP 49.04 ± 9.43 mmHg; score 3 mPAP 52.55 ± 9.52 mmHg; and score 4 79.20 ± 21.09 mmHg. the summary statistics and boxplots, reveals that there was no difference between the heart scores at harvest and their PAP measurements at the beginning of the feeding period. It was unlikely that earlier PAP (unless extremely high PAP) would be a good indicator of heart score at harvest. The significance of Figure 4.5 was noting the differences between heart score and the PAP scores, this indicated a view area of investigation. The first conclusion would be that a 9-month-old PAP was unlikely to tell producers about overall susceptibility to feedlot heart disease. The second point would be that PAP scores of 14 months may be too late to take measurements to identify cattle but are indicative of heart score, especially scores 3 and 4. These scores had a larger variation of PAP scores and ultimately begin top contain higher measurements that are unhealthy to the cattle. This could not be said about the later PAP scores collected at the end of the feeding periods. A linear model with 9 month or 14 month PAP as the predictor and heart score and lot as the predictor variable was utilized to see the differences between heart scores in individuals who had repeated measures as shown in Table 4.2 and presented as least square means based on the previous linear model.

Table 4.2: Least Square means of early PAP (9mo) and later PAP (14mo) on 178 head of angus influenced cattle who had repeated measures of PAP scores in feedlot. Means are averaged over lots by ending heart score.

Heart Scores	Early PAP (mmHg)	Late PAP (mmHg)
1	39.8 ± 0.348	43.4 ± 1.396
2	40.0 ± 0.340	47.9 ± 0.926
3	40.3 ± 0.490	51.5 ± 1.289
4	40.1 ± 1.260	67.4 ± 2.374

In the early PAP, measured as cattle began the feeding period, there were no differences between any of the heart scores. This could show how PAP measurements taken too early may not be a good indication of how cattle will do throughout the feeding period. In a high-altitude study of the repeated measures of PAP in Angus cattle at 1,500m and 2,500m found that yearling PAP at a moderate altitude was an important predictor for high altitude PAP for bulls aging to 18mo (Zimprich et al., 2020). The cohort was measured around 9 to 10 months of age, which could mean these cattle are too young for PAP to be an adequate predictor. There was also varying differences on the elevation being much lower at 1,080m, which could mean as previously also shown in Neary et al. 2015, these early PAP measurements may not yet have enough variability to predict later PAP measurements and heart scores. Ideally, early PAP measurements when cattle enter the feeding phase would be able to display which cattle are at risk for feedlot heart disease, but unfortunately this does not seem to be the case.

Later PAP had multiple differences within their heart scores, which parallels heart scores' relationship to PAP. The biggest difference was among scores 4 and 1, where scores of 4 had a least square mean of 67.4 mmHg whereas scores 1 had 43.4 mmHg. This high PAP trend within the heart scores supports Heffernan et al. (2020) with drastic spikes in heart score 4. Overall, PAP scores drastically changed from the early PAP measurements to late PAP measurements on the cohort of cattle no matter which heart score group, promoting more questions on identifying animals that rapidly increase from early PAP to late PAP. Utilizing a linear regression and analysis of variance was used to determine any significant factors that contribute to early and late PAP variables. A sex effect was found to be important ($P < 0.05$) in the early PAP model when accounting for sex, PAP age and heart score. Steers in this group were found to have lower PAP scores than heifers with an estimate of -1.04. PAP age, and heart score added no significance to the model. Cattle had a standard deviation of 16 days of difference in age and about 38.64 kgs of difference in weight at the time of first PAP. Heart scores were collected at the time of harvest and have been found to be correlated with later PAP; therefore, this was found to be somewhat expected when analyzing early PAP scores. Later PAP scores, when using sex, PAP age, and heart scores as effects concluded that only heart score was significant to the model ($P < 0.01$). There were no sex effect and PAP age did not contribute to the model.

The difference between PAP scores was used to find the change for each individual animal from the first measurement of PAP to the second measurement of PAP. This change was considered the PAP difference between each individual animal. The summary statistics on this difference showed that the average PAP score increased by 9.28mmHg. The minimum difference was -7 mmHg, and the maximum was 64 mmHg. It was unlikely that a PAP score would drop as the cattle grow and age; however, it was difficult to say why this occurred within some cattle. Many factors can affect PAP score such as stress, improper measurements, human error while recording scores etc., but most cattle had an increase in PAP score. Healthy heart scores increased on average by 7.51 mmHg and unhealthy heart scores increased by 15.73 mmHg. Individual heart scores utilizing HSD Tukey multiple comparison of means indicated significant differences within PAP scores

Cattle that become at risk would be a result of how quickly PAP changed over the given length of time. PAP differences were divided by 155 days (length of time in between PAP measurements). This gave an average change per day unit and identifies animals that had a greater rate of change than others. Individual cattle varied from -0.05 to 0.41 mmHg per day change. The rate of change by PAP score was determined by BIF guidelines for under 4,000ft, with a slight change that any measure over 55mmHg would be considered a high reading, although steers in this study are very fat in comparison to cattle on high altitude rangeland who would appear leaner. PAP rate of change was organized by cattle who displayed low (<45mmHg), moderate (<55), and high (>55 mmHg) PAP measurements. Low (n =74) PAP cattle averaged 0.02 mmHg per day increase, moderate (n =70) averaged 0.05 mmHg per day change increase, and high (n= 34) averaged 0.17 mmHg per day increase. Simple linear models were used to study hot carcass weight, ribeye area, backfat, marbling, feed conversion rate, average dry matter intake, and average daily gain differences among our sample by using PAP rate as the predictor variable and lot as a contemporary group. In all the models, PAP rate was not found to be an important factor *($P > 0.05$).* Average dry matter intake did display a tendency ($P < 0.1$) with an regression coefficient estimate to be -6.10, meaning cattle who had higher PAP rates ate less dry matter. The differences between PAP measurements between a 155-day period showcased the stress the heart obtains within a five-month span. Although feedlot cattle are not able to utilize PAP EPD at their elevation, and instead PAP can only be used as a screening measure, and the timing of cattle entering the feedlot. There was still little known about the overall effect of these high PAP cattle have on their performance, at least, with this sample size it was inconclusive on what the overall impact would be phenotypically. It was important to note that although there were not any significant differences between increased PAP rate changes, these relationships may begin to become more apparent in each grouping of PAP change of rate, especially high-rate change.

CONCLUSION AND IMPLICATIONS

Since the documentation of brisket disease in 1915 by Newsom and Glover, pulmonary arterial pressure has aided to the decrease of incidence of brisket disease and can further help researchers understand more about feedlot heart disease. Limited research on PAP measurements at low to moderate altitudes yields new questions on PAP's overall usage for feedlot producers as a preventative tool for cattle at risk of early feedlot death. Pulmonary arterial pressure measurements entering the feedlot period were not indicative of PAP measurements taken at the end of the feedlot period. There was little correlation and little variability in entering PAP measurements, concluding that PAP may not be as useful at identifying the cattle that are unable to maintain growth and performance demands. Pulmonary arterial pressure was also seen to change more rapidly in some individuals more than others. This means that at some point in the intensive feeding period, individuals begin rapidly increasing between time periods. It may be possible in the future to determine genetically which cattle may be more prone to these drastic increases more than others. Late PAP measurements and the rate of change between PAP could be correlated with heart scores, and in turn show more evidence to the implementation of heart scores practical use in the feedlot sector to development a cardiovascular fitness EPD to provide to feedlot management practices.

LITERATURE REVIEW

American Angus Association. 2019. Research PAP EPD launched by Angus Genetics Inc. Available from https://www.angus.org/Pub/Newsroom/Releases/020119-pap-epd-launch.aspx [accessed May 6, 2022].

BIF. 2019.*Guidelines: Pulmonary Arterial Pressure. 9th ed.* Beef Improvement Federation.

Dixon A.E., Peters U. The effect of obesity on lung function. 2018. *Expert Rev Respir Med*.12(9):755-767. doi: 10.1080/17476348.2018.1506331.PMID: 30056777.

Heffernan, K.R., M. G. Thomas, R. M. Enns, T. N. Holt, S. E. Speidel. 2020. Phenotypic relationships between heart score and feed efficiency, carcass, and pulmonary arterial pressure traits, Translational Anim. Sci. 4(1):S103–S107. doi:10.1093 tas/txaa114

Holt T., Callan R. 2007. Pulmonary Arterial Pressure Testing for High Mountain Disease in Cattle. Veterinary Clinics of North America: Food Animal Practice. 23(3):575-596. Doi:10.1016/j.cvfa.2007.08.001

Neary, J., Garry F., Holt T., Krasfur G., Morley P.,Brown R., Stenmark K., Thomas M., Enns R. 2015a. High Altitude Disease, PAP, Feedlot hypertension, and Respiratory Issues. The Range Beef Cow Symposium XXIV Proceedings.

Neary J. M., Garry F. B., Holt T. N., Brown R. D., Stenmark K. R., Enns R. M., and Thomas M. G. 2015b. The altitude at which a calfwasborn and raised influences the rate at which mean pulmonary arterial pressure increases with age. *J. Anim. Sci*. 93:4714–4720. doi:10.2527/jas.2015-9217

Neary J., Booker C., Wildman B., Morley P. 2016. Right-Sided Congestive Heart Failure in North American Feedlot Cattle. J Vet Intern Med. 30(1):326-34. doi: 10.1111. PMID: 26547263; PMCID: PMC4913666.

RStudio Team (2020). RStudio: Integrated Development Environment for R. RStudio, PBC, Boston, MA URL

Stehle A., Peel Breedlove D.S. Riley J.M. 2018. A profile of Cattle Feeding: Above the Averages. *AgEcon Search*. Western Economics Forum.

Will D.H., Hicks J.L., Card CS, Reeves J.T., Alexander A.F. 1975Correlation of acute with chronic hypoxic pulmonary hypertension in cattle. *J Appl Physiol*. 38:495–8.

Zeng, X, R. M. Enns, S. E. Speidel, M. G. Thomas. 2015. Angus Cattle at High Altitude: Relationship Between Age and Pulmonary Arterial Pressure. In: Proc. West. Sec. Am. Soc. Anim. Sci. 66:119–121.

Zimprich T., Speidel S., Schafer D., LaShell B.,Holt T., Enns R., Cunningham S., Thomas M. 2020. 276 Repeated Measures of PAP at Different Elevations in Beef Bulls in Colorado, *Journal of Animal Science*, 98(4):205–206, doi:10.1093.

CHAPTER 5 HERITABIITY OF HEART SCORES AND GENETIC CORRELATIONS WITH CARCASS TRAITS

SUMMARY

Feedlot cattle experience pulmonary hypertension risks as feedlot heart disease prevalence continues in low to moderate altitude production systems. With little explanation on the cause, cattle with severe pulmonary hypertension risk experience early feedlot death, poor performance, and health complications. The factors that cause pulmonary hypertension in fattening cattle are unknown, and irreversible once pulmonary hypertension begins. High altitude disease has been developed PAP as an indicator trait. This gave producers a tool to utilize for breeding selection decisions, but feedlot producers lack this tool at their elevations. For this reason, the development of heart score was created to potentially create a new set of criteria for evaluating heart health post-harvest to than make predictions on future breeding decisions. Calculating estimated progeny differences for sires could be done in the future with heart scores but before that, a development of the heritability and phenotypic correlations needed to be performed before genetic improvement can be accomplished. In this study of 1,506 head of cattle, heritability and genetic correlations with carcass traits were estimated given the following dataset. There were 88 Angus sires in these analyses. Information included traits of performance, carcass, and cardiovascular categories. The objective of this study was to:

1. Determine genetic correlations and covariances among phenotypic traits of interest and heart score.
2. Calculate heart score's heritability in multi trait animal model.

INTRODUCTION

High altitude cattle with cases of pulmonary hypertension often worsen in the constant hypoxic environment but for cattle at low to moderate altitude there was little explanation of why pulmonary hypertension would be observed. If not, a true high altitude induced hypoxic environment, then another reason must be intertwined specifically within growing, and fattening cattle. The American Angus Association introduced a PAP EPD (American Angus Association, 2020) to be used for sire selection for reducing pulmonary hypertension risk in cattle. This selection tool was brought on by PAP's moderate heritability which was found to be 0.24 to 0.34 (Crawford et al. 2016; Briggs et al.,2020; Pauling et al. 2018) and its minimal influence on growth traits meaning selecting for lower PAP bulls while maintaining selection performance standards (Crawford et al. 2016 and Shirly et al. 2008). Although producers in high altitude systems can select for PAP, collection of data may prove to be difficult for some since the procedure requires the insertion of a catheter into the jugular vein by a licensed and BIF certified veterinarian. From there, the catheter was fed into the right atrium, right ventricle, to the pulmonary artery where the measurement was taken (Holt and Callan, 2007). This process can be costly, labor intensive, and may not be a feasible option for all high-altitude producers, impeding the ability to collect data on PAP. At low to moderate altitudes, PAP measurements can only be used to identify high risk animals and has not been used a selection tool. As elevation increases, PAP measurements increase as the animal was adjusting and may or may not change. Therefore, it was not indicative of which animals will experience feedlot heart disease rather an indication of which animals are at risk of high-altitude disease. (Holt and Callen, 2007). To find a solution for feedlot heart disease, the development of a Gross Visual External Cardiac Evaluation System provided by Dr. Tim Holt of Colorado State Veterinary Teaching Hospital as presented in Heffernan et al. (2020), aims to record the morphology of the heart in feedlot cattle at harvest. The foundational research provided positive results for heart score's success in recording the severity of heart remodeling in harvested cattle. Following this research, an investigation of the sire differences within heart scores looked for the potential genetic relationship of the trait. The conclusive result of sire differences of heart scores suggested the further investigation of heart scores heritability and its correlations with performance and carcass traits (Kukor et al. 2021). Using a larger data set, the heritability and correlations of genetic and phenotypic information concluded with the hypothesis that similarly to PAP, heart score would have a moderate heritability with similar correlations between HS/PAP/phenotypic traits of interest reported by (Heffernan et al., 2020; Jennings et al., 2019; and Thomas et al., 2019).

MATERIAL AND METHODS

The data set in this study included 1,507 animals. Data were collected on multiple cohorts of cattle from Cactus Feed yard in Canyon, Texas during the years 2020-2022 (elevation ~1,080m). All animals in the study were Angus influenced and included heifers (n = 712) and steers (n = 793). Each trait had differing numbers of individuals collected within phenotypes (i.e. Hot Carcass Weight, Ribeye Area, Marbling Score, Back Fat, PAP, Heart Score) as shown in Table 5.1.

Table 5.1: Summary statistics for phenotypic data collected in study.

Trait	n	mean	SD	Min.	Max.
Heart Score	1,422	2.13	0.79	1.00	4.00
PAP (14mo) mmHg	362	49.61	12.91	32.00	151.00
Back Fat (mm)	1,445	18.03	5.33	4.06	41.66
Marbling Score	1,445	500.95	101.73	0.00	952.00
Hot Carcass Weight (kg)	1,454	403.38	50.30	213.64	560.64
Ribeye Area(mm^2)	1,445	9141.91	929.03	5374.18	12619.33

All cattle were fed similar diets in feedlot with no differences in their nutritional management. The dataset was cleaned utilizing only animals with heart score information, totaling 1,422 animals heart scores. The total pedigree size included in this model was 1592. There were 88 Angus sires and 0 records of the dams. The simple, single trait mixed model is shown below:

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Zu} + \boldsymbol{e}$$

Where y was the vector of observations (HCW, REA, etc.), X was a known incidence matrix relating observations in y to unknown fixed effects in β, β represented the vector of unknown fixed effects (harvest date, sex, and harvest age), Z represented the incidence matrix for relating random effects in u to y observations, u represented the direct additive genetic effects due to additive gene action, e represented the residual error in the model. In the model for this dataset, harvest date, sex, and harvest age were the fixed effects, individual id were the random effect, and heart score was the y vector.

Multi trait model expands the model to include all six traits of interest to be solved simultaneously and allowed covariances between traits to be calculated. Multi Trait BLUP model was expanded upon below:

$$\begin{bmatrix} y_1 \\ y_2 \\ y_3 \\ y_4 \\ y_5 \\ y_6 \end{bmatrix} = \begin{bmatrix} X_1 & 0 & 0 & 0 & 0 & 0 \\ & X_2 & 0 & 0 & 0 & 0 \\ & & X_3 & 0 & 0 & 0 \\ & & & X_4 & 0 & 0 \\ & \text{Sym} & & & X_5 & 0 \\ & & & & & X_6 \end{bmatrix} \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \\ b_5 \\ b_6 \end{bmatrix} + \begin{bmatrix} Z_{a1} & 0 & 0 & 0 & 0 & 0 \\ & Z_{a2} & 0 & 0 & 0 & 0 \\ & & Z_{a3} & 0 & 0 & 0 \\ & & & Z_{a4} & 0 & 0 \\ & \text{Sym} & & & Z_{a5} & 0 \\ & & & & & Z_{a6} \end{bmatrix} \begin{bmatrix} u_{a1} \\ u_{a2} \\ u_{a3} \\ u_{a4} \\ u_{a5} \\ u_{a6} \end{bmatrix} + \begin{bmatrix} e_1 \\ e_2 \\ e_3 \\ e_4 \\ e_5 \\ e_6 \end{bmatrix}$$

Notation on the single trait was constant with the notation in multi trait. The same fixed effects were utilized in this model across traits. There was extremely limited dam information which was why the availability to test for maternal effects was not yet conducted in the analyses. Similarly, to our single trait model, the multi-trait model was expanded where y_i represented the vector of observations for each ith trait, X_i represented the incidence matrix for fixed effects relating to the ith trait, b_i represented fixed effect solutions for ith trait in y observation, Z_{ai} represented the incidence matrix for random additive effects for ith trait, u are the solutions for the random additive effects to the observations and e_i are the residual errors for each trait.

Within the multi trait model there was the availability to establish covariances for both additive genetic effects and residual covariances as follows:

Genetic covariances

$$\mathrm{VAR}\begin{bmatrix} u_{a1} \\ u_{a2} \\ u_{a3} \\ u_{a4} \\ u_{a5} \\ u_{a6} \end{bmatrix} = \begin{bmatrix} \sigma_{a1} & \sigma_{a1a2} & \sigma_{a1a3} & \sigma_{a1a4} & \sigma_{a1a5} & \sigma_{a1a6} \\ & \sigma_{a2} & \sigma_{a2a3} & \sigma_{a2a4} & \sigma_{a2a5} & \sigma_{a2a6} \\ & & \sigma_{a3} & \sigma_{a3a4} & \sigma_{a3a5} & \sigma_{a3a6} \\ & & & \sigma_{a4} & \sigma_{a4a5} & \sigma_{a4a6} \\ & & & & \sigma_{a5} & \sigma_{a5a6} \\ & & & & & \sigma_{a6} \end{bmatrix} \otimes A$$

Residual Covariances

$$\mathrm{VAR}\begin{bmatrix} e_{1} \\ e_{2} \\ e_{3} \\ e_{4} \\ e_{5} \\ e_{6} \end{bmatrix} = \begin{bmatrix} \sigma_{e1} & \sigma_{e1e2} & \sigma_{e1e3} & \sigma_{e1e4} & \sigma_{e1e5} & \sigma_{e1e6} \\ & \sigma_{e2} & \sigma_{e2e3} & \sigma_{e2e4} & \sigma_{e2e5} & \sigma_{e2e6} \\ & & \sigma_{e3} & \sigma_{e3e4} & \sigma_{e3e5} & \sigma_{e3e6} \\ & & & \sigma_{e4} & \sigma_{e4e5} & \sigma_{e4e6} \\ & & & & \sigma_{e5} & \sigma_{e5e6} \\ & & & & & \sigma_{e6} \end{bmatrix} \otimes I$$

A represented Wright's numerator relationship matrix, σ_{ai} represented the additive genetic variance for the ith trait, σ_{aij} described the additive genetic covariances between ith and jth trait. Similar to the variance of additive genetic effects, the variance of residual effects was as follows, *I* was an identity matrix whose order was equal to the number of observations in y, σ_{ei} was the variance of residual error for ith trait, and σ_{eij} was the covariance between residual error of ith and jth trait. The Knonecker product operator was denoted by ⊗. Heritability and correlations were estimated using the statistical software package ASREML. Heritability was calculated for each trait utilizing genetic variance divided by phenotypic variance (phenotypic variance = genetic + residual error). Correlations were calculated by the following equation:

$$\frac{COV(a_{ij})}{\sqrt{VAR(a_i) \times VAR(a_j)}}$$

The same equation can be used to calculate the residual correlation as well as phenotypic correlations in the model. The Animal Breeding Toolkit (ABTK) **(Golden et al., 1995)** within the Center of Genetic Evaluation of Livestock, and ASReml **(Gilmour et al. 2009)** were used for the estimation of heritability for heart scores and all other traits in the data set. Heritability estimates were in conjunction with using ASReml 3.0 and animal breeder's toolkit,

RESULTS AND DISCUSSION

Knowing the heritability of heart score may prove to be a positive indication of the use of heart score as a phenotype to make breeding selection decisions. Utilizing an animal model, a moderate heritability was observed at 0.28 ± 0.10. Wald F tests suggested that harvest date and sex were significant fixed effects in the model ($P < 0.05$). Each harvest date only contained two lots. Each lot was separated by sex providing a set of contemporary groups without including lot in the model. The result of a moderate heritability for heart score indicates that there could be a potential to use this phenotype for genetic selection which breeding decisions can be done to select for cattle with healthy heart scores.

Research confirmed that heart score was important to mean PAP scores, with the heart scores of 1,2,3 being relatively similar but scores of 4 had an average 27 mmHg higher than those of the previous three scores (Heffernan et al. 2020). Noting the relationship between high, PAP scores and heart scores, there was an assumption of a strong genetic correlation between the two traits. A potential issue between comparing high altitude PAP literature and low altitude studies lies in PAP heritability's variation with the elevation in which animals are measured and housed at. Speidel et al. (2019) stated that lower elevations often yielded lower heritability estimates, compared to high elevation measurements. This same relationship between elevation and heart score could also exist but would be unable to be captured in this low elevation study. However, the heritability estimate can only be determined for cattle at elevations of approximately 1,100m within this study. Further analysis would need to be conducted to determine the range of heritability estimates for heart score. PAP heritability was found to be 0.29 ± 0.16, see Table 5.1, and has been reported in literature to range from 0.22 to 0.39 (Speidel et al., Shirley et al., AAA 2022) showcasing the PAP estimate to be within range. Carcass traits displayed moderate to high heritability estimates in our data set which are also in line with literature ranges. As shown in Table 5.1, Hot Carcass Weight (HCW), Ribeye Area (REA), Backfat Thickness(BF), and Marbling (MARB) had estimates of 0.61 ± 0.14, 0.43 ± 0.13, 0.60 ± 0.14, and 0.45 ± 0.13, respectively.

A beef carcass study review combined 72 papers for overall heritability estimates of carcass traits and found on average backfat (h^2 = 0.36), carcass weight(h^2 =0.40), and marbling score (h^2 = 0.37). Although researchers noted that heritability estimates vary based on what was included in the overall model (Utrera et al. 2004), a more recent study looked at heritability between five different breeds of beef cattle in Europe (Aberdeen Angus, Charolais, Limousin, Hereford and Simmental) and found carcass weight to have a heritability of 0.39 across breeds but overall Angus tended to have the highest heritability of 0.51 (Kause et al. 2014). Lastly, ribeye area heritability estimates tended to be higher with reports of Angus sired steers reaching a heritability estimate of 0.59 (Minick et al., 2001), which was almost identical to our single trait heritability estimate of ribeye area based on the Angus influenced cattle in this study. Overall, heritability assessed by the American Angus Association (2022) displays the overreaching heritability estimates for a multitude of traits. Pulmonary arterial pressure, HCW, backfat, marbling score, and ribeye area have the respective heritability estimates 0.39, 0.44, 0.33, 0.48, and 0.32. It was difficult to compare heritability estimates of cattle raised in varying environments, breeds, ages, etc, but based on literature and what was known about our controlled environment, these heritability estimates can be supported.

Genetic correlations and residual correlations are presented in the Table 5.2. Genetic correlations are above the diagonal, residual correlations are below the diagonal, and heritability estimates are along the diagonal.

Table 5.2: Genetic and residual correlations among traits. Genetic correlations are above the diagonal and residual correlations are below the diagonal. Across the diagonal are the heritability estimates for this model.

Trait[1]	HS	PAP	HCW	BF	REA	MARB
HS	0.28 ± 0.10	0.94 ± 0.17	0.63 ± 0.20	0.15 ± 0.24	0.27 ± 0.22	0.07 ± 0.24
PAP	0.14 ± 0.12	0.29 ± 0.16	0.66 ± 0.25	0.28 ± 0.29	0.15 ± 0.30	0.05 ± 0.30
HCW	-0.39 ± 0.20	-0.48 ± 0.27	0.61 ± 0.14	0.41 ± 0.16	0.51 ± 0.13	0.29 ± 0.18
BF	-0.07 ± 0.12	-0.11 ± 0.16	0.63 ± 0.13	0.43 ± 0.13	-0.24 ± 0.19	0.35 ± 0.19
REA	-0.28 ± 0.16	-0.19 ± 0.21	0.52 ± 0.18	0.15 ± 0.20	0.60 ± 0.14	-0.17 ± 0.19
MARB	-0.17 ± 0.12	-0.12 ± 0.15	0.41 ± 0.17	0.40 ± 0.13	0.31 ± 0.21	0.45 ± 0.13

[1]HS= heart score, PAP= pulmonary arterial pressure, HCW= hot carcass weight, BF= backfat thickness, REA= ribeye area, MARB= marbling score

Heffernan et al. (2020), described similar results with PAP relationship to heart score being positively related although, there are no current studies that describe the genetic correlation between these traits. Pauling et al., (2017) presented the genetic correlation between PAP and ultrasound backfat, intramuscular fat, and ultrasound ribeye area to be −0.03 ± 0.12, −0.04 ± 0.10, and 0.24 ± 0.12, respectively. These results are different than what was shown in PAP's genetic correlation within the study. Partially, again, these may be inconclusive due to the limited data available for PAP measurements. There are also differences in time of collection, one key difference being that these carcass characteristics were collected at a year of age and included both bulls and heifers, rather than steers. Cattle at a year old would be halfway through their feeding period, therefore not all potential growth was captured through ultrasound at 12months. As cattle continue in the feeding regime, more weight, adiposity, and cardiovascular stress would be present and different physiological challenges would be present for longer on 14-month-old cattle versus 12 months.

Similarly, heart score showcased a weak trend in its genetic correlations of 0.15± 0.24 (backfat), 0.07 ± 0.24 (marbling), and 0.27 ± 0.22 (ribeye area). The larger backfat, ribeye, and marbling characteristics lead to heavier muscled individuals, and these individuals could structurally be different than previous genetic selection goals due to the new addition of selection for excess weight caused by more muscling rather than tall structure size as seen in the late 1900s, in addition to the increased payments for increased muscling and fat. A more extreme case of heavier muscling was within double muscled cattle, who have been found to be less efficient in cardiovascular fitness as displayed in Amory et al. (1992). Findings in this study displayed a similar narrative of heavier cattle have an increase in PAP and increase in heart score, meaning these larger cattle are likely to have problems with pulmonary hypertension.

Based on the heritability and genetic correlations, affected cattle appeared to be heavier muscled cattle especially those selected for increase carcass traits. These cattle could be identified as the genetically superior individuals but are more likely to be predisposed to feedlot heart disease.

CONCLUSION AND IMPLICATIONS

Selection for heart score could prove to include more significant relationships to economically relevant traits such as hot carcass weight, and ribeye area. Although, selecting for lower heart scores will most likely not decrease marbling, carcass weights, and favorable carcass traits at a drastic rate, its moderate heritability allows for the selection of better cardiovascular fitness without a steep decline of economically relevant traits. Furthermore, the addition of heart scores in breeding decisions minimizes the potential risk of pulmonary hypertension for feedlot cattle reducing overall early feedlot death. Since the risk of pulmonary hypertension for high altitude was not fully expressed until sires or progeny are moved to these known altitudes, more research of how to bridge pulmonary hypertension occurrences with the utilization of heart scoring visual grading systems could be utilized with PAP to predict at risk cattle for feedlot heart disease at low to moderate elevation. In summary, heart score was moderately heritable, displaying a positive relationship for use in future selection goals. PAP and heart score research have weak to moderate correlations with carcass traits. Traits such as ribeye and hot carcass weights had some of the highest correlations with PAP and heart score. Heart score and PAP although highly correlated with each other did not display the same correlations with the traits, with heart score showcasing results similar to what PAP research has shown. Measurements of PAP may not be in enough abundance in this sample size to deduce accurate estimates. With a larger dataset, a more accurate depiction of these relationships should become more evident and provide a step towards developing a selection tool for feedlot heart disease.

The information in this study was important because this was the first genetic analysis and report of a heart trait for feedlot heart disease with promising results of being able to select for healthier cattle. With little to no options for feedlot cattle experiencing pulmonary hypertension complications, making breeding decisions to reduce the chance may be one of the only sustainable practices to consider for producers struggling with these devastating occurrences within their herd. The genetic correlations of support similar findings that drove the creation of PAP EPDs. Profits within the beef industry are not only driven by carcass qualities at processing facilities but also by simply whether animals born make it to their projected harvest date.

LITERATURE CITED

American Angus Association. 2019. Research PAP EPD launched by Angus Genetics Inc. Available from https://www.angus.org/Pub/Newsroom/Releases/020119-pap-epd-launch.aspx [accessed May 6, 2022].

American Angus Association. 2022. Angus National Cattle Evaluation: Fall 2022. Available from https://www.angus.org/Nce/Heritabilities [accessed August 6, 2022].

Amory H., Rollin F., Desmecht D., Linden A., and] Lekeux P. 1992. Cardiovascular response to acute hypoxia n double muscled calves. *Research in Veterinary Science,* 52(3): 316-324. doi: 10.1016/0034-5288(92)90031.

Briggs, E. A., Enns, R. M., Thomas, M. G., & Speidel, S. E. 2019. Genetic and phenotypic parameter estimates for feed intake and pulmonary arterial pressure. *Translational animal science*, *3*:1, 1655–1657. https://doi.org/10.1093/tas/txz049.

Crawford N. F., Thomas M. G., Holt T. N., Speidel S. E., and Enns R. M.. 2016. Heritabilities and genetic correlations of pulmonary arterial pressure and performance traits in Angus cattle at high altitude. J. Anim. Sci. 94:4483–4490. doi:10.2527/jas.2016-0703.

Gilmour A. R., Gogel B. J., Cullis B. R. and Thompson R.. 2009. ASReml user guide. Release 3.0. Hemel Hempstead (UK): VSN Int. Ltd

Golden, B.L., Snelling W.M., and Mallinckrodt C.H. 1995. Animal Breeder's Tool kit 2.0. User's Guide and Reference manual. Department of Animal Sciences. Colorado Sta University. Fort Collins, CO.

Kause A., Mikkola L., Strandén I., and Sirkko K. 2014. Genetic parameters for carcass weight, conformation, and fat in five beef cattle breeds. *The Animal Consortium.*9:1(35-42). doi:10.1017/S1751731114001992

Kukor I.M. , Thomas M.G., R Enns M.R., Holt T., Speidel S.E., Cleveland M.A., Holland B.P., Word A.B., Ellis G.B. 2021. Sire differences within heart and heart fat score in beef cattle, *Translational Animal Science*, 5(1): S149–S153, https://doi.org/10.1093/tas/txab147

Speidel S.E., Thomas M.G., Holt T., and Enns R.M. 2020. Evaluation of sensitivity of pulmonary arterial pressure to elevation using a reaction norm model in Angus Cattle. *J. Anim. Sci*. 98(5).

Holt T. N., and Callan R. J.. 2007. Pulmonary arterial pressure testing for high mountain disease in cattle. Vet. Clin. North Am. Food Anim. Pract. 23:575–596, vii. doi:10.1016/j.cvfa.2007.08.001

Heffernan, K. R., M. G. Thomas, R. M. Enns, T. Holt, and S. E. Speidel. 2020. Phenotypic relationships between heart score and feed efficiency, carcass, and pulmonary arterial pressure traits. Transl. Anim. Sci. 4(Suppl. 1):S103–S107. doi:10.1093/tas/txaa114

Jennings K. J., Krafsur G. M., Brown R. D., Holt T. N., Coleman S. J., Enns R. M., Speidel S. E., Stenmark K. R., and Thomas M. G.. 2019. Pulmonary hypertension in Angus steers: influence of finishing systems and altitudes. J. Anim. Sci. 96(Suppl 3):87. doi:10.1093/jas/sky404.192

Minick J.A., Wilson D.E., Dikeman M.E., and Pollak E.J. 2001. Heritability and Correlation Estimates of Carcass Data from Angus-Sired Steers. Beef Research Report 2001. Iowa State University.

Pauling R. 2017. Pulmonary arterial pressure in angus cattle: environmental influences and relationship with growth and carcass traits ProQuest. Dissertations Publishing [accessed April, 2022] http://search.proquest.com/docview/1975772534/?pq-origsite=primo.

Pauling R.C., Speidel S.E, Thomas M.G., Holt T.N., and Enns R.M. 2018. Elevation of moderate to high elevation effects on pulmonary arterial pressure measures in Angus cattle. *Journal of Animal Science.* 96(9): 3599-3605.

Thomas M. G., Culbertson M. M., Holt T., Brown R. D., Krafsur G. M., Speidel S. E., Enns R. M., Bowen R., Li M., and Stenmark K.. 2019. Metabolism and inflammation predict cardiopulmonary disease outcomes in fattening beef cattle. Animal model. In: 100th Conf. Res. Workers Anim. Disease, P165, Chicago, IL: USDA-NIFA; November 3–5, 2019.

Shirley K. L. Beckman D. W. Garrick D. J. 2008. Inheritance of pulmonary arterial pressure in Angus cattle and its correlation with growth. J. Anim. Sci.86:815–819. doi:10.2527/jas.2007-0270

R Core Team. 2019. R: a language and environment for statistical computing. Vienna (Austria) R Foundation for Statistical Computing. https://www.R-project.org/.

Utrera A.R. and Van Vleck L.D. 2004. Hertiability estimates for the carcass traits of cattle: A review. *Genetics and molecular research.* 3(3): 380-394. PubMed.