INTRODUCTION

Pulmonary arterial pressure (PAP) is a measure for pulmonary hypertension (PH) and is used to determine an individual’s susceptibility to high altitude disease (HAD), a consequence of reduced oxygen from the higher elevations and the potential inefficiencies of the modern bovine cardiopulmonary system. Right-sided heart failure that results from hypoxia at altitudes greater than 1,500 m is a common pathophysiological observation of HAD (Thomas et al., 2018). High altitude disease initiates pulmonary arterial remodeling, which ultimately results in death. Past research suggests that PAP measurements are moderately heritable, which is important when selecting bulls for high-altitude beef production systems (Shirley et al., 2008; Crawford et al., 2016; Pauling et al., 2018; Speidel et al., 2020). High-altitude beef production systems produce approximately 1.5 million calves per year. With HAD having an incidence rate of 3%–5%, complications from this disease would result in more than 75,000 animals affected (Holt and Callan, 2007; Williams et al., 2012). An issue with utilizing PAP as an indicator of susceptibility to HAD is the accuracy based on the varying altitudes where PAP was initially collected and age of the individual (Pauling et al., 2018; Speidel et al., 2020). The most accurate testing age for PAP is approximately 18 months at an elevation above 1,524 m; however, given the management of most beef production systems, PAP measurements are typically collected prior to 16 mo age and often at moderate altitude. Bull and heifer development procedures for most beef production systems typically PAP test cattle at approximately 1 yr of age (culling of animals with measurements > 50 mmHg; BIF, 2020).

The American Angus Association published the first breed-wide estimated progeny differences (EPD) for PAP (Pauling et al., 2018; American Angus Association, 2020). Development of EPD with an acceptable accuracy requires phenotypic information from a sire’s progeny. There are limited studies of breed differences in PAP. The plethora of data needed for a breed conclusion was not possible in these initial studies. Due to the need for data in estimation of EPD, PAP information from moderate and low altitude may be necessitated. The AAA evaluated PAP using data from moderate elevations as a correlated trait to high-elevation PAP EPD (Pauling et al., 2018). This study reported a genetic correlation of 0.83. This was the first study that reported the relationship of PAP at various elevations. Therefore, there is need to learn more about PAP and the sources of variation (breed, age, altitude, sire, etc.) that may influence breeding value estimations. With
expected progeny differences (EPD) for PAP measurement becoming available through breed associations, it is important to determine the implications of low to moderate elevation of PAP measurements on overall usefulness in estimating high-altitude PAP EPD and for the movement of bulls to and/or from moderate and high elevations.

A portion of the data herein was based on five-different PAP measurements collected from bulls in 2018 (Zimprich et al., 2020). The authors observed dynamics of PAP with changing elevation. The current study evaluates whether yearling PAP at moderate altitude is predictive of later life PAP measurements at high altitude, and the effectiveness of this measure in predicting PAP measured at a much higher elevation. This project’s over-arching goals were to determine if a bull’s high-altitude PAP can be predicted by a yearling measurement at moderate elevation using a linear model approach.

We are also determining the impact of changing altitude on a bull’s PAP measurements, the relationship between PAP at moderate altitude (1,525 m) to PAP at high altitude (2,470 m), and if the time an animal resides at high altitude influences the prediction.

MATERIALS AND METHODS

This study obtained approval from the Colorado State University Animal Care and Use Committee under protocol number 16-6757AA.

Cattle and Data

Pulmonary arterial pressure was measured on Angus and Hereford bulls (n = 48 and n = 41, respectively) at different ages and elevations as the bulls progressed from yearling to approximately 16 mo of age. Cattle were born at an elevation of 1,525 m located at Colorado State University’s Agricultural Research, Development, and Education Center (ARDEC) facility in Fort Collins, CO. Bulls used in this study were calved in the spring months ranging from March to May in 2017, 2018, and 2019. Post-weaning bulls were fed a typical gain test ration targeting 1.5 kg/d. Subsequently, bulls were moved to Fort Lewis College (Hesperus, CO) at an elevation of 2,470 m from June to August/September 2017, 2018, and 2019 where they grazed irrigated pasture, gaining about 0.5 kg/d. The bulls then returned to ARDEC in September of their respective years. Three mPAP measurements were collected from each bull over this time period: 1) yearling PAP at ARDEC, 2) after acclimating to high altitude (FLC), and 3) before returning to ARDEC from FLC. Bulls were acclimated to each elevation for at least 21 d according to the procedure described in Holt and Callan (2007). Each year, there was about 42 d between the yearling PAP observation and the high-altitude PAP observation 1; there was approximately 70 d between high-altitude PAP observation 1 and high-altitude PAP observation 2.

Data used in these analyses consisted of breed, sire, mean PAP (mPAP) measures, elevation, and age. These data are described in Tables 1 and 2. All PAP records (n = 234) were collected by T.N. Holt D.V.M (College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO) using procedures described in Holt and Callan (2007).

Statistical Analysis

Model selection was completed using a step-wise regression approach to determine the most important terms to be included in the model. The model utilized was as follows:

\[ y_i = \mu + \text{Age}_i + \text{Yearling PAP}_i + e_i \]

where \( \text{Age}_i \) was the days in age of the individual bull at high-altitude PAP observation, \( \text{Yearling PAP}_i \) was the individual’s yearling PAP measurement, and \( e_i \) was the residual specific to individuals with observations. The statistical software packages of R and ASReml 3.0 (Gilmour et al., 2009) were used to test differences in high-altitude mPAP within individuals at different ages accounting for the individual’s yearling PAP observation. ASReml was used to determine predicted PAP values. Fixed effects included in the analyses consisted of age of each animal at each collection date (in days), yearling PAP at moderate elevation, and breed. Higher orders of the fixed regression for both high-altitude PAP models were considered but did not account for additional variation in PAP (\( P > 0.05 \)). Contemporary groups were considered but did not account for variability in the dependent variable.

Table 1. Summary statistics of Angus bulls (arithmetic means)

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Average age (d) ± SD</th>
<th>N</th>
<th>Mean (mmHg)</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ARDEC</td>
<td>376 ± 16.11</td>
<td>48</td>
<td>41.96</td>
<td>4.90</td>
<td>35</td>
<td>57</td>
</tr>
<tr>
<td>2</td>
<td>FLC</td>
<td>419 ± 15.93</td>
<td>48</td>
<td>46.08</td>
<td>8.78</td>
<td>36</td>
<td>77</td>
</tr>
<tr>
<td>3</td>
<td>FLC</td>
<td>490 ± 21.23</td>
<td>27</td>
<td>44.75</td>
<td>5.49</td>
<td>37</td>
<td>57</td>
</tr>
</tbody>
</table>

ARDEC = 1,525 m; FLC = 2,470 m.
Table 2. Summary statistics of Hereford bulls (arithmetic means)

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Average age (d) ± SD</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ARDEC</td>
<td>377 ± 13.11</td>
<td>40</td>
<td>39.17</td>
<td>2.41</td>
<td>33</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>FLC</td>
<td>419 ± 16.23</td>
<td>41</td>
<td>41.36</td>
<td>5.25</td>
<td>37</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>FLC</td>
<td>489 ± 23.13</td>
<td>24</td>
<td>42.65</td>
<td>4.77</td>
<td>36</td>
<td>60</td>
</tr>
</tbody>
</table>

ARDEC = 1,525 m; FLC = 2,470 m.

Contemporary groups were assigned based on birth year. Spearman rank correlations and Pearson correlations for PAP were evaluated from the raw PAP values.

Pulmonary arterial pressure observations used in this study had a skewed right distribution which parallels reports using similar data (Pauling et al., 2018, Cockrum et al., 2019, Speidel et al. 2020). A plot of residuals vs. fitted values and a normal quantile–quantile plot were created. These plots suggested that raw phenotypes violate assumptions of normality. As a result of the violation, Tukey transformation analysis suggested that the raw PAP observations be raised to a power between −3.275 and −6.15 for accommodation of non-normality of data. Resulting parameter estimates were not representative of original observed data scale, and the back transformation was not logical due to nonlinearity between transformed parameter estimates and original data. Due to these issues, models will be presented from an evaluation of raw PAP phenotypes.

**RESULTS AND DISCUSSION**

To reiterate, number of observations, arithmetic means, standard deviation (SD), ages, as well as minimum and maximum values for PAP in both Black Angus and Hereford bulls are presented in Tables 1 and 2, respectively. There is reduced numbers of observations at time 3 which is due to no collection at that time point for one of the collection years. The most significant model for high-altitude PAP included age in days and the bull’s yearling PAP score at moderate altitude (P < 0.05) as shown in Table 3. This table also presents estimates and P-values for the fixed effects on high-elevation PAP. The model, which included age in days and yearling PAP, accounted for less variability as the bull spent more time at high altitude than it did for initial high-altitude PAP. This is showcased by the reduced partial $R^2$ values of both yearling PAP and age. Yearling PAP as a fixed effect for high-altitude PAP after acclimation (~21 d) had an $R^2$ value of 0.50, which was reduced to a value of 0.30 after the bulls were at altitude for ~ 90 d. These results illustrate that yearling PAP measurements are highly correlated in the shorter term at higher elevations, but as a bull approaches 18 mo of age at higher elevations, it is less indicative of PAP scores. This result suggested that the genetic mechanisms which influence PAP may be different at moderate elevations than the high elevation genetic mechanisms, as previously described by Speidel et al. (2020). Therefore, making it difficult to know if a bull is tolerating high altitude or PAP changed as a result of failure to adapt.

Figures 1 and 2 are scatterplots of high-altitude PAP plotted vs. the significant model components with a fitted regression line. The positive increasing regression lines indicate the relationships between yearling PAP or age (respectively) and each high-altitude PAP observation. Also note that within the figures is a boxplot to illustrate the variability of the data and identify outliers common within these types of data (Cockrum et al., 2019).

Pearson correlations (above diagonal) and Spearman’s rank correlations (below diagonal) between the raw PAP values are presented in Table 4. Correlations between yearling PAP and PAP measured at high altitude were moderately to highly correlated. Estimates (i.e., raw data correlations) between yearling PAP and PAP at high-elevation PAP measures 2 and 3 were 0.71 and 0.55, respectively, again suggesting that it is difficult to know if a bull can tolerate high altitude based on the lower (i.e., moderate) elevation PAP. The correlation between the raw PAP measures 2 and 3 at high altitude was 0.81. The magnitude of this correlation suggested that a high-altitude PAP may be a predictor for future PAP measurements at high altitude. Speidel et al. (2020) reported similar behavior in the correlations between the moderate altitude PAP observations and high-altitude PAP observations. Historically, PAP is considered to be the most

Table 3. Results of linear model estimates of PAP at 419 ± 16 d (High Altitude 1) and 490 ± 22 d (High Altitude 2) in bulls

<table>
<thead>
<tr>
<th>High altitude 1</th>
<th>Estimate</th>
<th>P-value</th>
<th>Partial $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 2</td>
<td>0.07758</td>
<td>0.033042</td>
<td>0.05175</td>
</tr>
<tr>
<td>Yearling PAP</td>
<td>1.28504</td>
<td>&lt; 0.0001</td>
<td>0.50423</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High altitude 2</th>
<th>Estimate</th>
<th>P-value</th>
<th>Partial $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 3</td>
<td>0.05569</td>
<td>0.04428</td>
<td>0.07699</td>
</tr>
<tr>
<td>Yearling PAP</td>
<td>0.79408</td>
<td>&lt; 0.0001</td>
<td>0.30491</td>
</tr>
</tbody>
</table>

Columns include sources of variation, modeled estimate, $P$-values, and partial coefficients of variations ($R^2$).
Yearling pulmonary arterial pressure in beef bulls in Colorado

Translate basic science to industry innovation

accurate indicator of an individual’s susceptibility to HAD if it is measured at high altitude and near 18 mo of age (Holt and Callan, 2007). These results were supported by this study. However, results also provide evidence to suggest that yearling PAP collected at a moderate altitude is a modest short-term predictor of PAP at high altitude and leaves uncertainty of the animal’s lifetime tolerance of high altitude. The altitude of the ARDEC facility (1,525 m) of CSU is moderate; therefore, questionable if it yields enough hypoxic stress to determine if a bull has PAP that will be acceptable or unacceptable for lifetime residence in a mountainous beef production system. Therefore, this challenge warrants additional research when considering the diversity of beef operations in the Western United States.

**IMPLICATIONS**

This study suggested that yearling PAP at moderate elevations was a modest and short-term indicator of future PAP performance in beef bulls when moving to high altitudes. Yearling PAP measurements are likely less indicative of PAP, and the longer bulls reside at high elevation. It should be noted that high-altitude PAP observations will likely have higher correlations and be a stronger indicator to future high-altitude PAP measures. Breed was not a significant variable in this specific study. This is likely due to limited numbers being evaluated in each breed. To further study breed influence, greater numbers of bulls being analyzed are necessitated. Overall, this study supports the research findings that were used in the development of the American Angus Association PAP

Table 4. Pearson correlations (above diagonal) and Spearman’s rank correlations (below diagonal) of predictions for PAP indication of additional PAP measurements

<table>
<thead>
<tr>
<th></th>
<th>1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>3&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
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<tr>
<td>1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.71</td>
<td>0.55</td>
<td></td>
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<tr>
<td>2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.76</td>
<td>0.81</td>
<td></td>
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<tr>
<td>3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.63</td>
<td>0.82</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>ARDEC (1,525 m);
<sup>b</sup>FLC (2,470 m).

Ages: 1) 377 ± 15 d; 2) 419 ± 16 d; and 3) 490 ± 22 d.
EPD, which defines the EPD as being a trait of yearling PAP for cattle of high altitude.

**ACKNOWLEDGMENTS**

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*Conflict of interest statement.* None declared.

**LITERATURE CITED**


