Introduction

1. Humans with group 3 PH characterized by alveolar hypoxia exhibit diversity in disease progression outcomes.
2. Similarly certain breeds and individuals among beef cattle, including the American Angus, demonstrate variable susceptibility to hypoxic-induced pulmonary vascular constriction, progressive remodeling of the pulmonary vasculature, pulmonary hypertension (PH) and right heart failure (HF).
3. Despite selection of breeding stock with low PH susceptibility, failure to thrive and death losses associated with PH and right HF remain problematic for unknown reasons.
4. Clinical and experimental evidence coupled with gross and microscopic cardiopulmonary lesions suggest inflammation plays a significant role in the pathogenesis of pulmonary vascular remodeling, PH, and right HF in cattle and recapitulates features of Group 3 PH in humans.

Hypothesis

The extent of pulmonary inflammation predicts the magnitude of fibroproliferative remodeling in the pulmonary vascular tree and the perivascular adventitia and intima of the right ventricle.

Methods

Three distinct phenotypes were identified at slaughter based upon mPAP values and clinical signs: (i) Non-hypertensive (n=10), mPAP range 36-46 mm Hg; (ii) PH without signs of RV dysfunction (mPAP 47-71 mm Hg); and (iii) PH with signs of RV failure (n=3), mPAP ≥72 mm Hg. Average RV systolic weight ratio was significantly increased for all PH animals compared to non-hypertensive, whereas L/R body weight was unchanged.

Cardiac Histopathology Indicates PH Progression

Low mPAP Steers with No Pulmonary Lesions

A. Normal right ventricular myocardium
B. Inconspicuous adventitia
C. No smooth muscle hypertrophy or adventitial proliferation
D. Inconspicuous pulmonary vein
E. Arteriole with normal tunica media and luminal diameter

High mPAP Steers with Cardiac Lesions

F. Prominent adventitial thickening
G. Pulmonary artery and vein with mildly thickened adventitia and prominent BAL
H. Conspicuous medial hypertrophy and luminal narrowing
I. Medial hypertrophy and adventitial proliferation highlighted with Masson's Trichrome stain
J. Pulmonary arteriole with prominent muscularization and expansion of the adventitia
K. Prominent adventitial thickening and vasa vasorum hyperplasia. The intermediate artery is larger than its associated artery
L. Prominent adventitial and vasa vasorum hyperplasia highlighted with Masson's Trichrome stain
M. Prominent medial hypertrophy and severe adventitial thickening
N. Severe adventitial expansion highlighted with Masson's Trichrome stain
O. Conspicuous pulmonary vein with prominent adventitia highlighted by Masson's Trichrome stain
P. Bronchus with prominent BAL
Q. Alveolar septa and lumina infiltrated and filled by moderate numbers of neutrophils and mononuclear cells
R. Inflammation, alveolar fibrosis, organizing fibrin exudate and hyperplasia

Conclusion

Beef cattle raised in chronic hypoxic environments provide a natural model of Group 3 PH where pulmonary inflammation and venous remodeling predict disease severity and outcomes and may provide novel therapeutic targets for the treatment of PH in humans and beef cattle.