Journal of Veterinary Internal Medicine
Open Access

J Vet Intern Med 2015

Right-Sided Congestive Heart Failure in North American Feedlot Cattle

J.M. Neary, C.W. Booker, B.K. Wildman, and P.S. Morley

Background: Anecdotal reports suggest the incidence of right-sided congestive heart failure (RHF) in feedlot cattle is increasing; however, the rate of occurrence and risk factors are largely unknown.

Objective: The purposes of this study were to evaluate the risk of RHF over time and among feedlots, to characterize some of the risk factors for RHF, and to investigate how risk factors may affect the timing of RHF occurrence.

Animals: The population at risk consisted of 1.56 million cattle that were placed in 10 Canadian feedlots during the years 2000, 2004, 2008, and 2012, and 5 US feedlots during the year 2012.

Methods: A retrospective observational study was conducted. Variables, including year of feedlot entry, were evaluated for association with RHF using zero-inflated negative binomial and logistic regression models. Factors affecting time to RHF were evaluated using Cox proportional hazard regression analyzes. Death from digestive disorders (DD) served as a control.

Results: The risk of RHF in Canadian feedlots doubled from the year 2000 to the year 2012 ($P = .003$). For every 10,000 cattle entering US feedlots in 2012, 11 cattle died from RHF and 45 cattle died from DD. The median time to RHF was 19 weeks. Cattle treated for bovine respiratory disease were 3 times more likely to die from RHF, and they died earlier in the feeding period.

Conclusions: A doubling of the incidence of RHF over a short time period is concerning, particularly for US feedlots situated at moderate altitudes in the High Plains.

Key words: Congestive heart failure; Fat; Hypoxia; Pulmonary hypertension; Respiratory disease.

Right-sided congestive heart failure (RHF), also known as high altitude disease or brisket disease, is initiated by hypoxia-induced pulmonary arteriolar narrowing.[1,2] Vessel narrowing increases resistance to blood flow, mean pulmonary arterial pressure and, ultimately, the risk of RHF. Cattle exposed to the hypobaric hypoxia of high altitude have a greater baseline risk of alveolar hypoxia and, consequently, are at greater risk of RHF than cattle at lower altitudes. Before the 1970s, RHF had only been reported in cattle at altitudes over 2,130 m[3,4]; it has since been reported at lower altitudes, however. In 1974, a study of 4 US feedlots located at an altitude of 1,600 m reported the attack risk of RHF to be 2.85 cases per 10,000 cattle entering the feedlot.[5] More recently, a study conducted at an altitude of 1,600 m reported RHF to be the second leading cause of death, behind pneumonia, in Holstein dairy heifers aged <1.5 years.[6] Furthermore, anecdotal reports suggest that the incidence of RHF in feedlot cattle is increasing. These reports are concerning because the majority of US feedlots are situated at moderate altitudes (800–1,600 m) in the High Plains.[7]

From the Department of Animal and Food Sciences, Texas Tech University, Lubbock, TX (Neary); the Feedlot Health Management Services Ltd, Okotoks, AB Canada (Wildman and Bookers); and Department of Clinical Sciences, Colorado State University, Fort Collins, CO (Morley).

Corresponding author: J.M. Neary, Department of Animal and Food Sciences, Texas Tech University, Lubbock, TX 79409-2141; e-mail: joe.neary@ttu.edu.

Submitted March 19, 2015; Revised September 18, 2015; Accepted October 13, 2015.

DOI: 10.1111/jvim.13789

Abbreviations:

RHF	right heart failure
DD	digestive disorders
BRD	bovine respiratory disease
UF	undifferentiated fever

The purposes of this study were 3-fold: to evaluate the risk of RHF over time and among feedlots; to investigate some of the risk factors for RHF; and, to determine how these risk factors affect the time to RHF occurrence. Treatment for bovine respiratory disease (BRD), date of feedlot entry, risk of BRD/undifferentiated fever (UF), and age on feedlot entry, were evaluated as potential risk factors for RHF.

Materials and Methods

Study Overview

Data from 10 Canadian feedlots were obtained from the years 2000, 2004, 2008, and 2012, and from 5 US feedlots from the year 2012. Cattle entering the feedlots were categorized by date of feedlot entry, age, sex, and risk of BRD/UF. All cattle that died in the feedlots were examined postmortem by a veterinarian and a primary cause of death recorded. For the purposes of this study, only the individual records of cattle that died from RHF or a digestive disorder were evaluated. From these data, the risks of RHF and digestive disorders (DD) were determined every 4 years from the year 2000 to the year 2012. The effects of respiratory disease, placement date, risk of BRD/UF, and sex, on the risk, and distribution, of RHF through the feeding period were evaluated. Death from DD served as a competing cause.

Study Population

The study population consisted of cattle placed in 10 feedlots located in western Canada during the years 2000, 2004, 2008, and

2012, and cattle placed in 5 feedlots in the western United States during the year 2012. These feedlots were chosen because they individually identified all cattle they managed, recorded detailed health information for all individuals in a specially designed computer information system (iFHMS), and a gross necropsy was performed by a licensed veterinarian on all animals that died.[a] These data were provided by the veterinary health management company responsible for oversight of health care in these populations.[a]

A total of 1.28 million cattle entered the participating Canadian feedlots over the years studied, and 273,319 cattle entered the participating US feedlots in 2012 (Table 1). The Canadian feedlots were located at altitudes ranging from 657 to 1,145 m. One US feedlot was located at an altitude of 596 m; the other 4 feedlots were located at altitudes ranging from 1,142 to 1,282 m (Table 1). The procurement and management of cattle within the feedlots studied was typical of those practices used at large commercial cattle feedlots. Pens of animals entering the feedlots had a range of body weights (225–400 kg), ages, frame sizes, and sexes. Based upon these factors, and historical patterns of illness in similar cattle, arriving groups were assigned an ordinal category of perceived risk for developing BRD/UF (low risk to very high risk), which was used to determine prevention and treatment protocols. For this study, these categories were dichotomized (low versus high risk).

The same standardized health and production procedures were used across all feedlots, as per the protocols developed by specialist feedlot veterinarians.[a] On arrival at the feedlot, all cattle received an ear tag with a unique identification number, a growth implant, a topical avermectin anthelmintic, and vaccines against bacterial and viral agents of respiratory disease. Cattle categorized as being at high risk of BRD/UF were administered a parenteral antibiotic as a prophylactic, or metaphylactic, treatment. Cattle were fed a ration that met or exceeded the National Research Council requirements for beef cattle.[8] Cattle were typically slaughtered at a body weight of 550–650 kg, approximately 120–250 days after feedlot arrival.

Data Collection and Disease Diagnosis

The population at risk was the number of cattle entering a feedlot during a calendar year: 2000, 2004, 2008, or 2012. All cattle that entered a feedlot within 1 of these years were followed until the day of slaughter, which might have been in the calendar year after their arrival at the feedlot. The population was grouped for analyses by: feedlot, placement year, placement period (January 1–April 30; May 1–August 31; and, September 1–December 31), age on feedlot placement (calf or yearling), sex (male or female), and risk of BRD/UF (high or low). Information that was collected for all cattle in the study population included individual identification, individual weights on feedlot arrival, group weights on feedlot exit, all preventive and therapeutic treatments (eg, vaccinations, deworming, medications administered), and any disease diagnoses. Trained feedlot personnel evaluated cattle for signs of illness at arrival and daily thereafter. Animals that were considered to be ill or injured were moved to a chute for closer examination. The primary illness was diagnosed and recorded in the health information system using standardized diagnosis categories. Illness consistent with BRD was identified when cattle exhibited signs of dyspnea, lack of response to stimulation, reluctance to move, abnormal carriage or posture of the head, or some combination of these signs. All cattle that died underwent necropsy examination, and a veterinarian used clinical history and physical findings to assign the cause of death using a standardized set of diagnosis codes. For the purposes of this study, postmortem diagnoses attributed to DD included cattle with ruminal bloat, enteritis, intestinal disorders, and peritonitis. Peritonitis was included in the DD as it was deemed that a digestive disorder was the most likely underlying cause of the peritonitis.

To minimize confounding associated with a common pathogenesis, cattle that died of DD served as a control group for the analysis of risk factors associated with RHF. The criteria used for the diagnoses of RHF and DD are provided in Table 2. For analysis purposes, each animal was assigned a single, primary cause of death. In addition to the information that was obtained from all cattle, the information obtained from cattle that died of RHF or a digestive disorder also included prior treatment for BRD (yes/no) and the number of days from feedlot entry to death.

Statistical Analyses

Analyses were performed using commercially available statistical software.[b] Data were summarized descriptively, including calculations of frequencies, and means for quantitative variables with associated 95% confidence intervals (95% CI). Three statistical

Table 1. The number of cattle that entered each feedlot according to year of feedlot entry.

Country	Feedlot	Altitude, m	Year 2000	2004	2008	2012	Total
Canada	1	1,006	30,933	29,107	64,926	44,740	169,706
	2	837	3,453	3,045	1,738	2,646	10,882
	3	1,018	20,933	23,682	25,538	13,368	83,521
	4	934	63,817	60,212	104,364	57,247	285,640
	5	917	23,281	34,761	51,394	23,597	133,033
	6	657	55,489	53,865	60,071	27,735	197,160
	7	1,145	9,858	9,716	6,464	5,252	31,290
	8	887	2,779	1,529	2,234	1,984	8,526
	9	1,102	65,582	60,148	86,947	49,380	262,057
	10	1,005	10,941	25,613	48,016	17,809	102,379
	Total		287,066	301,678	451,692	243,758	1,284,194
United States	11	1,161	–	–	–	91,088	–
	12	1,242	–	–	–	34,736	–
	13	1,282	–	–	–	44,164	–
	14	1,142	–	–	–	28,590	–
	15	596	–	–	–	74,741	–
	Total					273,319	273,319
Combined total						1,557,513	

Table 2. The postmortem lesions used for establishing the cause of death.

Cause of Death	Postmortem Lesions
Congestive heart failure	Brisket and ventral edema; hydroperitoneum; hydrothorax and secondary atelectasis; hepatomegaly and chronic passive congestion; intestinal and mesenteric edema; hydropericardium; right-ventricular hypertrophy and dilatation
Ruminal bloat	Underinflated lungs; cranial carcass congestion; caudal carcass pallor; edema of subcutaneous tissue and facial planes of hind limbs; rumen distended with gas; small, pale liver; small, pale heart
Enteritis	Hyperemia and edema of intestinal mucosa; fibrinous mucosa; luminal hemorrhage; dark, fluid-filled intestine; diffuse or segmented
Intestinal disorder	Intussusception; mesenteric rent; intestinal parasitism; lodged trichobezoar; stricture; intestinal torsion/volvulus
Peritonitis	Hydroperitoneum; fibrin deposition; adhesions; local or diffuse

Not all of the lesions listed were required for a diagnosis. Peritonitis was recorded as the "cause" of death when peritonitis was present, but an underlying cause of the peritonitis could not be identified.

models were used: zero-inflated negative binomial, logistic regression, and Cox proportional hazard regression. Each model provided unique information.

The zero-inflated negative binomial models revealed which risk factors were associated with RHF, but could not distinguish between risk factors specific to RHF and nonspecific risk factors for death loss. By using DD as a competing cause, we determined, through logistic regression analyses, which of the risk factors were specific to RHF. Finally, Cox proportional hazard regression analyses divulged how the various risk factors affected the rate of RHF occurrence through the feeding period. The latter findings were important because time at risk, or feeding duration, might have confounded risk factors in the logistic regression models. For example, cattle entering feedlots as calves were likely fed for longer than cattle entering as yearlings. Calves were, therefore, at risk of RHF for longer than yearlings. Consequently, calves and yearlings might have had the same odds of RHF even if the rate of RHF occurrence was greater in yearlings. Cox proportional hazard regression was necessary to disclose such information.

In all models, the individual animal was the unit of analysis. Two-way interactions between period of feedlot placement, risk of BRD/UF, sex, and age, were evaluated. Variance inflation factors were <2.0 for all variables indicating that the models were not adversely affected by multicollinearity. Clustering by feedlot was controlled as a fixed-effect in all models, providing feedlot-specific estimates of effect. Pen-level information was not available; therefore, robust variance estimators were used in all models to account for potential clustering at the pen-level and assure that interpretations are conservative. Wald tests ("test") were performed in all models to determine the statistical significance of multi-level categorical variables.

Zero-inflated negative binomial models ("zinb") were used to calculate attack risk ratios for RHF and DD according to period of feedlot placement, risk of BRD/UF, sex, age, year of placement (Canadian feedlots only), and feedlot. The number of cattle within a covariate pattern was the only variable included in the logistic part of all zero-inflated models. Covariate patterns with fewer cattle were more likely to have a zero count of RHF and DD. The results of the logistic part of the model were not pertinent to the study objectives; they are, therefore, not presented. Adjusted mean risks of RHF and DD were obtained for US cattle in 2012 and, for Canadian cattle for each year studied, while controlling for period of feedlot placement, risk of BRD/UF, sex, age, and feedlot. All variables remained in the final model irrespective of their statistical association with RHF. This allowed the comparison of risk factors between US and Canadian populations, and also allowed the relationship between the risk factors and outcome to be compared across the various models. Adjusted mean risks ("margins") of RHF were also obtained for each US and Canadian feedlot in 2012, while controlling for period of feedlot placement, risk of BRD/UF, sex, and age.

Case–control analyses, stratified by country, were performed using logistic regression models ("logistic") to investigate risk factors that were more specifically associated with RHF. Cases were cattle whose death was attributed to RHF, and controls were cattle that died from DD. The odds of RHF were calculated for period of feedlot placement, risk of BRD/UF, sex, age, treatment for BRD, and feedlot. All variables remained in the final model irrespective of their statistical association with RHF. Year of placement (Canadian model only) and feedlot were forced into the models as fixed effects to control for clustering.

Cox proportional hazard regression analyses ("stcox") were performed, stratifying on country, to determine which risk factors affected time to RHF. A case–control design was used; cases were cattle that died of RHF, and controls were cattle that died from DD. The risk factors evaluated included period of feedlot placement, sex, risk of BRD/UF, and treatment for BRD. The models were grouped by year of placement (Canada only), and feedlot. A backward elimination method was used so that in the final model all variables were considered statistically significant if $P < .05$. The proportional hazards assumption was validated by graphical assessment of the log-cumulative hazard plot.

Results

Risk of RHF Over Time

The adjusted risk of RHF doubled from the year 2000 to the year 2012, when controlling for period of feedlot placement, risk category, sex, age, and feedlot (Table 3). Between the years 2000 and 2012, the risk of RHF, bloat, nonbloat DD (enteritis, intestinal disorders and peritonitis), and all DD increased by 91, 70, 29, and 61%, respectively. The odds of RHF increased over time relative to the year 2000, when controlling for death loss from DD. Relative to the year 2000, the odds of RHF in the years 2004, 2008, and 2012 were 1.58 (95% CI = 1.11, 2,26), 2.69 (95% CI = 1.95, 3.70), and 1.51 (95% CI = 1.07, 2.13), respectively, when controlling for the likelihood of DD, feedlot, age, risk of BRD/UF, sex, period of feedlot placement, and treatment for respiratory disease.

Likelihood of RHF Among Feedlots in 2012

The adjusted risks of RHF and DD in US feedlots were 1.08 per 1,000 cattle (95% CI = 0.89, 1.28) and 4.54 per 1,000 cattle (95% CI = 3.52, 5.56), respectively.

Table 3. The adjusted[a] risk and robust 95% CI of RHF, bloat, nonbloat[b] DD and all DD determined using multivariable zero-inflated negative binomial regression for cattle in Canadian feedlots.

	Mean Attack Risk Per 1,000 Cattle (95% CI)			
Cause of Death	2000	2004	2008	2012
RHF	0.21 (0.11, 0.31)	0.28 (0.17, 0.39)	0.47 (0.27, 0.66)	0.40 (0.24, 0.56)
Bloat	1.05 (0.79, 1.31)	0.81 (0.65, 0.98)	1.30 (0.95, 1.64)	1.78 (1.23, 2.45)
Nonbloat DD	0.42 (0.27, 0.57)	0.65 (0.49, 0.82)	0.64 (0.44, 0.84)	0.54 (0.31, 0.78)
DD	1.37 (1.03, 1.71)	1.39 (1.12, 1.65)	1.81 (1.34, 2.28)	2.20 (1.52, 2.88)

DD, digestive disorders; CI, confidence intervals; RHF, right heart failure.

[a]Controlling for feedlot, age, risk of respiratory disease and undifferentiated fever, sex, and period of feedlot entry.

[b]Nonbloat DD included enteritis, intestinal disorders, and peritonitis.

Relative to cattle in US feedlots, cattle in Canadian feedlots had approximately half the risk of RHF and DD (Table 3). In both US and Canadian feedlots, the risk of death from RHF was approximately 5 times lower than the risk of death from DD.

There were substantial differences in the risk of RHF among US and Canadian feedlots ($P < .001$; Fig 1). Among the Canadian feedlots in 2012, Feedlot 4 had the greatest risk of RHF (adjusted risk = 0.99 per 1,000 cattle; 95% CI = 0.57, 1.42), and Feedlot 8 had the least risk (adjusted risk = 0.09 per 1,000 cattle; 95% CI = 0, 0.30). Canadian feedlots with an increased risk of RHF relative Feedlot 8 did not have significantly greater likelihood of death from RHF, when controlling for the likelihood of death from DD (Fig 1).

Among US feedlots, Feedlot 13 had the greatest adjusted risk of RHF (adjusted risk = 1.75 per 1,000 cattle; 95% CI = 1.29, 2.20), and Feedlot 15 had the least risk (adjusted risk = 0.42 per 1,000 cattle; 95% CI = 0.26, 0.58). Relative to Feedlot 15, cattle in the other 4 US feedlots were more likely to die of RHF, when controlling for death loss from DD ($P < .001$; Fig 1). This indicates that in US feedlots, the risk of RHF did not parallel the risk of DD.

Risk of RHF by Season of Placement, Risk of BRD/UF, Age, and Sex

Period of placement, BRD/UF risk category, and sex, showed the same direction of effect in US and Canadian feedlots (Table 4). Cattle placed in feedlots from May 1 to August 31, or from September 1 to December 31, had an adjusted risk of RHF that was at least 50% greater than cattle placed in feedlots from January 1 to April 30. In US feedlots, male cattle and cattle classified at placement as having a high risk of developing BRD/UF were approximately 2 and 3 times more likely to die of RHF than female cattle and cattle classified at placement as having a low risk of BRD/UF, respectively. In Canadian feedlots, sex and BRD/UF risk had the same direction of effect as US feedlots, but they had a reduced magnitude of effect (Table 4). The adjusted risk of RHF in cattle entering the feedlots as yearlings was 60% lower than calves in Canadian feedlots, but 138% greater than calves in US feedlots (Table 4).

Likelihood of RHF Occurrence

Cattle treated for BRD were approximately 3 times more likely to die from RHF than cattle that were not treated for BRD, when controlling for the likelihood of death from DD, year of placement, risk of BRD/UF, age, sex, period of feedlot placement, and feedlot (Table 5). Period of feedlot placement was significantly associated with the odds of RHF in both US and Canadian feedlots ($P < .001$). Cattle entering feedlots from May 1 to December 31 had a 51–127% greater risk of RHF than cattle that entered from January 1 to April 30. Cattle categorized as low risk of BRD/UF on feedlot arrival were twice as likely to die from RHF when compared to cattle categorized as high risk (Table 5). The odds of RHF were 39% greater in males relative to females in US feedlots ($P = .04$), but there was no sex difference in Canadian feedlots. Age on arrival at the feedlot was not associated with the likelihood of RHF in either US or Canadian feedlots (Table 5).

Time From Feedlot Arrival to Death From RHF

Death from RHF occurred throughout the feeding period but tended to occur later in the feeding period than death from DD (Fig 2). The median days to death from RHF and bloat were 132 and 129 in Canadian feedlots, and 133 and 107 days in US feedlots, respectively. Relative to the year 2000, the mean days to death from RHF did not significantly change over time, when controlling for period of placement, feedlot, BRD/UF risk, age, sex, and treatment for BRD ($P > .20$). Ruminal bloat accounted for 72 and 83% of deaths from DD in Canadian and US feedlots, respectively.

Although age on feedlot entry did not affect the likelihood of RHF (Table 5), the rate of RHF in yearlings was double that of calves (Table 6). Except for period of feedlot placement, all other factors associated with time to RHF showed a similar pattern in US and Canadian feedlots (Figs 3, 4).

Discussion

The results of this study support producer concerns that the incidence of RHF in feedlot cattle has

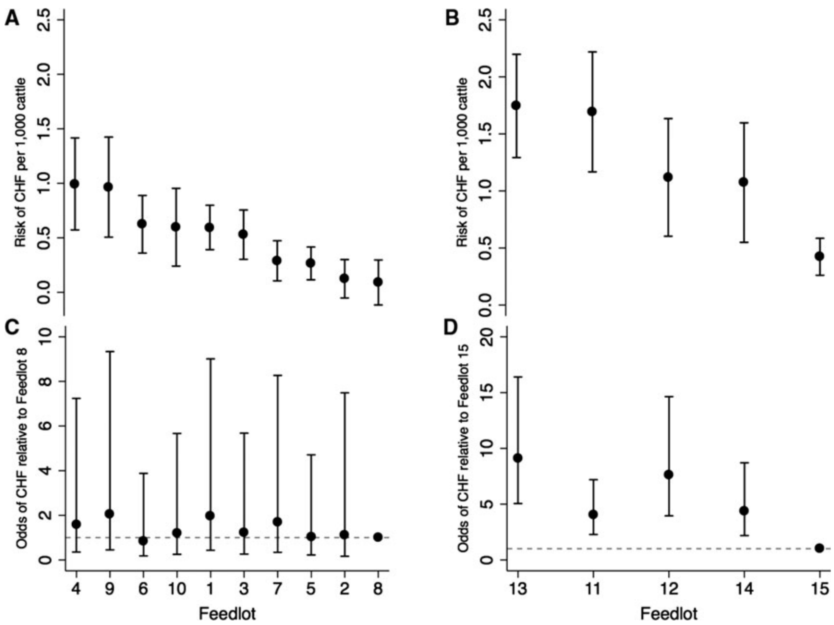

Fig 1. Adjusted mean estimate and robust 95% confidence intervals of the attack risk of right heart failure (RHF) per 1,000 cattle (Controlling for country, season of placement, bovine respiratory disease/undifferentiated fever [BRD/UF] risk category, sex and age.) entering (**A**) Canadian feedlots in 2012 and (**B**) US feedlots in 2012; and, the odds of RHF (Controlling for the likelihood of death from digestive disorders, period of feedlot placement, risk of BRD/UF, sex, age and treatment for BRD.) in, (**C**) Canadian feedlots, and (**D**) US feedlots, relative to the feedlot in each respective country with the lowest risk of RHF in 2012. Feedlots arranged in descending order of risk.

Table 4. The adjusted risk ratio and robust 95% CI for RHF in US and Canadian feedlots determined using multivariable zero-inflated negative binomial regression.

		Canada[a]		United States[b]	
Variable	Category	Risk Ratio (95% CI)	*P*-Value	Risk Ratio (95% CI)	*P*-Value
Placement period	January 1–April 30	Reference	.006	Reference	.03
	May 1–August 31	1.62 (1.00, 2.59)		1.58 (1.00, 2.50)	
	September 1–December 31	2.10 (1.33, 3.32)		1.62 (1.11, 2.36)	
Risk of BRD/UF	Low	Reference		Reference	
	High	1.20 (0.77, 1.87)	.42	2.89 (1.61, 5.18)	<.001
Age	Calf	Reference		Reference	
	Yearling	0.40 (0.26, 0.60)	<.001	2.38 (1.38, 4.09)	.002
Sex	Female	Reference		Reference	
	Male	1.19 (0.89, 1.58)	.23	2.21 (1.58, 3.08)	<.001

The number of cattle within a covariate pattern was significantly associated with the probability of a nonzero count of RHF.
BRD, bovine respiratory disease; CI, confidence intervals; RHF, right heart failure; UF, undifferentiated fever.
[a]All years; [b]2012 only.

increased: the risk of RHF in Canadian feedlots approximately doubled from the year 2000 to the years 2008 and 2012. Despite a 2-fold increase in RHF mortality, the number of cattle that died of RHF in 2012 was relativity minor when compared to DD: approximately 4-5 times more cattle died of DD than RHF. Although death loss from RHF was relatively minor, the occurrence of RHF in feedlot cattle is noteworthy for 2 reasons: First, before the 1970s, RHF was only reported in cattle at altitudes over 2,130 m;[3,4,9] therefore, a 2-fold increase in RHF over a 12 year period in feedlots located at low (657 m) to moderate (1,145 m) elevations deserves attention. Second, although RHF occurred throughout the feeding period, half of all cases occurred after 19 weeks; this makes death loss from RHF particularly costly. One might suspect that because cattle are being fed for longer, and to heavier finishing weights, the risk period for RHF has merely increased over time and, consequently, led to more RHF fatalities, particularly in the late feeding period. If so, the average time from feedlot arrival to death from RHF should have increased over time, but in our study, this was not observed. Unfortunately, because we know so little about the risk factors for this disease, attempts to reduce the incidence of RHF have been frustrating for both producers and veterinarians.

Table 5. The adjusted odds and robust 95% CI of RHF controlling for the likelihood of death from digestive disorders in 10 Canadian and 5 US feedlots determined using multivariable logistic regression, controlling for year of placement.

		Canada[a]		United States[b]	
Variable	Category	OR (95% CI)	*P*-Value	OR (95% CI)	*P*-Value
Placement period	January 1–April 30	Reference	<.001	Reference	<.001
	May 1–August 31	2.02 (1.38, 2.95)		1.51 (1.01, 2.26)	
	September 1–December 31	1.73 (1.26, 2.39)		2.27 (1.56, 3.30)	
Risk of BRD/UF	Low	Reference		Reference	
	High	0.45 (0.32, 0.64)	<.001	0.62 (0.37, 1.02)	.06
Age	Calf	Reference		Reference	
	Yearling	0.85 (0.61, 1.18)	.25	1.29 (0.80, 2.09)	.31
Sex	Female	Reference		Reference	
	Male	0.98 (0.79, 1.20)	.83	1.39 (1.01, 1.93)	.04
Treated for BRD	No	Reference		Reference	
	Yes	2.52 (2.05, 3.10)	<.001	3.14 (2.29, 4.30)	<.001

BRD, bovine respiratory disease; CI, confidence intervals; OR, odds ratio; RHF, right heart failure; UF, undifferentiated fever.
[a]All years; [b]2012 only.

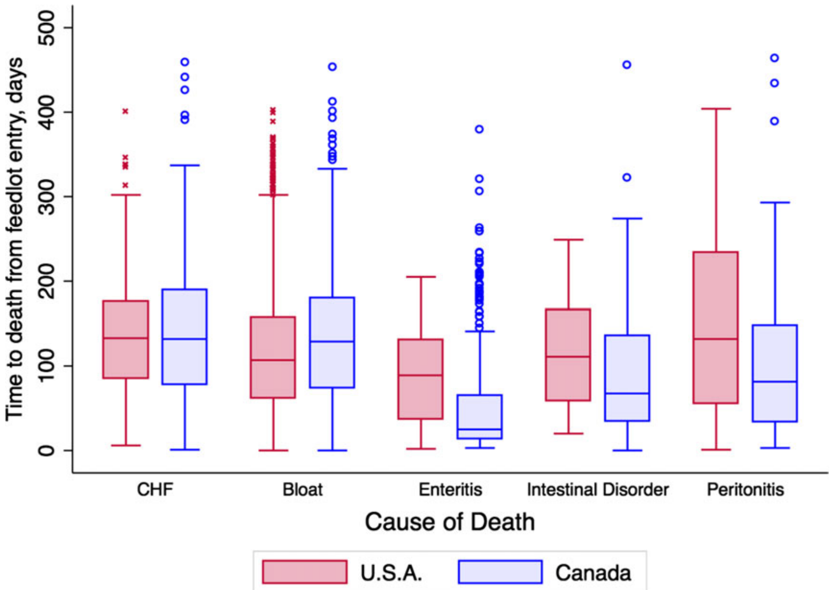

Fig 2. Box and whisker plot of days on feed to death from right heart failure (RHF), bloat, enteritis, intestinal disorder, and peritonitis in 10 Canadian feedlots over the years 2000, 2004, 2008, and 2012 and 5 US feedlots in 2012.

In cattle, alveolar hypoxia is considered to be the primary risk factor for pulmonary vascular remodeling and hypertension, which may ultimately cause RHF. Any factors predisposing cattle to alveolar hypoxia could, therefore, have explained the increase in RHF mortality observed over time in our study. Factors that may cause alveolar hypoxia include: hypobaric hypoxia, hypoventilation, and respiratory disease.

Hypobaric hypoxia cannot explain the increase in RHF death loss observed since the same Canadian feedlots were studied over the entire period. It could, however, explain why cattle had twice the risk of RHF in the US feedlots relative to Canadian feedlots. The US feedlots studied had the greatest range of altitudes and were generally located at the highest altitudes. Four of the 5 US feedlots studied were located at altitudes over 1,142 m; the fifth feedlot was located at just 596 m. An altitude difference of 686 m may explain why cattle in the feedlot located at the highest altitude (1,282 m) were 9 times more likely to die of RHF than cattle at the lowest altitude. Alternatively, the risk of RHF may have been greater in US feedlots at altitudes ≥1,142 m because they were more likely to have procured cattle from high altitude regions (>1,600 m) than the feedlot at 596 m. Prior mountain grazing is thought to increase the risk of RHF in feedlot cattle.[5] Canadian feedlots, on the other hand, were generally located at lower altitudes than the US feedlots and likely procured cattle from lower altitudes. They also had a maximum altitude difference of only 488 m, which likely explains why the risk of RHF, and the variation in RHF risk among feedlots, was small relative to the US feedlots.

Table 6. Adjusted hazard ratios and robust 95% CI for death from RHF for cattle that entered into 10 Canadian feedlots and 5 US feedlots determined using multivariable Cox proportional hazards modeling.

		Canada[a]		United States[b]	
Variable	Category	HR (95% CI)	*P*-Value	HR (95% CI)	*P*-Value
Placement period	January 1–April 30	Reference	.02	Reference	<.001
	May 1–August 31	1.66 (1.15, 2.39)		1.67 (1.18, 2.37)	
	September 1–December 31	1.12 (0.82, 1.55)		2.11 (1.55, 2.89)	
Risk of BRD/UF	Low	Reference		Reference	
	High	0.48 (0.35, 0.66)	<.001	0.42 (0.27, 0.64)	<.001
Age	Calf	Reference		Reference	
	Yearling	1.75 (1.24, 2.46)	.001	2.09 (1.41, 3.10)	<.001
Treated for BRD	No	Reference		Reference	
	Yes	2.32 (1.91, 2.82)	<.001	2.58 (2.00, 3.33)	<.001

BRD, bovine respiratory disease; CI, confidence intervals; HR, hazard ratio; RHF, right heart failure; UF, Undifferentiated fever.
[a]All years; [b]2012 only.

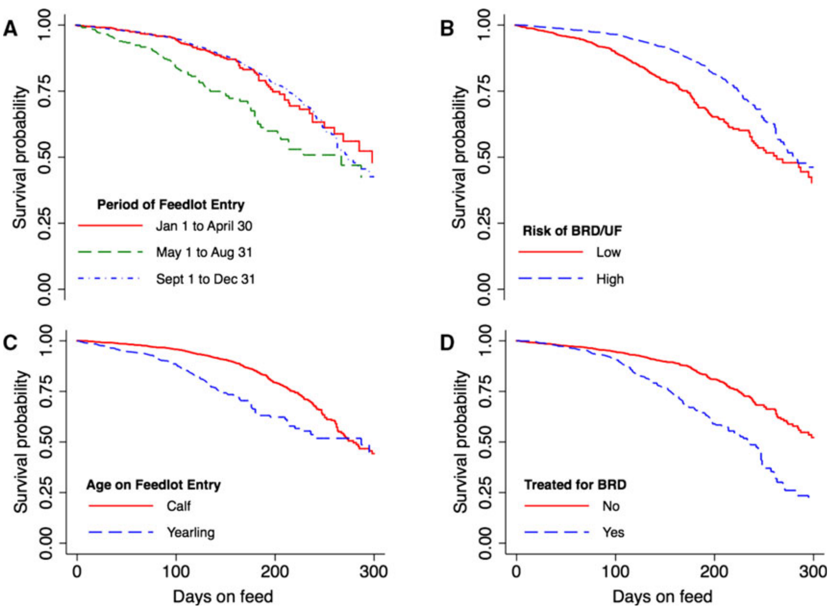

Fig 3. Kaplan–Meier curves, with robust variance estimators, comparing survival times among all cattle that died of right heart failure (RHF) in Canadian feedlots. (**A**) Cattle entering feedlots from May 1 to August 31 died from RHF earlier than cattle entering at any other time ($P \leq .01$). (**B**) Cattle categorized as being at high risk of respiratory disease (BRD) and undifferentiated fever (UF) died from RHF later in the feeding period than cattle at low risk ($P < .001$). (**C**) Cattle entering feedlots as yearlings died from RHF earlier than cattle entering as calves ($P = .002$). (**D**) Cattle treated for BRD died earlier from RHF than cattle not treated ($P < .001$).

Unfortunately, our study design did not allow us to investigate the relationship between RHF risk and feedlot altitude. There were too many potentially confounding variables associated with feedlot altitude, such as altitude from which cattle were procured, to make any conclusions. We can conclude, however, that although hypobaric hypoxia, or prior exposure to hypobaric hypoxia, might have accentuated the risk of RHF in feedlot cattle, neither explanation can adequately explain the increase in RHF mortality over time. This leaves BRD and hypoventilation as possible explanations.

Our results show that cattle treated for BRD were 2–3 times more likely to die of RHF than cattle that were not treated for BRD. Although it is biologically feasible that BRD predisposes to RHF,[10] a causal relationship in cattle has yet to be documented. One may suspect that the increase in RHF risk observed over time was partly attributable to an increase in the risk of BRD over the same time period. Our results, however, show that the likelihood of RHF increased over time even when controlling for BRD treatment.

The second possible explanation, hypoventilation, has been previously suggested as a risk factor for RHF.[5] It could be problematic in feedlot cattle for 2 reasons: First, ruminal engorgement after feeding could compress the lungs and, consequently, reduce effective alveolar ventilation; and second, feedlot cattle accumulate large amounts of body fat through the feeding period.[11] The accumulation of fat in the abdomen and over the

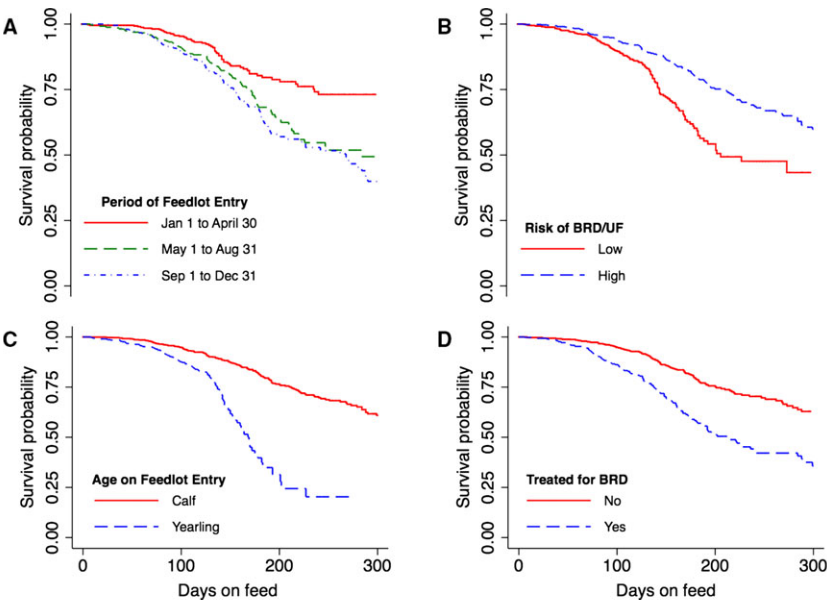

Fig 4. Kaplan–Meier curves, with robust variance estimators, comparing survival times among all cattle that died of right heart failure (RHF) in US feedlots. (**A**) Cattle entering feedlots from January 1 to April 30 died from RHF later than cattle entering at any other time ($P \leq .005$). (**B**) Cattle categorized as being at high risk of respiratory disease (BRD) and undifferentiated fever (UF) died later in the feeding period than cattle at low risk ($P < .001$). (**C**) Cattle entering feedlots died earlier than cattle entering as calves ($P = .001$). (**D**) Cattle treated for BRD died earlier that cattle not treated ($P < .001$).

thorax could increase the mechanical work of breathing.

There are several factors that point to body fat accumulation as a risk factor for RHF. First, RHF predominantly occurred after 4 months on feed, a period coinciding with maximal body fat percentages.[12] Second, yearlings had twice the rate of RHF relative to calves (calf-feds), but over their respective feeding periods, they were equally likely to die from RHF. Perhaps the most parsimonious explanation for these findings is that calves and yearlings are managed to a similar end point: fat cattle ready for slaughter. Yearlings, however, are typically fatter than calves on feedlot entry; this may have predisposed them to a greater risk of RHF earlier in the feeding period. Lastly, and rather paradoxically, cattle with a high risk of BRD/UF were 50% less likely to die of RHF than cattle considered to be a low risk. This seems nonsensical given that treatment for BRD increased the risk of RHF by 2–3 times; unless, however, the risk of BRD/UF was confounded by a risk factor that was protective against RHF such as genetics, body condition, or management differences.

A limitation of our study is that only 4 years of data were used to estimate the risk of RHF in Canadian feedlots. However, we are confident in the precision of our estimates given that our data consisted of 1.56 million cattle that were managed using standardized health management protocols, and were compiled by specialists in feedlot health.[a] Furthermore, although we did not account for potential clustering at the pen-level, our use of robust variance estimators in all models assure that the estimations obtained are conservative. Because, however, only 4 years of data were selected, we cannot rule out the possibility that year-to-year variation in climate or other factors contributed to variation in the risk of RHF. Even if year-to-year variation in climate affected our results, however, any bias in the risk of RHF over time would have occurred toward the null. Instead, we found that relative to the year 2000, the likelihood of RHF was consistently greater in subsequent years.

Another limitation is that because only Canadian feedlots were studied over multiple years we cannot make inferences regarding how the risk of RHF in US feedlots changed over the same time period. However, the available evidence suggests that the incidence of RHF in US feedlot cattle has increased substantially. In 1974, a study of 4 US feedlots located at an altitude of 1,600 m reported the risk of RHF to be 2.85 cases per 10,000 cattle entering the feedlot.[5] In our study of US feedlots, the risk of RHF was notably higher: ranging from 4 to 17 deaths per 10,000 cattle entering feedlots at altitudes ranging from 596 to 1,282 m, respectively.

Footnotes

[a] Feedlot Health Management Services Ltd, Okotoks, Alberta, Canada

[b] STATA version 12, Stata Corporation, College Station, TX

Acknowledgments

Conflict of Interest Declaration: Authors disclose no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

References

1. Alexander AF, Jensen R. Pulmonary vascular pathology of high altitude induced pulmonary hypertension in cattle. Am J Vet Res 1963;24:1112–1122.
2. Alexander AF, Jensen R. Pulmonary arteriographic studies of bovine high mountain disease. Am J Vet Res 1963;24:1094–1097.
3. Glover GH, Newsom IE. Brisket Disease (Dropsy of High Altitude). Colorado Agricultural Experiment Station; Fort Collins, CO, USA. 1915:3–24.
4. Hecht HH, Kuida H, Lange RL, et al. Brisket disease. II. Clinical features and hemodynamic observations in altitude-dependent right heart failure of cattle. Am J Med 1962;32:171–183.
5. Jensen R, Pierson RE, Braddy PM, et al. Brisket disease in yearling feedlot cattle. J Am Vet Med Assoc 1976;169:515–517.
6. Malherbe CR, Marquard J, Legg DE, et al. Right ventricular hypertrophy with heart failure in Holstein heifers at elevation of 1,600 meters. J Vet Diagn Invest 2012;24:867–877.
7. USDA. Cattle Fattened on Grain and Concentrates and Sold, 1997. Available at: http://www.agcensus.usda.gov/Publications/1997/Ag_Atlas_Maps/Livestock_and_Animals/map193.gif. Accessed March 5, 2015.
8. NRC. Nutrient Requirements of Beef Cattle: Seventh Revised Edition: Update 2000. Washington DC: The National Academies Press; 2000.
9. Blake JT. Occurrence and Distribution of Brisket Disease in Utah. Logan, UT: Utah State University Utah Agricultural Experiment Station Circular; 1968:2–15.
10. Holt T, Callan R. Pulmonary arterial pressure testing for high mountain disease in cattle. Vet Clin North Am Food Anim Pract 2007;23:575–596.
11. Rathmann RJ, Bernhard BC, Swingle RS, et al. Effects of zilpaterol hydrochloride and days on the finishing diet on feedlot performance, carcass characteristics, and tenderness in beef heifers. J Anim Sci 2012;90:3301–3311.
12. Owens FN, Gill DR, Secrist DS, et al. Review of some aspects of growth and development of feedlot cattle. J Anim Sci 1995;73:3152–3172.