Association between computer-aided lung auscultation and treatment failure risk in calves treated for respiratory disease

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Abstract — The use of computer-aided lung auscultation (CALA, Whisper Veterinary Stethoscope; Merck Animal Health, Madison, New Jersey, USA) is a relatively new approach to assist in confirming the diagnosis of bovine respiratory disease (BRD). For this prospective cohort study at 1 feedlot in the United States, a CALA score was generated for 2726 feeder cattle (calf-fed Holsteins and mixed-breed beef animals) at the time of the first BRD diagnosis and treatment. All cattle were treated according to the same BRD protocol prescribed for that facility and the protocol was not influenced by the CALA score. Data were collected for 120 d after enrollment. In this study, the risk of BRD retreatment and the risk of BRD mortality were each significantly ($P < 0.05$) associated with the CALA score at the time of first BRD diagnosis and treatment, and those risks increased (numerically and in some cases statistically) as the CALA score increased.

Résumé — Association entre l'auscultation pulmonaire assistée par ordinateur et le risque d'échec du traitement chez les veaux traités pour une maladie respiratoire. L'utilisation de l'auscultation pulmonaire assistée par ordinateur (CALA, Whisper Veterinary Stethoscope; Merck Animal Health, Madison, New Jersey, USA) est une approche relativement nouvelle pour aider à confirmer le diagnostic de maladie respiratoire bovine (BRD). Pour cette étude de cohorte prospective dans un parc d'engraissement aux États-Unis, un score CALA a été généré pour 2726 bovins d'engraissement (veau Holstein et bovins de race mixte) au moment du premier diagnostic et traitement de la BRD. Tous les bovins ont été traités selon le même protocole BRD prescrit pour ce site et le protocole n'a pas été influencé par le score CALA. Les données ont été collectées pendant 120 jours après l'inscription. Dans cette étude, le risque de retraitement pour BRD et le risque de mortalité associée au BRD étaient chacun significativement ($P < 0,05$) associés au score CALA au moment du premier diagnostic et traitement BRD, et ces risques augmentaient (numériquement et dans certains cas statistiquement) à mesure que le score CALA augmentait.

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The diagnosis of bovine respiratory disease (BRD) can be difficult due to limited accuracy of current diagnostic modalities. Manual lung auscultation is 1 diagnostic test traditionally used to assist in confirming the BRD diagnosis. However, the accuracy and reliability of manual auscultation among veterinary practitioners has recently been shown to be poor (1). Computer-aided lung auscultation (CALA, Whisper Veterinary Stethoscope; Merck Animal Health, Madison, New Jersey, USA) is a relatively new approach to assist in confirming the diagnosis of BRD. This technology is easily applied at the time of BRD diagnosis by trained, on-farm animal health personnel. The CALA system is composed of an automated stethoscope wirelessly connected to a chute-side computer. Once the animal is secured in the chute, the CALA device is placed on the right side of the animal's thorax (just caudal to the right forelimb) and an 8 s recording is collected by the system and analyzed by the system software. Within seconds, the CALA score for the animal appears on the computer screen. On average, it is estimated that this process requires an additional 30 s per animal among animals removed presumptively for BRD. The objective of this prospective cohort study at 1 feedlot in the United States was to investigate the association between CALA and treatment failure risk in calves treated for BRD.

In this study, a CALA score was generated for 2726 feeder cattle (calf-fed Holsteins and mixed-breed beef animals) at the time of the first BRD diagnosis and treatment. All cattle were

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Merck Animal Health is the sole owner of the Whisper Veterinary Stethoscope technology.

Table 1. Backward elimination model-building sequence using fixed effect of CALA score (1 to 5), breed ("B" = Holstein or beef), and rectal temperature ("Temp" ≤ 40.5°C or > 40.5°C); and their association with the risk of BRD retreatment. The sequence began with the 3-way interaction (Model 1); terms were sequentially removed until the Final model contained variables that met $P < 0.05$. For each subsequent model, the variable with the largest *P*-value was removed.

Classification variables	Model 1[a]		Model 2[a]		Model 3[a]		Model 4		Final model	
	F-stat	*P*-value	F-stat	*P*-value	F-stat	*P*-value	F-stat	*P*-value	F-stat	*P*-value
CALA × B × Temp	0.57	0.69	NA		NA		NA		NA	
CALA × Temp	0.18	0.95	0.79	0.53	NA		NA		NA	
CALA × B	1.03	0.39	1.04	0.39	1.24	0.29	NA		NA	
B × Temp	0.00	0.98	2.40	0.12	2.84	0.09	1.45	0.23	NA	
CALA	1.94	0.10	2.00	0.09	2.47	0.04	3.05	0.02	3.06	0.02
B	0.00	0.98	2.57	0.11	2.40	0.12	0.13	0.73	0.21	0.65[b]
Temp	0.00	0.98	4.48	0.03	14.98	< 0.01	14.37	< 0.01	13.28	< 0.01

[a] A random effect was implemented to account for clustering within the month of enrollment. Models 1 through 3 did not converge with the stated random effect and do not reflect adjustment for clustering within the month of enrollment. Model 4 and the Final model reflect adjustment for the random effect of enrollment month.
[b] The inclusion of breed in the Final model (despite a non-statistically significant outcome) reflects the likely confounding effect on the CALA estimate. When breed was removed from the model, the F-statistic for CALA was reduced by 45%, which was greater than the threshold of 30% determined *a priori* to the study to be considered as a possible confounding variable. Therefore, breed was considered to be a potential confounder and remained in the model to properly adjust the CALA estimate.
NA — not applicable.

Table 2. Backward elimination model-building sequence using fixed effect of CALA score (1 to 5), breed ("B" = Holstein or beef), and rectal temperature ("Temp" ≤ 40.5°C or > 40.5°C); and, their association with the risk of BRD mortality. The sequence began with the 3-way interaction (Model 1); terms were sequentially removed until the Final model contained variables that met $P < 0.05$. For each subsequent model, the variable with the largest *P*-value was removed.

Classification variables	Model 1[a]		Model 2[a]		Model 3[a]		Model 4		Final model	
	F-stat	*P*-value	F-stat	*P*-value	F-stat	*P*-value	F-stat	*P*-value	F-stat	*P*-value
CALA × B × Temp	0.13	0.97	NA		NA		NA		NA	
CALA × Temp	0.58	0.68	0.52	0.72	NA		NA		NA	
CALA × B	1.06	0.38	1.38	0.24	1.29	0.28	NA		NA	
B × Temp	0.00	0.98	1.25	0.26	2.02	0.16	1.23	0.28	NA	
CALA	3.93	< 0.01	4.68	< 0.01	5.12	< 0.01	10.85	< 0.01	10.85	< 0.01
B	0.00	1.00	21.89	< 0.01	23.68	< 0.01	18.26	< 0.01	17.45	< 0.01
Temp	0.00	0.98	0.68	0.41	10.21	< 0.01	7.37	0.01	6.34	0.02

[a] A random effect was implemented to account for clustering within the month of enrollment. Models 1 through 3 did not converge with the stated random effect; and, do not reflect adjustment for clustering within the month of enrollment. Model 4 and the Final model reflect adjustment for the random effect of enrollment month.
NA — not applicable.

treated according to the same BRD protocol prescribed for that facility and the protocol was not influenced by the CALA score. Data were collected for 120 d after enrollment. In this study, the risk of BRD retreatment and the risk of BRD mortality were each significantly ($P < 0.05$) associated with the CALA score captured at the time of first BRD diagnosis and treatment. In addition, those risks increased (numerically and in some cases statistically) as the CALA score increased.

The Whisper Veterinary Stethoscope is a computer-aided lung auscultation (CALA) system that records thoracic sounds; processes those sounds with a proprietary, machine-learning algorithm; and generates a score from 1 to 5 that reflects the overall severity of pulmonary disease. A score of 1 reflects lung tissue that is relatively healthy, whereas score 5 indicates severely compromised lung health.

The study was performed at 1 feedlot in the United States from July 29, 2015 to April 15, 2017, during which time 2726 cattle were evaluated. The experimental population was composed of calf-fed Holsteins (n = 2023) and mixed-breed, auction market-derived, beef steers and heifers (n = 703) that were enrolled in the study at the time of the initial BRD diagnosis and treatment. Body weight at the time of enrollment ranged from 71 to 699 kg. When observed in their feedlot pen, a tentative diagnosis of BRD was assigned based on subjective criteria (general appearance, attitude, gauntness, reluctance to move). Those animals were then individually separated from pen-mates and moved to the hospital facility. Animals with clinical signs not attributable to BRD were excluded from the study. During physical examination of each animal at the time of initial BRD diagnosis and treatment, a CALA score and rectal temperature were recorded for each animal by feedlot personnel. As per normal feedlot operating procedure, cattle were subsequently categorized with rectal temperatures ≤ 40.5°C or > 40.5°C. Criteria for diagnosis and the respective treatment protocol were based on prescribed standard operating procedures for the feedlot. The CALA score was not used to determine diagnosis or treatment.

Animals were monitored for 120 d after enrollment. Similar to initial assessment for respiratory disease, when animals were observed in their feedlot pen, a tentative diagnosis of BRD relapse was assigned based on the subjective criteria. Those animals were then individually separated from pen-mates and moved to the hospital facility where animals with no abnormal clinical signs referable to body systems other than the respiratory tract were diagnosed and treated for BRD a second time. As part of the standard feedlot protocol, a gross post-mortem

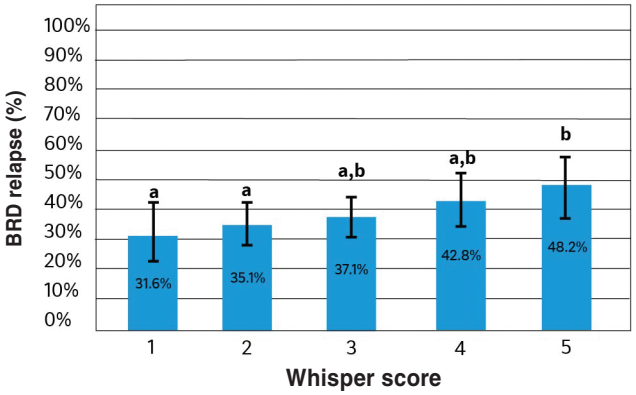

Figure 1. Model-adjusted estimates (%) of risk of BRD retreatment and 95% CI by CALA score. CALA scores with different letters indicate a significant difference ($P < 0.05$) between scores.

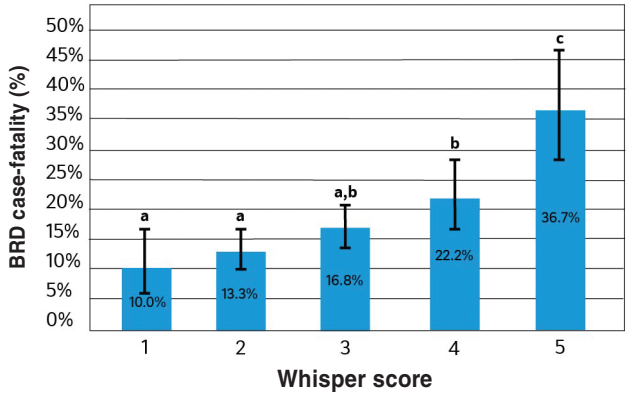

Figure 2. Model-adjusted estimates (%) of risk of BRD mortality and 95% CI by CALA score. CALA scores with different letters indicate a significant difference ($P < 0.05$) between scores.

examination was completed on all animals that died. In some instances, a veterinarian from Feedlot Health Management Services (Feedlot Health – Okotoks, Alberta) conducted the post-mortem examination on site and determined the cause of death based on clinical history and a gross post-mortem examination. In other instances, trained personnel prosected the dead animals using a standardized method to capture appropriate digital images as outlined in the written necropsy protocol provided by Feedlot Health. Subsequently, all digital images were electronically transferred to Feedlot Health and the cause of death for each animal was determined based on the clinical history and the gross post-mortem examination by a Feedlot Health veterinarian. Mortality due to BRD was defined as mortality due to bronchopneumonia, bronchointerstitial pneumonia, bronchopneumonia and arthritis, chronic bronchopneumonia, chronic mycoplasma-like bronchopneumonia, fibrinous pneumonia, chronic fibrotic pleuritis, infectious bovine rhinotracheitis, lung abscess, or viral interstitial pneumonia.

Data analyses were performed using generalized linear mixed models (GLIMMIX procedure; SAS, Cary, North Carolina, USA) with the animal as the experimental unit. Within each model, a binomial distribution was assumed, and a logit link was used. All necessary clustering effects were accounted for in all models. A backwards step-wise model building procedure was implemented to determine a final multivariable model. The fixed effects in the model statement included CALA score, breed (i.e., Holstein or beef), and rectal temperature ($\leq$ 40.5°C or $>$ 40.5°C). The denominator degrees of freedom were adjusted by the Kenward-Rogers method. Based on the available data, cattle were clustered at 2 levels: the lot and the time frame of enrollment. The lot was first evaluated as a random effect; however, subsequent analysis revealed that numerous lots contained only 1 calf that was enrolled in the study which created model convergence challenges. Therefore, a random effect was implemented to account for clustering among animals enrolled within the same month. Utilizing these 3 main effect variables (CALA score, breed, and rectal temperature), all biologically plausible 2- and 3-way interactions were assessed. An alpha level of 0.05 was used for inclusion of all parameters (main effects and interactions) in the final model statement. Confounding and collinearity among the variables in the final model were evaluated by standard methods (3). Least-square means were generated for CALA score estimates. Multiple comparisons among CALA scores were adjusted by the Tukey-Kramer method.

Across the sample population (N = 2726), the proportion of calves requiring BRD retreatment was 36.9% (n = 1005) and the BRD case-fatality was 15% (n = 410).

An overview of the model building procedures for the BRD retreatment and mortality outcomes is displayed in Tables 1 and 2, respectively. The risk of BRD retreatment was significantly ($P < 0.05$) associated with the CALA score at the time of initial BRD diagnosis and treatment (Table 1). The model-adjusted means reflecting the risk of BRD retreatment and associated 95% confidence interval (CI) for each of the 5 CALA scores are shown in Figure 1.

The risk of BRD mortality was significantly ($P < 0.05$) associated with the CALA score collected at the time of initial BRD diagnosis and treatment (Table 2). Model-adjusted estimates of BRD mortality risk and associated 95% CI for each of the 5 CALA scores are shown in Figure 2.

Under the conditions of this study using the Whisper Veterinary Stethoscope, the CALA score (scale of 1 to 5) collected at the time of initial BRD diagnosis and treatment was significantly associated with the risks of BRD retreatment and BRD mortality. These respective risks increased most notably as the CALA score increased from 3 to 5. Findings of this study were similar to those of previous research evaluating the relationship of the CALA score and the risk of BRD retreatment and mortality (2). DeDonder et al (2) observed a significant association between a greater Whisper score, collected at the time of initial BRD treatment, and the risks of requiring BRD retreatment and BRD mortality. In that study, cattle were followed to closeout. Further analyses revealed a strong correlation (R^2 = 0.89; $P < 0.0001$) between the ante-mortem CALA score and the magnitude of post-mortem lung lesions observed at slaughter (2).

Application of this technology at the time of BRD treatment is typically performed by feedlot lay staff. Findings from this study indicated that CALA scores generated by the Whisper Veterinary Stethoscope at the time of initial BRD diagnosis

and treatment are associated with the risks of subsequent BRD retreatment and BRD mortality. More research is necessary to identify the value proposition of implementing this technology in commercial feedlot production systems.

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