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Systematic thoracic ultrasonography in acute bovine respiratory disease of feedlot steers: impact of lung consolidation on diagnosis and prognosis in a case-control study

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Abstract

A study was conducted to evaluate the diagnostic and prognostic value of thoracic ultrasonography (TUS) in feedlot calves with clinical signs attributable to bovine respiratory disease (BRD). Twenty-nine BRD cases and 15 asymptomatic controls were evaluated using systematic TUS on the day of initial pull (day 0), and days 3, 6, 9, and 15. Four-second ultrasound loops were saved at 46 locations per animal and later evaluated off-line for evidence of lung pathology. Five TUS indicators of lung lesions and 4 indices of consolidation were evaluated for ability to differentiate between healthy controls and BRD cases, as well as predict death (negative outcome) among non-treated BRD cases.

The number of sites with consolidation (SITES), number of sites with pleural irregularities (PIRR), maximal depth of consolidation (DEPTH), maximal area of consolidation (AREA), and total consolidated area (TCA) were found to be significantly higher in BRD cases than controls at enrollment ($P<0.05$). These same parameters (SITES, PIRR, DEPTH, AREA, TCA) were found to be significantly higher at enrollment for BRD cases that died before the end of the 15-day observation period ($P<0.05$). Among BRD cases, 9 of 46 sites examined had an odds ratio of negative outcome significantly greater than 1 when consolidation was present at enrollment ($P<0.05$). This study demonstrates that TUS may prove useful in feedlot cattle for determining the extent of lung lesions and predict outcome in BRD cases.

Key words: bovine respiratory disease, thoracic ultrasonography, beef cattle, clinical diagnosis

Résumé

Une étude a été menée afin d'évaluer la valeur du diagnostic et du pronostic de l'échographie thoracique chez les veaux de parc d'engraissement avec des signes cliniques attribuables au complexe respiratoire bovin. L'étude comportait 29 cas avec le complexe respiratoire bovin et 15 témoins asymptomatiques qui ont évalués avec l'échographie thoracique systématique au moment de leur arrivée (jour 0) et aux jours 3, 6, 9, et 15. On a récupéré des enregistrements d'échographie thoracique de 4 secondes au niveau de 46 localisations chez chaque animal. Ces enregistrements ont ensuite été évalués hors ligne pour des signes pathologiques pulmonaires. On a évalué cinq indicateurs de lésions pulmonaires avec les échographies thoraciques et quatre index de consolidation afin de déterminer s'il était possible de distinguer les témoins en santé des cas atteints du complexe respiratoire bovin de même que de prédire la mort (issue négative) parmi les cas non-traités.

Le nombre de sites avec consolidation, le nombre de sites avec des irrégularités pleurales, la profondeur maximale de la consolidation, l'aire maximale de la consolidation et l'aire total de consolidation étaient significativement plus élevés chez les cas que chez les témoins à l'arrivée ($P<0.05$). Ces mêmes paramètres étaient aussi significativement plus élevés à l'arrivée chez les cas qui sont décédés avant la fin de la période d'observation de 15 jours ($P<0.05$). Parmi les cas, le rapport de cotes pour une issue négative était significativement plus grand que 1 pour 9 des 46 sites examinés lorsque la consolidation était présente à l'arrivée ($P<0.05$). Cette étude démontre que l'échographie thoracique peut être utile chez les bo-

vins en parc d'engraissement pour déterminer l'étendue des lésions pulmonaires et prédire l'issue de cas avec le complexe respiratoire bovin.

Introduction

Despite intensive research into management and prevention strategies, the bovine respiratory disease (BRD) complex remains the primary health concern for the cattle feeding industry during the early finishing phase of production.[14] One challenging aspect of BRD case management is the accurate and timely recognition of those animals at higher risk of experiencing adverse health outcomes, which include impaired growth,[21,22] relapse or treatment failure, and death.[2]

The practical application of any BRD diagnostic in a field setting is dictated by its diagnostic and prognostic accuracy, expense, speed, ease of use, and ability to be performed chute-side. Recent investigations have focused on ancillary tests using blood biomarkers[2,11,23] or diagnostic ultrasonography.[1,19] Thoracic ultrasonography (TUS) holds promise due to its reported accuracy for diagnosis of parenchymal lung lesions, especially consolidation associated with infectious bronchopneumonia.[4] Additionally, TUS is well correlated with gross lesions found at postmortem examination of dairy calves suffering from naturally occurring respiratory disease,[13,18] and may therefore be used for the antemortem assessment of the severity and extent of pulmonary lesions. Data is scant and controversial concerning the application of TUS in feedlot cattle. A recent study conducted in commercial feedlots in western Canada found no prognostic value of TUS; however, the investigators concluded TUS may be useful for evaluation of chronically diseased cattle.[1] In contrast, researchers recently demonstrated that ultrasonographic evidence of lung consolidation is negatively associated with average daily gain (ADG) in pre-weaned dairy calves.[17]

Ultrasonographic lesions associated with BRD consist of 1) alteration of the pleural surface of the lung, 2) varying degrees of lung consolidation due to inflammation and exudate deposits in the alveolar bed and small bronchi, 3) varying amounts of pleural fluid accumulation, and 4) cavitary lesions in cases of lung abscessation.[4,6,19] Because ultrasonography is an antemortem diagnostic tool that can be used to assess the extent of lung lesions,[19] and lung lesions and inflammation negatively impact growth,[15] we hypothesized that systematic TUS could be used as an indicator of disease severity in feedlot calves acutely affected with BRD.

The objective of this case-control study was to assess the utility of extensive, systematic TUS examination as a diagnostic and prognostic tool in feedlot steers suffering from signs consistent with acute BRD.

Materials and Methods

Procurement and Processing

The experimental protocol was developed, reviewed to ensure humane treatment of study animals, and approved by the Research Department, Johnson Research, LLC, Parma, Idaho.

During the summer of 2012, 3 truckload lots of multiple source, recently weaned beef steers were purchased from auction markets in California and transported to a research feedlot in southwestern Idaho (Table 1). All cattle were processed within 24 hours of arrival following standard feedlot protocol. Briefly, study animals were administered a pentavalent modified-live viral vaccine[a], 9-way clostridial bacterin-toxoid[b], injectable moxidectin[c], and a growth-promoting implant containing 200 mg trenbolone acetate and 40 mg estradiol[d]. Metaphylactic antimicrobial therapy and bacterin-toxoids typically used for prevention of disease associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and/or *Histophilus somni* were withheld in order to achieve the incidence of BRD required by the study protocol. Cattle were housed in groups of 14 to 20 head in open-air, dirt-floor pens with dimensions of 25 by 70 feet (7.6 by 21.3 m), thereby providing a total of 1750 feet^2 (162.6 m^2) of space per pen. A typical feedlot starter ration was delivered once daily in the morning to permanent concrete bunks lining the front of each pen, with bunk space provided at a rate of 15.0 to 21.4 inches (38.1 to 54.4 cm) per head.

Enrollment

All cattle were observed daily by an experienced animal health evaluator (RR) for clinical signs attribut-

Table 1. Procurement data by load.

Sale date	Origin	Processing date	Head (n)	Time on truck (hrs)	Median processing weight (lb) (min max)
June 27 2012	Galt, CA	June 29 2012	76	12	614.5 (481 to 749)
July 12 2012	Orland, CA	July 14 2012	78	15.5	589.5 (449 to 773)
July 25 2012	Aromas, CA	July 28 2012	78	15	591 (485 to 762)

able to BRD and assigned depression and respiratory scores consistent with regulatory standards used in pivotal antimicrobial approval studies (Table 2). Animals with less than 45 days-on-feed (DOF) were eligible for enrollment, and candidates were selected if they met the following criteria: depression score ≥ 1 and respiratory score ≥ 1, or a score ≥ 2 in either category; and rectal temperature ≥ 104.0°F (≥ 40.0°C). Candidates were subjected to a bronchial lavage (BL)[3] and TUS examination. Serial dilutions of recovered BL solution were plated on day 0 and then read after incubation at 98.6°F ± 5.4°F (37°C ± 3°C) and 10% CO_2 ± 3% for 18 to 36 hours. Final enrollment as a case was determined by demonstration of clinical signs, pyrexia, and *M. haemolytica* levels of ≥ 1.0 x 10^5 colony forming units (CFU) per mL of recovered BL fluid. Calves that did not qualify based on the CFU criteria, but in which pulmonary lesions were visualized on day 0 via TUS, were also enrolled on the study.

In order to eliminate the variable of treatment response, case animals did not receive antimicrobial treatment during the study. This allowed investigators to determine diagnostic and prognostic accuracy of TUS in naturally occurring BRD in feedlot calves with no effect of treatment. In addition, by not treating cases, a much smaller sample size was needed to determine statistically significant differences in ultrasonographic findings between survivors and non-survivors.

Cohorts consisted of 2 cases and 1 asymptomatic control. Following enrollment of the first case of a cohort, a period of 36 hours was allowed for enrollment of the second case before the cohort was closed. Control calves were randomly selected from the same load as the case animal, and qualified for enrollment only if depression and respiratory scores equaled 0, rectal temperature was < 104.0°F (< 40.0°C), and *M. haemolytica* was detected at a level of < 1.0x10^5 CFU per mL of recovered BL fluid. All control steers were treated prophylactically with tilmicosin phosphate[e] administered subcutaneously at the rate of 6.0 mg/lb (13.2 mg/kg) on the day of enrollment (day 0) and again 6 days later (day 6).

Ultrasonographic Examination and Evaluation

Enrolled steers were subjected to full TUS examinations at enrollment (day 0), and days 3, 6, 9, and 15 in order to assess the dynamic component of lung lesions during the early feeding period. Thoracic ultrasonography was performed in a manual squeeze chute using a portable ultrasound unit with a 66 mm array linear rectal probe (5 to 8 MHz)[f]. Preparation of the site to be scanned was performed using 70% isopropyl alcohol without clipping the hair.

Prior to initiating the trial, the research team reviewed TUS technique and clinical interpretation in order to achieve consensus on ultrasonographic lesions

Table 2. Depression and respiratory scoring system.

Depression score		
0	Healthy	No clinical signs attributable to bovine respiratory disease.
1	Mild	Animals showing mild signs of depression may stand or lie isolated from the other cattle in the pen with ears or head drooped. They will respond to visual stimulation during scoring and readily move away from the observer. Mild dehydration (sunken appearance of the eyes).
2	Moderate	Animals show similar signs of drooped ears and head, but are slower to respond to the observer. May have difficulty in getting up, lack of effort to stretch, and may knuckle when walking. More pronounced dehydration.
3	Severe	Moribund
Respiratory score		
0	Healthy	No clinical signs attributable to bovine respiratory disease.
1	Mild	Serous nasal or ocular discharge. Dry cough and/or elevated respiratory rate. Subtle excessive salivation.
2	Moderate	Purulent or mucopurulent eye and/or nasal discharge, productive cough, and forced respiratory effort. Excessive salivation.
3	Severe	Open-mouth breathing, dyspnea, excessive salivation.

and measurements. The TUS method used in the current study was previously reported in dairy calves; it was found to be accurate in the assignment of lung lesion scores, even when performed by novice ultrasonographers.[9] A total of 46 locations (23 per side) on the thorax spanning intercostal spaces 4 to 10 were examined. Each intercostal space was divided in 5 locations from dorsal to ventral: 1) the level of the tuber coxae, 2) mid-distance between the shoulder joint and the dorsal border of the scapula, 3) the level of the shoulder joint, 4) mid-diaphysis of the humerus, and 5) the point of the elbow (Figure 1). Using the 13th rib as a landmark, the TUS examination was performed starting in the 10th intercostal space (ICS) and proceeding cranially. Images were captured from all imaging locations in each respective ICS, moving from dorsal to ventral, before proceeding to the next ICS. In order to ensure scanning location consistency, a grease marker was used to mark the rib caudal to the ICS of interest. A maximal depth of 11.8 cm was set for all ultrasonographic examinations.

A 4-second loop of ultrasound footage was stored for each location and evaluated off-line by the same operator (RR) after the study period was complete in order to reduce bias. Each loop was evaluated using the identical procedure to assess for the presence of lung consolidation, comet-tail artifacts, pleural irregularity (defined as a corrugated pleural line as opposed to the smooth line found in healthy animals[4,7]) or thickening, pleural fluid accumulation (defined as observation of the pleural cavity),[4] and cavitary lesions indicative of abscessation.[10] The total number of comet-tail artifacts per field was noted and the maximum value for each steer was used for further analysis (TAIL). The maximal depth of pleural fluid accumulation was noted if detected (PLEFF); the number of sites with pleural thickening (THICK) and/or pleural irregularity (PIRR) was also compiled. Since only 1 surviving case steer had more than 1 site with pleural thickening (n = 8), THICK was classified as a dichotomous variable (0 = absence of pleural thickening; 1 = pleural thickening present in at least one site) for further analysis.

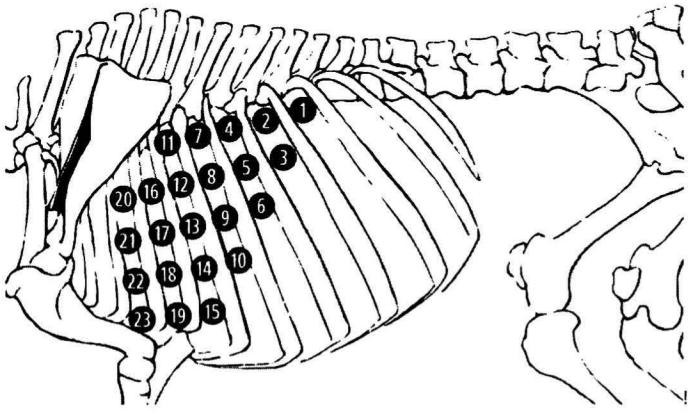

Figure 1. Diagram of ultrasound locations on the left hemithorax. Locations were labeled from 1 to 23 and repeated on the right side of the animal.

The maximal depth of consolidated lung was noted for every steer (DEPTH, cm). The area of consolidated lung was calculated for each location using the 1 cm^2 grid of the ultrasound unit and manually counting the squares. The maximal area of consolidation per animal was determined for each examination (AREA, cm^2). A global index of lung consolidation was created using the sum of consolidated area from all locations (TCA: total consolidated area per steer, cm^2). The number of sites with consolidation present (SITES) was also recorded.

Following final TUS observation on day 15, surviving case steers were treated with injectable tilmicosin[e] (6.0 mg/lb or 13.2 mg/kg, subcutaneously). Any steer that became recumbent and could not reach food and water, or any animal deemed to have a grave prognosis by the primary investigator during the study period, was humanely euthanized. Steers that were euthanized or found dead during the study period were necropsied to confirm the presumptive diagnosis of BRD. These steers were considered to have severe forms of BRD, and were classified as non-survivors (negative outcome) for further analysis.

Statistical Analysis

Ultrasonographic examinations were stored on a memory card until analysis. Examination findings were compiled in a commercially available spreadsheet software program[g]. Data were subsequently exported to other commercially available software programs[h,i] for full statistical analysis.

Outcomes of interest for the present study were 1) the ability of TUS to accurately distinguish cases from control steers, 2) the ability of TUS to accurately determine disease severity and subsequently predict mortality in morbid steers, and 3) the identification of TUS locations that have greater value for establishing case prognosis.

In order to determine the most efficient means of implementing TUS in a commercial feedlot setting, additional analyses were performed assessing the accuracy of ultrasonographic findings. The concordance of results between the right and left sides of the thorax was assessed using the kappa agreement for consolidated lung diagnosis in the right and left lungs. The intra-class correlation coefficients (ICC) were determined for single and average measurements to assess the relationship between the number of consolidated sites from the right and left sides of the thorax.

In addition, each location was classified as either having consolidation present on day 0 or not. This di-

chotomous classification did not take into account the degree of consolidation. An odds ratio was calculated at each site using logistic regression to evaluate the relationship between negative outcome and consolidation for each ultrasound location (LOGISTIC procedure in SAS). Wald 95% confidence intervals were estimated for the odds ratios.

A descriptive analysis of the data was performed. Because the data were not normally distributed and therefore did not meet the assumptions for normality, non-parametric statistical analysis was performed. A Wilcoxon rank sum analysis was employed to compare the continuous, non-normally distributed ultrasonographic parameters in cases compared to control steers, and in survivors compared to non-survivor steers (TAIL, PIRR, PLEFF, DEPTH, AREA, TCA, SITES). For dichotomous variables (THICK, ABSCESS), descriptive statistics were used.

The diagnostic accuracy of ultrasonographic parameters of consolidation that differed significantly depending on case outcome was then analyzed using receiver-operating characteristic (ROC) curves. The different areas under the ROC curves were compared using non-parametric analysis as previously described[12] in order to determine the most accurate parameter of interest among ultrasonographic indicators of consolidation.

In order to take into account the dynamic nature of lung lesions (i.e. depth of consolidation; the easiest measurement to capture chute-side) between different observation time points, a survival analysis was performed for sick calves using negative outcome before the end of the study as the outcome of interest. Lung consolidation was also assessed using Cox regression for proportional hazard analysis with DEPTH as a time dependent covariate (PHREG procedure in SAS). The proportional hazard assumption was determined for assessing the absence of significance of the interaction DEPTH*TIME, with TIME representing the various intervals (days 0 to 3; days 3 to 6; days 6 to 9, and days 9 to 15) between observations.

The level of significance for all statistical analysis was set at $P<0.05$.

Results

A total of 29 cases and 15 control steers were included in the study. Of the 29 cases enrolled in the study, 12 did not survive the 15-day study period. Two of the 12 non-survivors were euthanized due to welfare concerns. All non-survivors were necropsied and confirmed to have succumbed to complications of primary BRD.

Average TUS image quality was good, and the approximate time to conduct the full examination was 45 minutes (which included time to screen the 23 sites on each side of the thorax and to store the 46 resulting 4-second cineloops). Evidence of consolidation was found in 22 of 29 cases, with a median of 3 sites per steer (range 0 to 15 sites) and in 3 of 15 controls (median 0; range 0 to 2 sites). No abscesses were found at the time of initial pull. Evidence of PTHICK was found in 4 of 25 cases, but was not found in any control steers. A summary of additional lung lesion indicators (TAIL, PIRR, PLEFF) and consolidation indices (DEPTH, AREA, TCA, SITES) is presented in Table 3.

The median number of consolidated sites on the right side of the thorax was 1 (range 0 to 8) in case steers and 0 (range 0 to 1) in control steers. On the left side of the thorax, the distribution of lesions was similar in BRD steers (median 1; range 0 to 8) and control steers (median 0; range 0 to 2). Despite these apparent similarities, the kappa agreement between the right and left sides for ultrasonographic diagnosis of consolidation was moderate (0.500; 95% confidence interval (CI) from fair to good (0.251 to 0.749)). The ICC was 0.663 (95% CI: 0.458 to 0.801) for single measurement and 0.797 (95% CI: 0.629 to 0.889) for average measurement.

A total of 9 individual locations yielded an OR > 1 ($P<0.05$) when relating the presence of consolidation on day 0 to a negative outcome (Figure 2). These included 5 sites on the left side of the animal (L9, L10, L14, L18, and L19) and 4 sites on the right side (R14, R18, R19, and R22) (Table 4). When consolidation was present in locations L18, L19, R18, and R19 concurrently, the OR of a negative outcome increased to 9.685 (95% CI: 4.420 to 21.221).

The accuracy of the various indicators of consolidation for predicting mortality in case steers was assessed by calculating the area under the ROC curve. Area under the ROC curve did not differ significantly for DEPTH (0.814; 95% CI 0.626 to 0.933), AREA (0.765; 0.571 to 0.901) or TCA (0.814; 0.626 to 0.933). Pairwise comparisons between area under the ROC curve were made using a non-parametric Mann-Whitney U test for DEPTH to AREA ($P=0.29$), DEPTH to TCA ($P=1.0$), and AREA to TCA ($P=0.28$). Optimal cutoffs for these 3 parameters are presented in Table 5. Notably, setting the maximal depth cutoff at 5 cm would have a sensitivity of 75% and a specificity of 82% for the prediction of non-survivors. DEPTH used as a time-dependent covariate was significantly associated with the hazard of dying (hazard ratio (HR)=2.24; 95% CI:1.35 to 3.66 per 1 cm increase, $P=0.001$) in survival analysis.

Discussion

Results of the current study suggest systematic TUS examination at the time of first pull in feedlot calves provides useful prognostic information in cases of naturally occurring BRD when no treatment is administered. Among the ultrasonographic predictors of

Table 3. Ultrasonographic findings at enrollment in 29 steers with clinical suspicion of acute BRD and in 15 clinically healthy steers. Examination in cases and control steers (A), and in survivor and non-survivor (negative outcome) BRD cases (B).

A							
Ultrasonographic	**Acute BRD steers (n=29)**			**Control steers (n=15)**			
parameter	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	***P* value**
TAIL* (n)	0	0	7	0	0	2	0.25
PIRR† (n)	4	0	16	1	0	4	0.0006[a]
PLEFF‡ (cm)	0.5	0	5	0	0	5	0.16
DEPTH§ (cm)	5	0	10	0	0	5	0.0001[a]
AREA‖ (cm^2)	17	0	65	0	0	13	0.0002[a]
TCA¶ (cm^2)	28	0	252.5	0	0	13	0.0002[a]
SITES# (n)	3	0	15	0	0	2	<0.0001[a]
B							
Ultrasonographic	**Non-survivors (n=12)**			**Survivors (n=17)**			
parameter	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	***P* value**
TAIL* (n)	1	0	4	0	0	7	0.06
PIRR† (n)	7.5	1	15	3	0	16	0.045[a]
PLEFF‡ (cm)	0.5	0	3.5	0.7	0	5	0.81
DEPTH§ (cm)	7.5	2	10	4.5	0	9	0.005[a]
AREA‖ (cm^2)	34	6	65	15	0	47.5	0.02[a]
TCA¶ (cm^2)	75	6	252.5	21	0	70	0.005[a]
SITES# (n)	7	1	15	2	0	12	0.008[a]

[a]Denotes values are statistically different ($P<0.05$)
*TAIL: number of comet-tail artifacts per site
†PIRR: number of sites with pleural irregularity present
‡PLEFF: maximal depth of pleural fluid accumulation per animal
§DEPTH: maximal depth of consolidated lung per animal
‖AREA: maximal area of consolidated lung per animal
¶TCA (total consolidated area): sum of consolidated area from all sites per animal
#SITES: number of sites with consolidation present per animal

interest associated with the risk of non-survival following first pull, indicators of lung consolidation (DEPTH, AREA, and TCA) were most negatively associated with clinical prognosis.

Only 1 study has been performed in commercial feedlots assessing the utility of ultrasonographic examination at processing, on the day of first pull, and then 2, 4, and 6 weeks later.[1] That study used a focused examination of 3 sites on the right thorax and concluded TUS examination at first pull held no diagnostic or prognostic value; however, it could be reserved for assessment of chronically diseased cattle in order to confirm respiratory disease and assess the extent of lung pathology. The current study indicates that there may be a significant loss of information concerning consolidation assessment when TUS examination is conducted on only 1 side of the thorax (moderate kappa level agreement: 0.500; 95% CI: 0.251 to 0.749). A previous report suggests ultrasonographic lesions may be overinterpreted (false positive) when using frozen TUS images rather than videos; this may affect the diagnostic accuracy of the reader.[20] Moreover, TUS examination conducted using a 3.5 MHz sectorial probe as previously reported,[1] may result in image distortion and low definition for analysis of superficial structures such as the thorax.[5]

It is important to note that treatment was withheld from clinically ill animals. This feature of the study protocol was necessary in order to observe the progression of ultrasonographic lesions associated with naturally occurring BRD, thereby providing a basis of

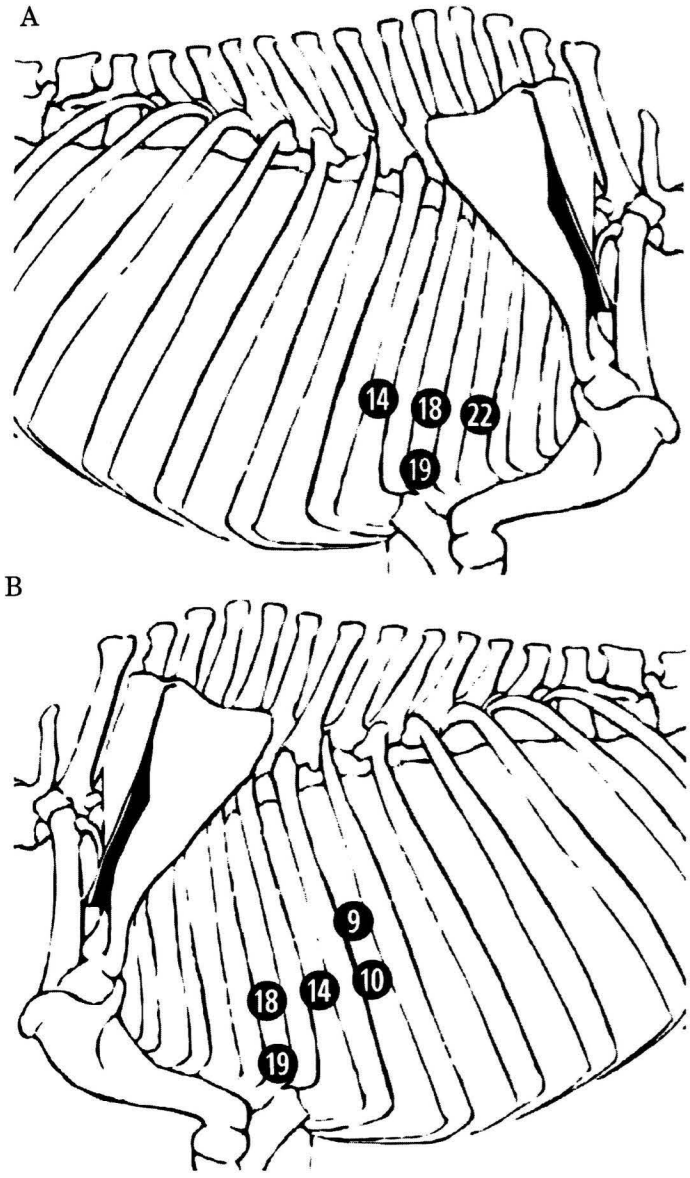

Figure 2. Locations with OR significantly greater than 1 ($P<0.05$) for predicting negative outcome (death) before the 15-day study period ended when consolidation was present at enrollment. Right hemithorax (A) and left hemithorax (B).

knowledge on this topic. However, it may impact the external validity of our findings, and serve to explain some over-fitting of our model, as the non-treated cases were perceivably at greater risk of experiencing an adverse clinical outcome. This component of the protocol was also necessary to achieve statistically significant results that can be used to direct further investigation into the technology. Due to the extensive process used in this initial study to evaluate the entire viewable lung field, an adequate number of non-survivors was needed for statistical analysis while using a smaller total number of animals. While this study provides insight into what may occur in cattle with BRD under certain management practices, it does not reflect the conventional management of BRD in the majority of cattle in current North American cattle feeding systems. Future studies should evaluate the progression of BRD ultrasonographically when case animals are treated with antimicrobials.

Controls in the present study were prophylactically treated with an antimicrobial. It is arguable that metaphylactic treatment of controls inserts a variable that may confound the statistical analysis between the 2 groups. However, because the primary aim of the present study was to evaluate lung lesions over time in animals with BRD, the authors believe that prophylactic treatment of controls allowed comparison between diseased lungs in animals with BRD to healthy lungs in control animals. Response to treatment was not an outcome of interest in the present study, therefore the authors concluded that appropriate comparisons can be made between cases and controls as to the difference in ultrasonographic findings between healthy and diseased lungs.

Time and labor required to conduct a TUS examination as described in this study currently precludes its use in commercial feedlots. Notably, our protocol required that individual video loops be saved at each of 46 locations on the thorax, thus considerably increasing the time required to conduct each examination. While this was a necessary procedure given the hypothesis-generating nature of the study, results suggest significant time could be saved in the future by restricting TUS examinations to those sites with the greatest diagnostic

Table 4. Odds of negative outcome (death) when consolidation was present at enrollment by ultrasound location for those sites where OR was found to be significantly greater than 1, $P<0.05$ (L: left, R: right).

Location	Odds ratio est.	95% CI
L9	15.496	1.515 to 158.457
L10	10.712	1.711 to 67.085
L14	5.400	1.229 to 23.727
L18	7.560	1.699 to 33.629
L19	10.712	1.711 to 67.085
R14	7.499	1.158 to 48.559
R18	30.000	4.633 to 194.255
R19	6.067	1.422 to 25.886
R22	7.560	1.699 to 33.629

Table 5. Diagnostic accuracy of ultrasonographic indicators of lung consolidation at enrollment as predictor of negative outcome (death) in 29 steers suffering from clinical respiratory disease.

DEPTH* (cm)	Sensitivity	95% CI	Specificity	95% CI
≥0	100.00	73.5 to 100.0	0.00	0.0 to 19.5
>1.5	100.00	73.5 to 100.0	35.29	14.2 to 61.7
>2	91.67	61.5 to 99.8	35.29	14.2 to 61.7
>3.5	91.67	61.5 to 99.8	41.18	18.4 to 67.1
>4	83.33	51.6 to 97.9	47.06	23.0 to 72.2
>4.5	83.33	51.6 to 97.9	52.94	27.8 to 77.0
>5§	75.00	42.8 to 94.5	82.35	56.6 to 96.2
>6	66.67	34.9 to 90.1	82.35	56.6 to 96.2
>7	50.00	21.1 to 78.9	94.12	71.3 to 99.9
>9	8.33	0.2 to 38.5	94.12	71.3 to 99.9
>9.5	8.33	0.2 to 38.5	100.00	80.5 to 100.0
>10	0.00	0.0 to 26.5	100.00	80.5 to 100.0
AREA† (cm^2)	**Sensitivity**	**95% CI**	**Specificity**	**95% CI**
≥0	100.00	73.5 to 100.0	0.00	0.0 to 19.5
>3	100.00	73.5 to 100.0	35.29	14.2 to 61.7
>9	75.00	42.8 to 94.5	35.29	14.2 to 61.7
>16	75.00	42.8 to 94.5	64.71	38.3 to 85.8
>17	66.67	34.9 to 90.1	64.71	38.3 to 85.8
>22§	66.67	34.9 to 90.1	76.47	50.1 to 93.2
>24	58.33	27.7 to 84.8	76.47	50.1 to 93.2
>31	58.33	27.7 to 84.8	94.12	71.3 to 99.9
>42	16.67	2.1 to 48.4	94.12	71.3 to 99.9
>47.5	16.67	2.1 to 48.4	100.00	80.5 to 100.0
>65	0.00	0.0 to 26.5	100.00	80.5 to 100.0
TCA‡ (cm^2)	**Sensitivity**	**95% CI**	**Specificity**	**95% CI**
≥0	100.00	73.5 to 100.0	0.00	0.0 to 19.5
>3	100.00	73.5 to 100.0	35.29	14.2 to 61.7
>9	83.33	51.6 to 97.9	35.29	14.2 to 61.7
>19	83.33	51.6 to 97.9	47.06	23.0 to 72.2
>20.5	75.00	42.8 to 94.5	47.06	23.0 to 72.2
>31.5§	75.00	42.8 to 94.5	76.47	50.1 to 93.2
>48	66.67	34.9 to 90.1	76.47	50.1 to 93.2
>50.5	66.67	34.9 to 90.1	82.35	56.6 to 96.2
>51	58.33	27.7 to 84.8	82.35	56.6 to 96.2
>70	58.33	27.7 to 84.8	100.00	80.5 to 100.0
>252.5	0.00	0.0 to 26.5	100.00	80.5 to 100.0

*Maximal depth of consolidated lung recorded during the examination of the steer.
†Maximal area of consolidation per site recorded during the examination of the steer.
‡Sum of the different area of consolidated lung found during the examination of the steer.
Se: sensitivity; Sp: specificity; 95% CI: 95% confidence interval.
§Optimal cutoff optimizing Se/Sp.

and prognostic value. Additionally, results of the present study agree with previous reports of satisfactory TUS images being obtained with minimal site preparation (ie. using only alcohol).[9,17] In human medicine, various rapid scanning protocols have been proposed for thoracic examination in the emergency room, including Rapid Assessment of Dyspnea with Ultrasound (RADiUS).[16] The aim of RADiUS is to focus on the most important prognostic and therapeutic indicators that can be accurately and rapidly measured in order to improve case management.

Of the various parameters found to be significantly associated with the risk of negative outcome, DEPTH appeared to be the most valuable and simplest parameter to collect. This finding is consistent with previous studies conducted using veal calves.[9] In the present study, 3 indicators of lung consolidation (DEPTH, AREA, and TCA) had the same prognostic accuracy. Interestingly, neither AREA nor TCA had greater predictive accuracy compared to DEPTH. This is of practical interest, since DEPTH is simple to collect and can be measured rapidly (less than 5 minutes per steer), especially if the examiner is focusing the TUS examination on the mid- to ventral thorax where bronchopneumonia lesions are typically found.[22] Further investigation into the significance of DEPTH in clinical BRD cases may provide future value for directing management decisions for individual animals.

A previous study that utilized replacement dairy calves demonstrated that consolidation was associated with reduced ADG in calves in which a previous exam during the pre-weaning period demonstrated no ultrasonographic evidence of lung consolidation.[17] However, this study was not designed to assess the usefulness of monitoring pulmonary consolidation as a predictor of reduced ADG in feedlot steers. Since ultrasonographic assessment of lung lesions is highly correlated with pathologic findings[13,18,19] and lung lesions are associated with poor performance,[8,22,24] it is reasonable to infer that TUS has the potential to detect animals with subclinical forms of BRD, even in the absence of outward clinical signs.

Of the 15 control steers enrolled in this study, 3 had evidence of lung consolidation at day 0 despite normal clinical signs. Similarly, researchers previously reported finding ultrasonographic lesions in 9 of 58 (16%) healthy feedlot cattle during the observation period.[1] The impact of these lesions in otherwise clinically normal animals warrants further investigation.

Conclusion

The present study has demonstrated that 1) systematic TUS is possible in feedlot calves and can be applied chute-side, 2) bilateral examination of the thorax is important when assessing thoracic evidence of lung consolidation, 3) the cranioventral thorax represents the most valuable location for identifying lung lesions that could have an impact on mortality, and 4) among the various lesions that may be detected by TUS, DEPTH is most closely associated with clinical outcome and also the easiest parameter to measure. Results from this study indicate TUS has potential applications in commercial feedlots, and is worthy of additional study in more typical production scenarios.

Endnotes

[a]Bovi-Shield Gold 5®, Pfizer Animal Health, New York, NY
[b]Calvary™ 9, Merck Animal Health, Summit, NJ
[c]Cydectin®, Boehringer Ingelheim Animal Health, St. Joseph, MO
[d]Revalor® XS, Merck Animal Health, Summit, NJ
[e]Micotil® 300, Elanco Animal Health, a subsidiary of Eli Lilly and Co., Greenfield, IN
[f]Ibex Pro, EI Medical, Loveland, CO
[g]Microsoft Excel 2010, Microsoft Corp., Redmond, WA
[h]SAS, Version 9.2, SAS Institute Inc., Cary, NC
[i]MedCalc, v.12.4.0 Mariakerke, Belgium

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ADVERSE REACTIONS: No adverse reactions were observed during clinical trials.

ANIMAL SAFETY:
In cattle safety studies, clinical signs of depression, incoordination and muscle fasciculation were observed in calves when doses of 15 or 25 mg/kg were administered for 10 to 15 days. Clinical signs of depression, inappetance and incoordination were observed when a dose of 50 mg/kg was administered for 3 days. An injection site study conducted in feeder calves demonstrated that the formulation may induce a transient reaction in the subcutaneous tissue and underlying muscle. In swine safety studies, incidental lameness of short duration was observed in all groups, including the saline-treated controls. Musculoskeletal stiffness was observed following the 15 and 25 mg/kg treatments with clinical signs appearing during the second week of treatment. Clinical signs of lameness improved after treatment ceased and most animals were clinically normal at necropsy. An injection site study conducted in pigs demonstrated that the formulation may induce a transient reaction in the subcutaneous tissue.

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