

Incremental Value (Bayesian Framework) of Thoracic Ultrasonography over Thoracic Auscultation for Diagnosis of Bronchopneumonia in Preweaned Dairy Calves

S. Buczinski, J. Ménard, and E. Timsit

Background: Thoracic ultrasonography (TUS) is a specific and relatively sensitive method to diagnose bronchopneumonia (BP) in dairy calves. Unfortunately, as it requires specific training and equipment, veterinarians typically base their diagnosis on thoracic auscultation (AUSC), which is rapid and easy to perform.

Hypothesis/Objectives: We hypothesized that the use of TUS, in addition to AUSC, can significantly increase accuracy of BP diagnosis. Therefore, the objectives were to (i) determine the incremental value of TUS over AUSC for diagnosis of BP in preweaned dairy calves and (ii) assess diagnostic accuracy of AUSC.

Animals: Two hundred and nine dairy calves (<1 month of age) were enrolled in this cross-sectional study.

Methods: Prospective cross-sectional study. All calves from a veal calves unit were examined (independent operators) using the Wisconsin Calf Respiratory Scoring Criteria (CRSC), AUSC, and TUS. A Bayesian latent class approach was used to estimate the incremental value of AUSC over TUS (integrated discrimination improvement [IDI]) and the diagnostic accuracy of AUSC.

Results: Abnormal CRSC, AUSC, and TUS were recorded in 3.3, 53.1, and 23.9% of calves, respectively. AUSC was sensitive (72.9%; 95% Bayesian credible interval [BCI]: 50.1–96.4%), but not specific (53.3%; 95% BCI: 43.3–64.0%) to diagnose BP. Compared to AUSC, TUS was more specific (92.9%; 95% BCI: 86.5–97.1%), but had similar sensitivity (76.5%; 95% BCI: 60.2–88.8%). The incremental value of TUS over AUSC was high (IDI = 43.7%; 5% BCI: 22.0–63.0%) significantly improving proportions of sick and healthy calves appropriately classified.

Conclusions and Clinical Importance: The use of TUS over AUSC significantly improved accuracy of BP diagnosis in dairy calves.

Key words: Bovine respiratory disease; Calf pneumonia; Diagnostic tests; Integrated discrimination improvement; Latent class model.

Infectious bronchopneumonia (BP) in young calves is a major health problem in dairy and veal calf industries worldwide.^{1,2} This disease represents the second most likely cause of morbidity after digestive diseases in preweaned dairy heifers (on average, 18.3% calves were treated for this condition).³ In addition, it is the leading cause of morbidity in veal calves, with an incidence of 0.95 cases per 1,000 calf days at risk.⁴

Accurate antemortem diagnosis of BP in dairy and veal calves remains challenging for both producers and veterinarians.^{5,6} For producers, diagnosis of BP is typically based on visual signs of respiratory disease (anorexia,

Abbreviations:

AUSC	thoracic auscultation
BCI	bayesian credible interval
BP	bronchopneumonia
COVN	covariance of auscultation and ultrasonography in calves without bronchopneumonia
COVP	covariance of auscultation and ultrasonography in calves with bronchopneumonia
CRSC	clinical respiratory scoring criteria
IDI	integrated discrimination improvement
Se	sensitivity
Sp	specificity
TUS	thoracic ultrasonography

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depression, nasal and ocular discharges, cough, and ear position), associated or not with increased rectal temperature. However, this diagnostic approach often lacks both sensitivity (Se) and specificity (Sp). Consequently, several clinical examination scores have been developed to improve its accuracy,^{1,6} with moderate success.⁷ For veterinarians, diagnosis of BP is typically based on presence of visual signs of respiratory disease and abnormal lung sounds at thoracic auscultation (AUSC), including increased bronchial sounds, crackles, wheezes, or absence of respiratory sounds.⁸ Thoracic auscultation is rapid and easy to perform under field conditions, but abnormal lung sounds can also result from causes other than respiratory disease, which calls into question accuracy of AUSC for BP diagnosis.

Thoracic ultrasonography (TUS) is another test that can be used by veterinarians to diagnose BP. It detects

signs of lung consolidation (eg, related to inflammation and exudate in lung parenchyma) adjacent to the pleura. It can be performed on-farm and takes from 1 to 3 min per calf, depending on operator experience. In a recent study in preweaned dairy calves,⁷ TUS was specific (SpTUS: 93.9%; 95% Bayesian credible intervals [BCI]: 88.0–97.6%) and relatively sensitive (SeTUS: 79.4%; 95% BCI: 66.4–90.9%) for BP diagnosis. Unfortunately, TUS is not widely used by veterinarians because it requires specific training and equipment (ie, portable ultrasound apparatus). Furthermore, the incremental value of TUS in addition to AUSC for diagnosis of BP is unknown. Such information is crucial to assess and quantify potential improvement in diagnostic accuracy obtained by using TUS over AUSC versus AUSC only and thus determine whether TUS over AUSC should be promoted among veterinarians.

The challenge to quantify the incremental value of TUS over AUSC is that there is no perfect reference test for antemortem diagnosis of BRD. In the absence of a perfect reference test, Bayesian latent class analysis is considered one of the best methods to assess diagnostic test accuracy and is frequently used in human and veterinary medicine.^{9–11} This method assumes that the true disease status is unknown (latent) and needs to be estimated from the data. Furthermore, Bayesian analysis enables incorporation of prior scientific information on parameters to estimate.

The objectives of this study were to assess, using a Bayesian latent class approach, (i) incremental value of TUS over AUSC for BP diagnosis in preweaned dairy calves; and (ii) diagnostic accuracy of AUSC. We hypothesized that the use of TUS over AUSC significantly improves accuracy of BP diagnosis.

Materials and Methods

Study Design

All management and procedures were reviewed and approved by the Animal Ethical Care Committee, University of Montreal, Faculty of Veterinary Medicine (14-Rech-1727) and were in accordance with guidelines of the Canadian Council on Animal Care.

This study was conducted as a cross-sectional study where all calves present in the facility were included. This design, also called “one-gate,” is recommended for determining unbiased test accuracy parameters.¹² Dairy veal calves ($n = 209$) were examined 12 days after arrival at a preweaning veal calf unit (average body weight on arrival = 48.1 kg, range = 33.1–65.3 kg). Each calf was examined for BP by 3 tests: a clinical evaluation using the Wisconsin Calf Respiratory Scoring Criteria (CRSC),¹ AUSC, and TUS.⁷ Two investigators performed the CRSC test, 1 investigator performed AUSC (JM), and 2 trained investigators performed TUS (good inter-observer agreements for TUS).¹³ All investigators were blinded to all other test results.

Data Collection

Clinical evaluation was performed using the CRSC as described,⁷ with a cut-off of 5 or more defining a positive test.¹ The AUSC was performed on the entire thoracic projection as described,⁸ using a conventional stethoscope.^a An abnormal AUSC was defined by presence of increased bronchial sounds or

presence of abnormal sounds (ie, crackles and wheezes or total absence of lung sounds) or both. The TUS was performed using an ultrasound unit with a 7.5 MHz, linear-array transducer.^b The thoracic area scanned was slightly modified from a previous study,⁸ as it also included the right lung field cranial to the heart (1st–2nd intercostal spaces), as described.¹⁴ An abnormal TUS was defined by the presence of any area of consolidated lung with a depth ≥ 1 cm (using the 1-cm grid of the ultrasound apparatus; Fig 1).⁷

Data Analysis

Descriptive results of each diagnostic test (CRSC, AUSC, and TUS) were reported in a contingency table. In the absence of a perfect reference test, diagnostic accuracy of AUSC (Se, Sp) and incremental value of TUS over AUSC were evaluated using a Bayesian framework.¹⁵ The accuracy of AUSC was assessed using a 1 population, 2 tests Bayesian latent class model analysis. The latent variable was true BP status, which was assessed by 2 imperfect tests, namely TUS and AUSC. Informative priors on TUS were based on a previous study⁷ and were reported in terms of beta distribution (Table 1). Best guesses for SeTUS and SpTUS were 79% (5th percentile value = 65%) and 94% (5th percentile value = 88%) corresponding to beta distributions $\beta(27.02, 7.92)$ and $\beta(80.58, 6.08)$, respectively. Noninformative priors (ie, objective) were used for SeAUSC and SpAUSC; uniform distribution, $\beta(1,1)$. The prior used for BP prevalence (P_{BP}) was a uniform distribution between 10 and 80% (low informative prior). Because both TUS and AUSC evaluate presence of abnormal lung parenchyma associated with BP, a positive conditional dependence between

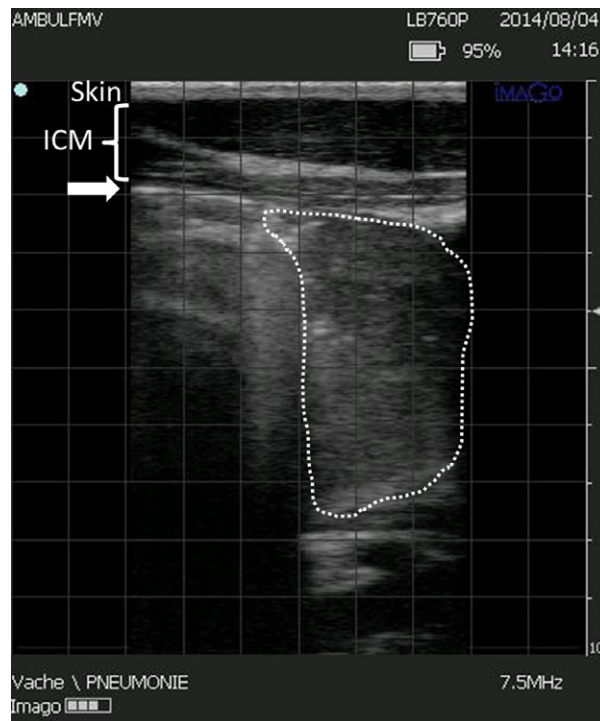


Fig 1. Ultrasound findings of lung consolidation in a preweaned Holstein calf (linear probe, 7.5 MHz). The skin, intercostal muscles (ICM), and pleural line (arrow) are observed. Consolidated lung parenchyma is outlined by the dotted line. The screen is divided by 1 cm grid (gray squares). The maximal depth of lung consolidation in this picture is 5–5 squares (cm).

Table 1. Prior densities and median posterior estimates (95% Bayesian credibility interval [BCI]) of bronchopneumonia (BP) prevalence (P_{BP}) and test sensitivity (Se) and specificity (Sp) of thoracic auscultation (TUS) and thoracic auscultation (AUSC) for BP diagnosis of 2 Bayesian latent class models.

	Main Model ^a		Less Informative Model ^b	
	Prior Densities	Posterior Estimates ^c	Prior Densities	Posterior Estimates
Se _{TUS}	$\beta(27.02, 7.92)$	76.5 (60.2–88.8)	$\beta(23.57, 8.52)$	70.7 (52.8–85.1)
Sp _{TUS}	$\beta(80.58, 6.08)$	92.9 (86.5–97.1)	$\beta(23.57, 8.52)$	82.5 (75.3–89.8)
Se _{AUSC}	$\beta(1, 1)$	72.9 (50.1–96.4)	$\beta(1, 1)$	69.0 (23.4–98.3)
Sp _{AUSC}	$\beta(1, 1)$	53.3 (43.3–64.0)	$\beta(1, 1)$	49.2 (39.2–60.7)
P_{BP}	$U(0.1, 0.8)$	24.2 (13.5–37.3)	$U(0.1, 0.8)$	15.2 (10.2–30.0)
COVP ^d	$U(0, a)$	6.0 (0.2–16.1)	$U(0, a)$	5.7 (0.2–17.6)
COVN ^d	$U(0, b)$	1.6 (0.0–4.9)	$U(0, b)$	4.7 (0.6–8.8)
Se _{diff} ^e	–	4.2 (–24.2 to 26.0)	–	2.0 (–33.4 to 47.0)
Sp _{diff} ^f	–	39.3 (28.0–50.0)	–	33.2 (22.1–43.6)

^aMain model: priors Se_{TUS} mode = 79% (95% lower bound: 65%); priors Sp_{TUS} mode = 94% (95% lower bound: 88%); P_{BP} : uniform distribution between 10 and 80%; noninformative priors for AUSC and covariance parameters.

^bLess informative model: priors Se_{TUS} and Sp_{TUS} mode = 75% (95% lower bound 60%); P_{BP} : uniform distribution between 10% and 80%; noninformative priors for AUSC and covariance parameters.

^cPosterior densities are indicated as percentages (95% Bayesian credible intervals).

^dCOVP/COVN: covariance of the test for positive (p) or negative (n) BP cases; $a = \min(\text{Se}_{AUSC}, \text{Se}_{TUS}) - \text{Se}_{AUSC} \times \text{Se}_{TUS}$; $b = \min(\text{Sp}_{AUSC}, \text{Sp}_{TUS}) - \text{Sp}_{AUSC} \times \text{Sp}_{TUS}$.

^eSediff = Se_{TUS} – Se_{AUSC}.

^fSpdiff = Sp_{TUS} – Sp_{AUSC}.

both tests was taken into account (COVP: covariance of both tests in calves with BP; and COVN: covariance of both tests in calves negative for BP).^{16,17} Distribution of covariance parameters was defined as:¹⁶

$$\text{COVP} \sim U(0, \min(\text{Se}_{AUSC}, \text{Se}_{TUS}) - \text{Se}_{AUSC} \times \text{Se}_{TUS}), \quad (1)$$

$$\text{COVN} \sim U(0, \min(\text{Sp}_{AUSC}, \text{Sp}_{TUS}) - \text{Sp}_{AUSC} \times \text{Sp}_{TUS}). \quad (2)$$

The incremental value of TUS over AUSC was evaluated using the same Bayesian latent class model,¹⁵ controlling for a conditional dependence between AUSC and TUS. This model determined the integrated discrimination improvement (IDI) of TUS over AUSC, an important measure to compare 2 nested models.¹⁸ The IDI represents the sum of the average increase in predicted probability among patients with the outcome and the average decrease in predicted probability among patients without the outcome.¹⁸ The IDI calculation was based on predictive values obtained from a model using both AUSC+TUS versus a model using only AUSC:

$$\text{IDI} = (P_{AUSC+TUS, BP+} - P_{AUSC, BP+}) + (P_{AUSC, BP-} - P_{AUSC+TUS, BP-}). \quad (3)$$

Therefore, IDI was the difference of discrimination slopes between these 2 models.

To assess model sensitivity to prior information on TUS accuracy, a second model using weaker priors for Se_{TUS} and Sp_{TUS} was created (ie, less informative model). Both Se_{TUS} and Sp_{TUS} were set at 75% in this model, with a 95% confidence that these parameters were >60% ie, $\beta(23.57, 8.52)$. Priors for BP prevalence and covariance parameters were identical to the initial model (ie, main model).

Bayesian computations were implemented using public-domain software.^c The first 5,000 iterations were discarded as burn-in, whereas the next 95,000 were used to obtain posterior distributions. Convergences of models were assessed by (i) visual inspection of the history and density plots and (ii) Brooks-Gelman-Rubin statistic. Four chains were run with different initial

values. Posterior distributions of each parameter were reported as medians and corresponding 95% BCI.

Results

Cross-classifications of calves based on CRSC, AUSC, and TUS are shown (Table 2). Only 7 calves had a CRSC score ≥ 5 (3.3%). Abnormal AUSC was detected in 111 of 209 cases (53.1%) and ultrasonographic evidence of lung consolidation (≥ 1 cm depth) was detected in 50 of 209 calves (23.9%).

Results of Bayesian latent class models are shown (Table 1). The Se_{AUSC} and Sp_{AUSC} were 72.9% (95% BCI: 50.1–96.4%) and 53.3% (95% BCI: 43.3–64.0%), respectively, whereas Se_{TUS} and Sp_{TUS} were 76.5% (95% BCI: 60.2–88.8%) and 92.9% (95% BCI: 86.5–97.1%; Fig 2). Thoracic ultrasonography was significantly more specific than AUSC for BP diagnosis (Spdiff: 39.3%; 95% BCI: 28.0–50.0%), but there was no difference in Se between TUS and AUSC (Sediff: 4.2%; 95% BCI: –24.2 to 26.0%; Table 1).

The addition of TUS over AUSC significantly increased proportions of sick and healthy calves correctly classified (Table 3). The average increase in predicted probability among calves with BP was 33.0% (BCI: 16.1–47.8%) and the average decrease in predicted probability among calves without BP was 10.5% (BCI: 4.0–18.3%). Therefore, the overall estimate of the IDI was 43.7% (95% BCI: 22.0–63.0%). Changes in disease probability after AUSC only and after AUSC combined with TUS are shown (Fig 3). By adding TUS over AUSC, the probability of a calf to have BP increased from 33.2% (AUSC+ and no TUS performed) to 80.7% (if AUSC+ and TUS+).

The model with less informative priors gave posterior medians included in the 95% BCI of the posteriors of

the main model, except for SpTUS (Table 1). Therefore, prior information on TUS accuracy did not strongly influence posterior estimates of AUSC accuracy. Furthermore, the IDI using less informative priors remained high (21.4%, 95% BCI: 6.2–43.1%) demonstrating that even if TUS was less specific (82.5 versus 92.9%), its use over AUSC improved accuracy of BP diagnosis compared to AUSC alone.

Discussion

This study provides unique information on ante-mortem diagnosis of BP in dairy calves. Previous

Table 2. Cross-classification of 209 preweaned dairy calves according to thoracic auscultation (AUSC), thoracic ultrasonography (TUS), and clinical evaluation findings using the Wisconsin Calf Respiratory Scoring Criteria (CRSC).¹

	AUSC+ ^a	AUSC–	Total
TUS+ ^b			
CRSC+ ^c	7	0	7
CRSC–	33	10	43
TUS–			
CRSC+	0	0	0
CRSC–	71	88	159
Total	111	98	209

^aAUSC was defined as positive in the presence of increased bronchial sounds and/or in the presence of any abnormal sounds (eg, crackles, wheezes, or absence of lung sounds).

^bTUS was considered positive if lung consolidation depth was ≥ 1 cm at 1 or more sites.

^cCRSC was defined as positive if score was 5 or more.

studies have compared AUSC and TUS findings in sheep¹⁹ or in chronic pneumonia cases in adult cows.²⁰ We present here the incremental value of TUS over AUSC for BP diagnosis evaluated in preweaned dairy calves. Based on Bayesian latent class models, we showed that TUS was more specific (92.9%) than AUSC (53.3%) and that its use over AUSC significantly improved accuracy of BP diagnosis (IDI: 43.7%). Based on these findings, the use of TUS in addition to AUSC should be promoted among veterinarians to improve accuracy of BP diagnosis in preweaned dairy calves.

Precautions were taken in this study to avoid biases in estimating Se and Sp of diagnostic tests. First, investigators were blinded to other test results to avoid review bias. In nonblinded studies, animals with unexpected results can be retested, which can lead to overoptimistic Se and Sp estimates.²¹ Second, to avoid information bias, a latent class analysis was performed to account for the absence of a perfect reference test for ante-mortem BP diagnosis. If classification errors in the reference test are ignored, serious bias may be introduced in assessment of the accuracy of the new test.¹⁰ For example, in a case of a reference test with a Sp $< 100\%$, samples falsely detected as positive by this imperfect test might be correctly classified as negative by a more specific new test, thus leading to a biased estimate of Se (in this case, too low) of the new test. However, with the latent class approach used, the true disease status of animals was unknown (ie, latent) but was estimated from the data. Finally, the “one-gate” design included healthy and sick calves at various stages of the disease, which prevented the spectrum of disease bias.¹²

The incremental value of a new test over a reference test is high when the new test is more Se or Sp (or

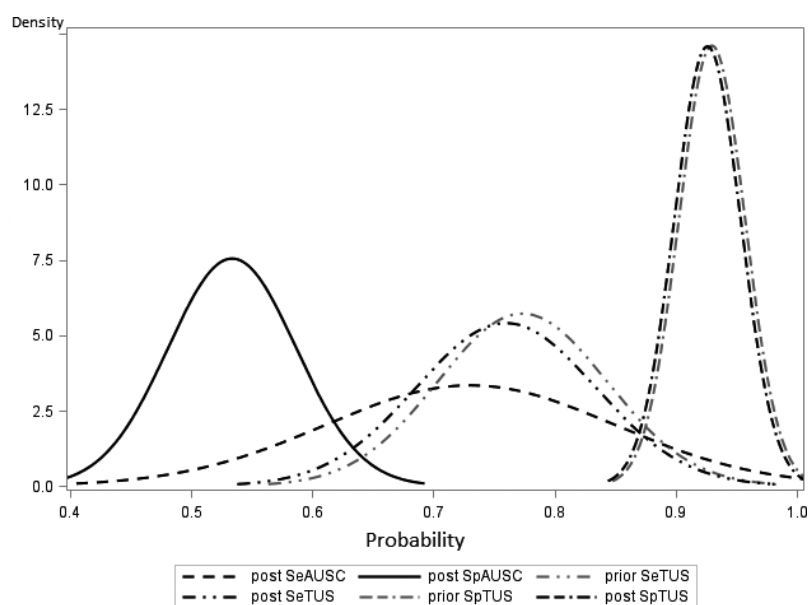


Fig 2. Prior and posterior densities for sensitivities (Se) and specificities (Sp) of thoracic auscultation (TUS) and thoracic auscultation (AUSC) for diagnosis of bronchopneumonia in preweaned dairy calves. The priors for auscultation sensitivity and specificity were non-informative priors (uniform density between 0 and 1).

Table 3. Median posterior estimates and 95% Bayesian credibility interval (BCI) of integrated Discrimination Improvement (IDI) statistics for bronchopneumonia (BP) diagnosis when thoracic auscultation (AUSC) was interpreted alone or in combination with thoracic ultrasonography (TUS) in 2 Bayesian latent class models.

	IDI in BP+ (95% BCI)	IDI in BP- (95% BCI)	IDI (95% BCI)
Main model ^a	33.0 (16.1–47.8)	10.5 (4.0–18.3)	43.7 (22.0–63.0)
Less informative model ^b	18.8 (5.2–36.3)	3.3 (0.8–9.0)	21.4 (6.2–43.1)

^aMain model: priors Sensitivity (Se)_{TUS} mode = 79% (95% lower bound: 65%); priors Specificity (Sp)_{TUS} mode = 94% (95% lower bound: 88%); Prevalence_{BP}: uniform distribution between 10 and 80%; noninformative priors for AUSC and covariance parameters. ^b: Less informative model: priors for Sensitivity (Se) and specificity of TUS mode = 75% (95% lower bound: 60%); Prevalence BP: uniform distribution between 10- 80%; non-informative priors for AUSC and covariance parameters.

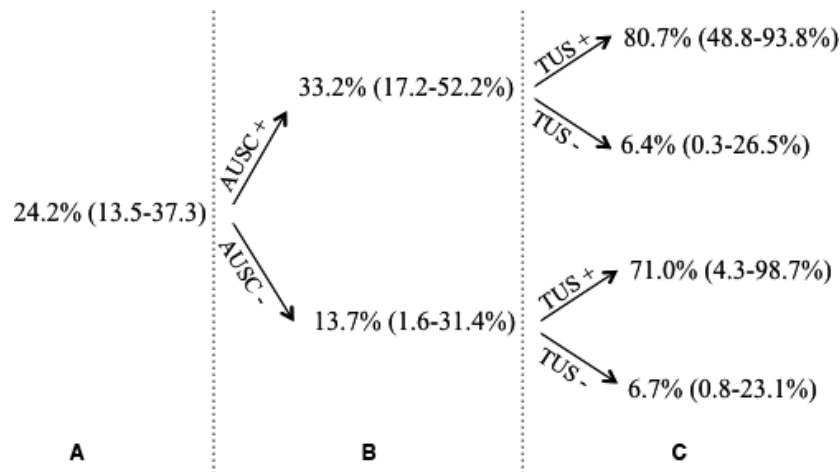


Fig 3. Probability of bronchopneumonia (A) in the present study population, (B) after thoracic auscultation alone (positive or negative; AUSC) and (C) after AUSC combined with thoracic ultrasonography (TUS). Probabilities were derived from Bayesian latent class models,¹⁵ including both AUSC and TUS or AUSC alone.

both) than the reference test.¹⁵ It is therefore not surprising that the incremental value TUS over AUSC was high, as Sp of TUS was higher than AUSC. However, it is noteworthy that IDI can change with disease prevalence.¹⁵ In this study, IDI of TUS over AUSC was especially high because prevalence of BP was low (ie, higher chance of false positive) and TUS was more Sp than AUSC. However, if BP prevalence was higher, the incremental value of TUS over AUSC would have probably been reduced (as Se of TUS and AUSC did not differ).

The Se of AUSC in this study was higher than anticipated. In a previous study with dairy calves, the Se of lung auscultation to diagnose BP (defined as lung consolidation ≥ 1 cm detected by ultrasonography) was only 5.9% (range, 0–16.7%).⁸ This apparent discrepancy was attributed to bronchial sounds being included in lung sounds interpretation in the present study, whereas in the previous study, only crackles, wheezes, or absence of respiratory sounds were interpreted as abnormal. Increased bronchial sounds are usually the first and most common abnormal lung sound that occurs in animals with respiratory disease, which accounts for its high Se to diagnose BP.^{22,23}

Unfortunately, interpretation of increased bronchial sounds suffers from a lack of Sp, as illustrated by the present study. Increased bronchial sounds typically

result from areas of consolidation or atelectasis that increase sound transmission through lung tissue (ie, increased tissue density).²³ However, they can also result from causes other than respiratory disease, including exercise, anxiety, fever, anemia, and high ambient temperatures that increase velocity of air flow (ie, hyperventilation). Increased bronchial sounds should therefore be interpreted with caution, and preferably in calves that have visual signs of BP, to improve its positive predictive value (ie, proportion of animals with increased bronchial sounds that truly have BP). It is noteworthy that interpretation of bronchial sounds is also very subjective in humans, with a low to fair interobserver agreement.²⁴ This emphasizes the advantage of using more objective measurements such as TUS that have good interobserver agreement (ie, reproducibility).

Thoracic auscultation could nevertheless be an improvement over the use of a clinical examination score alone. In the present study, AUSC detected 33 calves that had lung consolidation at TUS, but were negative when examined by clinical examination using the Wisconsin CRSC scoring system. Unfortunately, determination of the incremental value of AUSC over CRSC was not possible, because of (i) low prevalence of abnormal CRSC and (ii) 2 scorers, which could have introduced a bias in score attribution (low interobserver

agreement and thus nonconstant accuracy of CRSC between observers).²⁵

In conclusion, AUSC was sensitive (72.9%), but not specific (53.3%) to diagnose BP. Adding TUS over AUSC significantly improved the accuracy of BP diagnosis and therefore should be promoted among veterinarians (especially in context of low BP prevalence to confirm presence of lung consolidation).

Footnotes

^a 3M Littmann Cardiology, Littman Canada, Concord, ON, Canada

^b Imago, Echo Control Medical, Angoulême, France

^c WinBUGS version 1.4.3, MRC Biostatistics Unit, Cambridge, UK.

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

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