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Effect of ultrasonographic lung consolidation on health and growth in dairy calves: A longitudinal study

A. Sáadatnia,[1] G. R. Mohammadi,[1]* M. Azizzadeh,[1] A. Mirshahi,[1] A. A. Mohieddini,[2] and S. Buczinski[3]
[1]Department of Clinical Science, Faculty of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran 9177948974
[2]Private veterinary practitioner, Tehran, Iran 3314143581
[3]Département des Sciences Cliniques, Faculté de Médecine Vétérinaire, Université de Montréal, St-Hyacinthe, QC J2S 2M2, Canada

ABSTRACT

Bovine respiratory disease (BRD) is a common and complex disease process in calves. Subclinical disease exists and early detection can be challenging due to inconsistent or nonexistent clinical signs. Thoracic ultrasonography (TUS) is often used and has the potential to improve the identification of respiratory diseases. Combining systematic TUS with clinical examination allows distinguishing BRD, including upper respiratory tract disease (clinical signs of respiratory disease, but no significant lung consolidation), clinical pneumonia (clinical signs of respiratory disease along with lung consolidations), and subclinical pneumonia (no clinical signs, but lung consolidations). Data on subclinical pneumonia are scarce, particularly outside of the North American or European contexts similar to Iran in west Asia with a dry and semi-arid climate and intensive breeding systems similar to North America which breeding calves begin in individual boxes, then moving to group pens, and finally to free stall or open shed housing systems. The first objective of this longitudinal study was to use weekly ultrasonography to monitor calves from birth until weaning in an Iranian dairy herd. The second objective was to look for any association between individual lung consolidation episode or cumulative consolidation episodes on preweaning growth. Thoracic ultrasonography was performed on calves (n = 221) weekly from birth to weaning (8 wk), and scanning occasions for each calf were equally distributed with 1-wk intervals (using consolidation threshold $\geq$3 cm as a specific lung consolidation definition, and $\geq$1 cm as a more sensitive threshold). Calf body weights were recorded using a weight tape. Other information recorded were transfer of passive immunity (TPI) using serum Brix (%) $\geq$8.4% as adequate TPI within the first week after birth and the treatment history of the calves. The main strategy for modeling was to determine how long-term lung consolidation affects average daily gain (ADG) during the preweaning period. A linear model was used to determine the effect of the number of weeks with consolidation on ADG. Using consolidation threshold of $\geq$3 cm, the mean ($\pm$SD) of total ADG for calves with no consolidation episode, 1 consolidation episode, and 2 or more consolidation episodes were 0.45 ($\pm$0.10), 0.39 ($\pm$0.10), and 0.38 ($\pm$0.11) kg/d, respectively. In the final multivariable regression analysis model and based on consolidation threshold of $\geq$3 cm, calves with 1 and 2 or more consolidation episodes had significantly lower ADG $\pm$ standard error (SE) of 0.04 $\pm$ 0.02 kg/d, and 0.06 $\pm$ 0.02 kg/d, respectively compared with animals with no consolidation episode. A total of 20% of calves (46/229 calves that entered the study) were treated for respiratory disease based on clinical signs (based on farmer examination). The final model also included specific confounders related to ADG and their interactions with lung consolidation (TPI and BRD treatment). An overall of 86% of adequate TPI was obtained. Bovine respiratory disease treatment based on farmer diagnosis had a larger negative effect on preweaning ADG than ultrasonography-diagnosed consolidation episodes (lower ADG $\pm$ SE of 0.10 $\pm$ 0.03 kg/d). When using a more sensitive consolidation threshold ($\geq$1 cm as consolidation), the number of weeks with consolidation was also negatively associated with the ADG in the multivariable linear regression model with significant difference of 0.05 $\pm$ 0.02 kg/d for nonconsolidated calves versus calves consolidated for 2 or more weeks and insignificant difference of 0.01 $\pm$ 0.02 kg/d for nonconsolidated calves versus calves with 1 consolidation episode.
Key words: bronchopneumonia, lung consolidation, preweaning, average daily gain

INTRODUCTION

Bovine respiratory diseases (**BRD**) are one of the health issues in dairy calf breeding systems that can

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*Corresponding author: gmohamad@um.ac.ir

have a wide range of short and long-term economic consequences. Short-term consequences include increased treatment (Van Donkersgoed et al., 2008) and labor costs along with reduced growth (Buczinski et al., 2021), recurrence, mortality, pathogen spread and time spent monitoring and implementing treatments (McGuirk, 2008). Long-term consequences include decreased survival to the first calving (Adams and Buczinski, 2016), decreased future reproductive performance (Hayes et al., 2019), and decreased milk production (Dunn et al., 2018). Important variation of herd prevalence of BRD in preweaning dairy calves have been observed with ranging from 0 to 90% (Lago et al., 2006; Heins et al., 2014). Among the different sources of variation of BRD prevalence, part of the observed differences could be due to pathogens case mix or diagnostic methods for case definition (Ollivett et al., 2015). Treatment records that determine importance of the disease is highly dependent on the dairy farmers' ability to detect true cases and avoiding false positive cases (i.e., calves incorrectly diagnosed as requiring treatment). Active pneumonia is typically diagnosed based on the presence of visual signs of respiratory disease as well as abnormal lung sounds, such as increased bronchial sounds, crackles, wheezes, or absent lung sounds which are of interest to veterinarians (Berman et al., 2019). However, a study of pre-weaned dairy calves revealed that auscultation is not accurate enough, with a sensitivity of less than 6% to detect ultrasonographic lung consolidation (Buczinski et al., 2014). Another study found that lung auscultation by veterinarians had poor diagnostic accuracy and very low inter-rater reliability in diagnosing pneumonia (Pardon et al., 2019). Also, clinical signs of BRD can be transient and difficult to diagnose in a significant proportion of calves (Pardon and Buczinski, 2020). However, decreased ADG in the absence of reported clinical signs and the presence of postmortem lung lesions suggests the presence of subclinical respiratory disease and its role in economic losses in beef and veal calves (Wittum et al., 1996; Leruste et al., 2012). As a logical result, an accurate diagnosis of pneumonia in calves is an important challenge. To date, 2 clinical scoring systems, including Wisconsin (McGuirk, 2008) and California (Love et al., 2014) have been developed for (1) standardizing case definition and (2) improving the accuracy and early detection of dairy calves with BRD. In dairy calves, some studies have reported prevalence of subclinical pneumonia (calves without clinical signs of BRD but with evidences of ultrasonographic lung lesions) with a wide range of variation. For example, one study reported 73/103 (70.8%) calves with subclinical pneumonia (Cramer et al., 2020). Similarly, in another study the incidence of subclinical pneumonia was much higher than expected. In this study, 69.1% of the calves with pneumonia on thoracic ultrasonography (**TUS**) did not develop clinical signs of pneumonia (Jourquin et al., 2022). Thoracic ultrasonography has recently been advocated as a promising (Babkine and Blond, 2009), quick, objective (Ollivett et al., 2015), and practical (Ollivett and Buczinski, 2016) tool for on-farm BRD detection, which helps to determine the correlation between clinical signs and lung lesions (Ollivett, 2018). The California scoring system's diagnostic sensitivity and specificity (95% CI) were estimated to be 72.6% (65.2–78.9) and 87.4% (82.6–91.1), respectively (Love et al., 2016), while different studies have reported TUS sensitivity ranging from 86 to 94% and specificity ranging from 98 to 100% (Rabeling et al., 1998; Ollivett et al., 2015). Ultrasound is a noninvasive procedure (Ollivett et al., 2015) and when combined with respiratory scoring, allows the differentiation of BRD into 4 subtypes including healthy (normal respiratory score and normal TUS), upper respiratory tract infection (positive respiratory score and a normal TUS), clinical pneumonia (positive respiratory score and abnormal TUS), and subclinical pneumonia (normal respiratory score and an abnormal TUS; Ollivett and Buczinski, 2016). Thoracic ultrasonographic findings and clinical findings are weakly correlated (Rhodes et al., 2021). Thoracic ultrasonography is useful to monitor the prevalence and severity of pneumonia over time and to assess the effects of management changes such as ventilation, vaccination, changes in treatment protocols, and calf care provider performance (Ollivett and Buczinski, 2016). Recently, a US study concluded that calves with lung consolidation $\geq$1 cm^2 had lower ADG (mean $\pm$ SE) of 0.12 $\pm$ 0.05 kg/d compared with calves without lung consolidation, where ADG was 0.85 kg/d (Cramer and Ollivett, 2019). In an Irish study on 7 dairy farms with variable preweaning ADG, calves with consolidation $\geq$1 cm^2 but not full lobar consolidation had lower ADG (mean $\pm$ SE) of 0.13 $\pm$ 0.05 kg/d compared with calves with no consolidation (median farm ADG: 0.34 kg/d, range from 0.02 to 0.80 kg/d; Rhodes et al., 2021). Focusing on the diagnosis of lung ultrasonographic lesions and especially consolidation could therefore be of interest because a reduced preweaning ADG is associated with later detrimental effects on cow productivity (Gelsinger et al., 2016). The association between TUS and growth is complex and may also depend on various specific management factors or BRD agents present in a specific farm or geographic area. Information on TUS in dairy calves are scant in geographical areas other than North America and Western Europe. In Iran, where the dairy sector is of great importance, information on this topic is missing. Moreover, most of the studies do not extensively look for duration of lung consolidation during the preweaning period as potentially affecting its effect on ADG, with the exception of Rhodes et al. (2021), who used 3 examination periods at 21, 42, and 63 d and reported a lower preweaning growth in animals displaying lesions throughout the study, with 7 kg less than calves without consolidation at any time point, and Jourquin et al. (2022), who, by defining chronic pneumonia as the presence of consolidated lung tissue (≥1 cm) for 30 consecutive days or more in calves derived from different farms, found that calves with chronic pneumonia had a lower ADG ± standard deviation (SD) of 0.17 ± 0.03 kg/d compared with calves that never developed pneumonia after 12 wk of arrival. They also found that calves with chronic pneumonia had a lower cold carcass weight ± SD of 10.3 ± 4.4 kg compared with animals without chronic pneumonia. Therefore, the first objective of this study was to weekly monitor calves from birth until weaning in a specific Iranian herd with known problems of clinical and subclinical pneumonia, using ultrasonography and treatment history. The second objective was to look for the association between individual lung consolidation episode or cumulative lung consolidation episodes on preweaning growth. Finally, a third objective was to describe short-term evolution of lung consolidation from time at first BRD treatment when calves were clinically detected by the farmer.

MATERIALS AND METHODS

Farm Characteristics and Animal Management and Recruitment

This research project was authorized by the local ethical research committee (IR.UM.REC.1401.202). The commercial dairy farm was located on the west side of Tehran, Iran, and had an average of 2,000 milking cows with an average of 11,600 kg of milk per lactation. Data for this longitudinal study were collected between June 2021 and January 2022. Specific farm management of calves consisted of raising both males and females, and both were under the same management and housing conditions. Calves were separated from their dam within 30 min after birth and moved to sawdust-bedded individual pens. Umbilical cord disinfection with a solution containing 1.5% chlorhexidine was performed immediately after birth. Calves were offered 4 L of single-source or pooled pasteurized colostrum either voluntarily or, if they did not drink, using an esophageal tube, within 1 h of birth, followed by another 2 L 12 h later, and then unpasteurized transition milk (milkings 2 to 6 postcalving; Godden, 2008) twice a day for 3 to 5 d (each meal, 2 L). After this period, feeding management included providing 4 to 8 L of unpasteurized milk per day, divided into 2 meals fed by bucket. From 3 to 5 d of age, calves had free access to starter (20% crude protein) and clean, fresh water. Male calves were generally sold at 2 to 3 wk of age while still in individual pens. However, female calves were moved as a group into sawdust-bedded pens containing 10 to 12 calves in each pen at 3 to 6 wk of age. Therefore, only female calves were kept in the herd until the end of their productive life, and they were included in this study. Every day, clean sawdust was used to replace the dirty part of the bedding in all individual and group pens. All calves were weaned at around 8 wk of age. All calves had their birth weight measured with a 0.1-kg accuracy scale (Newtech Indiamart, India, Delhi). During the study, a farm veterinarian collected jugular venous blood from 1- to 2 d-old calves by jugular venipuncture, using a 20-gauge, 1-inch hypodermic needle and glass tube without anticoagulant as part of a routine farm procedure to measure serum total protein (percent Brix) as an indicator of passive transfer of maternal antibodies (adequate transfer of passive immunity [**TPI**] if Brix ≥8.4%, inadequate TPI if Brix <8.4%). At approximately 20°C, blood tubes were centrifuged at 3,000 × g for 15 min. An optical refractometer (VBR62, Movel Scientific Instrument Co. Ltd., Ningbo, China) was used to measure total protein in serum using Brix (%) scale.

Data Collection

Sample Size. The sample size for this prospective longitudinal study was calculated based on data from a previous study, which found a 0.1-kg/d difference of ADG between 2 groups of calves with and without lung consolidation in their multivariable model (Cramer and Ollivett, 2019). Assuming a standard deviation of 0.2 kg/d, 63 calves with at least 1 episode of consolidation and 63 calves without any consolidation during the study period would be required, based on a 95% confidence interval (CI) and 80% power to detect a 0.1-kg/d difference between 2 groups. To achieve this goal, female calves were consecutively included to the study between the ages of 5 and 10 d (mean ± SD: 7.1 ± 1.2 d), and all calves were weekly subjected to thoracic ultrasound and weighing for 8 wk (before they were weaned). The minimal enrolment age of 5 d was a priori selected to avoid potential abnormal images such as atelectasis or extensive comet tails that could potentially be associated with the neonatal adaptation to extrauterine life (Jung and Bostedt, 2004). Because the study was conducted in a farm with a high risk of

BRD, we aimed to find 63 calves without lesions, and to increase the power of the study and accounting for loss of follow-up, we decided to include 15 more normal cases. So, to reach 78 cases without any consolidation, 151 consolidation cases with different depths and persistencies were found during the 8-wk period. Finally, total ADG was calculated for each calf.

Disease Recording System During the Study Period. During the study, calves were monitored by an experienced calf manager, who visually observed calves daily for clinical signs. All treatments were recorded on paper treatment records by the calf manager. All calves in the pens were considered eligible for the study regardless of their external clinical status. Diarrhea was defined as loose feces that stayed on top of bedding or watery feces that sifted through bedding. Umbilical treatment was established when umbilical cord was present and enlarged, with pain, heat, or malodorous discharge. In addition, when calves presented with labored breathing and coughing associated with any general sign of illness (e.g., depression or delayed or decreased feeding capacity), the calf manager treated them for a respiratory event. The calf manager administered antibiotics for the diseases mentioned in this study in accordance with a treatment protocol in cooperation with farm veterinarian. For respiratory events, treatment included enrofloxacin 10% (5 mg/kg s.c.) plus tylosin 20% (10 mg/kg i.m.) plus flunixin meglumine 5% (2.2 mg/kg i.m. or i.v.) plus chlorpheniramine 1% (0.5 mg/kg IM) and oral bromhexine 1% (10 mL/calf p.o.). The mean ± SD duration of clinical pneumonia treatment was 6.7 ± 1.5 d. The treatment for diarrhea was oral solution of sulfadimidine 33.3% at a dose of 220 mg/kg for the first day and 110 mg/kg for the second, third, and fourth days plus enrofloxacin 10% (5 mg/kg, s.c.). The treatment for umbilical infection was penicillin G sodium at a dose of 15,000 IU/kg, i.v., or ceftiofur hydrochloride at a dose of 2.2 mg/kg, i.m.. Finally, calf treatment data were collected from farm records.

Ultrasonography and Weighing Calves During the Study Period. Thoracic ultrasonography on calves was performed weekly using a portable linear rectal ultrasound set at a depth of 10 cm, frequency of 7.5 MHz, and gain of 27 dB (near 20 dB; far 30 dB; WED-3000, Veterinary Ultrasound Scanner, Shenzhen, China). At each visit, all TUS exams were completed by a single researcher (author AS). Approximately 200 mL of 90° industrial alcohol was applied to unclipped hair on both sides of the thorax as a transducing agent. To prevent drying, the probe was placed inside a rectal glove containing ultrasonographic coupling gel. The thorax was scanned on both sides, beginning dorsally at the level of the scapula in the tenth intercostal space (**ICS**) and progressing cranially toward the right first ICS or the left second ICS (Ollivett et al., 2015). The specific focus of thoracic ultrasonography was on lung consolidation. To get a perception of the lesion extension, the thorax was divided into 3 sections: caudal to the heart (right and left) and right cranial lung lobe (cranial to the heart, beneath the right forelimb). The cranial part of the left cranial lung lobe was not scanned due to the uncommon presence of consolidation in that lobe and the possibility of the thymus being present and confusing it with consolidation (Ollivett and Buczinski, 2016). We recorded the maximum depth of consolidation at each of these 3 locations. The electronic caliper on the ultrasound unit was used to measure the depth of lung consolidation in a dorsoventral plane on a centimeter scale. The lesions were further divided into 4 scores based on the maximal depth of consolidation (score 0 = <1 cm, score 1 = 1–<3 cm, score 2 = 3–<5 cm, score 3 = ≥5 cm). For remaining analyses, ultrasonography results were reported as dichotomous variable using a specific threshold (≥3-cm consolidation, score 2 and 3) and a sensitive threshold (≥1-cm consolidation, score 1, 2, 3). The specific threshold (≥3 cm) was the main threshold of interest because it has been previously reported as associated with future decreased milk production (Dunn et al., 2018). Calf body weights were recorded using a previously validated tape (ANImeter Tape, Bladel, the Netherlands). The tape was pulled tight around the calf's heart girth, with the calf standing. Each calf was measured once per visit. Finally, 8 ultrasound and weight reports were recorded for each calf.

Statistical Analysis

All statistical analyses were performed using the open access statistical R version 4.0.5 (https://cran.r-project.org/), using various packages for data manipulation (Tidyverse Suite; Wickham et al., 2019). Modeling was performed using the lme4 package (Bates et al., 2015). Descriptive data were obtained for the calves' population and presented as mean (±SD) for normally distributed variables (ADG, birth weight), or as median (first quartile, third quartile) for non-normally distributed variable (serum Brix value). The modeling approach accounted for TPI and antimicrobial treatment during the trial as possible confounders of consolidation effects on ADG. The effect of the number of weeks with consolidation on ADG was determined using a linear model. The main modeling strategy was to determine the effect of prolonged lung consolidation on ADG. For descriptive purposes, the dynamics of lung lesions and their severity were evaluated. Looking for the effect of lung consolidation and various outcomes, maximal consolidation depth was then categorized as ≥3 cm (score 2 + score 3) versus <3 cm (score 0 + score 1) as previously suggested (Ollivett, 2014), as well as ≥1 cm (score 1 + score 2 + score3) versus score 0. The number of weeks with observed lung consolidation (≥3-cm depth) was defined as a trichotomous outcome based on the frequency observed (no consolidation episode during the trial, 1 consolidation episode, and 2 or more consolidation episodes). Specific confounders associated with ADG and their interaction with lung consolidation (adequate [≥8.4%] versus inadequate TPI [<8.4%], BRD treatment) were also added in the model and kept in the final model if associated with the outcome ($P < 0.05$) or if changing the specific estimates by more than 20%. The final fit of the model was assessed using a visual assessment judging of the normality of residuals' distribution. The same model strategy was performed using a consolidation depth threshold of ≥1 cm. The association between birth weight and diarrhea on the number of weeks with consolidation was tested using a Kruskall-Wallis test and a chi-squared test for both consolidation thresholds. Finally, as a last objective of the study, a specific focus was put on the assessment of the evolution of the maximal consolidation depth of calves when detected as sick and treated by the calf manager. For this section, because of imbalanced data set and impossibility to use any simple linear or nonlinear model, the proportion of calves with significant consolidation (using ≥3 cm vs. <3 cm and ≥1 cm vs. <1 cm consolidation depth, respectively) during the last ultrasonographic examination preceding the treatment and the week after initiation of the treatment was reported.

RESULTS

Descriptive Statistics

The final data set consisted of 1,768 TUS reports from 221 calves over a period of approximately 6.5 mo (summer, fall, and 16 d in winter) from 1 farm.

The mean (SD) temperature (32.5 ± 2.1°C), relative humidity (25.2 ± 8.4%), and wind speed (2.6 ± 1 m/s) were observed in summer. The mean (SD) temperature (17.5 ± 7.7°C), relative humidity (46.2 ± 20.4%), and wind speed (2.4 ± 1.9 m/s) were observed in fall, and mean (SD) temperature (6.5 ± 0.7°C), relative humidity (51.4 ± 10.5), and wind speed (1.2 ± 0.8 m/s) were noted for the 16-d winter period.

Of the 229 calves that entered the study, 221 calves finished the study, and 8 calves were removed during the study period due to various diseases (n = 4: 1 meningitis case, 3 pneumonia; median age at death 18 d [8–36 d]) or positive bovine viral diarrhea (**BVD**) test (n = 4; median age at removal 13 d [7–29 d]). Because the BVD virus is endemic in the study area, BVD testing is routinely performed in the farms of that area. The mean ± SD of birth weight for all calves was 38.8 ± 4.3 kg. The mean ± SD Brix (%) concentration for TPI was 9.2 ± 0.9 (median [interquartile range]: 9 [8.80–9.84]). In 41 of 221 calves (18.6%) no blood sample could be collected for logistical reasons. Overall, inadequate TPI was found in 14% (25/180) of the calves.

The mean ± SD of ADG for all calves in this study was 0.45 ± 0.11 kg/d during the 8-wk preweaning period. During this time, 8 calves received treatment specifically for BRD, 24 calves received treatment specifically for umbilical problems, and 111 calves received treatment specifically for diarrhea. Also, 4 calves received treatment for BRD plus umbilical problems (at different times), 33 calves for BRD plus diarrhea, 8 calves for umbilical problems plus diarrhea, and 1 calf for BRD plus diarrhea plus umbilical problems. In total, 46 calves received treatment for BRD. A total of 40 calves did not receive any treatment during the study.

Lung Consolidation Over the Study Period

The individual lung consolidation dynamic (progression of the maximal depth of consolidation) is presented in Figure 1 and characterized by an increase over time of consolidation in these calves. Figure 2 presents the distribution of the percentage of calves with various consolidation score during the study period.

The distribution of calves depending on the number of weeks with consolidation depth ≥3 cm or ≥1 cm in relation with preweaning ADG is depicted in Figure 3.

Based on consolidation threshold ≥3 cm, a total of 127 (57.5%) calves had no lung consolidation episode, 48 (21.7%) had only 1 episode of lung consolidation, and 46 (20.8%) had 2 or more episodes.

Birth weight ($P = 0.13$ and $P = 0.55$, Kruskal-Wallis test for 3-cm and 1-cm thresholds, respectively) and diarrhea treatment ($P = 0.13$ and $P = 0.93$, chi-squared test for 3-cm and 1-cm thresholds, respectively) were not associated with the consolidation profile.

Lung Consolidation and Calf Growth

The mean total ADG (±SD) for calves with no consolidation episode, 1 consolidation episode, and ≥2 consolidation episodes was 0.45 (±0.10), 0.39 (±0.10), and 0.38 (±0.11) kg/d when using ≥3 cm as consolidation threshold. In the final multivariable regression

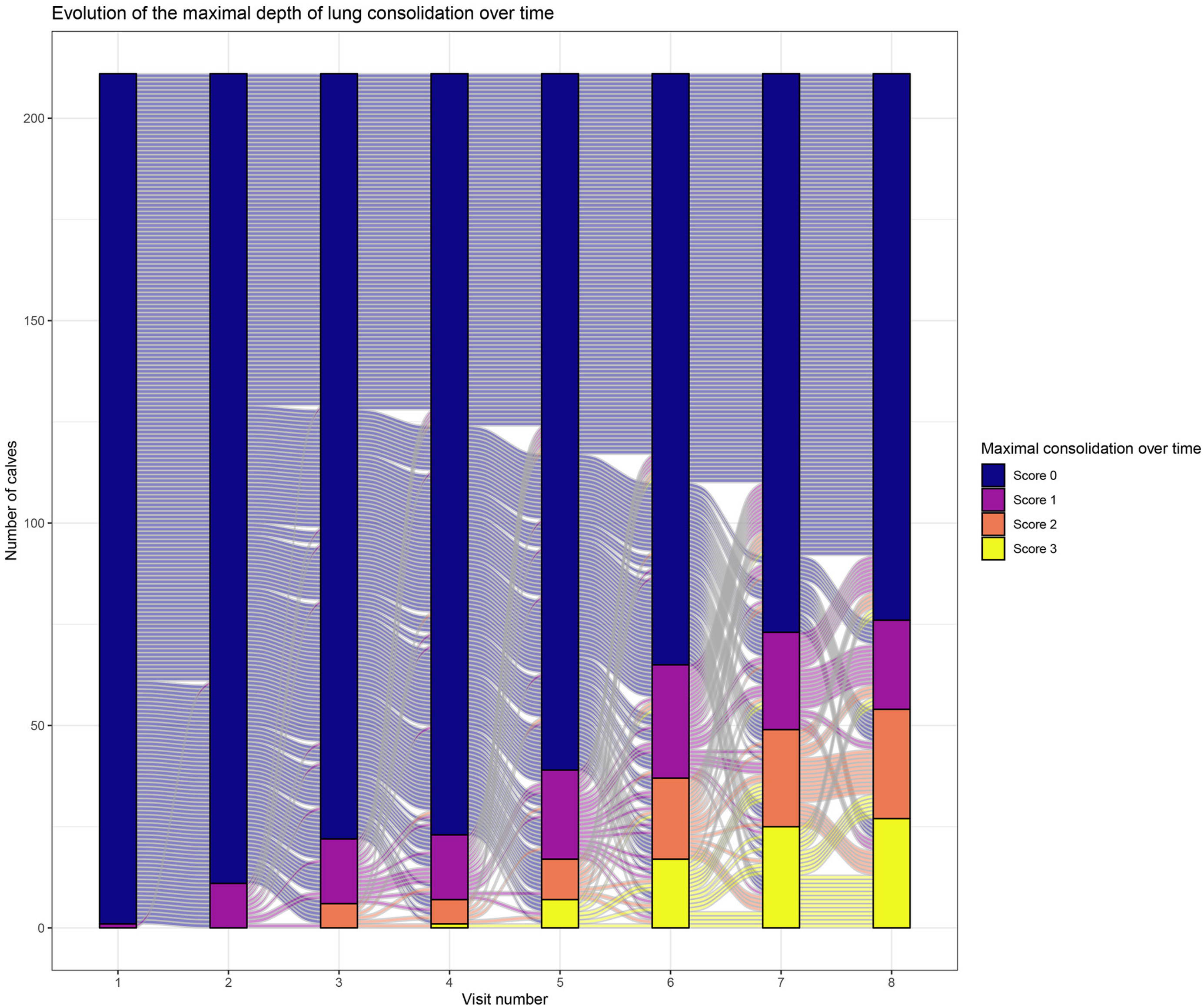

Figure 1. Evolution of the maximal depth of lung consolidation score over time (alluvial plot). Each line represents the evolution of the status of each of the 221 calves that completed the study over 8 visits. (It took 6.5 mo to complete 8 visits for 221 calves.) A score of 0 was attributed for a calf with <1-cm maximal depth of consolidation, 1 for a calf with 1- to <3-cm maximal depth of consolidation, 2 for a calf with 3- to <5-cm maximal depth of consolidation, and 3 for a calf with maximal depth of consolidation ≥5 cm.

model and based on consolidation threshold of ≥3 cm, calves with 1 and 2 or more consolidation episodes had significantly lower ADG ± standard error of 0.04 ± 0.02 kg/d, P-value = 0.02 and 0.06 ± 0.02 kg/d, P-value = 0.002, respectively, compared with animals with no consolidation episode. Also, the mean total ADG (±SD) for calves with no consolidation episode, 1 consolidation episode, and ≥2 consolidation episodes was 0.46 (±0.10), 0.43 (±0.10), and 0.38 (±0.10) kg/d, respectively, when using ≥1 cm as consolidation threshold as presented in Figure 4.

Univariable associations between various recorded preweaning variables and preweaning ADG are presented in Table 1. When using the lower consolidation threshold (≥1 cm depth) in the final multivariable linear regression model, the effect of 1 consolidation episode did not differ from no consolidation episode (reduced ADG of 0.01 ± 0.02 kg/d, P-value = 0.60), whereas 2 or more consolidation episodes were associated with a reduced ADG of 0.05 ± 0.02 kg/d (P = 0.003). The results from the multivariable linear regression analysis are indicated in Table 2. The number of lung consolida-

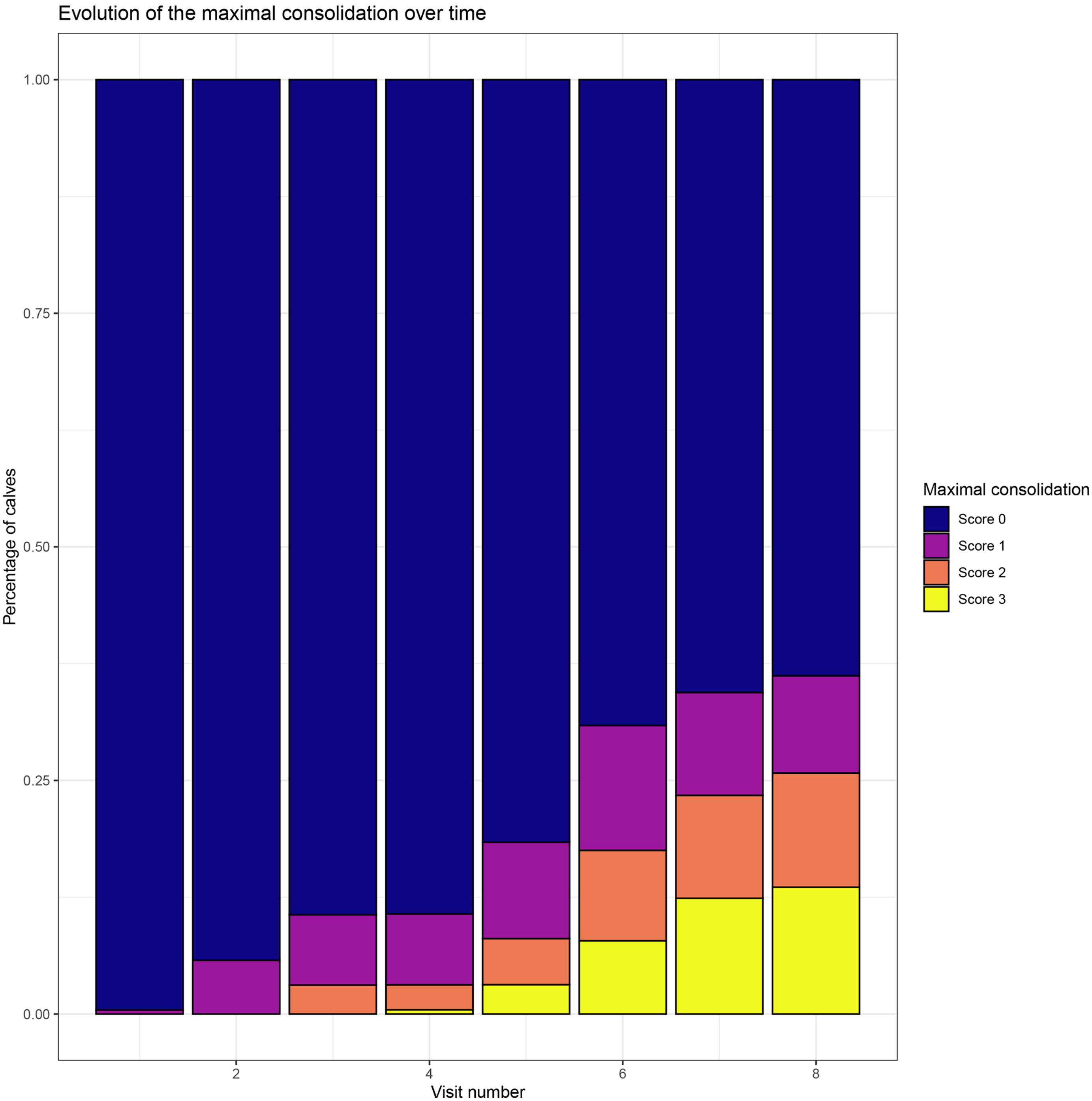

Figure 2. Distribution of the maximal depth of lung consolidation score over time. The proportion of 221 calves that completed the study with specific ultrasonographic score over 8 visits is presented. The score of 0 was attributed for a calf with <1-cm maximal depth of consolidation, 1 for a calf with 1- to <3-cm maximal depth of consolidation, 2 for a calf with 3- to <5-cm maximal depth of consolidation, and 3 for a calf with maximal depth of consolidation ≥5 cm.

tion episodes (≥3 cm depth), treatment for respiratory disease, and inadequate TPI were negatively associated with ADG.

When focusing more specifically on lung consolidation in treated calves, the median (interquartile range) consolidation depth at treatment was 1.7 (0.1–3.3) cm.

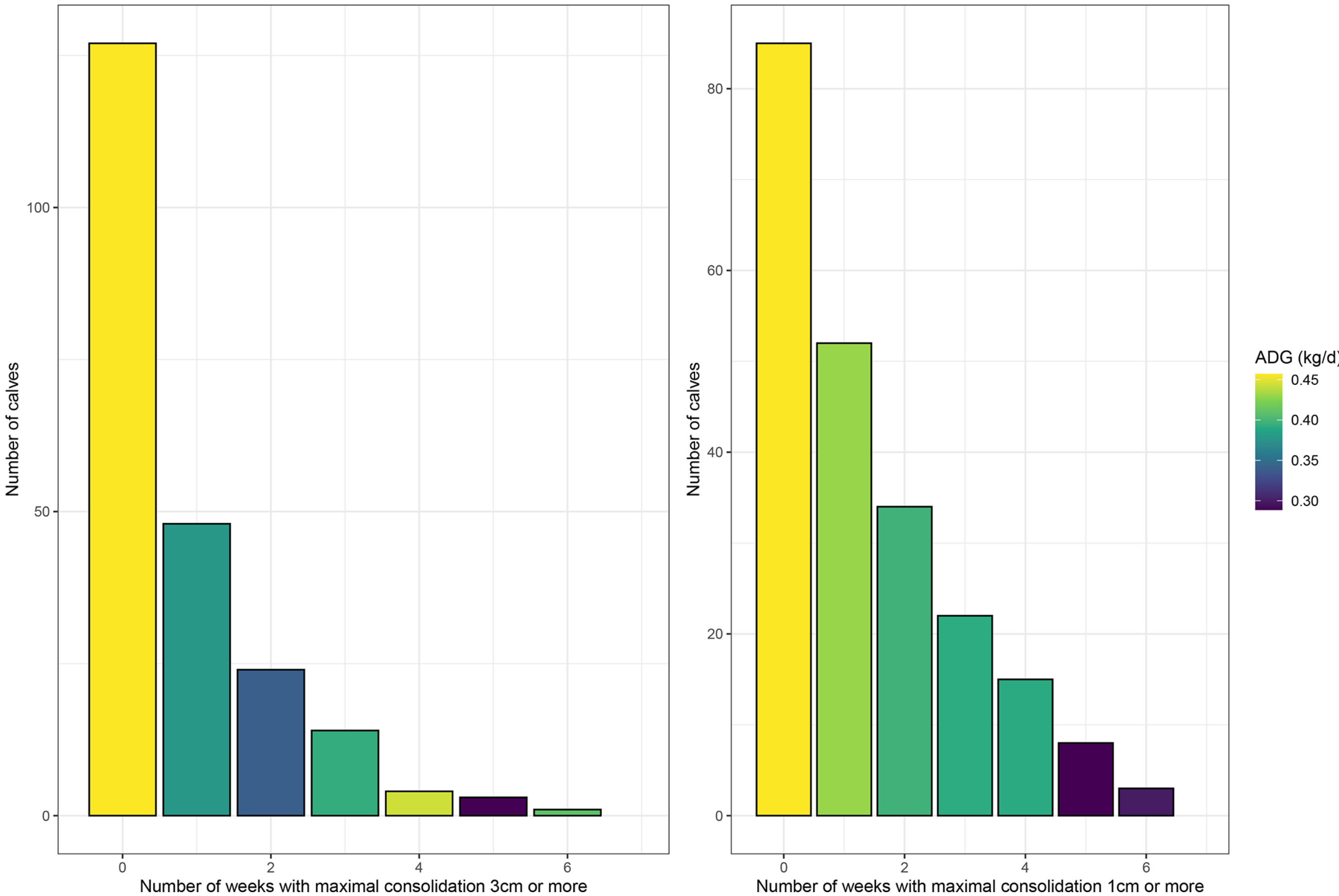

Figure 3. Distribution of calves based on the number of weeks with maximal consolidation depth ≥3 cm or ≥1 cm and preweaning ADG. The color of the bars indicates the mean ADG of calves present in this specific category.

The mean ± SD age at first BRD treatment was 42 ± 16 d (range: 12–58 d).

Evolution of Consolidation Over Time in BRD-Treated Calves

The evolution of consolidation profiles before and after pneumonia treatment is presented in Figure 5. No evolution of consolidation pattern was observed over time (P = 1.0 and P = 0.57 for ≥3 cm and ≥1 cm, respectively).

DISCUSSION

Lung Consolidation and Preweaning Growth

To the authors' knowledge, this is the first longitudinal study that used ultrasonography and treatment history to monitor calves weekly from birth until weaning in Iran. In the present study, we found that calves with 1 and 2 or more consolidation episodes had a decreased ADG of 0.04 and 0.06 kg/d, respectively, using consolidation cut-off of ≥3 cm (Ollivett, 2014), when compared with animals with no consolidation episode after controlling for treatment and TPI. Interestingly, when using a lower consolidation threshold of ≥1 cm, this negative effect of lung consolidation was still observed in our study despite the difference being more pronounced for 2 or more consolidation episodes. It is, however, important to mention that 65% of calves with only 1 episode of consolidation ≥1 cm were diagnosed between wk 6 and 8, which may limit the ability to see a negative effect of the preweaning ADG for this specific threshold. When looking at the study results at glance, it is not unreasonable to hypothesize that extensive consolidation is associated with more negative outcomes and that chronicity of disease (assessed by consolidation episodes) is an important factor in decreasing the growth and production of dairy calves. Therefore, even if our observational setting cannot prove causality, ensuring that consolidation does not progress to the 3-cm stage and not entering the chronic

Table 1. Results of univariable analysis to determine the association between health events and ADG (kg/d) during the preweaning period in dairy calves

Item	Estimate	SEM	*P*-value
Transfer of passive immunity			
Inadequate transfer of passive immunity (Brix <8.4%)	−0.050	0.023	0.033
Treatment of clinical disease			
Diarrhea	−0.023	0.015	0.14
Omphalitis	−0.028	0.019	0.14
Bronchopneumonia	−0.127	0.028	<0.001
Lung consolidation (≥3cm)			
1 consolidation episode	−0.058	0.017	<0.001
≥2 consolidation episodes	−0.069	0.018	<0.01
Lung consolidation (≥1cm)			
1 consolidation episode	−0.027	0.018	0.13
≥2 consolidation episodes	−0.075	0.016	<0.001

phase either, with 1-cm or 3-cm threshold, could potentially be a way to limit negative outcomes associated with consolidation.

In a previous study, Rhodes et al. (2021) used 3 assessment points at 21, 42, and 63 d and found that calves with a TUS score of 3+ (based on the 6-level ultrasound score, USS6; Ollivett and Buczinski, 2016) grew 0.13 kg/d less than their counterparts at any time point. Total ADG of all calves in that study was 0.50 kg/d. Additionally, a prior study that included calves from the time of purchase (23 [SD: 6.2] days of age) until weaning at 53 d, as well as assessment points at approximately 23, 37, and 51 d of age, revealed that calves with severe lung lesions (lung lobe completely consolidated or pulmonary emphysema) grew 0.12 kg/d less than those without lung lesions during the preweaning period (Cuevas-Gómez et al., 2021) and that the total ADG of all calves was 0.75 kg/d. Finally,

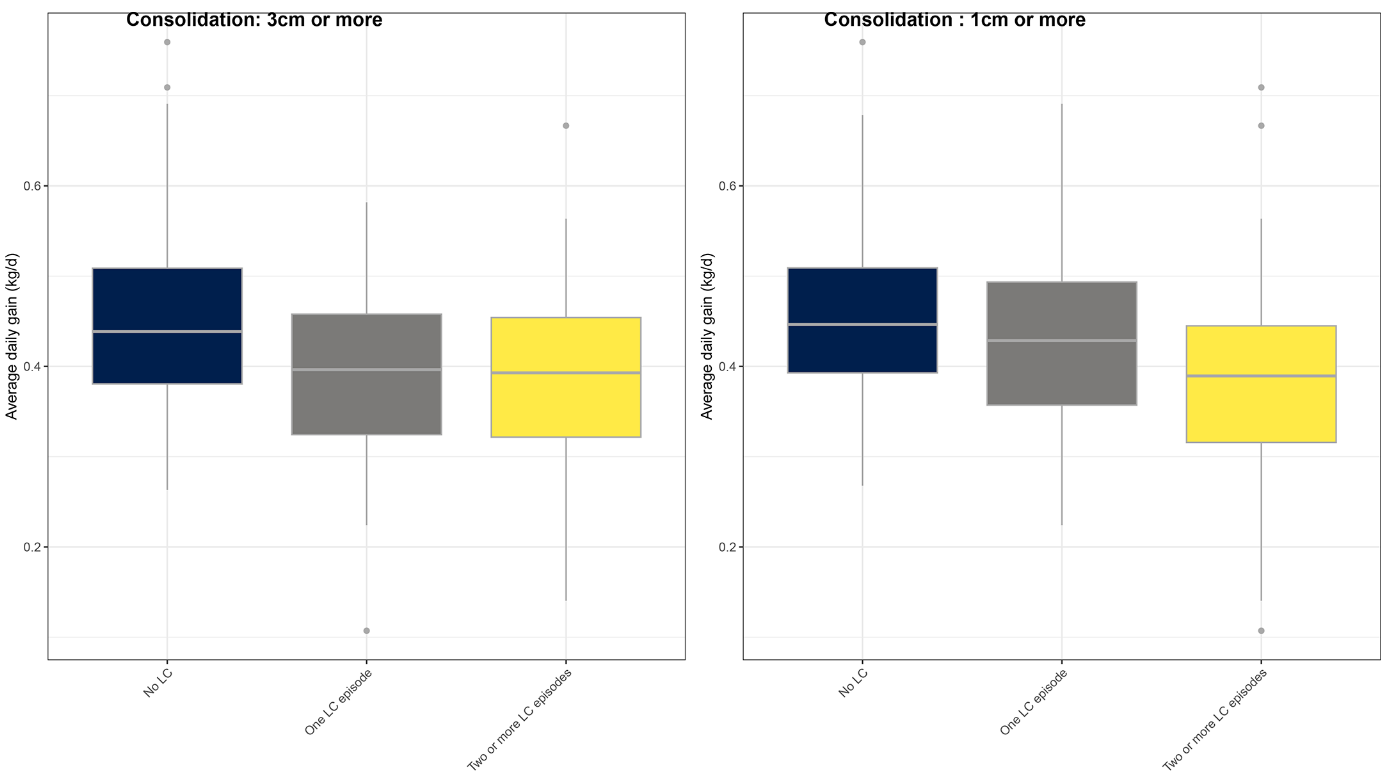

Figure 4. Preweaning ADG for calves with no consolidation episode, 1 consolidation episode, and 2 or more consolidation episodes during the 8-wk period (using depth ≥3 cm or depth ≥1 cm as consolidation thresholds). LC: lung consolidation. In the box plots, the midline represents the median, the two edges of the box represent the lower and upper interquartile range (IQR), and whisker edges are the last data points within 1.5× the IQR. The dots indicate outlier data.

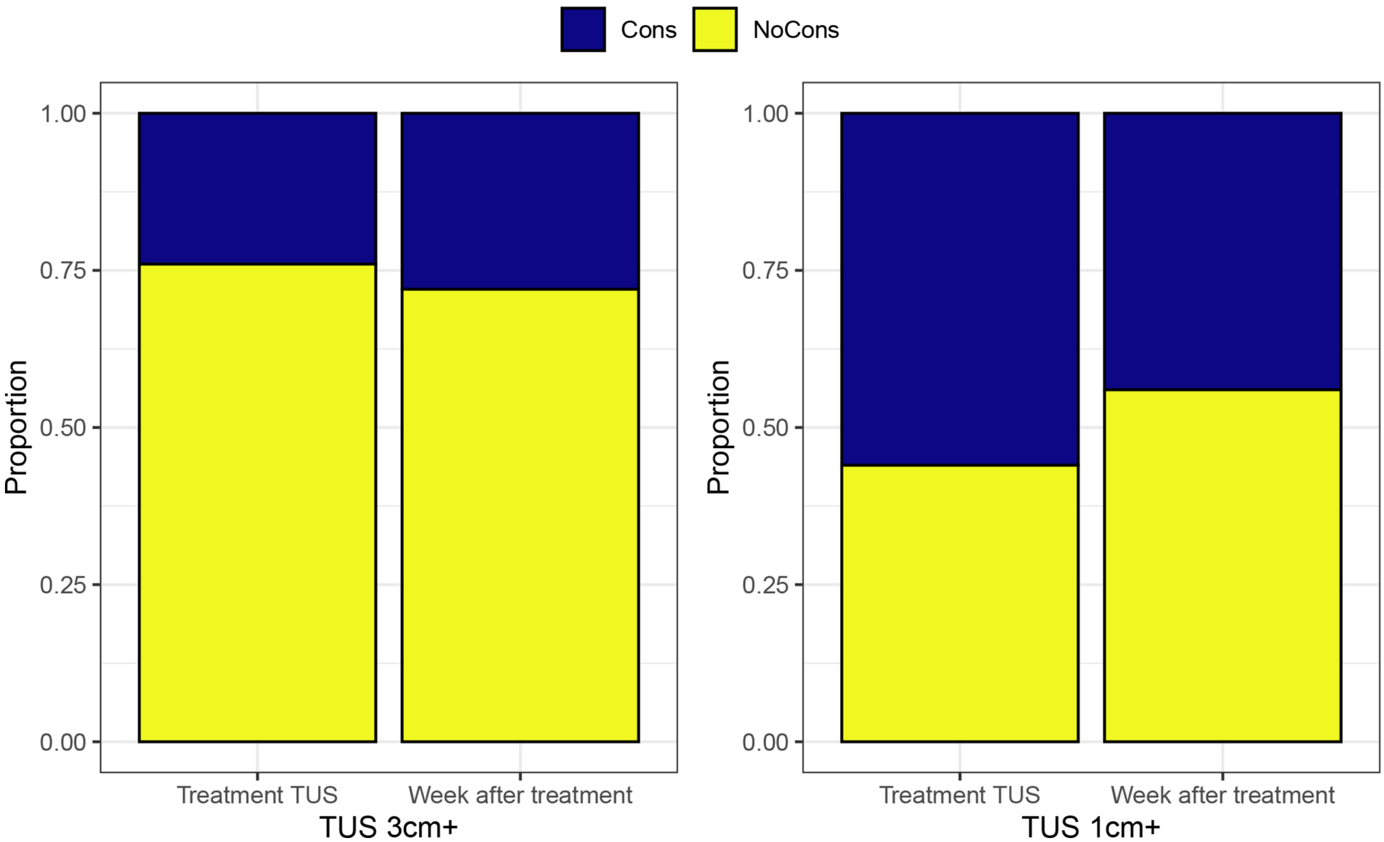

Figure 5. Consolidated (blue) and nonconsolidated (yellow) calves at the closest TUS before treatment and the week after treatment. Using both consolidation levels (1-cm or 3-cm threshold), the proportion of consolidated calves did not dramatically change between the 2 examination weeks (exam before treatment and after treatment). Cons: consolidation; NoCons: nonconsolidated; TUS: thoracic ultrasonography.

Cramer and Ollivett (2019) showed that preweaning calves with lung consolidation ≥1 cm^2 based on their first BRD event had a 0.12-kg/d ADG reduction (total ADG of all calves in that study: 0.93 kg/d). These studies were conducted in different areas with different definitions of lung lesions and different farm managements (as shown by variation of total ADG). Interestingly, the ratio of decreased ADG in calves with lesions versus no lesions is generally around 10 to 20% of the total ADG.

Effects of Clinical Treatment and Transfer of Passive Immunity on ADG

Unsurprisingly, in the final multivariable model, inadequate TPI (Brix <8.4%) also had a negative effect on ADG (0.04 kg/d less). Inadequate TPI has previously been associated with decreased preweaning ADG. In a systematic review, Raboisson et al. (2016) found that inadequate TPI was associated with a decreased ADG from −0.08 to −0.05 kg/d.

Table 2. Results of multivariable models for determining the effects of weeks with consolidation on the preweaning ADG, using ≥3 cm or ≥1 cm consolidation depth as case definition[1]

	Consolidation threshold ≥3 cm			Consolidation threshold ≥1 cm		
Item	Estimate	SEM	*P*-value	Estimate	SEM	*P*-value
Intercept	0.454	0.010	<0.001	0.454	0.012	<0.001
1 consolidation episode	−0.043	0.019	0.025	−0.011	0.020	0.596
≥2 consolidation episodes	−0.060	0.019	0.002	−0.050	0.018	0.003
Inadequate transfer of passive immunity (Brix <8.4%)	−0.045	0.021	0.037	−0.038	0.022	0.089
Treatment of clinical pneumonia	−0.103	0.028	<0.001	−0.104	0.029	<0.001

[1]Values represent both consolidation thresholds to define lung consolidation (≥ vs. <).

The main model results for the present study showed that BRD treatment based on farmer diagnosis has a much larger negative effect on preweaning ADG than consolidation episodes diagnosed by ultrasonography (0.10 kg/d less vs. 0.04 kg/d less for 1 episode and 0.06 kg/d less for ≥2 episodes). This could be a logical observation because in one study, lung lesions appeared before the appearance of clinical respiratory signs in 61% of cases (14/23; Cuevas-Gómez et al., 2021), and in another study, 64% of the calves developed clinical pneumonia after ultrasonographic detection of lung lesions (Cramer and Ollivett, 2019). Therefore, if we consider enzootic bronchopneumonia as a continuous process, clinically detected cases may be the most severe cases, which have a larger negative effect on ADG. As a result, this variable could be judged as a severity indicator, and it seems that efforts to use TUS techniques in farms to detect calves with (subclinical) pneumonia before the disease becomes clinical could be beneficial and have the potential to prevent further reduction in ADG.

Because the model analysis for the current study was controlled by the BRD treatment history, we can be confident that the effect of consolidation on ADG was not confounded by treatment (which is associated with more easily detectable clinical signs).

Lung Consolidation Patterns After Initiating BRD Treatment

As a last objective of the present study, we aimed to look for the evolution of consolidation patterns starting from the first treatment event. However, it is difficult to find a specific pattern of lung consolidation following treatment for clinically detected calves. We concluded that it is unclear whether the consolidation pattern changes or follows a specific pattern after treatment (Figure 5). Although this was an observational finding with very limited power of our analysis as the third objective of this study, it was consistent with the results of Jourquin et al. (2022) in 2 ways. In that study, male dairy calves exposed to *Mycoplasma bovis* and bovine respiratory syncytial virus could completely reaerate on TUS, and also, once fully recovered, the negative effects on ADG were no longer detectable. However, significant therapy failure was observed for various antimicrobial group treatments. However, it has been reported in humans that the monitoring of consolidation over a 48-h period could be a good indicator of evolution (Buonsenso et al., 2020). Unfortunately, we do not have specific data in this regard in calves, but it seems that it may be more complicated than in humans and will most likely depend on the pathogens involved. The design of the current study does not allow us to determine reaeration of consolidated lung in this calf population. The weekly ultrasound exam was not coordinated with treatment performed by the calf manager, and therefore the findings on the evolution of lung lesions before and after the treatment associated with the limited number of calves does not allow us to draw firm conclusions on that aspect.

We could not specifically look for the effect of chronic consolidation (30 d or more with lung lesion, as defined by Jourquin et al., 2022) due to limited sample size. Moreover, the evolution of BRD pathogens in a specific dairy farm may be different from farms comingling calves from different origins and experiencing a respiratory outbreak as in Jourquin et al. (2022).

Study Limitations

Unfortunately, it was not possible to collect and sample calves for microbiological analyses in this study. For this reason, part of the findings of this study could also be affected by specific dynamics of the agents present in this farm. The specific agents associated with BRD complex in Iran are generally the same (Roshtkhari and Mohammadi, 2012; Jamali et al., 2014) as those traditionally reported in Europe and North America (Pardon and Buczinski, 2020). Interestingly, the farm was also concurrently infected by BVD virus, and therefore it could not be excluded that transient immunosuppression periods occurred during the study. Our definition of consolidation duration assumes that the same episode of lung consolidation is observed between 2 examination periods. However, we cannot rule out that some calves healed and could be reinfected during the 1-wk window between 2 different thoracic ultrasonographic examinations.

The external validity of this study to other farms or geographical areas is therefore limited. The absence of specific clinical definition of the clinical threshold used in the farm for case detection and treatment regarding pneumonia is also a limitation of this study. Moreover, it should be kept in mind that the overall ADG found in this study was relatively low versus ADG previously reported in other studies focusing on the association between TUS and growth. However, the association was in the same proportion as that previously reported in studies with higher preweaning ADG (i.e., roughly a 10–20% decrease of ADG associated with any lung consolidation episode). This study therefore gives interesting results that need to be prospectively collected from a larger farm sample in this area.

CONCLUSIONS

Based on weekly monitoring of a specific population of preweaning dairy calves, animals with 2 or more consolidation episodes had lower ADG than animals with 1 consolidation episode, and animals with 1 consolidation episode had lower ADG than animals with no consolidation episode. Furthermore, we found that BRD treatment based on calf manager diagnosis was associated with substantially lower preweaning ADG than consolidation episodes diagnosed by ultrasonography.

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ORCIDS

A. Sáadatnia https://orcid.org/0000-0002-3011-1057
G. R. Mohammadi https://orcid.org/0000-0002-3209-2611
M. Azizzadeh https://orcid.org/0000-0001-9192-5022
A. Mirshahi https://orcid.org/0000-0001-6372-6931
A. A. Mohieddini https://orcid.org/0000-0002-1515-3830
S. Buczinski https://orcid.org/0000-0002-8460-4885