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Development of Clinical Signs based Scoring System for Assessment of Omphalitis in Neonatal Calves.

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Abstract

Omphalitis contributes significantly to morbidity and mortality in neonatal calves. Diagnosis of omphalitis is based on the local signs of inflammation – pain, swelling, local heat and purulent discharge. An abattoir trial identified an optimal, sign based, scoring system for diagnosis of omphalitis. A sample of 187 calves aged between 7 and 15 days old, were clinically examined for signs of umbilical inflammation and compared with postmortem examination of navels.

On post-mortem findings, 64 calves (34.2%) had omphalitis. In the examined omphalitis cases, the most commonly affected umbilical structure was the urachus (78.1%). Multivariable logistic regression revealed that thickening of the umbilical stump over 1.3 cm (P <0.001), discharge (P<0.001), raised local temperature (P=0.003) and the presence of umbilical hernia (P=0.024) were correlated and positive predictors of omphalitis. Discharge from the umbilical stump was associated with intra-abdominal inflammation (P =0.004).

Assigning weights based on the multivariable logistic regression coefficients, a clinical scoring algorithm was developed. The cumulative score ranged from 0 to 9. Using this scoring system, calves were categorised as positive if their total score was ≥ 2. This scoring method had a sensitivity of 85.9%, specificity of 74.8 % and correctly classified 78.6 % of all calves.

Introduction

At birth, the calf is sterile and is born in a pathogen-rich environment. The umbilicus is a sensitive porte d'entre for these pathogens to invade the calf's body. Navel ill or inflammation of the umbilicus can remain localised or diffuse into generalised peritonitis. In addition, it can ascend to the liver or be a source of septicaemia (House, 2009; Madigan, 2009). Omphalitis has been described as inflammation of any of the three component structures of the umbilicus - the two umbilical arteries, the umbilical veins and the urachus (Madigan, 2009). In omphalitis, the urachus is the most commonly affected structure in calves and the umbilical arteries least frequently affected (Trent and Smith, 1984). Additionally, there may be inflammation or swelling of the surrounding tissues, or other intra-abdominal structures may also be involved. The infection of any of these structures will manifest with the overt signs of inflammation – heat, swelling, purulent discharge and pain and could significantly contribute to neonatal morbidity and mortality (Virtala and others, 1996; Miessa and others, 2003). The common causal agents of omphalitis are opportunistic bacteria *(*Hathaway and others, 1993*)* and in the past, various figures for incidence or mortality due to omphalitis has been reported. Donovan and others (1998), reported cumulative incidence of 11%, while Virtala and others (1996), gave a higher incidence of 14 %. In a veal calf system, Pardon and others (2012) recorded an incidence rate of 0.01 omphalitis cases per 1000 calf days at risk. Thomas and Jordaan (2012), reported omphalitis as the main reason for pre-slaughter mortality in 23% of calves. According to the same authors, omphalitis was also the most common cause of post-slaughter wastage (97 out of 180 calves i.e. 54% of condemned carcases).

Despite the major impact omphalitis has on neonatal calf health, and consequently, on various production parameters (e.g. growth rates), there is a lack of peer-reviewed research in the area of navel ill diagnostics and specifically on the association between clinical signs and omphalitis. Farmers associate navel ill with the visible swelling of the umbilicus, pain, and discharge, or delays in drying up (Laven, 2015). This most common description of navel ill is practical and easy to use on the farm and allows for simple evaluation of navel ill without the need for specialised diagnostic techniques or expensive and complicated equipment. Additionally, it has the benefit of including inflammations affecting all structures of the umbilicus i.e. omphalophlebitis, omphaloarteritis, and urachitis. Although some neonates could appear completely normal, with dry external navel, they could be severely ill from intra-abdominal inflammation of the urachus, umbilical arteries and/or veins (House, 2009; Steiner and LeJeune, 2009). This makes it difficult to rely on topical signs of inflammation only, for reaching a clinical diagnosis and the reliability of these signs has to be further evaluated. Robinson and others (2015) have published clinical data on the normal umbilicus and its healing rates within the first twenty-four hours of life. However, no clinical protocol or clinical signs algorithm for detection of navel ill in calves has been assessed or validated in the past.

Considering the importance of early and accurate detection of omphalitis and with the aim to create a scoring system similar to the scoring systems for Bovine Respiratory Disease (McGuirk, 2008; Aly and others, 2014; Love and others, 2014), this paper describes a study that evaluates the reliability of clinical signs used by farmers and vets to assess the umbilicus (and/or the navel stump), with the ultimate goal to present an individual sign approach or a composite algorithm to diagnose omphalitis.

Animals, Materials, and Methods

For the purpose of determining the diagnosis of the navel region, it was decided to evaluate the navel on post-mortem. This enabled us to reach a detailed diagnosis of the navel, as well as the deeper involvement into the abdomen of calves. This study population can be defined as healthy calves suitable for human consumption. However, omphalitis (and specifically omphalitis affecting internal umbilical structures) is frequently unobserved by farmers or omitted on clinical examination and therefore only detected after submission to the abattoir at post-mortem. An abattoir in South Wales was recruited that takes young male calves on a commercial basis (approx. age of slaughter 10-14 days), as this type of livestock is not economically viable to rear or fatten. The Buderer's method (Buderer, 1996) was used to calculate the sample size and the need for adequate sensitivity (Se) and specificity (Sp) through incorporating the omphalitis prevalence. As previously reported (Virtala and others, 1996; Miessa and others, 2003), the prevalence of omphalitis ranges between 5 and 15 %. The sample size for this study was calculated as 183 calves, based on the higher figure of 15 % prevalence.

Antemortem clinical exam

The age of calves in the examined group varied between 7 and 15 days. All calves were Holstein-Friesian bull calves. They originated from local farms and were presented for slaughter on the day of examination. Clinically, omphalitis was defined as “inflammation of any of the umbilical structures – including the umbilical arteries, umbilical vein, urachus, or tissues immediately surrounding the umbilicus” (Madigan, 2009). The calves were examined for the topical clinical signs of omphalitis. The topical signs that were recorded were; pain, swelling (thickness) of the umbilical stump, raise in temperature (local heat) and the presence of pus (discharge). Change of tissue colour (redness), even though present in some cases, was omitted as difficult to visualise, due to thick hair coat and therefore less practically relevant.

Additionally, cases of an umbilical hernia, patent urachus, concurrent inflammatory conditions (joint ill, lameness) and concurrent systemic illness (if present) were also recorded for each calf. Kyphosis was recorded as a sign of intra-abdominal pain, and deep abdominal palpation was performed to detect abdominal wall tension and abdominal pain as a distinct entity from umbilical stump pain. Pain was assessed through palpation (firm squeeze) of the umbilical stump (always before abdominal palpation) and the elicited pain response - flinch and kyphosis. Flinch, kyphosis, kicking, etc. are subjective behavioural responses to a “noxious” i.e. potentially tissue-damaging stimulus and as such are imperfect indicators of measurable pain response (Mellor and others, 2000; Hudson and others, 2008). However, similarly to other behavioural responses, they have the advantage of occurring immediately after palpation (examination) and can be measured non-invasively (Stewart, 2008).

Heat was measured with a non-contact IR digital infrared thermometer [Standard ST 88618 Dual Laser (N85FR)], and two continuous scanning measurements were taken for each calf; one at the umbilical stump and one at the mid-point of the sternum (as a reference point for external body temperature). Two recordings were made at each location, and the highest reading for each was recorded. Cut off points for normal stump temperature were explored based on measures of central tendency of the study data set and the highest sensitivity and specificity of elevated temperature as a test determinant for detection of omphalitis. Calves with a stump temperature 0.5 ° C higher than the referent sternal temperature were considered potentially affected with navel ill.

The thickness of the umbilical stump was measured at mid-point between the base of the stump and the end of the stump using Vernier digital callipers and recorded in centimetres with a precision of two decimals. Based on previous normal physiological data reported by Robinson and others (2015) and the sensitivity and specificity derived from the sample data, swelling over 1.3 cm was considered pathological and therefore calves with swelling over this threshold positive for navel ill (Robinson and others, 2015). The presence or absence of umbilical hernia was established through palpation, and any palpable opening was recorded as a positive result.

The discharge was assessed according to its physical characteristics as serous, mucoid, purulent, and haemorrhagic (sanguineous) or as a combination of these. The volume and the origin of discharge were also described and recorded. Patent urachus was distinguished from discharge and draining abscesses through evaluation for the origin of the discharge, the depth of the passage or abscess and the presence of urine draining from the umbilical stump.

Post mortem examination

A gross post-mortem examination was performed on all calves, and any visible tissue changes due to inflammatory reaction (both extra-abdominally and intra-abdominally) were recorded following the established guidelines of pathological anatomy (Biss and others, 1994; Maxie and Miller, 2016). All navels were sliced, and the appearance of the cut surface described. Each affected umbilical structure (urachus, umbilical arteries, umbilical veins or surrounding soft tissues) were noted separately and for each individual calf, specifying if the inflammatory reaction was intra or extra-abdominal (or both) along with a description of the size and location of the lesions and the severity of the inflammatory process. The presence of any visible (gross) post-mortem tissue change (lesion), in any of the umbilical structures, was defined as a case of omphalitis. “Intra-abdominal” omphalitis was defined as any gross post-mortem lesion of the intra-abdominal umbilical structures (artery, veins or urachus), with or without other organs involvement (liver, bladder) but in the absence of externally visible lesions, detectable in the live animal pre-slaughter.

Statistical analysis and algorithm development

Individual inflammatory signs were assessed as diagnostic tools for detection of omphalitis through calculating percentage agreements and sensitivity and specificity. These were assessed by comparison with the gross post-mortem findings of navel ill at the abattoir.

Each clinical sign was dichotomised (present or absent) and univariable logistic regression was used to evaluate the relationship between the main clinical signs and the outcome (presence or absence of omphalitis at post mortem) i.e. to estimate the relative odds of post-mortem lesions occurring, with each clinical sign present. The individual clinical signs were investigated for potential collinearity before creating a working model, and once they satisfied this criterion, the five statistically significant clinical signs were fitted in the regression model. Variance inflation factor (VIF) higher than 5.0 was considered a positive indicator for the presence of collinearity (Rogerson, 2014).

Multivariable logistic regression (Petrie and Watson, 2006) was performed to assess the relationship between the main clinical signs combined and the presence of omphalitis at post-mortem. After stepwise removal of the non-significant variables, the goodness of fit of the final multivariable logistic model was evaluated by using the Hosmer -Lemeshow test (Hosmer and Lemeshow, 1982, 1989, 2004).

The final multivariable logistic regression model was used to create a scoring system for omphalitis by taking into account the relative contributions of each of the clinical symptoms. A score weight was assigned to each abnormal clinical sign, and the size of this score was defined as the logarithmic scale value of the corresponding regression coefficient (β or beta weight) rounded to the nearest integer (Segev and others, 2008; Love and others, 2014). The absence of each sign was assigned 0 points, and the total score value for each individual calf was calculated as the sum of the score weights for each recorded clinical sign. This summed value (i.e. the total score value for each calf) was further used to calculate the probability of positive result for each of the examined calves.

The score cut-off points were investigated through calculating sensitivity, specificity and positive and negative likelihood ratios for each possible cut-off point of the total score. ROC curve plots were fitted to the total calf score (i.e. summed values) and overall predictive accuracy (c-statistic) values for all possible cut-off points were calculated (Greiner and others, 2000). The optimal cut-off point was finally determined as the score that had the highest probability of a correct result, the highest c-statistical value and had correctly identified the greatest proportion of calves over all of the threshold points (Love and others, 2014). This methodology was adapted from previous research (Segev and others, 2008; Love and others, 2014). Additionally, the same process was applied for intra-abdominal omphalitis. All analyses were conducted using IBM® SPSS® Statistics 23.0 2015 (IBM Corp., Armonk NY, USA).

Ethical approval

Informed consent was obtained from an FSA approved Welsh abattoir to perform the clinical and post-mortem examinations. The Clinical Research and Ethical Review Board (CRERB) of the Royal Veterinary College, University of London has examined and approved the protocol *(URN* 2016 1484).

Results

In total 187 calves were evaluated over a period of eight consecutive days. The overall sample prevalence of navel ill in this study was found to be 34.2 % at post-mortem (64 of all calves). The prevalence of intra-abdominal involvement in the omphalitis cases was 29.7 % (19 out of 64 calves). The overall percentage prevalence of omphaloarteritis at post-mortem was 7.0 % (n= 13), of omphalophlebitis – 14.4 % (n= 27) and of urachitis – 26.7 % (n= 50). All three structures were affected in 17.2 % (n= 11) of omphalitis calves. Omphaloarteritis was, therefore, the least and urachitis the most frequently observed condition. The sample mean for the size of the navel in the current study was 1.3 cm with SD of 0.7 cm.

Of all examined calves, only four presented with joint ill and elevated rectal temperature (over 39.3 °C). Three of those were with all four legs affected (multiple joints) and had concurrent omphalitis. One calf had a swelling of a single tarsal joint but had no detectable signs of omphalitis and no umbilical lesions at post-mortem. All four calves were with palpably enlarged joints but not severely lame which explains why they may have failed detection prior to transport.

Of examined calves, 68.4 % presented with at least one of the main clinical symptom (128 calves). A substantial number of calves exhibited both pain and thickened umbilical stump – 49 or 26.2% of all calves. 29 calves (15.5% of all calves) exhibited both thickened umbilical stump and raised local temperature (>0.5° C rise in stump temperature over the referent sternal temperature). Individually, 70 of all calves (37.4 %) exhibited pain when firm pressure ("squeeze") was applied at the stump, and 37 of these were found to have omphalitis at post-mortem (57.8 % of cases). These numbers for swelling were 66 (35.3 % of all examined calves) vs. 38 (59.4 % of omphalitis cases), for local heat 65 (34.75 %) vs. 37 (57.8 %) and for umbilical hernia 12 (6.4%) vs. 8 (12.5 %).

The majority of evaluated calves with discharge (32 calves or 17.1 %) presented with visible fibrino-suppurative (pus-like) discharge. Only three calves presented with a combination of haemorrhagic and purulent discharge (9.4 % of all navels with discharge) and no calves presented with clear serous type of discharge. Consequently, these categories were combined into a single value (purulent discharge i.e. pus) for further analysis. At post-mortem, 93.8% of all calves with discharge (n=30) were confirmed with either purulent abscessation along the umbilical cord (intra-abdominal omphalitis; n=9 or 30%) or with an abscess at the umbilical stump (n=21 or 70% of cases with discharge).

Regression modelling for omphalitis

Univariable binary logistic regression revealed a statistically significant association between the main individual clinical signs of pain, swelling, heat, discharge, the presence of umbilical hernia and the presence of omphalitis at post-mortem (Table1). All analysed clinical signs with the exception of umbilical hernia were correlated with omphalitis at the p <0.001 level.

Table 1. Univariable logistic regression parameters for the main clinical signs as indicators of omphalitis.

Sign	**Regression Coefficient**	**Standard Error**	**Wald Statistic**	**P-Value**	**Odds Ratio**	**95 % CI**	
						Lower	**Upper**
Pain	1.32	0.32	16.48	0.000	3.74	1.98	7.06
Swelling [1]	1.60	0.33	23.09	0.000	4.96	2.58	9.53
Heat [2]	1.54	0.33	21.41	0.000	4.65	2.42	8.91
Discharge[3]	3.98	0.76	27.71	0.000	53.38	12.14	234.75
Hernia	1.45	0.63	5.22	0.022	4.25	1.23	14.71
Urachus[4]	1.37	1.24	1.23	0.267	3.94	0.35	44.25
Palpation[5]	-0.48	0.60	0.65	0.420	0.62	0.19	2.00

1: Swelling of the umbilical stump over 1.3 cm in diameter.
2: Rise of stump temperature with 0.5 °C above the reference sternal temperature.
3: Purulent and/or haemorrhagic.
4: Patent urachus.
5: Palpation for abdominal pain.

The visible presence of pus (discharge) was ranking highest (β = 4.0, P < 0.001), followed by swelling (β= 1.60, P < 0.001), pain (β = 3.0, P < 0.001) and heat (β = 1.5, P < 0.001). To a lesser degree concurrent umbilical hernia was also associated with omphalitis (β = 1.5, P = 0.022). Patent urachus (P = 0.267) and abdominal palpation for abdominal pain (P= 0.420) were not associated with omphalitis and excluded from further consideration.

The multivariable logistic regression (Table 2) identified four clinical indicators to be statistically significant and correlated with omphalitis at post-mortem. These were swelling, local heat, discharge and umbilical hernia. The most significant contributor in this multivariable model was discharge (β= 4.0, P < 0.001) and the smallest contributor was local heat (β = 1.3, P = 0.003).

The model explained 57.0 % of the variance in the navel ill sample (R^2 = 0.57) and correctly classified 65.8 % of all studied cases of omphalitis. The Hosmer-Lemeshow test confirmed the goodness of fit of this model (Chi-Square = 5.38; P = 0.250). There was no multicollinearity detected, with VIF ranging between 1.1 and 1.5 for all clinical signs.

The above four clinical indicators were subsequently used to create a scoring system for omphalitis as described and presented in Table 3. The probability of positive result, the probability of negative result, positive and negative likelihood ratios, the total percentage of correctly classified calves and the total predictive accuracy values for nine different score cut-off points are presented in Table 4.

The algorithm performed best at a cut-off point three classifying correctly 81.8 % of all examined calves, however, the c-statistic suggests a slightly better performance at the cut-off point of 2. Binary logistic regression for each score group and assessment of the Wald ratio confirmed that higher scores were associated with higher probability of navel ill.

Table 2. Multivariable logistic regression model parameters of the clinical signs as indicators of omphalitis.

Sign	Regression Coefficient	Standard Error	Wald Statistic	P-Value	Odds Ratio	95 % CI	
						Lower	Upper
Swelling [1]	1.72	0.43	15.73	0.000	5.59	2.39	13.09
Heat [2]	1.30	0.44	8.98	0.003	3.69	1.57	8.65
Discharge [3]	4.14	0.81	26.40	0.000	62.59	12.92	303.22
Hernia	1.73	0.77	5.09	0.024	5.64	1.25	25.38
Intercept	-2.65	0.38	47.53	0.000	0.07	-	-

1: Swelling of the umbilical stump over 1.3 cm in diameter.
2: Rise of stump temperature with 0.5 °C above the reference sternal temperature.
3: Purulent and/or haemorrhagic.

Table 3. Summary description of the clinical scoring method for detection of omphalitis based on the binary assessment (Present/Absent) for swelling of the umbilical cord or stump, local heat, the presence of pus and concurrent umbilical hernia.

Description of the proposed clinical scoring system for detection of Omphalitis		
Clinical qualifiers (signs)	**Description of qualifiers**	**Score weights (points)**
SWELLING	**Thickening of the umbilical stump**	
Thickened stump	Diameter of the stump is over 1.3 cm	**2**
No thickening	Diameter of the stump is less than 1.3 cm	**0**
LOCAL HEAT	**Raised surface temperature of the stump**	
Raised stump temperature	Stump temperature 0.5 ° C higher than the reference sternal temperature	**1**
Stump temperature not raised	Stump temperature lower than 0.5 ° C above the reference sternal temperature	**0**
DISCHARGE (PUS)	**Pus or abscess on the umbilical stump**	

Pus present	Pus can be visibly detected at the stump	**4**
Pus absent	Pus cannot be visualised at the stump	**0**
UMBILICAL HERNIA	**An umbilical hernia with palpable orifice**	**Score weights (points)**
Hernia present	An umbilical hernia can be palpated	**2**
Hernia absent	An umbilical hernia cannot be palpated	**0**

Table 4. Diagnostic performance of the scoring system to correctly identify calves with omphalitis.

Diagnostic performance of the scoring system to correctly identify calves with omphalitis					
Score cut off point (≥)	**Specificity**	**Sensitivity**	**Positive likelihood ratio (LR+)**	**Total % of calves correctly classified**	**Predictive Accuracy (c- statistic)**
1	95.3%	59.3%	2.3	71.7%	0.773
2	85.9%	74.8%	3.4	78.6%	0.804
3	67.2%	89.4%	6.4	81.8%	0.783
4	53.1%	96.7%	16.3	81.8%	0.749
5	42.2%	99.2%	51.9	79.7%	0.707
6	23.4%	99.2%	28.8	73.3%	0.613
7	15.6%	100.0%	-	71.1%	0.578
8	3.1%	100.0%	-	66.8%	0.516
9	3.1%	100.0%	-	66.8%	0.516

Regression modelling for intra-abdominal omphalitis

The association of the clinical signs to intra-abdominal inflammation was evaluated following the same methodology, except for the development of the algorithm. The univariable logistic regression revealed that local heat and purulent discharge were individually correlated to internal umbilical inflammation (Table 5). However, the multivariable analysis indicated that only discharge (β = 1.7; P=0.001) was significantly correlated to intra-abdominal navel ill. The odds ratio for discharge was 5.67 with a confidence interval between 2.08 and 15.46. The Intercept value of the regression model was – 2.7. Individually, the presence of discharge predicted 89.8% of the studied intra-abdominal cases of omphalitis (R^2 = 0.12; P=0.001). Since only one of the clinical signs (discharge) was significant for intra-abdominal navel ill, no scoring system specific for detection of internal omphalitis is proposed here.

Table 5. Univariable logistic regression parameters for the clinical signs as indicators of intra-abdominal omphalitis.

Sign	Regression Coefficient	Standard Error	Wald Statistic	P-Value	Odds Ratio	95 % CI	
						Lower	Upper
Pain	0.46	0.49	0.88	0.348	1.58	0.61	4.10
Swelling [1]	0.56	0.49	1.32	0.250	1.75	0.67	4.56
Heat [2]	1.07	0.49	4.67	0.031	2.90	1.10	7.63
Discharge [3]	1.74	0.51	11.52	0.001	5.67	2.08	15.46

Sign	Regression Coefficient	Standard Error	Wald Statistic	P-Value	Odds Ratio	95 % CI	
						Lower	Upper
Abdominal Palpation	0.80	0.69	1.35	0.245	2.24	0.58	8.68
Hernia	1.15	0.83	1.91	0.167	3.16	0.62	16.15
Patent Urachus	-19.04	23205.42	0.00	0.999	0.00	0.00	-

1: Swelling of the umbilical stump over 1.3 cm in diameter.
2: Rise of stump temperature with 0.5 °C above the reference sternal temperature.
3: Serous, mucoid, purulent, and haemorrhagic types were combined into single values.

Discussion

Previously reported prevalence data on the anatomical structures affected were similar to the current study (Trent & Smith, 1984). The presented data and subsequently suggested clinical scoring algorithm can be a valuable method for veterinary surgeons and farmers to score omphalitis reliably. The findings will make it easier and more accurate to score calves for the presence of omphalitis and possibly affected intra-abdominal structures. The clinical assessment of navel swelling is relatively straightforward and easy to perform and can be effectively applied in clinical practice. Although the assessment of local temperature (heat) may not be as easy to perform or interpret in general practice, availability and affordability of contactless thermometers (or thermal imaging devices) will make these measurements easier in the future.

As individual clinical signs usually have lower sensitivity and specificity as indicators of inflammation, the proposed composite algorithm would be preferred in the clinical examination of calves. At the threshold of 2 or larger, the sensitivity of the "all signs" algorithm (swelling, local heat, purulent discharge and umbilical hernia), was 85.9 % and the specificity was 74.8 %, suggesting that this algorithm is useful not only as an initial diagnostic tool in individual animals but also on a herd level to underpin veterinary advice on navel hygiene. Omphalitis scoring could also inform on the use of further tests in the clinician's decision-making process, such as ultrasonography, and inform on the prognosis and treatment (Steiner and LeJeune, 2009). Since the choice of tests and prognosis should consider the severity of inflammation and suspicion for the involvement of internal abdominal structures, the presence of discharge (an inflammatory sign that is specifically associated with inflammation of the intra-abdominal structures) can support an early decision for a therapeutic or surgical intervention (Rings, 1995).

The highest c-statistical value was used to determine the optimal cut-off point in this study, however, the optimum cut-off for a test, based on maximising the proportion of correctly classified individual animals, depends on the prevalence of cases. We acknowledge that maximising the c-statistic is equivalent to optimising equally on positive and negative animals i.e. equivalent to a prevalence of 0.5 and therefore the highest c-statistical value may not be the optimum cut-off for the whole population. In future research, the intercept (e^b0) can be chosen instead as a cut-off point, and it would provide the maximum of correctly classified cases and non-cases in a dataset with β-weights used as maximum likelihood estimators.

The accuracy of detection is also dependent on cut-off points for the individual clinical signs. These can be validated for the appropriate populations and sensitivities and specificities used according to clinical aims. The method of producing the proposed scoring system for detection of navel ill has been trialled and tested in other areas such as Bovine Respiratory Disease (Love and others, 2014) and has a distinct advantage over parallel and serial testing. In some clinical circumstances, algorithms consisting of either symptom present (serial testing) as opposed to concurrent symptoms (parallel testing) can raise the sensitivity, whereas second and third assessment of the positives at a later time (sequential clinical assessment) can raise the specificity (with a net loss of sensitivity). Additionally, compared to a single observation, sequential clinical assessment can evaluate the rate of drying up of the umbilical cord (Hides and Hannah, 2005), and also evaluate the healing and treatment response (Grover and Godden, 2011).

In our final model, all clinical signs were treated as binary variables (with yes/no result on clinical examination). But if cut - off points are to be defined these should be re-evaluated under different conditions. Based on a comparison of the median sample estimates, the Sensitivity and Specificity for swelling and the logistic regression results for this group of calves, we recommend a cut-off point of 1.3 cm for swelling (if used alone or in combination for detection of omphalitis). This result is the same as previously suggested by Grover and Godden (2011), but more than the reported healthy mean at 24 hours after birth by Robinson and others 2015. (7.6 mm). Our data corroborate with these authors that umbilical cord remaining over 1.3 cm, later than 24 hours from birth, is a cause for concern. Umbilical cord drying times are variable, but according to Hides & Hannah (2015), 91% of healthy umbilical cords are considered to have completely shrivelled and dried by four days old. Hence, we consider that the measurements of navel thickness, and consequently thickness cut-offs, in calves between 7 and 15 days old are unlikely to be confounded by age.

The high prevalence of omphalitis in this study (34.2%) is probably a result of these being male dairy calves, raised in general, under poorer husbandry conditions than female calves and so this prevalence may not be directly comparable to other populations. Also, this study is based on calves that were healthy enough to be transported to an abattoir, and therefore, some calves with severe omphalitis or unfit for transportation may have been missed. While our selection criteria may not be applicable to older calves, the goal of the proposed scoring system is early detection and treatment. Examination of older calves would not be useful in achieving this goal.

The UK welfare regulations state that calves should be at least ten days old before transportation for slaughter. Also, calves cannot be transported if “the navel has not completely healed” (Ref. DEFRA, 2012). The presence in this study of calves as young as seven days and with painful, wet, or swollen navels indicate possible non-compliance with these standards by local farmers or suppliers. The very small number of calves with joint ill and elevated rectal temperature (four calves) may have escaped detection before transport because they were not severely lame.

In clinical practice, ultrasound examination of the abdomen can be used to detect intra-abdominal navel ill, but this may be impractical on a farm or when the assessment is to be done on many calves. Informed prognosis and early intervention can be crucial to avoid complications and achieve desirable growth rates, the assessment for discharge can be a quick and easy method to predict the presence of intra-abdominal omphalitis.

The next step of the validation of the algorithm is to test its performance in other populations (breed and gender), different climatic conditions and different geographical areas. The other area where further detail would be required is the level of interference for the improvement of umbilical hygiene.

Conclusions

This research is the first of its kind to quantify the magnitude of the association between the clinical signs and omphalitis with or without intra-abdominal involvement. It defines the inflammatory symptoms of swelling, heat and discharge (with the additional assessment for umbilical hernia) as good predictors for omphalitis developing within two weeks from birth. The assessment of these signs in combination can achieve overall accuracy of 81.8 % in identifying calves affected with omphalitis. Since relevant to omphalitis complications such as bacteraemia, (poly) arthritis can be avoided through early detection and treatment, a scoring algorithm is proposed to improve the detection and early diagnosis of omphalitis. This algorithm facilitates prognosis, informs on subsequent treatment options or necessary prevention measures and therefore it could be judiciously applied in clinical practice as a diagnostic combination for omphalitis.

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References:

ALY, S. S., LOVE, W. J., WILLIAMS, D. R., LEHENBAUER, T. W., VAN EENENNAAM, A., DRAKE, C., KASS, P. H. & FARVER, T. B. (2014) Agreement between bovine respiratory disease scoring systems for pre-weaned dairy calves. *Animal Health Research Reviews, 15, 148-150.*

BISS, M., ALLEY, M., MADIE, P. & HATHAWAY, S. (1994). Lesions in the carcases and viscera of very young slaughter calves condemned at post-mortem meat inspection. *New Zealand Veterinary Journal, 42, 121-127.*

BUDERER, N. M. (1996) Statistical methodology: I. Incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. *Academic Emergency Medicine, 3, 895-900.*

DEFRA, (2012) Live Transport: Welfare Regulations. Available at: *https://www.gov.uk/guidance/farm-animal-welfare-during-transportation.* Last accessed March 03, 2017.

DONOVAN, G. A., DOHOO, I. R., MONTGOMERY, D. M. & BENNETT, F. L. (1998). Calf and disease factors affecting growth in female Holstein calves in Florida, USA. *Preventive Veterinary Medicine, 33, 1-10.*

GREINER, M., PFEIFFER, D. & SMITH, R. D. (2000) Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. *Preventive Veterinary Medicine, 45, 23-41.*

GROVER, W.M. & GODDEN, S. (2011) Efficacy of a new navel dip to prevent umbilical infection in dairy calves. *Minnesota dairy health conference, 17-19 May 2011, St. Paul, MN, USA.* (Retrieved from the University of Minnesota Digital Conservancy, *http://hdl.handle.net/11299/118901)*.

HATHAWAY, S. C., BULLIANS, J. A., JOHNSTONE, A. C., BISS, M. E. & THOMPSON, A. (1993) A pathological and microbiological evaluation of omphalophlebitis in very young calves slaughtered in New Zealand. *New Zealand Veterinary Journal, 41, 166-170.*

HIDES, S.J., HANNAH, M.C. (2005) Drying times of the umbilical cords of dairy calves. *Australian Veterinary Journal, 83, 371-373.*

HOSMER, D. W. & LEMESHOW, S. (1989) Assessing the fit of the model. In: Applied logistic regression. New York, John Wiley & Sons, Inc., pp.30-34.

HOSMER, D. W. & LEMESHOW, S. (2004) Assessing the fit of the model. In: Applied logistic regression. New York, John Wiley & Sons, Inc., p.143.

HOUSE, J.K. (2009) Umbilical enlargement. In: Smith B.P. ed. Large Animal Internal Medicine, 4th ed., St Louis, Mosby Elsevier Co. p.364.

HUDSON, C., WHAY, H., HUXLEY, J., (2008) Recognition and management of pain in cattle. *In Practice,* 30**,** 126-134.

LAVEN, R. (2015) Joint Ill / Navel Ill. NADIS Livestock Health Bulletin. Available online at: *http://www.nadis.org.uk/bulletins/joint-ill-navel-ill.aspx?altTemplate=PDF.* Last accessed February 22, 2017.

LEMESHOW, S. & HOSMER, D. W. (1982) A Review of the goodness of fit statistics for use in the development of logistics regression models. *American Journal of Epidemiology, 115, 92-106.*

LOVE, W.J., LEHENBAUER, T.W., KAAS, P.H., VAN EENENNAAM, A.L., ALY, S.S. (2014) Development of a novel clinical scoring system for on-farm diagnosis of bovine respiratory disease in pre-weaned dairy calves, *Peer Journal 2, e238.*

MADIGAN, J.E. (2009) Patent urachus, omphalitis, and other umbilical abnormalities. In: Smith B.P. ed. Large Animal Internal Medicine, 4th ed., St Louis, Mosby Elsevier Co., 2009 pp. 321-322.

MAXIE, M.G. & MILLER, M. A. (2016) Gross Examination. Introduction to the diagnostic process. In: Maxie M.G. ed., Jubb, Kennedy, Palmer's Pathology of domestic animals. 6th ed., Vol. 1, St Louis, Mosby Elsevier Co., pp. 4-8.

MCGUIRK, S. M. (2008). Disease management of dairy calves and heifers. *Veterinary Clinics of North*

America: Food Animal Practice, 24, 139-153.

MELLOR, D.J., Cook, C.J., Stafford, K.J. (2000). Quantifying some responses to pain as a stressor. In: Moberg, G.P. & Mench, J.A. Eds., The biology of animal stress: basic principles and implications for animal welfare, *CABI Publishing, Wallingford, UK, pp. 171-198.*

MIESSA, L.C., SILVA, A.A., BOTTEON, R.C.C.M., BOTEON P.T.L. (2003) Morbidity and mortality by umbilical cord inflammation in dairy calves. *A Hora Veterinaria, 23, 16-18.*

PARDON, B., DE BLEECKER, K., HOSTENS, M., CALLENS, J., DEWULF, J. & DEPREZ, P. (2012) Longitudinal study on morbidity and mortality in white veal calves in Belgium. *BioMed Central, Veterinary Research, 8, 26.*

PETRIE, A. & WATSON, P. (2006) Linear correlation and regression. In: Statistics for Veterinary and Animal Science. 2nd ed., Oxford, Blackwell Publishing, pp. 121-157.

RINGS, D. M. (1995) Umbilical Hernias, Umbilical Abscesses, and Urachal Fistulas. *Veterinary Clinics of North America: Food Animal Practice, 11, 137-148.*

ROBINSON, A. L., TIMMS, L. L., STALDER, K. J. & TYLER, H. D. (2015) Short communication: The effect of 4 antiseptic compounds on umbilical cord healing and infection rates in the first 24 hours in dairy calves from a commercial herd. *Journal of Dairy Science, 98, 5726-5728.*

ROGERSON, P. A. (2014) Introduction to regression analysis. In: Statistical methods for geography: a student's guide. London, Sage Publications. p. 266.

SEGEV, G., KASS, P.H., FRANCEY, T. & COWGILL, L.D. (2008) A novel scoring system for outcome prediction in dogs with Acute Kidney Injury Managed by Haemodialysis. *Journal of Veterinary Internal Medicine 22, 301-308.*

STEINER, A. & LEJEUNE, B. (2009) Ultrasonographic assessment of umbilical disorders. *Veterinary Clinics of North America: Food Animal Practice, 25, 781-794.*

STEWART, M. (2008). Non-invasive measurement of stress and pain in cattle using infrared thermography: a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Animal Science at Massey University, Palmerston North, New Zealand.

THOMAS, G. W. & JORDAAN, P. (2013). Pre-slaughter mortality and post-slaughter wastage in bobby veal calves at a slaughter premises in New Zealand. *New Zealand Veterinary Journal, 61, 127-132.*

TRENT, A.M. & SMITH D.F. (1984) Surgical management of umbilical masses with associated umbilical cord remnant infections in calves. *Journal of the American Veterinary Medical Association, 185, 1531-1534*.

VIRTALA, A.M., MECHOR, G. D., GROHN, Y. T. & ERB H. N. (1996) The effect of calfhood diseases on the growth of female dairy calves during the first three months of life in New York State. *Journal of Dairy Science, 79, 1040-1049.*