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Development of clinical signs-based scoring system for assessment of omphalitis in neonatal calves.

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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

35 contribute to neonatal morbidity and mortality (Virtala and others, 1996; Miessa and others, 2003).
36 The common causal agents of omphalitis are opportunistic bacteria (Hathaway and others, 1993) and
37 in the past, various figures for incidence or mortality due to omphalitis has been reported. Donovan
38 and others (1998), reported cumulative incidence of 11%, while Virtala and others (1996), gave a
39 higher incidence of 14 %. In a veal calf system, Pardon and others (2012) recorded an incidence rate
40 of 0.01 omphalitis cases per 1000 calf days at risk. Thomas and Jordaan (2012), reported omphalitis
41 as the main reason for pre-slaughter mortality in 23% of calves. According to the same authors,
42 omphalitis was also the most common cause of post-slaughter wastage (97 out of 180 calves i.e. 54%
43 of condemned carcasses).

44 Despite the major impact omphalitis has on neonatal calf health, and consequently, on various
45 production parameters (e.g. growth rates), there is a lack of peer-reviewed research in the area of
46 navel ill diagnostics and specifically on the association between clinical signs and omphalitis. Farmers
47 associate navel ill with the visible swelling of the umbilicus, pain, and discharge, or delays in drying up
48 (Laven, 2015). This most common description of navel ill is practical and easy to use on the farm and
49 allows for simple evaluation of navel ill without the need for specialised diagnostic techniques or
50 expensive and complicated equipment. Additionally, it has the benefit of including inflammations
51 affecting all structures of the umbilicus i.e. omphalophlebitis, omphaloarteritis, and urachitis.
52 Although some neonates could appear completely normal, with dry external navel, they could be
53 severely ill from intra-abdominal inflammation of the urachus, umbilical arteries and/or veins (House,
54 2009; Steiner and LeJeune, 2009). This makes it difficult to rely on topical signs of inflammation only,
55 for reaching a clinical diagnosis and the reliability of these signs has to be further evaluated. Robinson
56 and others (2015) have published clinical data on the normal umbilicus and its healing rates within the
57 first twenty-four hours of life. However, no clinical protocol or clinical signs algorithm for detection of
58 navel ill in calves has been assessed or validated in the past.

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

64 **Animals, Materials, and Methods**

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

77 Antemortem clinical exam

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

87 Additionally, cases of an umbilical hernia, patent urachus, concurrent inflammatory conditions (joint
88 ill, lameness) and concurrent systemic illness (if present) were also recorded for each calf. Kyphosis
89 was recorded as a sign of intra-abdominal pain, and deep abdominal palpation was performed to
90 detect abdominal wall tension and abdominal pain as a distinct entity from umbilical stump pain. Pain
91 was assessed through palpation (firm squeeze) of the umbilical stump (always before abdominal
92 palpation) and the elicited pain response - flinch and kyphosis. Flinch, kyphosis, kicking, etc. are
93 subjective behavioural responses to a “noxious” i.e. potentially tissue-damaging stimulus and as such
94 are imperfect indicators of measurable pain response (Mellor and others, 2000; Hudson and others,
95 2008). However, similarly to other behavioural responses, they have the advantage of occurring
96 immediately after palpation (examination) and can be measured non-invasively (Stewart, 2008).

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

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

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

117 Post mortem examination

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

130 ***Statistical analysis and algorithm development***

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

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

141 Multivariable logistic regression (Petrie and Watson, 2006) was performed to assess the relationship
142 between the main clinical signs combined and the presence of omphalitis at post-mortem. After
143 stepwise removal of the non-significant variables, the goodness of fit of the final multivariable logistic
144 model was evaluated by using the Hosmer -Lemeshow test (Hosmer and Lemeshow, 1982, 1989,
145 2004).

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

154 The score cut-off points were investigated through calculating sensitivity, specificity and positive and
155 negative likelihood ratios for each possible cut-off point of the total score. ROC curve plots were fitted
156 to the total calf score (i.e. summed values) and overall predictive accuracy (c-statistic) values for all
157 possible cut-off points were calculated (Greiner and others, 2000). The optimal cut-off point was
158 finally determined as the score that had the highest probability of a correct result, the highest c-

159 statistical value and had correctly identified the greatest proportion of calves over all of the threshold
160 points (Love and others, 2014). This methodology was adapted from previous research (Segev and
161 others, 2008; Love and others, 2014). Additionally, the same process was applied for intra-abdominal
162 omphalitis. All analyses were conducted using IBM® SPSS® Statistics 23.0 2015 (IBM Corp., Armonk
163 NY, USA).

164 ***Ethical approval***

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

168 ***Results***

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

177 Of all examined calves, only four presented with joint ill and elevated rectal temperature (over 39.3
178 °C). Three of those were with all four legs affected (multiple joints) and had concurrent omphalitis.
179 One calf had a swelling of a single tarsal joint but had no detectable signs of omphalitis and no
180 umbilical lesions at post-mortem. All four calves were with palpably enlarged joints but not severely
181 lame which explains why they may have failed detection prior to transport.

182 Of examined calves, 68.4 % presented with at least one of the main clinical symptom (128 calves). A
183 substantial number of calves exhibited both pain and thickened umbilical stump – 49 or 26.2% of all
184 calves. 29 calves (15.5% of all calves) exhibited both thickened umbilical stump and raised local
185 temperature (>0.5° C rise in stump temperature over the referent sternal temperature). Individually,
186 70 of all calves (37.4 %) exhibited pain when firm pressure (“squeeze”) was applied at the stump, and
187 37 of these were found to have omphalitis at post-mortem (57.8 % of cases). These numbers for
188 swelling were 66 (35.3 % of all examined calves) vs. 38 (59.4 % of omphalitis cases), for local heat 65
189 (34.75 %) vs. 37 (57.8 %) and for umbilical hernia 12 (6.4%) vs. 8 (12.5 %).

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

197 ***Regression modelling for omphalitis***

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

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

203

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.

204

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

210 The multivariable logistic regression (Table 2) identified four clinical indicators to be statistically
 211 significant and correlated with omphalitis at post-mortem. These were swelling, local heat, discharge
 212 and umbilical hernia. The most significant contributor in this multivariable model was discharge ($\beta =$
 213 4.0 , $P < 0.001$) and the smallest contributor was local heat ($\beta = 1.3$, $P = 0.003$).

214 The model explained 57.0 % of the variance in the navel ill sample ($R^2 = 0.57$) and correctly classified
 215 65.8 % of all studied cases of omphalitis. The Hosmer-Lemeshow test confirmed the goodness of fit of
 216 this model (Chi-Square = 5.38; $P = 0.250$). There was no multicollinearity detected, with VIF ranging
 217 between 1.1 and 1.5 for all clinical signs.

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

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

226

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

228

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.

229

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

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

233 *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

234 **Regression modelling for intra-abdominal omphalitis**

235 The association of the clinical signs to intra-abdominal inflammation was evaluated following the same
 236 methodology, except for the development of the algorithm. The univariable logistic regression
 237 revealed that local heat and purulent discharge were individually correlated to internal umbilical
 238 inflammation (Table 5). However, the multivariable analysis indicated that only discharge ($\beta = 1.7$;
 239 $P=0.001$) was significantly correlated to intra-abdominal navel ill. The odds ratio for discharge was
 240 5.67 with a confidence interval between 2.08 and 15.46. The Intercept value of the regression model
 241 was -2.7 . Individually, the presence of discharge predicted 89.8% of the studied intra-abdominal cases
 242 of omphalitis ($R^2 = 0.12$; $P=0.001$). Since only one of the clinical signs (discharge) was significant for
 243 intra-abdominal navel ill, no scoring system specific for detection of internal omphalitis is proposed
 244 here.

245 *Table 5. Univariable logistic regression parameters for the clinical signs as indicators of intra-abdominal*
 246 *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.

247

248 **Discussion**

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

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

268 inflammation of the intra-abdominal structures) can support an early decision for a therapeutic or
269 surgical intervention (Rings, 1995).

270 The highest c-statistical value was used to determine the optimal cut-off point in this study, however,
271 the optimum cut-off for a test, based on maximising the proportion of correctly classified individual
272 animals, depends on the prevalence of cases. We acknowledge that maximising the c-statistic is
273 equivalent to optimising equally on positive and negative animals i.e. equivalent to a prevalence of
274 0.5 and therefore the highest c-statistical value may not be the optimum cut-off for the whole
275 population. In future research, the intercept (e^{b_0}) can be chosen instead as a cut-off point, and it
276 would provide the maximum of correctly classified cases and non-cases in a dataset with β -weights
277 used as maximum likelihood estimators.

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

289 In our final model, all clinical signs were treated as binary variables (with yes/no result on clinical
290 examination). But if cut - off points are to be defined these should be re-evaluated under different
291 conditions. Based on a comparison of the median sample estimates, the Sensitivity and Specificity for
292 swelling and the logistic regression results for this group of calves, we recommend a cut-off point of
293 1.3 cm for swelling (if used alone or in combination for detection of omphalitis). This result is the same
294 as previously suggested by Grover and Godden (2011), but more than the reported healthy mean at
295 24 hours after birth by Robinson and others 2015. (7.6 mm). Our data corroborate with these authors
296 that umbilical cord remaining over 1.3 cm, later than 24 hours from birth, is a cause for concern.
297 Umbilical cord drying times are variable, but according to Hides & Hannah (2015), 91% of healthy
298 umbilical cords are considered to have completely shrivelled and dried by four days old. Hence, we
299 consider that the measurements of navel thickness, and consequently thickness cut-offs, in calves
300 between 7 and 15 days old are unlikely to be confounded by age.

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

308 The UK welfare regulations state that calves should be at least ten days old before transportation for
309 slaughter. Also, calves cannot be transported if “the navel has not completely healed” (Ref. DEFRA,
310 2012). The presence in this study of calves as young as seven days and with painful, wet, or swollen
311 navels indicate possible non-compliance with these standards by local farmers or suppliers. The very
312 small number of calves with joint ill and elevated rectal temperature (four calves) may have escaped
313 detection before transport because they were not severely lame.

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

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

322

323 ***Conclusions***

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

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