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Early risk factors, development, disappearance and contents of umbilical outpouching in Danish pigs

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HIGHLIGHTS

- Umbilical outpouchings are mainly due to umbilical herniation and/or formation of abscesses or fibrosis.
- Early risk factors such as female gender, signs of immaturity and the condition of the umbilicus early in life are associated with the development of an umbilical outpouching.
- Spontaneous regression of umbilical outpouchings occur in pigs.

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ABSTRACT

The main objective of the study was to identify early risk factors associated with the development of umbilical outpouchings (UOs) in pigs. Secondly, to describe 1) the nature of UOs, 2) the age when UOs become visible, and 3) at which age UOs spontaneously may regress and disappear.

A longitudinal study following pigs (n=3031) from birth to slaughter was carried out in two commercial Danish herds.

In total, 8 % (n=255) of the pigs developed an UO between birth and death (spontaneous, euthanasia or slaughter). The odds for developing an UO was significantly lower for males than females (OR, 0.7; 95% CL, 0.5-0.9). Pigs born immature (OR, 3.4; 95% CL, 1.3-8.2) or observed with: 1) clinical sign of omphalitis (OR, 1.8; 95% CL, 1.1-2.8), 2) a elongated moist umbilical cord at birth (OR, 5.1; 95% CL, 2.6-9.8) or 3) a healed or healing protruding umbilicus in the second week after birth (OR, 1.9; 95% CL, 1.4-2.6) were associated with significant higher odds of developing an UO. No significant association (p-value >0.05) was found between the development of UOs and sow parity, litter size, birth weight and length of the umbilical cord. The nature of the UOs were mainly due to umbilical herniation and/or formation of abscesses or fibrosis. The majority of UOs became visible within the first 10 weeks of age (80%, n=234). Spontaneous regression of the UOs occurred in 14% (n=36) of the pigs; 83% (n=30) disappeared between the 4th and 14th week.

Identifying piglets with high odds of developing UOs makes it possible to identify to which pig special attention should be paid during the daily management.

1. Introduction

Umbilical hernia and differential diagnoses presenting as umbilical outpouchings (UOs) are frequent pathological conditions in pigs (Mattsson et al., 2013; Searcy Bernal et al., 1994; Vestergaard and Wachmann, 2002). The prevalence of UOs between herds varies. In a Danish cohort study of crossbreed pigs (Landrace x Yorkshire x Duroc) the occurrence of UOs was approximately 4.2% when no precautions were taken to prevent UOs (Vestergaard and Wachmann, 2002). Searcy-Bernal et al. (1994) found the prevalence of UOs in a Californian herd to be 1.5%, whereas Mattsson et al. (2013) found the prevalence in one Swedish herd to be 10.1%. Searcy-Bernal et al. (1994) examined pigs (n=2958) every week from birth until exit from the study, and most of the UOs were identified between 9 and 14 weeks of age. Mattsson et al. (2013) examined pigs (n=2660) from five different herds and identified the majority of the UOs when the pigs were between 9 and 10

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weeks of age. Most umbilical hernias in children resolve spontaneously, and the incidence of umbilical hernia decreases with advancing age (Cilley and Shereef, 2004). It is unclear to what extent UOs resolve spontaneously in pigs, but both Mattsson et al. (2013) and Searcy Bernal et al. (1994) reported a decreasing incidence of UOs with advancing age in pigs.

UOs differ in origin and presentation (Andersen, 2014), and the pathogenesis of UOs is complex. A number of pathological conditions appear as an UO. The five main conditions are hernia umbilicalis, enterocystoma, peritoneal proliferations, subcutaneous abscesses, and subcutaneous fibrosis (Andersen et al., 2014). These conditions occur alone or in combination and may be located intra-abdominally, extra--abdominally or as a combination of the two (Andersen et al., 2014).

Hernia umbilicalis is characterized by a persistent abdominal wall opening at the umbilicus, in which a protruding pouch of the peritoneum and skin forms a hernial sack, with or without contents (Uzal et al., 2016). Enterocystoma is characterized by one- or multi-cystic complexes (remains of the yolk sac) containing more or less serous, bloodstained fluid (Petersen, 1938). Knowledge regarding peritoneal proliferations is incomplete, but the proliferations may appear oblong, with rounded edges or more paddle-shaped with a closing vesicle. Often they appear combined with an umbilical hernia (Andersen et al., 2014). Subcutaneous abscesses at the umbilicus are a common complication of omphalitis (Ameh and Nmadu, 2002). In the healing process, the abscesses will turn into subcutaneous fibrotic masses (Andersen, 2014). In case of non-reducible UOs, the causative pathological condition cannot be determined by clinical examination (Glick and Nygaard, 2016).

UOs may compromise animal welfare, and the severity is mainly due to the presence of skin lesions on the UOs (Barington et al., 2016) and the type of pathological condition causing the UOs (Schild et al., 2015). Potentially, fatal complications such as: 1) strangulation, where the hernia-content compromises the blood supply, 2) obstruction of the intestines preventing the bowel content to pass through the herniated area of the gut, and 3) adhesions of e.g. the intestines or omentum (Hansen, 2014; Mattsson et al., 2013; White, 2010) are associated with severe pain in humans (Velasco et al., 1999), and it is reasonable to assume, that this also applies to other species.

Pigs with UOs represent a financial loss (Searcy-Bernal et al., 1994; Straw et al., 2009) due to increased mortality rate (Mattsson et al., 2013; Straw et al., 2009), decreased growth performance and early slaughter (Searcy-Bernal et al., 1994).

Shortly after birth, some piglets may have a higher risk of developing UOs than others. Searcy Bernal et al. (1994) reported an association between umbilical lesions (omphalitis or an umbilical abscess) and the development of an UO of more than 1cm. Similar results have been found in other species, such as humans and cattle (Ameh and Nmadu, 2002; Steenholdt and Hernandez, 2004). Previous studies have reported that administration of antibiotics to newborn piglets reduces the occurrence of UOs in pigs (Szczotka et al., 2019; Yun et al., 2017). Furthermore, Searcy-Bernal et al. (1994) and Rutten-Ramos and Deen (2006) proposed a genetic hypothesis, due to an observed familial clustering of pigs with an UO.

In general, evidence-based knowledge on risk factors associated with the development of UOs in pigs is inadequate. Prophylactic administration of antibiotics to newborn pigs is not a future-orientated strategy, and because a number of different pathological conditions may be the cause of an UO, genetic selection is not feasible. Scientific data elucidating the dynamics associated with the development and disappearance of UOs during early life of pigs and associated risk factors are not available. The identification of early risk factors associated with the development of UOs, makes it possible to identify to which pig special attention should be paid during the daily management. Further, it may assist efforts to establish management-strategies, for practical use, and as a result reduce the incidence of UOs.

The primary aim of the present study was to identify early risk factors associated with the development of UOs and to describe and determine 1) the nature of the UOs, 2) the age when UOs become visible and 3) at which age UOs spontaneously may regress and disappear.

2. Material and methods

The study was performed as a prospective field trial in two commercial farrow-to-finish herds, with production units located in the eastern part of Denmark. The experimental protocol complied with Danish Ministry of justice law concerning experimental animal (Licence no. 2017/ 15-0201-01372). Data were collected from December 2017 until August 2018.

2.1. Animals and housing

Two sow herds, delivering Danish crossbred offspring (Landrace/ Yorkshire x Duroc), were selected based on a history of a high prevalence of pigs with UOs. Herd A was a Specific Pathogen Free (SPF) herd (SPF-sus, 2017). Herd B was a conventional herd with unknown health status. In both herds, sows were housed in a standard indoor system, involving sows loose in the gestation unit followed by box fixation in the farrowing unit. Piglets were weaned at 3-4 weeks of age. In all production systems, the feed fulfilled the Danish Nutrient standards of 2017 (SEGES, 2017) and was mainly formulated with wheat, barley and soybean meal. Enrichment material for weaners and finishers consisted of wooden pins.

2.1.1. Herd A

Herd A consisted of approximately 1050 sows. Boxes in the farrowing unit had partially slatted plastic floors. Next to the sow, a covered nest-area was organized in the corner for nursery pigs – containing a heating lamp, and a rubber mat, scattered with a vegetable- and potatofiber product (Nordic Fiber-Hyg). A milk cup, a water-drinking bowl, and a feeding trough for nursery pigs were located next to the corner. Milk was available in the milk cups approximately 24 hours after birth and until weaning. Approximately one week after birth, feed was available ad libitum. At weaning, pigs were transported (16 km) by lorry to a herd with two weaner sections. Both sections were organized with a climate control system and a resting- and activity area. One section was organized with small pens, each containing approximately 12 weaners. The flooring consisted of 50% slatted floor and 50% solid concrete floor. The other section was organized with pens containing 20-25 weaners. The flooring consisted of two-third slatted plastic floor and one-third solid concrete floor. When pigs reach 30 kg, they were moved to the finisher sections. Each section contained 20 pens, and in each pen approximately 14 pigs were housed. The flooring in the finisher section consisted of 75% slatted concrete floor and 25% solid floor.

2.1.2. Herd B

Herd B consisted of approximately 1600 sows. Boxes in the farrowing unit were organized with 50% solid concrete floor and 50% metal grate. Next to the sow, a covered area was organized in the corner for nursery pigs – containing a heating lamp, and a rubber mat, scattered with wood- /potato-flour and disinfection (Staldren®). After birth, the nursery pigs had easy access to milk and water, available in an iron supplementation system and a water-drinking bowl, respectively. A feeding trough for nursery pigs was placed near the corner. Feed was available ad libitum one week after birth. At weaning the pigs were transported to two different weaner stations within 22 km. These were organized for weaners with a climate control system, a covered resting area with solid concrete floor and an activity area with metal or plastic grate. Each pen contained approximately 30-40 weaners immediately after weaning, and afterwards they were split into smaller groups. At approximately 30 kg, the pigs were transported to three different finisher locations within 22 km from the weaner locations. At all three locations, the flooring consisted of either solid, slatted or partially slatted concrete floor. Two of the locations were mainly organized with pens without covering areas and contained 10-18 pigs. The third finisher location was built with an innovative housing system with controlled environment including air cleaning systems and adjustable coverings, defined resting, defecation and activity areas. Each pen contained 10-16 pigs.

2.2. Study design

The study was designed as prospective cohort study following pigs from birth to slaughter. As the number of farrowings per week were lower in herd A and the approximated prevalence of UOs reported from the herd owners beforehand, was lower in herd A (approx. 5%) compared to herd B (approx. 7%), it was decided to enroll pigs born during a period of two weeks in herd A (n= 1915) and during a one-week period in herd B (n=1116). The cohort was slaughtered at approximately 6 months of age.

Within the first 24 hours of life, pigs were weighed and earmarked and their canine teeth were abraded. The length of the umbilical cord of all piglets was registered ($< / \geq$ 5cm) and cut to leave a small part of 2-5 cm in length. Prophylactic antibiotic treatment was not administered to the piglets. Tail docking was together with a supplementary iron-injection (Uniferon® 200 mg/ml) and oral administration of a coccidiostaticum (Baycox Vet. 50 mg/ml, Toltarox® 50 mg/ml) carried out 3-4 days after birth.

2.3. Data collection and clinical recordings

An umbilical outpouching was defined as a protrusion of more than 0.5 cm in height in the umbilical region, measured longitudinally from basis to apex of the UO.

Within 24 hours from farrowing (t0), the following was registered for each animal 1) sow ID-number, 2) litter size (number of piglets (incl. stillborn)), 3) parity of the sow (1, 2, $\geq$3), 4) birth weight (g), 5) sign of immaturity (bulging forehead: yes, no), 6) gender (male, female), 7) length of umbilical cord ($<$ 5 cm, $\geq$ 5 cm), 8) umbilical condition at birth (normal, rupture, omphalitis, moist) defined in Table 1. In regard to "umbilical condition at birth", the pigs could only appear in one of the defined categories in order of severity. Rupture was considered most severe followed by omphalitis and moist, i.e. if a piglet was recorded with omphalitis and moist umbilical cord, the umbilical condition was categorized as "omphalitis". In the second week (7-14 days) after birth the umbilicus of each pig was carefully inspected, and the umbilical condition was registered once again (normal, umbilical outpouching, healed/healing umbilical protrusion, omphalitis) defined in Table 1.

Table 1
Definitions of the umbilical conditions recorded in newborn piglets and recorded in piglets in the second week after birth.

Umbilical conditions in newborn piglets	Description	Illustration
Normal	Umbilicus with an attached, dry umbilical cord (wet if quite newborn)	
Rupture	Umbilical cord detachment, rupture or bleeding from the umbilical cord or umbilicus	
Omphalitis	Presence of erythema, swelling, or purulent discharge from the umbilical cord or periumbilical tissue	
Moist	Umbilical cord was moist, when the pig itself and littermates had dry skin	
Umbilical conditions in second week after birth		
Normal	Healed umbilicus	
Umbilical outpouching	Protrusion $>$ 0.5 cm in height	
Healed/healing umbilical protrusion	Protrusion $\leq$ 0.5 cm in height, with or without crust	
Omphalitis	Presence of erythema, swelling, or purulent discharge from the umbilical cord or periumbilical tissue	

Further, it was registered whether the piglets were separated from the biological mother, within the first two weeks, in the farrowing unit.

The umbilical area of all pigs was inspected once a month, until they either died spontaneously, were euthanized or slaughtered (approx. 6 months of age). As soon as an UO on a pig was identified, the pig received a second identification tag. To ensure animal welfare, pigs with UOs were clinically examined once a month, otherwise they were not treated or managed differently from pigs without an UO.

A veterinarian and a technician were involved in the clinical examinations; the technician restrained the animal in a pig nose snare, and the veterinarian examined the UO for wounds or spontaneous regression of the UO.

Due to animal welfare, pigs were euthanized if: 1) wounds $>$ 1cm across were identified on the UO, 2) the size of the UO affected the gait and movement of the pigs, or 3) the pigs were generally affected. When pigs with UOs died spontaneously, were euthanized or slaughtered, a post-mortem examination was performed, and the pathological manifestation of the UOs was recorded.

2.4. Data description and statistical analyses

In the following sections, an introducing data description and statistical analysis are presented, according to the two different objectives. Statistical analyses were performed in R version 3.6.1 Win (RStudio-Team, 2016). In statistical analyses a p-value $<$ 0.05 was used as level of significance.

2.4.1. Introducing data description

The principal epidemiological characteristics of the two herds were presented. The number of pigs developing an UO was reported and the cumulative incidence of UOs was calculated as the proportion of pigs, which developed an UO in the period from birth to slaughter (approx. 6 month). The causes of death were presented and the case fatality rate was calculated as the percentage of UO-pigs that died before scheduled slaughter.

2.4.2. Objective 1: early risk factors associated with the development of an umbilical outpouching

The risk factors associated with the development of an UO were identified using a mixed effect logistic model with sow as random effect to account for genetic clustering within litters. Mixed models were implemented using the lme4- and lmtest package (Bates et al., 2015; Zeileis and Hothorn, 2002). The following generalized mixed model equation was used

$\text{Logit}\ (Pij) = \beta 0 + \beta 1\ Xij + \ldots + \beta Xij + \mu sowi$ where Logit (Pij) is the log probability of the i-th pig from the j-th sow, β0 is the random intercept and μsowj is the random effect (variance component) of the individual sow/litter. The Xij's are the predictor values for the i'th pig from the j-th sow.

Initially, sow parity was categorized into three groups (1, 2, $\geq$3). Post hoc, based on the quantiles for birth weight pigs were split into four groups containing pigs sized: ($<$ 1100g), [1100-1300g), [1300-1500g), and ($\geq$1500g). In addition, post hoc, pigs were split into four groups based on the quantiles for litter size (incl. stillborn): ($<$ 19), [19-21), [21-24), ($\geq$24).

In the second week after birth, the main umbilical conditions of the piglets were either a normal umbilicus (n=2047) or a healed or healing umbilical protrusion (n=474). All piglets with omphalitis (n=14) also had an umbilical protrusion. Therefore, we developed a new binary variable called "healed/healing umbilical protrusion" describing whether a piglet had a healed or healing umbilical protrusion at the second week of life, and the new variable replaced the initial categorizing of umbilical conditions in second week after birth.

The potential risk factors: Sow parity, litter size (incl. stillborn), birth weight, gender, moved to a foster sow, length of umbilical cord, umbilical condition at birth and the presence of a healed/healing umbilical protrusion in the second week were individually screened for the effect of developing an UO by univariate logistic regression using the R function glm(). Herd (A, B) was screened as well to take the effect of herd into account. Variables with a p-value ≤ 0.25 and variables and interaction terms of relevance were incorporated in a mixed effect logistic model to investigate the association with the development of an UO.

The original logistic model was carefully reduced; variables not contributing to the model (p-value > 0.05) were eliminated one by one. The reduced model was compared with the original model using a likelihood ratio test included in the lmtest package. If the reduced model fitted as well as the original model, the reduced model was accepted.

To identify confounding variables, the estimated coefficients of variables in the reduced model were compared to coefficients in the original model. A confounding variable provided important adjustments of the effect of remaining variables and was considered as such, if the significant coefficients changed more than 20%. Confounders were retained in the final model.

To find out to what extent the observed data varied from the data predicted from the multivariable model, a Pearson standardized residuals plot was used, looking for data points that were extreme in some way relative to the rest of the data. The impact of identified observations with extreme residual values was assessed by comparing the model with and without the observations.

2.4.3. Objective 2: Describe 1) the nature of umbilical outpouchings, 2) the age of detection, and 3) the age of spontaneous regression of umbilical outpouchings

The nature of the umbilical outpouchings was presented as the proportion of different pathological manifestations observed post mortem. The age of detection and regression of UOs was described and presented on an overall basis with barplots and between gender (males and females) with boxplots. The difference between males and females and the age of detection/regression was analysed. Prior to performing the analysis, the assumptions were evaluated to ensure an appropriate and reliable comparison. Testing normality was performed using a Shapiro-Wilk normality test with the shapiro.test () function from the 'stats' package in R and QQ plots were implemented using the ggplot () – function in R. If the Shapiro-Wilk test p-values were < 0.05, for both genders and the QQ plot for males and females was showing a deviation from the theoretical normal diagonal line, the data was defined as skewed distributed instead of normally distributed. If normality was present, the difference between males and females and the age of detection/regression was evaluated with an independent samples t-test using the t.test () – function in R, otherwise, the Mann-Whitney U test was implemented using the wilcox.test () – function in R. In order to avoid multiple-comparison a Bonferroni corrected p-value of 0.025 (0.05/2) was used instead of the original p-value of 0.05.

3. Results

Initially, 3031 live born piglets from 161 litters were included in the study at birth. The principal epidemiological characteristics of the two herds are shown in Table 2. Within the first two weeks of life, 13.7% (414/3031) of the piglets died. In total, 8.4% (255/3031) of the pigs developed an UO between birth and death (spontaneously, euthanasia or slaughter) (cumulative incidence). In herd A, 5.2% (99/1915) developed an UO, and 14.0% (156/1116) of the pigs in herd B developed an UO. A total of 5.1% (13/255) of the pigs was omitted due to lack of records or they were unavailable at follow up visits (lost earmark, moved or death between visits).

Of the OU-pigs which were followed until death (n=242), 57.4% (139/242) died or were euthanized before slaughter (case-fatality rate) whereof 10.7% (26/242) died spontaneously and 46.7% (113/242) of the pigs were euthanized due to welfare concern. In 37.2% (90/242) of the UO-pigs, the main cause for euthanasia was wounds on the UO. The remaining UO-pigs, 42.6% (103/242) were sent for slaughter. In total, 86.0% (208/242) of the UO-pigs were examined post mortem. The remaining quantity of the UO-pigs (34/242) was not examined post mortem because individual identification of the pig was missing from the slaughtering or the umbilical area was damaged.Table 3

3.1. Early risk factors associated with the development of an umbilical outpouching

The risk factor "healed/healing umbilical protrusion" was registered in the second week after birth, for which reason only data from pigs alive in the second week were included in the analysis. As mentioned above, 255 pigs developed an UO, but since one UO-pig died within the first two weeks of age, only 254 pigs with an UO were enrolled in the analysis. An overview of early risk factors included in the analysis for piglets alive in the second week (n=2617) is presented in Table 4.

The results from the univariable analyses showed that litter size, parity, birth weight and length of the umbilical cord were not statistically associated with the development of an UO (p-value > 0.25) and were therefore excluded from the mixed logistic model. The multivariable model for the association between an UO and early risk factors is presented in Table 5. The odds of developing an UO were significantly lower for males than females (OR, 0.7; 95% CL 0.5 - 0.9), and immature piglets were associated with significantly higher odds of developing an UO (OR, 3.4; 95% CL 1.3 - 8.2) than piglets with no signs of immaturity.

Piglets with sign of omphalitis (erythema, swelling, or purulent discharge) (OR, 1.8; 95% CL 1.1 - 2.8) or with a moist umbilical cord (when the pig itself and littermates had dry skin) (OR, 5.1; 95% CL 2.6 - 9.8) at the examination within the first 24 hours of life, had significantly higher odds of developing an UO compared to piglets with an attached, dry umbilical cord and no swelling or discoloration in the umbilical area. Piglets with an umbilical cord detachment, rupture or bleeding within the first 24 hours of life tended to have higher odds of developing an UO (p-value = 0.06) compared to piglets with an attached, dry umbilical cord.

In the second week after birth, the odds of developing an UO were significantly higher for piglets with a healed or healing umbilical protrusion compared to piglets without a healed or healing umbilical protrusion (OR, 1.9; 95% CL, 1.4 - 2.6).

By contrast, there was no significant (p-value = 0.2) effect of the risk factor "moved to a foster sow" and the variable was excluded from the model. All two-way interaction terms were also insignificant (p-value >

Table 2
Epidemiological characteristics of the study population.

	Herd A	Herd B
Litter (n)	99	62
Parity (mean ±SD)	3.45 ±1.9	2.90 ±1.5
Litter size (mean ±SD)	22.25 ±3.7	20.22 ±3.9
Live born (n)	1915	1116
Stillborn (n (%))	235 (10.9)	87 (7.8)
Weight live born (g (mean ±SD))	1240 ±335	1293 ±349
Mortality within 2 weeks of life (n (%))	249 (13.0)	165 (14.8)

Table 3
The proportion of diagnoses based on 208 post-mortem examinations of pigs with an umbilical outpouching or a resolved umbilical outpouching.

Diagnoses	No. of animals (%)
Umbilical hernia	85 (40.87)
Umbilical hernia and abscess/fibrosis	28 (13.46)
Umbilical hernia and enterocystoma	7 (3.37)
Enterocystoma	20 (9.62)
Abscess/subcutaneous fibrosis	28 (13.46)
Other findings ex. preputial diverticulitis	6 (2.88)
No pathological findings	34 (16.35)

Table 4
Potential risk factors investigated in pigs, for an association with the development of an umbilical outpouching between birth and death (spontaneously, euthanasia or slaughter). In the second week after birth, 2617 pigs were alive and examined to be enrolled in the analysis.

Variable/levels	Umbilical outpouching Yes(n (%))	No(n (%))	No. of animals (%)
Total pigs alive in 2nd week	254(9.7)	2363 (90.3)	2617(100)
Herd			
A	99(5.9)	1567 (94.1)	1666(100)
B	155 (16.3)	796(83.7)	951(100)
Litter size (n)			
(< 19)	47(10.0)	424(90.0)	471(100)
(19-21)	59(10.4)	506(89.6)	565(100)
(21-24)	76(9.4)	736(90.6)	812(100)
(≥ 24)	72(9.4)	697(90.6)	769(100)
Sow parity			
1	41(9.2)	404(90.8)	445(100)
2	62(10.3)	538(89.7)	600(100)
≥ 3	151(9.6)	1421 (90.4)	1572(100)
Birth weight (g)			
(< 1100)	64(10.1)	571(89.9)	635(100)
(1100-1300)	52(8.9)	531(91.1)	583(100)
(1300-1500)	69(10.9)	567(89.2)	636(100)
(≥ 1500)	69(9.1)	693(90.9)	762(100)
NA	0(0.0)	1(100.0)	1(100)
Gender			
Female	148 (11.6)	1126 (88.4)	1274(100)
Male	106 (7.9)	1235 (92.1)	1341(100)
NA	0(0.0)	2(100.0)	2(100)
Signs of immaturity			
No	247(9.6)	2336 (90.4)	2583(100)
Yes	7(20.6)	27(79.4)	34(100)
Umbilical length (cm)			
< 5	66(8.8)	682(91.2)	748(100)
≥ 5	162(9.6)	1531 (90.4)	1693(100)
NA	26(14.8)	150(85.2)	176(100)
Umbilical condition at birth			
Dry	202(8.4)	2205 (91.6)	2407(100)
Rupture	3(21.4)	11(78.6)	14(100)
Omphalitis	28(19.9)	113(80.1)	141(100)
Moist	21(38.2)	34(61.8)	55(100)
Umbilical protrusion (2nd week)			
No	177(8.3)	1967 (91.7)	2144(100)
Yes	77(16.3)	396(83.7)	473(100)
Moved to a foster sow			
No	80(7.8)	951(92.2)	1031(100)
Yes	167 (11.3)	1309 (88.7)	1476(100)
NA	7(3.4)	103(93.6)	110(100)

0.05) and excluded from the model. The reduced model did not differ statistically (p-value = 0.7) from the original model in a likelihood ratio test. Further, the coefficients of the reduced model did not change markedly from the original model, which means that no confounding was present between the eliminated variables and the included variables in the model. A qq-plot of the intercept and standard error of the estimated random effect (sow/litter) showed a roughly linear prediction close to zero and no definite outliers. From this knowledge, the model assumptions were accepted.

3.2. The nature of umbilical outpouchings, 2) the age of detection, and 3) the age of spontaneous regression of umbilical outpouchings

In total, 86.0% (208/242) of the UO-pigs were examined post mortem, and the following pathological manifestations were observed: 40.9% (85/208) were diagnosed with an umbilical hernia and 13.5% (28/208) with an umbilical hernia combined with an abscess or fibrosis. In 13.5% (28/208) of the pigs an abscess or fibrosis was present as the only pathological manifestation, and in 9.6% (20/208) an enterocystoma was present as the only pathological manifestation. In 16.3% (34/208) of the pigs, no lesions were observed post mortem (Tabel 3).

The age of detection and age of spontaneously resolving of the UO in the pigs are shown in Fig. 1. In the second week after birth, 39.0% (100/255) of the UOs were detected and 80.4% (205/255) of the UOs were detected during the first 10 weeks of life. In 14.1% (36/255) of the pigs, the UO spontaneously disappeared, of which 83.3% (30/36) disappeared between week 4 and 14.

The side-by-side boxplot in Fig. 1 presents the distribution in males and females for the age of detection of UOs (A) and the age of spontaneously resolving of UOs (B), respectively. Boxplot A in Fig. 1 indicates outliers in the group of females and the mean value is at the 75th percentile, indicating data is highly skewed in the age of detection. Supported by the Shapiro-Wilk test p-values < 0.05, for both genders and a QQ plot for males and females showing a deviation from the theoretical normal diagonal line, the data was defined as not normally distributed. Therefore, the difference between male and female and age of detection was tested using a Mann-Whitney U test. The test revealed insignificant differences in the age of detection in males (n= 107, median=5, mean = 6.8, min=2, max=22) compared to females (n= 148, median= 4, mean= 5.8, min=1, max=22), W=6968, P-value= 0.09.

Boxplot B in Fig. 1 indicates normally distributed data, supported by the Shapiro-Wilk test p-values for males (P-value= 0.21) and females (P-value= 0.16) and QQ-plots with no deviation from the theoretical normal diagonal line. The difference between male and female and age of spontaneously resolving was tested using a t-test. The test revealed insignificant differences in the age of spontaneously resolving of UOs in males (n= 107, median=10, mean=10.4, min=4, max=22) compared to females (n= 148, median=11, mean=10.8, min=4, max=19), t-value (df)=0.22 (21.6), P-value= 0.08.

4. Discussion

In the present cohort study, 8.4% of the pigs developed an UO, a comparable prevalence at 8.3% has also been found in a Swedish study (Mattsson et al., 2013). However, in a previous Danish study, a cumulative incidence of 4.2% was present, when no precautions for UOs were taken (Vestergaard and Wachmann, 2002). The most plausible explanation for this difference is the selection strategy of herds and the great variation of UO between herds. Herds with a history of frequent occurrence of UOs were selected for the present study and the Swedish study, whereas Vestergaard and Wachmann (2002) selected herds with a history of 3-5% UOs recorded from the routine meat inspections at the abattoir.

We observed a poor prognosis concerning pigs with an UO because 57% of the UO-pigs died or were euthanized. This is a prominently higher number than found in other studies. Mattsson et al. 2013 reported, that 20% of the UO-pigs died spontaneously or were euthanized before slaughter, and in the study by Searcy Bernal et al. 1994, no pigs with UOs died before slaughter. The reason might be different management criteria for slaughter and euthanasia. In the last-mentioned study, most UO-pigs were sold soon after detection (Searcy Bernal et al., 1994), which reduced the time at risk developing complications to the UO. In the present study, 37% of the UO-pigs were euthanized after detection of wounds on the UO. This criterion agreed upon the Danish legislation concerning transport of animals in 2017 (Anonymous, 2008),

Table 5
Estimates for fixed effects and random effects using a mixed generalised logistic model for early risk factors associated with the development of an umbilical outpouching.

Variable	Level	Estimate (β_x)	(95% CI)	Std. error	OR (exp (β_x))	(95% CI)	*P*-value
Intercept		-2.9	(-3.2;-2.6)	0.2	0.1	(0.0;0.1)	< 0.001
Gender	Female	-	-				
	Male	-0.4	(-0.7;-0.1)	0.1	0.7	(0.5;0.9)	0.004
Signs of immaturity	No	-	-				
	Yes	1.2	(0.3;2.1)	0.5	3.4	(1.3;8.2)	0.008
Umbilical condition at birth	Normal	-	-				
	Rupture	1.3	(-0.2;2.6)	0.7	3.7	(0.8;13.3)	0.058
	Omphalitis	0.6	(0.1;1.0)	0.3	1.8	(1.1;2.8)	0.021
	Moist	1.6	(1.0;2.3)	0.3	5.1	(2.6;9.8)	<0.001
Umbilical outpoucing (2nd week)	No	-	-				
	Yes	0.6	(0.3;1.0)	0.2	1.9	(1.4;2.6)	<0.001
Herd	A	-	-				
	B	1.1	(0.7;1.4)	0.2	2.9	(2.1;4.1)	<0.001
Random effects		Variance		Std. dev.			
sow		0.3		0.6			

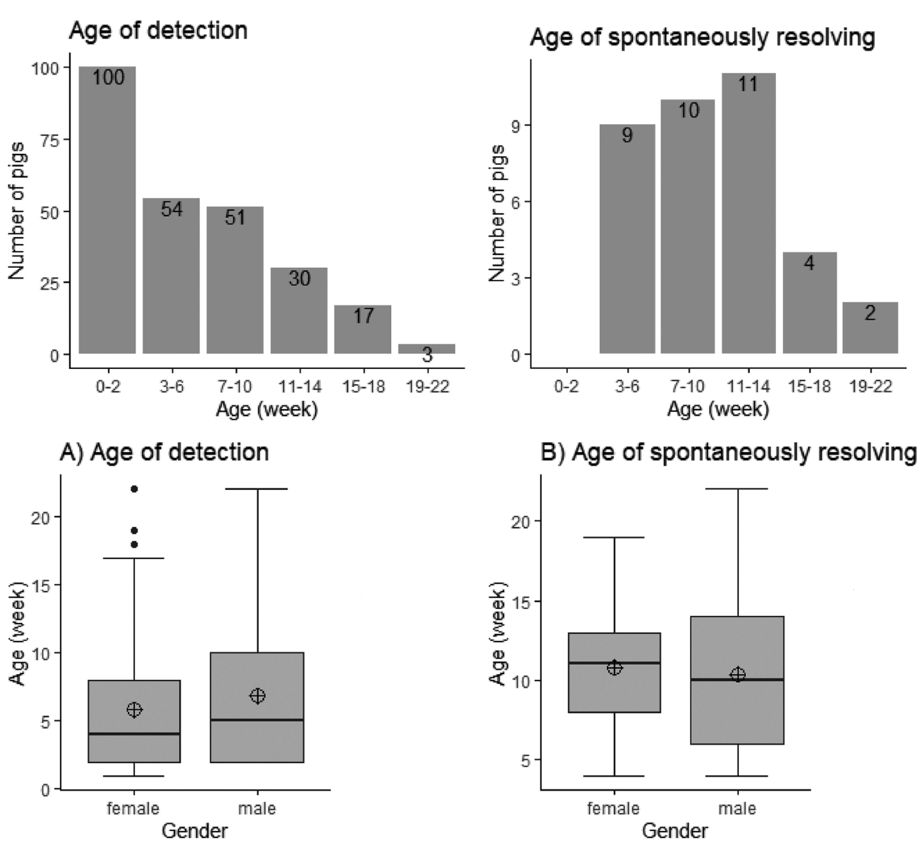

Fig. 1. Presenting the age at detection of umbilical outpouchings and the age at regression of umbilical outpouchings in pigs, from two commercial Danish swineherds. The side-by-side boxplot presents the distribution in males and females for the age of detection of UOs (A) and the age of spontaneously resolving of UOs (B), respectively. Boxplot A below seem to indicate three outliers in the group of females (dots). Furthermore, the mean (circle with +) value are at the 75th percentile, thus indicates that the data is highly skewed. Boxplot B indicate normally distributed data.

specifying that UO-pigs with wounds are not fit for transportation, which may explain the high mortality rate in the present study.

The odds of developing an UO were significantly lower for males than for females. This association is in accordance with previous studies (Hansen 2014). The same tendency was observed by Searcy Bernal et al. (1994) and Vestergaard and Wachmann (2002). Some speculated reasons might be a lower strength of the abdominal wall (m. rectus) or a later closure of the umbilicus in females compared to males or a sex-linked genetic variation in females. Pigs with signs of immaturity (bulging forehead) were at higher risk for developing an UO. Similarly, premature children are at higher risk for developing an UO (Cilley and Shereef, 2004). Because umbilical cord blood in preterm pigs has a lower leukocyte count and impaired responses to inflammatory challenges (Nguyen, 2016), it is likely that the UOs in preterm pigs are a result of early omphalitis and consequently, insufficient closure of the umbilicus. Piglets with signs of omphalitis (erythema, swelling, or purulent discharge) or with moist umbilical cords (when the pig itself and littermates had dry skin) within the first 24 hours of life, were at significantly higher risk for developing an UO. Pigs with a healed or healing umbilical protrusion in the second week of life were also at higher risk for developing an UO. Searcy Bernal et al. (1994) found a significant association between umbilical lesions and herniation on an individual basis. In the present study, an association between a moist umbilical cord stump and an UO was found. In other words, pigs with prolonged drying time of the umbilical cord stump were at higher risk of developing an UO. Because the porcine umbilical cord stump is a potential bacterial colonization site (Larsen et al., 2019) – it is possible that a moist umbilical cord stump is more exposed to bacteria compared to a dry umbilical cord stump, and consequently omphalitis is more likely to occur. A previous Norwegian study reported an increased probability of dying before weaning if piglets were born with a broken umbilical cord (Rootwelt et al., 2013). In the present study, piglets with a broken umbilical cord (detachment, rupture or bleeding) within the first 24 hours of life tended to have a higher risk of developing an UO. Only 14 piglets were categorized with a broken umbilical cord, and the limited number of piglets in this group can explain the lack of significance between a broken umbilical cord and the development of an UO.

An association between previous umbilical inflammation and the development of an umbilical hernia is described from different studies focusing on preventive antibiotic treatment of UOs (Szczotka et al., 2019; Vestergaard and Wachmann, 2002; Yun et al., 2017). Therefore, it is tempting to assume that our findings are a result of an early umbilical inflammation or infection and the development of an UO.

The risk factor “pigs moved to a foster sow” was not significantly associated with the development of an UO in our study. In Danish herds, cross fostering is a frequent management procedure, necessary in controlling large litters. In a previous study, pigs cross fostered were found more likely to die before slaughter and of greater risk of disease compared to pigs that were not cross fostered (Calderón Díaz et al., 2017). In our study, 89 % of the pigs born in herd B and still alive in the second week were moved to a foster sow, and we were therefore not able to show a potential association between cross fostering and the development of an UO.

Even though Miller et al. (2012) suggested that gilt born piglets in general are more susceptible to disease post weaning than sow born piglets due to their lower birth weight and reduced humoral immune responsiveness, no significant association was found between sow parity or birth weight and the development of an UO. Furthermore, Beaulieu et al., 2010 reported a decline in mean birth weight as litter size increased and as a consequence, the piglets colostrum intake declined (Dividich et al., 2017). The reduced colostrum intake in large-litter born piglets might cause higher susceptibility to diseases post weaning, but in the present study, litter size was not associated with the development of an UO.

The dominant pathological condition in UO-pigs was an umbilical hernia (41%) followed by umbilical hernia combined with an abscess or subcutaneous fibrosis (14%), or solely an abscess or subcutaneous fibrosis (14%). Similarly, Hansen (2014) who examined the nature of outpouchings in 148 spontaneously dead or euthanized pigs from 26 different herds post mortem, reported a majority of umbilical hernia (41%), followed by a diagnosis of umbilical hernia combined with an abscess (20%) and umbilical hernia combined with an enterocystoma (20%). Andersen et al. (2014) collected UOs from a Danish abattoir and found enterocystoma (28%) as the dominant pathological condition causing an UO followed by umbilical hernia (17%). This suggests that UO-pigs with enterocystoma more often reach the abattoir than UO-pigs with an umbilical hernia. This may be explained by the fact that umbilical hernias seem to cause fatal complications such as strangulation or obstruction of the intestines more often compared to other causes of UO. Moreover, Schild et al. (2015) found a behavioral difference in pigs with umbilical hernia compared to pigs with other causes of UO, probably due to discomfort from strangulation or obstruction of the intestines, which is also reported in humans (Velasco et al., 1999).

The majority of the UOs were detected during the first 10 weeks of life. In a previous Californian study, involving 44 pigs with an UO, the majority of UO’s became visible between the 9th and 14th week of age (Searcy Bernal et al., 1994). The difference is most likely a result of variation between herds and different definitions of an UO. In 14% of the pigs, the UO resolved spontaneously before slaughter. Spontaneous regression of UO is reported in children (Cilley and Shereef, 2004), where 80% of congenital umbilical hernias close spontaneously within the first 3 years of life. The prevalence of spontaneously resolving UOs reported in the present study is lower than reported for children. A possible explanation is that all kinds of UOs are reported and not only umbilical hernia. In the present study, the regression was based on a cut-off value (height <0.5 cm) no matter the size of the pig, and the majority of UOs spontaneously regressed between the 4th and 14th week of age. The cut-off value is of major importance because the umbilicus after regression often will present as a protruding umbilicus. If instead the cut-off value increased gradually in line with the growth of the pig, a higher number of UOs would have been reported as spontaneously regressed at an earlier stage.

In general, these findings show that early risk factors such as female gender, signs of immaturity and the condition of the umbilicus early in life are associated with the development of an UO. Umbilical hernia was the most frequent cause of the UOs, and the pigs with umbilical hernia seem more likely to die before slaughter. The identification of early risk factors is essential, in order to know which piglets to focus on in the daily routines. Piglets with signs of immaturity, such as a bulging forehead, are often time consuming and a considerable effort is required for survival. The risk of developing an UO is significantly higher in piglets with signs of immaturity, omphalitis, moist umbilical cord or a healed or healing umbilical protrusion, and additional precautions should be taken such as ensure the piglets are born in a dry, warm, and sanitary environment, which facilitates a short drying up of the umbilical cord and reduces the risk of infection. In the present study, a substantial part of UO observed in the farrowing unit disappeared during the weaner period. Therefore, farmers should consider not to cull healthy pigs with an UO until the pig leaves the weaner station.

5. Conclusion

The findings of the present study showed that umbilical hernia was the major pathological manifestation causing an umbilical outpouching (UO) in Danish pigs. In this study, the majority of UOs were present and permanent when the pigs left the weaner unit, which makes an evaluation of UOs optimal at that time point. Several risk factors such as gender, immaturity, omphalitis, prolonged drying up of the umbilical cord and an umbilical protrusion at week two were associated with the risk of developing an UO. Identifying pigs with high odds of developing an UO is essential in the daily work, knowing to which pigs special precaution should be taken.

Declaration of Competing Interest

The authors declare that there are no existing conflicts of interest according to research and authorship of this article.

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