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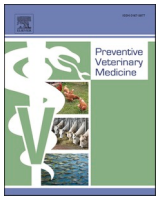

Survival of pigs with different characteristics of umbilical outpouching in a prospective cohort study of Danish pigs

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ABSTRACT

Umbilical hernia and other conditions clinically evident as umbilical outpouchings (UOs) affect the welfare and economy in Danish pig production. The objectives of the current study were to characterize the associations between 1) time of detection of the UOs and the odds of dying before scheduled slaughter; 2) time of death, irrespective of the cause, and clinical signs of the UOs, i.e. general condition, size, reducibility, form and skin-color of the UOs; and 3) occurrence of wounds on the UOs and clinical signs: general condition, size, reducibility, form and skin-color. A cohort of Danish conventional pigs with UOs (n = 255) were followed from the detection of an UO until spontaneous death, euthanization or slaughter of the pig. The pigs were clinically examined once a month, and when pigs with an UO died spontaneously, were euthanized or slaughtered, the causes and date of death were recorded. The effects of the clinical manifestations on overall survival were assessed using a Cox proportional hazards model.

In total 57 % of the pigs died spontaneously or were euthanized before slaughter. The median age of spontaneous death or euthanasia was 85 days. The UOs were detected at different ages, with half of the pigs (52 %) detected in the farrowing section. No significant association was found between death before scheduled slaughter and the time of detection. Three different clinical manifestations were found to have a prognostic value for overall survival until slaughter, i.e. skin-color of the UO, a general condition of the pig and the size of the UO. An interaction was present between the size and the skin-color of the UO.

Wounds on the UO were the most frequent complication resulting in euthanasia (37 %). The odds for developing a wound on the UO were higher for pigs in a general bad condition compared to pigs in a good condition (OR, 5.4; 95 % CL 2.5–11.3), and for pigs with an UO large in size compared to pigs with a small UO (OR, 4.8; 95 % CL 3.0–7.5). The identification of prognostic clinical signs in pigs with an UO is useful in the assessment and decision-making in relation to the future prospects of pigs with UOs.

1. Introduction

Umbilical hernia and other conditions including enterocystoma, peritoneal proliferations, subcutaneous abscess and fibrosis are clinically evident as umbilical outpouchings (UOs) (Andersen et al., 2014). UOs have been reported ranging from 1.5 % (California) to 10.1 % (Sweden) (Searcy Bernal et al., 1994; Mattsson et al., 2013; Straw et al., 2009), with an occurrence of 4.2 % in Danish crossbreed pigs (Landrace x Yorkshire x Duroc) (Vestergaard and Wachmann, 2002), when no precautions had been taken to control the occurrence.

Multifactorial causes and origins complicate efficient treatment and prevention strategies for UOs. For example, an infectious cause of UOs has been proposed (Searcy Bernal et al., 1994; Szczotka et al., 2019; Yun et al., 2017), whereas others have suggested a genetic predisposition for the development of UOs (Rutten-Ramos and Deen, 2006; Searcy Bernal et al., 1994). In the grower-finisher period, a case-fatality of 20 % in pigs with UOs has been reported (Mattsson et al., 2013). In that study, the mean diameter of the UOs post mortem was 12.5 cm. Similar results were found in a Danish study of 148 pigs with an UO, where the post mortem mean diameter of the UOs was 14.4 cm (Hansen, 2014). Apart from mortality, skin lesions on OUs are also affecting the welfare of pigs, and these lesions are more frequently occurring on OUs with a diameter

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of more than 15 cm compared to smaller OUs (Barington et al., 2016; Hansen, 2014). Moreover, the occurrence of umbilical hernia has been linked to increased discomfort in pigs (Schild et al., 2015) and humans (Miller et al., 1995). In humans, pain is especially reported if complications such as strangulation or obstruction of the intestines occur (Miller et al., 1995).

If UOs are detected early, some farmers cull the pigs in order to avoid welfare implications (Morrow et al., 2006), whereas other farmers are slaughtering pigs with UOs at an early age, and thereby reduce the time at risk for developing complications. However, early selling for slaughter provides a lower market value (Searcy Bernal et al., 1994). Pigs with UOs may be detected late in the grower-finisher period (Atkinson et al., 2017), whereas others, which have been detected earlier, are raised with an UO until close to market weight. Nevertheless, at that time culling may be necessary, due to severe complications or because they are unfit for transportation due to current regulations (Anonymous, 2005). In general, animals with pathological processes shall not be considered fit for transport and in particular if they are unable to move independently without pain, or to walk unassisted, or if they present a severe open wound (Anonymous, 2005). In addition, the Danish national guidelines addresses the diameter of the UOs as a criterion for transportation of pigs. Hence, pigs with UOs greater than 15 cm in diameter require special facilities during transportation, e.g. they should be separated from pigs without UOs, stabled on soft bedding during transportation, and the fitness for transport needs an veterinary evaluation prior to the transportation (Anonymous, 2008).

The aim of this study was to identify prognostic factors for mortality of pigs with an UO. The general condition of the pig, the size of the UO and the presence of wounds on the UO were the basic clinical manifestations for evaluating severity and fitness for transport of pigs with UOs. In the present study, a cohort of conventional pigs with OUs was followed from the occurrence of an UO until spontaneous death, euthanization or slaughter. The objectives were to characterize the associations between 1) time of detection of the UOs and the odds of dying before scheduled slaughter; 2) time of death, irrespective of the cause, and clinical signs, i.e. general condition of the pig and size, reducibility, form and skin-color of the UOs; and 3) occurrence of wounds on the UOs and clinical signs: general condition of the pig and size, reducibility, form and skin-color of the UOs. This knowledge should be practically applicable for farmers in order to decide when pigs with specific manifestations of UOs should be culled or fattened for slaughter.

2. Material and methods

2.1. Study population

The work was carried out as a prospective cohort study in two conventional Danish swine herds from December 2017 until August 2018. The two herds (Herd A and Herd B) were selected based on the type of herd (farrow-to-finish) and the fact that they had reported a continuously high prevalence of pigs with UOs (>3 %). Despite the farrow-to-finish concept, pigs were moved and housed at different locations in both herds. Herd A consisted of approximately 1050 sows and was characterized as a high health herd (SPF-herd) (SPF-sus, 2017). Herd B consisted of approximately 1600 sows with unknown health status. At both herds, the offspring were Danbred crossbreds (Landrace/Yorkshire x Duroc). A detailed description of the herds and inclusion of pigs in the field trial has recently been described (Hovmand-Hansen et al. (2021)).

The study was carried out in agreement with an ethical approval granted by the Danish Ministry of Justice law concerning experimental animal (Approval no. 2017/ 15-0201-01372).

2.2. Study design and data collection

Initially, a cohort of 3031 newborn pigs, born during a two-week period at Herd A (n = 1915) and during a one-week period at Herd B (n = 1116) were followed from birth until spontaneous death, euthanasia or slaughter (approx. at 6 month of age). Within 24 h from birth, each piglet received an identification mark and was carefully inspected. The following was recorded for each animal: 1) birth weight (g), 2) gender (male, female), 3) sign of immaturity (bulging forehead: no, yes), 4) length of the umbilical cord (< 5 cm, ≥ 5 cm), 5) umbilical condition (normal, rupture, omphalitis, moist), 6) litter size, 7) sow ID-number, and 8) sow parity (1,2, ≥3,). In the second week after birth, the condition of the umbilical area was inspected and registered for each piglet as either "normal", "a healed/healing umbilical protrusion", "omphalitis" or an "UO". An UO was registered if a protrusion in the umbilical area of more than 0.5 cm was present (measured longitudinal from basis to apex of the UO). In these cases the piglet received an additional identification mark. A veterinarian or a technician inspected all pigs once a month for the presence of new UOs. When pigs were registered with an UO they were pooled together with the pigs with OUs detected during the first weeks, and clinically examined once a month until spontaneous death, euthanasia or slaughter. In total, 255 pigs were identified with UOs from birth to slaughter (herd A; n = 99, herd B; n = 156), which represented 8.4 % (255/3031) of the pigs. Pigs with an UO were housed, feed and managed without any special treatment.

To ensure animal welfare, pigs were euthanized if: 1) the UO affected gait and movement, 2) the pig was severely affected, or 3) wounds greater than 1 cm across the wound surface were identified on the UO. The criteria for euthanasia were specified in according to current regulations (Anonymous, 2008, 2005). When pigs with an UO died spontaneously, were euthanized or slaughtered, the causes and date of dead was recorded and post mortem examinations were conducted.

2.3. Clinical examination

During the clinical examination, the general condition of the pig together with the following clinical signs of the UO were recorded: size, reducibility, form, skin-color and wounds.

During the examination, a technician restrained the animal meanwhile a veterinarian recorded clinical data. To ensure a complete examination, weaners were anaesthetized (Ketador Vet. 100 mg/mL & Stresnil Vet. 40 mg/mL) and positioned on the back, and finishers were standing in an upright position restrained by a nose snare. The general condition was determined by observing the skin, hair coat, eyes and behavior. If the haircoat was smooth, clean and uniform and the eyes were not sunken and without discharge, the snout was pink and moist and the behavior of the pig was bright, alert and responsive, the pig was described as being in a good condition. If this was not met by observing either the skin, hair coat, eyes or behavior, the pig was in a bad condition. The size of the UO was registered with a tape measure. The height (cm) was measured from basis to apex of the UO and the circumference (cm) was measured horizontal around the widest position at the UO. The form of the UO was defined as globular, conical or irregular. The reducibility of the UO was established by hand, trying to press the content of the UO back into the abdominal cavity (reducible, partly reducible or irreducible). The occurrence of skin changes was scored by the following definitions: 1) skin-color (reddish, bluish, "normal skin-color"), 2) skin lesions (superficial scratches, wound, no wound), and 3) number of wounds (1 wound, > 1 wound). The wounds were measured, longitudinally and across, with a tape measure.

2.4. Data description and statistics

To identify prognostic factors for mortality of pigs with an UO, different statistical models were applied, according to the three different objectives. In the following sections, an introducing data description summarize: 1) Age of detection and causes of dead and 2) data from the repeated clinical examinations. Finally, statistics for Objective 1, 2 and 3 are presented. Data processing and the statistical analyses were performed in R version 4.0.2 (R Core Team, 2020). In all statistical analyses,

a p-value < 0.05 was used to define significance.

2.4.1. Age at detection and causes of death

Initially, the distribution of pigs with UO was calculated based on the time of detection. The time of detection was categorized according to age group. Pigs with an UO detected from birth until 28 days of age were categorized "detected in the farrowing unit", those with an UO detected between 29 days and 72 days of age were categorized "detected in the weaning section", whereas pigs with an UO detected after 72 days of age were categorized "detected in the finisher unit".

The distribution of the causes of death and the age of death were calculated and reported, but for analytical purposes, the outcome was defined as death before scheduled slaughter (yes, no).

2.4.2. Repeated clinical examinations

During the clinical examinations, the following clinical signs were repeatedly measured and examined for their potential influence on overall survival; the general condition of the pig, size of the UO, skin-color, form, reducibility and wounds on the UO. The general condition of the pig (good, bad) was maintained, but for clarity and in order to ensure a reasonable amount of data in all groups, the rest of the variables were reclassified as follows: skin-color ("normal skin-color", "red/blue skin-color"), reducibility ("reducible/partly reducible", "irreducible"), form ("globular/conical", "irregular" and wounds ("≥1wound", "no wound/scratches"). The descriptive statistic of size of the UO (circumference (cm) and height (cm)) were presented and initially maintained on a continuous scale. It appeared in the validation process of the cox regression model (see below), that the variables; age of the pig and size of the UO, violated the cox proportional hazards assumptions. Therefore a Pearson's correlation test in R (cor.test function) was used to assess 1) the strength of a linear association between the height and circumference of UO and 2) the association between the size (circumference/height) of the UO and the age of the pig. A time-varying-effect was observed if the size was significantly associated with the age of the pig, and in that case it was decided to categorize the variable circumference in according to the median circumference of the UOs in different age groups. For practical reasons, the age groups were based on age and location: farrowing unit (age 0−28 days), weaning section (age 29−72 days) and finisher unit (age $>$ 72 days). UOs with a circumference (cm) above or equals to the median in the respective age groups were categorized as "large" and UOs below the median were categorized as "small". A total number of examinations of each variable and the number and percentage of deaths in each of the categories; general condition and size, skin-color, reducibility and form of the UO, were calculated to illustrate the effect of clinical signs.

2.4.3. Objective 1: the association between time of detection of the UOs and the odds of dying before scheduled slaughter

In order to investigate the association between time of detection and the odds of dying before scheduled slaughter, a univariable logistic analysis was performed using the R function glm (). The likelihood ratio test, McFadden's pseudo-R^2 and using the most parsimonious model were used to assess the model fitness.

2.4.4. Objective 2: the association between clinical signs in pigs with UOs and time of death

A cox proportional hazards model was used to estimate the effect of the clinical signs (general condition, size, skin-color, form and reducibility) on "time to death" in pigs with an UO. The endpoint in the analysis was defined as euthanasia or spontaneously death irrespectively of the stated cause of death. Pigs that were lost to follow up during the study or slaughtered at the end of the study were included in the survival analysis until their last clinical examination. Thereafter they were censored from the analysis. "Time at risk" was measured in days from the UO was detected and until death (spontaneous death/ euthanization) or censoring (slaughter/lost for follow up). Repeated examinations of the same pig resulted in clustered survival time data. To account for the presence of cluster-effect, the pig ID number was incorporated in the model as a cluster-term (i.e. frailty variable), adjusting for the within-cluster correlation in the model. The survival package in R (Therneau, 2020) was used to run a Cox Proportional-Hazard model. A multivariable model for clustered "time to event data" was constructed and all variables and 2-term interactions of relevance (see below) were incorporated in the cox regression analysis, which subsequently was reduced using a backward elimination based on the likelihood ratio test. Potential confounding and interaction were evaluated. Confounding was considered present, if changes of more than 20 % in the coefficients in the model with the potential confounder were identified. Confounding variables were retained in the model. Collinearity between all predictors was evaluated by variance inflation factor test in the car-package in R. Variance inflation factors (VIFs) between one and five were considered as a moderate correlation, and not severe enough to warrant a corrective action. Whereas VIFs greater than five were considered critical and the highly correlated variables should either be removed or combined. Interaction was tested by adding interaction terms between the size of the UO and the other predictors after an initial causal diagram. An estimate of the hazard ratio was accessible upon the set of coefficients in the model. The assumptions of the cox proportional hazard model were evaluated by Schoenfeld test based on the Schoenfeld residuals for each variable in the model. The impact of identified outlying measurement was assessed by comparing the model with and without the measures.

2.4.5. Objective 3: the association between clinical signs and wounds on the UO

The clinical sign "wound" on the UO was not incorporated in the cox proportional hazard model, because wounds on the UOs were a part of the criteria for euthanasia. Instead, the clinical signs associated with the development of wounds on the UO (outcome) were identified using a mixed effect logistic model with pigs ID as random effect to account for repeated measures on the same animal. The lme4- and lmtest package (Bates et al., 2015; Zeileis and Hothorn, 2002) were implemented for mixed model analyses in R.

The potential risk factors: general condition, skin-color, reducibility, form and size of the UO were individually screened for the effect of developing a wound on the UO by univariate logistic regression using the R function (glm). Variables with a p-value ≤ 0.25 and interaction terms of relevance, entered a mixed effect logistic model to investigate the association with the development of wounds on the UO. A backward elimination approach was applied to eliminate variables not contributing to the model (p-value > 0.05). The reduced model and the original model were compared by a likelihood ratio test (lmtest package). Confounding was considered present if changes of more than 20 % in the coefficients in the model with the potential confounder was identified. Confounders were retained in the model. The goodness of fit was evaluated from Pearson standardized residuals plot, looking for outlying data points relative to the rest of the data. If extreme residual values were identified, the impact were assessed by comparing the model with and without the values.

3. Results

In total, 255 pigs were detected with an UO $>$ 0.5 cm between birth and death (scheduled slaughter, spontaneously death or euthanization), 5 % (13/255) of the UO-pigs were lost to follow up during the observation period or because records were incomplete; these were omitted or censored in the statistical analyses. In 15 % (36/242) of the pigs, the UO spontaneously fully resolved or regressed to a height below 0.5 cm. Necropsies were performed on 82 % (208/255) of the pigs, the remaining animals (47/255) were not examined post mortem due to missing identification or a damaged umbilical area. The main diagnosis were: umbilical herniation in 58 % (120/208) either alone in 41 % (85/208) or in combination with an abscess or fibrosis in 14 % (28/208) or

with an enterocystoma in 3% (7/208). A solitary abscess or fibrosis was present in 14 % (28/208) of the pigs, and an enterocystoma was present in 10 % (20/208). In 3% (6/208) of the pigs preputial diverticulitis was present, whereas in 16.3 % (34/208) of the pigs, no lesions were observed at necropsy.

3.1. Association between the time of detection of UOs and death before scheduled slaughter

The UOs were detected at different ages: 52 % (125/242) were detected in the farrowing unit, 28 % (68/242) were detected in the weaning section, and 20 % (49/242) of the UOs were detected in the finisher unit. In total, 57 % (139/242) of the pigs with an UO died before slaughter; 11 % (26/242) died spontaneously and 47 % (113/242) were euthanized due to a welfare concern. The median age at spontaneously death or euthanasia was 85 days. Wounds on the UO where the main cause for euthanasia, followed by other causes such as size of the UO (Table 1). At the end of the study, 43 % were sent for slaughter under normal conditions. The results from a univariable logistic regression showed that the odds of death (spontaneous death/ euthanasia) before slaughter was not associated with the time of detection (Table 2). The goodness of fit of the statistical model was accepted based on predictions from the fitted model and a Mcfadden's pseudo-R squared ($R^2 = 0.00$).

3.2. Repeated clinical examinations

Of the 255 pigs developing an UO, six pigs died before the first clinical examination, and 249 pigs had at least one clinical examination before death or censoring (ranging from 1 to 9 examinations). In total 942 clinical examinations were carried out, but 166 examinations were excluded due to incomplete examination records, mainly because the UO spontaneously resolved. The remaining data represents 776 clinical examinations and the pigs were examined 3.1 times on average (SD = 1.8). Even though 139 pigs died in the study period, the survival time data represents 132 death (events): six pigs died before the first clinical examination, and one pig that spontaneously died, had incomplete records at the last examination before death.

The median height of UOs was 3.0 cm. An UO was initially defined as a protrusion greater than 0.5 cm in height, but some of the UOs decreased in size after detection, which lead to a minimum height of 0.3 cm and a maximum height of 19.0 cm (sd = 3.1). The median circumference of the UOs was 19.3 cm, ranging from 3 cm to a maximum of 58 cm (sd = 13.1). The distributions of age, height, and circumference of the UOs, along with their correlations are shown in Fig. 1. A linear association was found between circumference and height in UOs (R = 0.9 (95 % CL 0.88; 0.91) $P < 0.001$) and to avoid multicollinearity, only the circumference (cm) was included in the subsequently statistical analyses. The circumference of the UO was positively associated with the age of the pig (R = 0.7 (95 % CL 0.6; 0.7) $P < 0.001$) and consequently it was decided to categorize the variable circumference in "small" and "large" according to the median circumference of the UOs in different age groups. The median circumference (cm) of the UO-pigs, examined in the farrowing unit (age 0−28 days), was 7.0 cm (sd = 2.6). The median circumference of the UOs examined in the weaning section (age 29−72) was 10.0 cm (sd = 9.2), and the median circumference of the UOs examined in the finisher unit (age > 72 days) was 29.0 cm (sd = 13.0). The descriptive statistics of circumference (cm) and height (cm) of the UO are presented in Table 3.

The distribution of the total number of examinations and total number of deaths (spontaneous, euthanization) for the explanatory variables; general condition of the pig, size of the UO and skin-color of the UO is provided in Table 4.

Table 1
Overview of the causes of death in 242 pigs with an umbilical outpouching.

Causes of death	Number of pigs (%)	Median age (days) (min;max)	SD
Spontaneously dead	26 (10.7)	30.5 (9;138)	46.7
Euthanized			
- Wound(s) > 1cm	73 (30.2)	90.0 (39;166)	33.4
- Size affecting mobility	13 (5.3)	88.0 (67;138)	24.1
- Wound(s) > 1 cm and size affecting mobility	17 (7.0)	93.0 (59;138)	22.2
- Severe general condition	2 (0.8)	57.5 (48;67)	13.4
- Other reasons	8 (3.3)	67.0 (18;153)	39.1
Slaughtered	103 (42.6)	168.5 (158;178)*	5.6*
Total	242 (100)		

* Five pigs missing registration on age at slaughter.

Table 2
Results from the univariable logistic analysis of the association between time of detection of the umbilical outpouchings (UOs) and death before scheduled slaughter in 242 Danish pigs.

	Detected UO	Death before scheduled slaughter		p-value
Time for detection	n (%)	Yes (n (%))	No (n (%)) *Resolved UO n (%)*	
Location (age)				
- Farrowing unit (age 0–28 days)	125 (52)	71 (29)	54 (22) *0 (0)*	
- Weaning section (age 29–72)	68 (28)	40 (16)	28 (12) *18 (7)*	0.97
- Finisher unit (age > 72 days)	49 (20)	28 (12)	21 (9) *18 (7)*	0.79
Total	242 (100)	139 (57)	103 (43) *36 (15)*	

OR = odds ratio; 95 % CL: 95 % confidence limits.

The hazard of death before slaughter in pigs with UOs are presented in a Cox Proportional Hazard (survival) model (Table 4). The result show that the general condition of the pig, size of the UO and skin-color of the UO, had a significant effect on survival. The hazard ratio (HR), for pigs with an UO in a bad condition was significantly higher compared to UO-pigs, in a good condition (HR, 8.0; 95 % CL, 5.5–11.7). An interaction term was present between the size and the skin-color of the UOs, for which reason the HR are presented as combinations of these. The HR, for pigs with a "small" UO with a red/blue skin-color was higher compared to UO-pigs with a "small" UO and "normal" skin-color, (HR, 2.4; 95 % CL, 1.2–5.0). In addition, the hazard ratio for pigs categorized with "large" UOs, was also significant increased at any given time point before slaughter compared to pigs with a "small" UO, no matter if the skin-color was "normal" (HR, 3.8; 95 % CL, 2.4–5.9) or "red/blue" (HR, 2.8, 95 % CL, 1.5–5.4).

By contrast, the hazard of death was not significantly different between pigs with reducible and irreducible UOs and between UOs with globular/conical and irregular form. Consequently, the variables were eliminated from the model. Confounding and collinearity were not observed and no violation of the hazards assumptions was observed in the Schoenfeld test (global p = 0.14) and no outlying values with influence on the model were found.

3.3. Objective 2: the association between clinical signs in pigs with UOs and time of death

3.4. Objective 3: the association between clinical signs and wounds on the UO

In total 37 % (90/242) of the pigs were euthanized because of wounds on the UO (Table 1). Data from all examinations (n = 776) of pigs with an UO were included in the analysis of clinical signs associated with the development of wounds. The results from the initial univariable analyses showed that skin-color was not associated with the

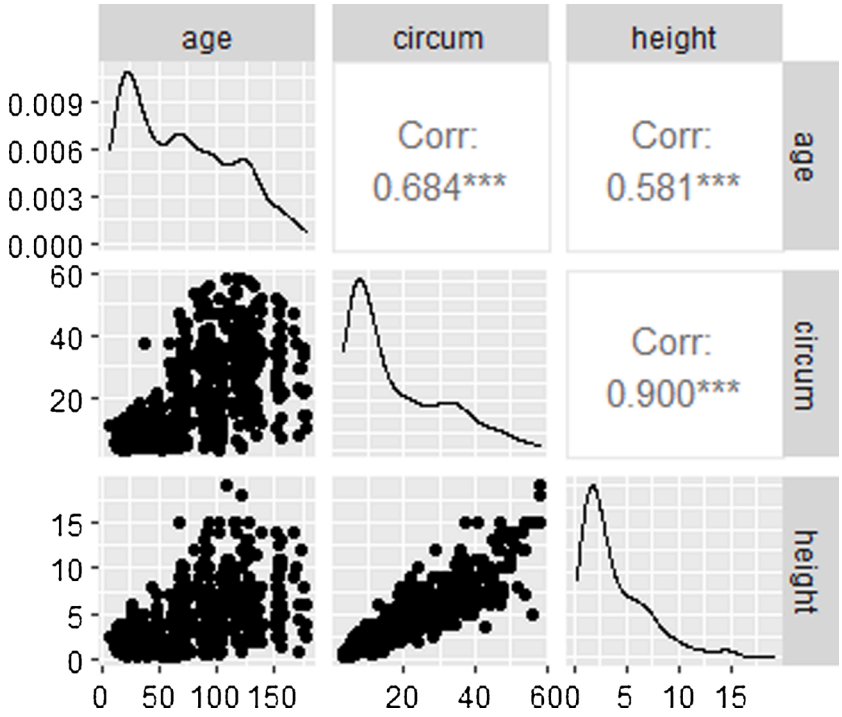

Fig. 1. Correlogram. Correlation, distribution and correlation coefficient between the age (days) of the pig, and size of the umbilical outpouching (circumference and height (cm)), recorded at 776 clinical examinations in two Danish herds.

Table 3
Descriptive statistics of circumference and height of umbilical outpouchings in pigs recorded at 776 clinical examinations in different age groups.

		Circumference				Height	
Location	No. of examinations (No. animals)	Median (cm) (min;max)	SD	Small UO No. < median	Large UO No. ≥ median	Median (cm) (min;max)	SD
Farrowing unit (age 0–28 days)	199 (113)	7.0 (3.0;16.0)	2.6	86	113	2.0 (0.4; 6.0)	0.9
Weaning section (age 29–72)	260 (174)	10.0 (3.0;47.0)	9.2	122	138	2.0 (0.3; 15.0)	2.4
Finisher unit (age > 72 days)	317 (145)	29.0 (3.0;58.0)	13.0	156	161	6.0 (0.5; 19.0)	3.4
Total	776 (249)	13.0 (3.0;58.0)	13.1	364	412	3 (0.3; 19.0)	3.1

development of wounds ($p = 0.6$). Therefore, this variable was not offered to the mixed logistic model. In addition to the distribution of the total number of examinations and wounds on the UOs, the results of the multivariable model are presented in Table 5.

The odds of developing a wound on the UOs were significantly higher among pigs in a bad general condition compared to pigs in a good general condition (OR, 5.4; 95 % CL 2.5–11.3), and pigs examined with a "large" UO were associated with significant higher odds for developing a wound (OR, 4.8; 95 CL, 3.0–7.5) than pigs with a "small" UO. The odds for developing a wound on the UO was significantly lower in pigs with a reducible UO (OR, 0.3; 95 % CL, 0.2 to 0.5) compared to pigs with an irreducible UO. By contrast, no effect of the clinical sign "form" of the UO was found. All interaction terms were insignificant and no confounding was observed. The model assumptions were fulfilled since no outliers were observed and the qq-plot of the intercept and standard error of the estimated random effect (pig ID) showed virtually a linear prediction close to zero.

4. Discussion

Today, the management and decision-making concerning pigs with UOs have mainly been based on personal experience, current regulations, current pig meat prices, and practicality in regards to housing systems (access to soft bedding or sick-pens) and the opportunity of early selling or slaughter.

In the present study, nearly 60 % of pigs with UOs died or were euthanized before slaughter, and 50 % of these died or were euthanized after 85 days of age. These deaths constitute important economic losses. The goal is to avoid fattening pigs with UOs until close to market weight, which may die spontaneously or are euthanized due to severity and complications, respectively. Therefore, the aim of the current study was to identify easily accessible clinical signs on UO-pigs that could be used to predict the risk of dying (spontaneously/euthanasia) before scheduled slaughter. Firstly, the time for detection of the UO was assumed to influence the odds of dying before scheduled slaughter, because early appearance of the UO often result in a longer time at risk for developing fatal complications (Hansen, 2014; Mattsson et al., 2013; White, 2010). A longer time at risk also facilitate an increase in size of the UO and development of severe skin-lesions, which consequently is affecting the welfare of the pig and/or the fitness for transportation (Anonymous, 2008, 2005). In the present study, this hypothesis was however rejected, as no association was found between the odds of dying before scheduled slaughter and the time of detection, irrespective of the UO-pig were detected in the farrowing section (age 0–28 days), the weaning section (age 29–72 days) or the finisher section (>72 days). A plausible explanation might be that 15 % of the UOs resolved spontaneously by age. The regression of umbilical hernia is also described in children, in which up to 80 % of congenital umbilical hernias close spontaneously within the first 3 years of age (Cilley and Shereef, 2004). According to Hovmand-Hansen et al. (2021), approximately 80 % of the

Table 4
Descriptive statistics and results of the multivariable Cox proportional hazards model estimating the effect of clinical signs of the UO on overall survival (irrespective of the stated cause of death) in a prospective cohort study of 249 pigs with an umbilical outpouching (UO).

Variable and level		Total number of examinations (%)			Number of deaths (%))	
General condition						
- Good		734 (94.6)			104 (78.8)	
- Bad		42 (5.4)			28 (21.2)	
Size of UO[a]						
- Small		364 (46.9)			33 (25.0)	
- Large		412 (53.1)			99 (75.0)	
Skin-color of the UO						
- Normal		655 (84.4)			110 (83.3)	
- Red/blue		121 (15.6)			22 (16.7)	
		Estimate/ coefficient (*b*)	Std. error coefficient (b)	Hazard ratio (Exp(*b*))	95 % CI	P-value
Adjusted Cox regression: interaction model						
General condition						
- Good		Baseline		1	–	
- Bad		2.08	0.24	8.0	(5.5; 11.7)	<0.001
Size : skin-color						
- Small size - Normal color		Baseline		1	–	
- Small size - Blue/red color		0.89	0.45	2.4	(1.2; 5.0)	0.014
- Large size - Normal color		1.33	0.23	3.8	(2.4; 5.9)	<0.001
- Large size - Blue/red color		1.02	0.34	2.8	(1.5;5.4)	0.002
N = 776	Events = 132			Cluster/robust variance = 61.22		

[a] The size of the UOs was defined from the median circumference of the UO in following age groups: Farrowing location (age 0−28 days) the UO is defined as big if circumference ≥ 7.0 cm. Weaner location (age 29−72 days) the UO was defined as big if circumference ≥ 10.0 cm. Finisher location (age > 72 days) the UO was defined as big if circumference ≥ 29.0 cm.

Table 5
Descriptive statistics for the occurrence of wounds with different clinical manifestations, and estimates for fixed effects and random effects using a mixed generalized logistic model for the association between the clinical manifestations of the UO and development of wounds.

	Wounds on the UO		Estimate (β_x)	Std. error	OR (exp (β_x))	95 % CI	P - value
	Yes (n (%))	No (n (%))		Coefficient (β_x)			
Fixed effect							
Intercept			−2.22				
General condition							
- Good	125 (16.1)	609 (78.5)	Baseline	–	1		
- Bad	17 (2.2)	25 (3.2)	1.68	0.38	5.4	(2.5;11.3)	<0.001
Size of UO[a]							
- Small	36 (4.6)	328 (42.3)	Baseline	–	1		
- Large	106 (13.7)	306 (39.4)	1.56	0.23	4.8	(3.0;7.5)	<0.001
Reducibility of the UO							
- No	108 (13.9)	390 (50.3)	Baseline	–	1		
- Yes	34 (4.4)	244 (31.4)	−1.30	0.25	0.3	(0.2;0.5)	<0.001
	N_{Exam} = 776	N_{wounds} = 142	N_{pigs} = 249				
Random effects				Variance	Std. dev.		
				0.18	0.43		

[a] The size of the UOs is define from the median circumference of the UO in following age groups: Farrowing location (age 0−28 days) the UO is defined as big if circumference ≥ 7.0 cm. Weaner location (age 29−72 days) the UO is defined as big if circumference ≥ 10.0 cm. Finisher location (age > 72 days) the UO is defined as big if circumference ≥ 29.0 cm.

spontaneously resolved UOs take place before 14 weeks of age. The fact that some UOs resolves and some UOs deteriorates makes it difficult to predict the odds of dying before scheduled slaughter exclusively on the time of occurrence.

One of the objectives of this study was to analyze the effect of recorded clinical manifestations in UO-pigs on survival, without considering the cause of death. The findings in the survival model indicate that pigs in a bad condition, with a large size UO and a skin-color of red or blue on the UO have a significantly higher hazard of dying before slaughter compared to pigs in a good condition with a small size UO and a normal skin-color of the UO.

The multivariable results showed that the general condition of the pig (good/bad) was associated with the hazard of death before scheduled slaughter in pigs with UOs. A reasonable explanation could be that the underlying cause of the UOs is affecting the growth and well-being of the pig, e.g. if complications such as strangulation or obstruction of the intestines occur. In the present study only two pigs were euthanized because of a “severe” condition. Most of the registrations of a “bad” condition in UO-pigs were obtained in the farrowing unit or at weaning in relation to undernourishment, bristly hair, dehydration sign and diarrhea. The findings may indicate that pigs with an UO are more vulnerable to other diseases. In addition, the results from a Norwegian genetic study by Grindflek et al. (2018) suggested an involvement of immunological factors in the development of UOs in pigs. If the immunological response is affected in UO-pigs, this could explain the susceptibility to other diseases. Pigs with a large UO had a significantly

higher hazard of dying before slaughter compared to pigs with a small UO. This is comparable to the observations by Mattsson et al. (2013) who reported a larger size (diameter) of the UO and a larger hernial opening in pigs that died or were euthanized from the UO compared to pigs that went for slaughter.

Pigs with a reducible UO were hypothesized to have a higher hazard of dying before slaughter because the reducibility or the ability to push the hernia-content back into the abdominal cavity by hand is related to the diagnose hernia umbilicalis, which is associated with discomfort in pigs (Schild et al., 2015) and are likely to cause fatale complications (Hansen, 2014; Mattsson et al., 2013; White, 2010). Another hypothesis was that the form of the UO somehow was linked to the cause of the UO and, therefore, could affect the hazard of death. In the present study, the reducibility and the form of the UO indicated, however, no significant effect of the hazard of death. The reducibility was easy to establish in the farrowing section and the weaning section, especially when the pig was turned over on the back for clinical examination, but as the pig and the UO became heavier and the clinical examination was in an upright position it could be difficult to reduce the hernia-content. In some finishers, the UOs were irreducible at the clinical examination, but reducible at the post mortem examination, which probably makes the method unreliable for finishers. If complications such as strangulated or obstructed intestines or adhesions of hernia-content occur, the UOs become irreducible, which consequently make complex umbilical hernia difficult to distinguish from cyst-complexes, abscesses and fibroses, which are irreducible.

In the present study, pigs were housed without special treatment and in order to ensure animal welfare, pigs with wounds greater than 1 cm across the wound surface were euthanized. Skin-lesions on the UOs were the main reason for euthanasia of pigs. The results from a generalized mixed logistic analysis showed that the general condition of the pig and the size of the UO were significantly associated with the development of wounds on the UOs. Similarly, Hansen (2014) who examined the nature of UOs in 148 pigs post mortem, found an association between UOs greater than 15 cm (diameter) and the presents of wounds. A reasonable explanation could be that pigs in a bad condition may be more motivated to lie down compared to pigs in a good condition, which facilitate the development of wounds caused by abrasion at the floor or applied by tread from pen-mates. Pigs with large UOs can easier get a wound on the UO due to abrasions at the floor and stable fixtures or by tread or push from pen-mates. Reducibility of the content of the UO was found as a protective factor for the development of wounds on the UO. A plausible explanation might be that a reducible UO also is movable, and easily can be displaced when the pigs lie down or are pushed by pen-mates, which decreases the pressure at the skin.

We have carried out a prospective cohort study, where the housing and management of the pigs reflect real life production. The use of multivariable survival analysis and mixed generalized logistic analysis allowed us to control and investigate several factors simultaneously and make allowance for the continuous observations on the same animals. This study focused on death before scheduled slaughter in pigs with UOs and incorporated the “time” factor in the analysis. By fitting an extended cox hazards model with the clinical signs, collected over time and used in the exact chronological order. The pigs could enter and leave the analysis at different ages depending on the detection of an UO, regression of the UO or death of pigs with UOs.

5. Conclusion

In the present prospective cohort study of Danish pigs with umbilical outpouchings (UOs) more than half of pigs with an UO died or were euthanized before scheduled slaughter. The odds of dying before scheduled slaughter was not associated with the time of detection. Three different clinical manifestations were found to have a prognostic value for overall survival until slaughter. A generally bad condition in pigs with an UO resulted in a significant increase in the hazard of death compared to UO-pigs in a good condition. The effect of size and skin-color of the UOs was depending on one another. The hazard ratio for pigs categorized with a large UO was significantly increased at any given time point before slaughter compared to pigs with a small UO, no matter of the skin-color of the UO. Pigs with a small UO and a reddish or blueish skin-color of the UO were higher compared to UO-pigs with a small UO without discoloration. The form and reducibility of the UOs were not found to have any prognostic value on survival. Wounds on the UOs were the most frequent complication resulting in euthanasia. A generally bad condition of the pig and large size of the UOs were found as risk factors for developing a wound on the UO. Reducibility of the content was found as a protective factor for the development of wounds. The identification of prognostic clinical signs in pigs with an UO is useful in the assessment and decision-making in relation to the future prospects of pigs with UOs.

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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