The duration and clinical course of udder cleft dermatitis

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Abstract

Udder cleft dermatitis (UCD) is an exudative dermatitis of the skin at the anterior junction of the frond quarters of the udder and the abdominal wall. Although UCD is well known in veterinary practice, little is published about this condition. Therefore the goal of this trial was to determine the duration and clinical course of UCD. Cows on five farms were repeatedly observed over a 45 week period. Photographs were taken of UCD lesions and scored according to a new scoring system. Later, a healthy, mild and severe classification was made, based on the presence of a breach in the skin. The average within-herd prevalence of UCD in the trial was 37%. Prevalence increased with parity. The incidence found was low, 1.85 episodes/100 cows/week. The duration is the major contributor to the high prevalence: Only half of the cows with a form of UCD were recovered after a 35 week period. A huge difference was found in the time to recovery between mild UCD and severe UCD, with the latter group hardly recovering at all; only 22% of the cows with severe UCD were recovered after a 38 week period. Episodes of UCD started more often around parturition (period from >305 days in milk to <61 days in milk). The severe stage of UCD started more often in fresh cows (0-60 days in milk) and was more likely to occur in heifers and second parity animals. 76% of the severe lesions were preceded by mild stage of UCD.

Introduction

Udder cleft dermatitis (UCD), otherwise known as ulcerative mammary dermatitis, udder foul or intertrigo, is an exudative ulcerative dermatitis (1-3). The most of the lesions are situated at the anterior junction of the frond quarters of the udder and the abdominal wall (4-6). All dairy cows seem to be susceptible for UCD (3, 4). Affected cows suffer from this painful process, and complications can be serious; the breached skin of the udder is a port of entry for bacteria, which increases the risk of mastitis. If the skin surrounding the V. subcutanea abdominis is breached, the cow can bleed out (5, 6). UCD is a problem in the dairy industry; a preliminary report with the Animal Health Centre in Deventer reports that UCD is present in 85% of all Dutch dairy farms. They reported within-herd prevalence can extend to 22% of all dairy cows (3, 5, 6).

Little is known about UCD; only few veterinary medicine textbooks describe the lesion, and give a hypothesis about causation (1, 2). Authors speculate that oedema and friction between the quarters of the lactating udder causes micro trauma. This trauma, possibly in combination with a secondary infection, is thought to be sufficient to cause disease. Other publications state about outbreaks of UCD. Articles of Boyer and Singleton (1998) and Beattie and Taylor (2000), describe that UCD is seen in herds with concurrent outbreaks of bovine digital dermatitis and superfoul (7, 8). However there is no clear indication that treponema's, mange or other bacteria (like F. Necrophorum) are the causative pathogen for UCD. Many potential pathogens are cultured from the lesions, but none of them are clearly associated with UCD (4, 9-11).

Several risk factors for the development of UCD have been described (3, 5,6, 12). At cow level the formation of the udder, like the depth and udder attachment seems to be important; strong attached anterior quarters are protective for UCD, as are shallow udders (3, 5, 6, 12). Also common risk factors like breed (Swedish Red cows vs Swedish Holstein), parity and high production level seem to be present (6, 12). At farm level the use of footbaths and a high year production seem to be risk factors (3, 5, 6, 11, 12).

However, the development and progression of udder cleft dermatitis has never been described. None of the authors have given an indication of the duration of the disease. It remains unknown how long cows are affected by UCD and what factors influences recovery. After the preliminary research by the Animal Health Center in Deventer, the production agency for the consumption of products of animal origin (PVV) gave funding to continue research. One of the important research questions was how UCD develops time. Therefor the object of this trial was to determine the duration and clinical course of UCD.

Materials and methods

The research project was conducted in the university large animal veterinary practice (Utrecht, the Netherlands). Only clients of the practice participated with the trial. Dairy farmers were approached to participate in the trial if there was a history of problems with UCD. Requirements for selection were: a within herd prevalence exceeding 6%, an average production-level exceeding 7500 kg/cow/year, a neat disease administration and the possibility of fixating all cows at the feed fences. A total of five farms were selected.

Data were collected in 2013, from week 4 until week 49. Farms were visited weekly until week 17; afterwards they were visited every other week. During the last two visits (week 47 and 49/50), only affected animals were photographed. Each farm was visited 30 or 31 times. The farms were visited by one regular researcher (SS), escorted by interns from the veterinary practice. All cows were fixated at the feeding fence. Cows were inspected using a hand mirror. If a cow was affected, a picture was taken using a mirror and camera which were assembled at a stick (See photograph 1 in Attachment 1 – Figures).

The intern would spread the two udder halves to have a clear view of the wound. In addition, a ruler with a piece of paper with the identification number of the cow was held in the frame of the picture. All photographs were scored by two persons, who trained to obtain a good level of agreement.

Initially, the scoring system as described by Amersfort et al. was used to score the photographs(3). This scoring system did not suffice very well, because a lot of variation between different photographs was lost in the single score of the photograph. Moreover, the agreement between the scores of the same photographs was very poor. Therefore, a new scoring system was developed during the trial. Photographs were scored at seven characteristics: Coverage of the wound, the presence of granulation tissue, the presence of scar tissue, the presence of erythema, the length of the lesion, the length of the wound and the location of the wound (See table 1, attachment 1 -Figures). The location of the wound is divided in six areas based on the Y-shaped predilection area of UCD. The length of the affected skin can differ from the length of the wound that is present. The wound can be surrounded by inflamed skin; therefore two characteristics were scored. These results were entered in a database, together with the most recent results of the milk production registration (MPR). Later the data of the cows that were not photographed were entered to complete the database. Parity was categorised in heifers, second parity cows and older cows. Days in milk (DIM) were categorised according to the MPR classes for DIM: 0-60 days in milk, 61-120 days in milk, 121-200 days in milk, 200-305 days in milk, exceeding 305 days in milk.

A period in which the cow is affected by UCD is called an episode of UCD. An episode consists of a series of photographs; A single observation "affected" (the cow showed signs of UCD), with the previous and following observation being "healthy", is regarded as an error. Therefore, an episode of UCD exists of two or more consecutive observations "affected". Several cows had more than one episode, being healthy in between. Between two episodes, there had to be more than one observation "healthy". If there was only one observation moment without a photograph, the healthy observation was regarded as an error.

Episodes were classified in based on severity. If a cow had at any point a breached skin (one or more photographs had a score "length of the wound" > 0), the episode was classified as severe. If not, the episode was classified as mild. Episodes were also classified based on a known start and/or ending; the duration of these episodes will be underestimated. A subset of animals with a known start of UCD was used to determine which animals develop UCD and what characteristics the first lesions.

Data were analysed with SPSS 22. Prevalence and incidence were calculated per farm visit. The following formula was used:

 $N_{new episodes at visit v} / (N_{unaffected animals at visit v-1} X$ $N_{days between visit v and visit v-1}$ Because of the low incidences found, the unit was converted from N new episodes/cows/day to N new episodes / 100 cows/ week. A univariable analysis was done to determine characteristic of cow that developed UCD.

A time variant covariant cox regression analysis was done to determine the duration of UCD. In this model the severity of UCD was entered as a time variant covariant. A survival analysis was done to determine the duration and chance to make the transition from mild UCD to severe UCD. Also a transition matrix is made, to express the chance of transitions between healthy, mild UCD and severe UCD.

Results

Descriptives

The five farms that were selected had an average herd size of 56-91 animals. Characteristics of the farms are described in table 2 (See attachment 1 – Figures). In total 457 cows were observed during the trial (182 heifers, 88 second parity animals and 187 third or more parity animals, upon entry at the trial). 239 cows developed a form of UCD. Several animals had more than one episode; 39 cows went through two episodes of UCD, 4 cows' experienced 3 episodes of UCD during the trial, and 1 cow went through four episodes of UCD. A total of 11064 observations (healthy and affected by UCD) were done during the trial.

Photographs

A total of 4290 photographs were taken. Erythema was present in 3914 photographs (91.2%). Granulation tissue was present in 1574 of the photographs (36.7%) and scar tissue was found in 1583 of the photographs (36.9%). Most of the wounds were covered with exudate, followed by coverage with tallow/grease (Graph 1 – Attachment 1). Lesions are predominantly found in the core, as can be seen in graph 2 (Attachment 1). Most lesions were 5-15 cm long, as can be seen in graph 3 (Attachment 1), 73.9% of the photographs contained lesions in this range. Wounds were present in 2423 photographs (56.5%); most of the wounds were smaller than 10 cm (2207 photographs, 91.1%) (Graph 4, Attachment 1).

Because of the long duration of UCD, the lesions cannot be fully characterised by the data from all the photographs. The repeated observations from chronically affected cows can overemphasize characteristics. Therefore, a single farm visit per farm was randomly selected, in order to obtain a representative cross section of mild and severe lesions.

One observation moment per farm was randomly selected in order to obtain a cross section of mild and severe lesion. At the selected visits, 65 cows were mildly affected and 84 cows were severely affected. Results can be seen in table 3 (Attachment 1). In mild lesions, the most common coverage is tallow/grease (66%). There is no granulation tissue present in these lesions, but in most of the lesions erythema is present (83%). Scar tissue is present in 31% of the mild lesions. The mild lesions do not exceed 15 cm in length. Most lesions are present in the pit (77%). Severe lesions are more often covered by exsudate (61%) or by crusts (27%). There is an increase in the presence of granulation tissue (62% of the lesions) and scar tissue (51.2%), and a decrease in the presence of erythema (51.2%). There is hardly any difference in the length of lesions of mild and severe lesion, nor is there in the location of the lesion. Mild lesions and severe lesions differed significantly in coverage (chi-square is 133.55, df=4), granulation tissue (chi-square is 61.81, df=1) scar tissue(chi-square is 6.26, df=1) and erythema (chi-square is 16.39, df = 1).

Episodes

In total 289 episodes of UCD were observed. The distribution of the episodes on farm level is expressed in Table 4 (Attachment 1). From the 289 episodes, 78 had an unknown start and unknown ending; all of these episodes had a duration exceeding 45 weeks. 92 episodes had a known start and a known ending. Episodes of UCD were categorised in mild and severe. 149 Episodes were categorised as severe, 140 episodes were mild. The distribution at farm level is presented at table 5 (Attachment 1).

150 episodes had a known start. 44 of these episodes started out in heifers (29.3%), 32 of these started in second parity cows (21.3%) and 74 in older parity cows (49.3%) (See graph 5, Attachment 1). This distribution over parity did not differ significantly from the distribution of parity within the overall sampling group. Fifty of these episodes developed a severe lesion during the episode. The start of this severe stage occurred in 18 heifers (38%) and in 17 second parity cows (34%) (See graph 5, Attachment 1). This was significantly different from the distribution of parity within the sampling group (chi-square was 9.7028, df=2, p<0,05).

45 of the 150 episodes with a known start, occurred in cows exceeding 305 days in milk (DIM), and 26 occurred in fresh cows (DIM<61 days) (See graph 6, attachment 1). This tested statistically different from the distribution of DIM within the overall sampling group (chi-square was 11.06, df=4, p<0.05). The effect of lactation stage is more obvious in the 50 episodes that became severe; in 42% of these episodes, the severe stage started out in fresh cows (DIM <61 days) (See graph 6, attachment 1). This was significantly different from the distribution of DIM within the overall sampling group (chi-square was 35.36, df=4, p<0,05).

Prevalence and incidence

The average within-herd prevalence was 37%, with a range of 28-45%. The prevalence's within farms can be found in table 6 (Attachment 1). The 95% confidence interval of the farms overlapped, with the exception of farm 2. This farm had a significantly lower prevalence. The prevalence increased with parity; heifers had an average prevalence of 16.15% (range 4.23-23.08%), second parity cows had an average prevalence of 34.6% (range 7.69-42%). Third parity or more animals had a prevalence of 49.82% with a range of 39.68-58.92%. Severe UCD had a higher prevalence than mild UCD; the average prevalence of animals with severe UCD was 21.1% (range: 13.0-24.2%), while the average prevalence of animals with mild UCD was 15.9% (range 8.9-20.3%). The mean incidence over all the farms was 1.850 episodes /100 cows /week. The incidence fluctuates over the trial period, ranging from zero new cases per visit to 6.01 episodes / 100 cows / week.

Transitions

Each observation is classified in healthy, mildly affected and severely affected. Each previous observation is compared with the next. A total of 10607 transitions were observed. The results are given in Table 7, attachment 1.

A previous healthy cow had a chance of 2.3% to be mildly affected at the current observation (Table 7, attachment 1). The chance to become severely affected at the current observation was 0.5%. A mildly affected cow had a 7.6% chance of recovery (healthy in the next observation), and a 6.2% chance of becoming severely affected. But it was most likely to remain mildly affected (86.2%).The same goes for severely affected cows; 93.1% of the severely affected cows remains severely affected at the next observation. There was a 5.2% chance of a transition to mildly affected and a 1.7% chance of recovery. 77% of all the severe stages of UCD were preceded by a mild stage of UCD.

The characteristics of lesions from before and after the transition were compared with the characteristics of mild and severe lesions from the cross section, to see if transition is accompanied with a change in characteristics of the lesions. Two transitions were investigated, namely the transition from mild to severe and the other way around. Three comparisons were made per transition:

- Characteristics before the transition versus representative lesions from the cross section.
- Characteristics after the transition versus representative lesions from the cross section
- Characteristics before the transition versus characteristics after the transition.

A chi-square test was used for the first two comparisons. For the third comparison, a McNemar chi-square test was used for dichotomous characteristics (granulation tissue, erythema and scar tissue). The other characteristics were tested with a normal chi-square test. The results are discussed per transition.

The transition from mildly affected to severely affected.

The mild lesions before the transition had more often the coverage exudate or crusts than lesions from the representative mild lesion from the cross section (chisquare is 9.72, df=4). Other characteristics of the mild lesions did not differ from the cross section. After the transition, the severe lesions had less often granulation formation and scarring. Also, the length of the lesions was significant more often smaller than 15 cm in diameter than the lesions from the cross section. This is also the case for the length of the wounds; the wounds were more often smaller than 10 cm in diameter than the wounds in the cross section.

The transition from mild to severe lesions is accompanied with a change in coverage (9.81% of the lesions continue to have the same coverage after the transition), an increase in the presence of granulation tissue (from 1.8% before to 39.3% after, p < 0.001) and the presence of erythema (from 80.4% before 95.5% after, p < 0.001).

The transition from severely affected to mildly affected.

The severe lesions before the transition to mild are more often covered with crusts than the severe lesions in the cross section. They also have less often granulation tissue and have more often erythema than the severe lesions in the cross section. After the transition, the mild lesions are more often covered by crusts than the mild lesions from the cross section. Other characteristics do not significantly differ from the mild lesions from the cross section.

The transition from severely to mildly affected by UCD is accompanied with a change in the presence of granulation tissue (36.9% to 0.8%, p<0.001) and the presence of erythema (91% to 74.6%, p< 0.001). The coverage changes in 84.44% of the cases, p=0.045, df =9.

Duration

The results of the cox regression analysis are given in graph, any form of UCD, mild or severe, is entered in the graph 7 (Attachment 1). Only 50% is recovered after a 38 week period. The results are split for mild and severe lesions; this can be seen in graph 8 (Attachment 1). Fifty percent of all the mild lesions are recovered after 12 weeks, but for the severe lesions, recovery takes a long time: only twenty-two percent was recovered after thirty-five weeks.

A Kaplan-Meijer analysis was done to determine the time it took for a mild lesion to transfigure to a severe wound. The survival function can be seen in graph 9 (Attachment 1). The average duration was 28 weeks, although many of the episodes were censored, because of recovery or because the trial ended before the lesion transfigured.

Discussion

As can be seen in the results, the duration of an episode of UCD is extensive; only 50% recovered of an episode of UCD after 38 weeks. This is the major contributor to the high prevalence: the incidence found is low, only 1.85 /100 cows at risk / week. The long duration might also be the reason that older parity animals have a higher prevalence. The prevalence of UCD seems to increase with parity, from 16% in heifers to 50% in older parity animals. These results are consistent with the results found by Person Waller et al. and Warnick et al (4, 12). The duration of the condition can exceed the length of a single lactation. The long duration might also the reason that it appears that heifers and second parity animals are more prone to develop severe episodes. This effect is also described by Person Waller et al., who mention that the proportion of cows with severe UCD was highest in second parity animals (12). This was concluded from the group of animals with a known start of UCD; however, as fifty percent of older parity cows, is affected by UCD, only half of the population older parity animals, is at risk to develop UCD. To firmly conclude that heifers are more prone to develop severe UCD, incidence for severe forms of UCD must be stratified for parity. But the number of known new (severe) cases of UCD in our data was too low to validly determine this effect on incidence. What is contradictive with this observation is that the distribution of parity within the 150 episodes with a known start of any form of UCD, did not differ from the distribution of parity within our trial. This would indicate that older parity animals develop a mild form of UCD more often than younger animals, because the number of animals at risk decreases with parity. Again, incidence must be stratified to firmly conclude that older parity animals are more prone to develop mild UCD, but our data did not allow validating this, because of low numbers of new episodes. As said before, the duration of UCD is the major component of the high prevalence. Therefore, any attempt to decrease prevalence, should be sought in decreasing the duration of UCD.

The first photographs in the trial were evaluated with the scoring system as described by Olde Riekerink et al. 2014 (6). Several veterinarians scored the photographs, which resulted in very different results. Also, the variations within the clinical course of an individual cows were lost in the overall score. Therefore, several characteristics were scored individually. In the final analysis of the results, it turned out that several of the characteristics transfigure with the development of wounds. The presence of a wound also had a drastic effect on the duration of UCD. Therefore the classification was altered to mild/ severe. Most of the severe cases originated from mild cases (76%). However, it is possible that the 24% that originated from healthy cows had a short mild stage that occurred during the two observation moments (7-14 days). It seems likely that certain risk factors, like changes in size and metabolism of the udder or effects on the immune system around parturition, contribute to speed of development of severe UCD. The transition to a severe stage of UCD was most often seen in the period around parturition. Many of the severe forms of UCD appeared in the first 60 days after calving (42%). This is in correspondences with reports of Olde Riekerink et al., who found a relationship of UCD with the dry period (6).

The transition from mild to severe UCD is accompanied with a change in coverage, the presence of granulation tissue and erythema. Mild lesions are more likely to have exudate as coverage than general mild lesions from the cross section; this could be an indication that mild lesions seem to get infected with pathogens, which results in an open wound. Several authors corresponded over potential pathogens for UCD; treponema's are cultured from this lesions, along with other bacterial pathogens as well (4, 7-11). However, a primary cause is responsible for the mild lesions, which are in many cases the predecessor for severe lesions. It would be interesting to see how these mild lesions appear in histology and what can be cultured from these mild lesions. This could clarify the aetiology of UCD.

The selected farms are not the best representation of the presence of UCD within the Netherlands. The production level of the five farms exceeds the average farm production level in the Netherlands. The average on Dutch farms was 8,084 kg milk/cow/year (sd. 1,191) (13). Farms were selected if the production exceeded 7,500 kg milk/cow/year. The selected farms had a production over 8648 kg milk/cow/year, which makes them produce in the top 27% of all Dutch dairy farms. Several authors mention farm production level as a risk factor for the prevalence of UCD (5, 6, 12). If this had an effect on the prevalence of UCD could not be determined, as the prevalence in our trial was in anyway higher than the average Dutch prevalence because of the selection criteria (The estimated within herd prevalence of UCD must exceed 6%). This is more than the average of 5.2% found by the AHS. The estimated prevalence of the farmers turned out to be the tip of the iceberg, as the prevalence's found in our study varied form 32-42% for all cases of UCD, and the prevalence of severe cases varied form 13-24%.

However, the goal of our trial was not to estimate prevalence of UCD, but to describe the clinical course for UCD. The high prevalence helped to observe more cases. It is possible that risk factors associated with a high production level also have an effect on the development or duration of UCD.

Conclusion

Udder cleft dermatitis is a condition which affects cows for an extended period of time; the duration exceeds a 38 week period in 50% of the cases. The incidence is low, 1.85 episodes / 100 cows at risk/week. Severe lesions are more likely to appear around parturition and in fresh cows, although UCD can affect dairy cows of all ages. Heifers and second parity animals were more likely to develop a severe stage of UCD. The severe stage is most of the time progressed by a mild stage, which is known by a sebum/greasy coverage and erythema. The severe stage is known by an ulcerative exudative coverage.

Literature

1. Blowey, R. W., Edmondson, Peter, .. Mastitis control in dairy herds. Wallingford, Oxfordshire, UK; Cambridge, MA: CABI; 2010.

2. Rebhun's diseases of dairy cattle [Internet]. St. louis, Mo.: Saunders/Elsevier; 2007.

3. K. van Amersfort. Prevalence and riskfactors of udder cleft dermatitis in 20 dutch dairy herds. Utrecht: 2011.

4. Warnick LD, Nydam D, Maciel A, Guard CL, Wade SE. Udder cleft dermatitis and sarcoptic mange in a dairy herd. J Am Vet Med Assoc. 2002;221(2):273,276. 11 ref.

5. Lam T, Olde Riekerink R. Prevalentie en risicofactoren van udder cleft dermatitis (smetplekken). Intern eindrapport. Deventer: GD Deventer; 2011. Report No.: Projectnummer: 1080134.

6. R.G.M. Olde Riekerink, K. van Amersfort, O.C. Sampinon, G.A. Hooijer, T.J.G.M. Lam, short communication – Prevalence, risk factors and a field scoring system for udder cleft dermatitis in dutch dairy herds, 2014, J. Dairy Sci. 97 (8): 5007-5011 7. Boyer P, Singleton G. Digital dermatitis, superfoul and severe necrotic dermatitis of the udder in dairy cows. Vet Rec. 1998;142(6):147,148. 1 ref.

8. Beattie KG, Taylor DJ. An investigation into intertrigo (necrotic dermatitis or 'foul udder') in dairy cows. Cattle Practice. 2000;8(4):377,380. 6 ref.

9. Stamm LV, Trott DJ. Treponema and bovine skin disease: Papillomatous digital dermatitis and ulcerative mammary dermatitis. In: .

10. Stamm LV, Walker RL, Read DH. Genetic diversity of bovine ulcerative mammary dermatitis-associated treponema. Vet Microbiol. 2009;136(1/2):192,196. 19 ref.

11. Evans NJ, Timofte D, Carter SD, Brown JM, Scholey R, Read DH, et al. Association of treponemes with bovine ulcerative mammary dermatitis. Vet Rec. 2010;166(17):532,533. 17 ref.

12. Persson Waller K, Bengtsson M, Nyman A-. Prevalence and risk factors for udder cleft dermatitis in dairy cattle, 2014, J Dairy Sci, 97 (1): 310-318.

13. https://www.crv4all.nl/over-

crv/publicaties/jaarverslagen/crv-jaarstatistieken-2013/

Attachment 1 - Figures



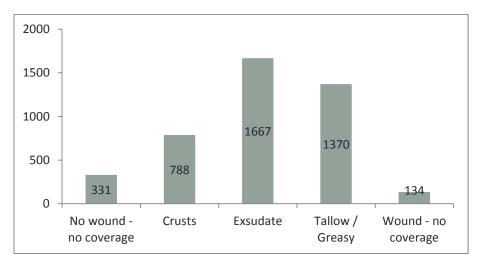
Photo 1, Materials for taking photographs on farm.

Score	Coverage	Granulation tissue	Scar tissue	Erythema	Length of the laesion (cm)	Length of the wound (cm)	Location
0	No cover – No wound	No	No	No	No laesion	No wound	-
1	Crusts	Yes	Yes	Yes	1 to 6	1 to 5	Core
2	Exsudate				6 to 15	6 to 10	Short axis of the Y
3	Tallow/Greasy				>15	>10	Long axis of the Y
4	No cover and a wound						Long and short axis of the Y, complete Y
5							Short axis and core
6							Long axis and core

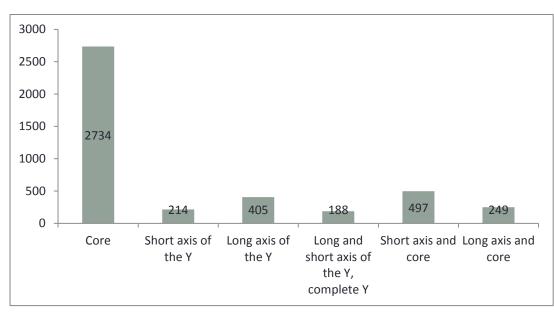
Table 1, Scoringsystem for photographs.

Farm	N animals	305-days production	Floor	Boxes	Milking method	Excess to pasture
1	56	9151 kg	Slatted flooring	Rubber mats with sawdust and chalk	2x5 Parallel parlor	Yes
2	79	9163 kg	Slatted flooring	Deep beds with straw and eggshells	2x6 Herringbone parlor	No
3	66	10378 kg	Slatted flooring	Matrasses with sawdust	2x5 Herringbone parlor	Yes
4	89	8648 kg	Slatted flooring	Rubber mats with sawdust	2x6 Herringbone parlor	Yes
5	91	9252 kg	Slatted flooring	Rubber mats and waterbeds with chopped straw and chalk	Robotic milking	No

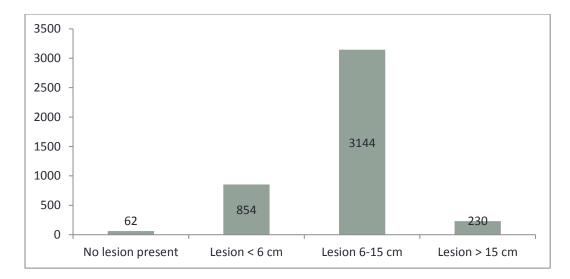
Table 2, Farm characteristics of the selected farms.



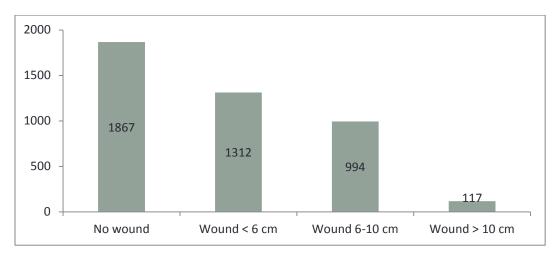
Graph 1, All photographs (N = 4290) - Distribution of coverage



Graph 2, All photographs (N = 4290) - Distribution of location



Graph 3, All photographs (N = 4290) - Distribution of length of lesion



Graph 4, All photographs (N = 4290) - Distribution of length of wound

		Characteristics of lesions												
	Cov	erage		lation sue	Scar tissue Erythema		Length of the laesion		Length of the wound		Location			
Score	Mild lesions	Severe Lesions	Mild lesions	Severe Lesions	Mild lesions	Severe Lesions	Mild lesions	Severe Lesions	Mild lesions	Severe Lesions	Mild lesions	Severe Lesions	Mild lesions	Severe Lesions
0	20	0	65	32	45	41	11	41	0	2	65	0		
1	2	23	0	52	20	43	54	43	11	14	0	46	49	62
2	1	51							53	63	0	35	1	7
3	42	1							1	5	0	3	6	6
4	0	9											1	2
5													7	5
6													0	2
Total	65	84	65	84	65	84	65	84	65	84	65	84	64	84

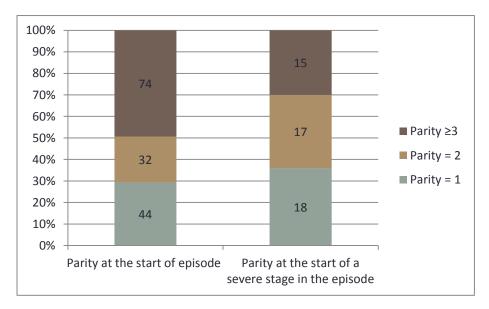
Table 3, Distribution of Characteristics of mild and severe lesions in a cross section of the photographs.

Chaut	End		Total				
Start		1	2	3	4	5	•
Unknown	Known	11	12	9	15	14	61
	Unknown	12	11	18	18	19	78
Known	Known	11	23	17	23	18	92
	Unknown	11	13	17	23	18	58
Total		45	59	50	66	69	289

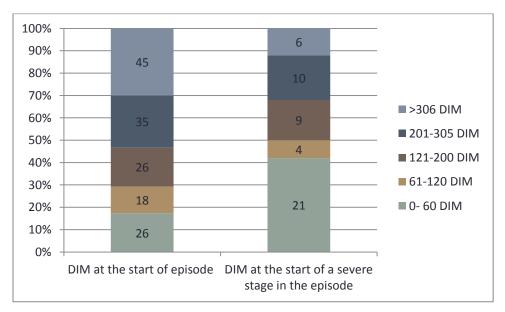
Table 4, the distribution of N episodes (total N =289) over farms. Episodes were stratified based on a known/unknown start and ending.

Farm		N Mild episodes	N Severe Episodes	
	1	19	26	45
	2	42	17	59
	3	22	28	50
	4	24	42	66
	5	33	36	69
All		140	149	289

Table 5, the distribution of mild and severe episodes on farm level.







Graph 6, the distribution of DIM Classes within episodes with a known start (N=150).

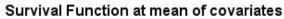
	Minimum prevalence	Maximum Prevalence	Average Prevalence	N Observations	Standard deviation
Farm 1	33,0%	51,0%	42,5%	30	5,0%
Farm 2	22,0%	41,0%	31,5%	30	4,2%
Farm 3	31,0%	53,0%	40,2%	31	6,5%
Farm 4	26,0%	46,0%	36,0%	31	5,6%
Farm 5	25,0%	43,0%	37,2%	31	5,2%
All farms	28%	45%	37%	31	5%

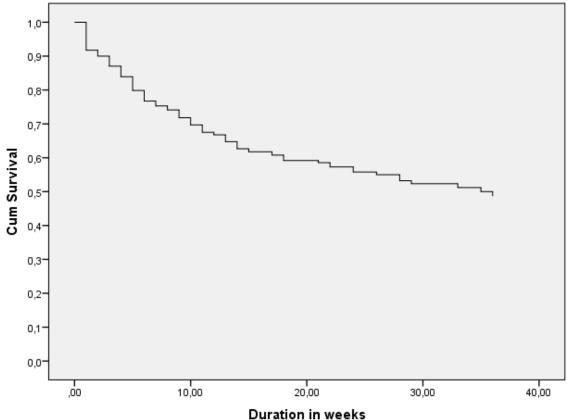
Table 6, Within herd prevalence.

Healthy	Healthy	6259	97.2
	Mildly affected	146	2.3
	Severely affected	35	0.5
Mildly affected	Healthy	136	7.6
	Mildly affected	1552	86.2
	Severely affected	112	6.2
Severely affected	Healthy	41	1.7
	Mildly affected	122	5.2
	Severely affected	2204	93.1

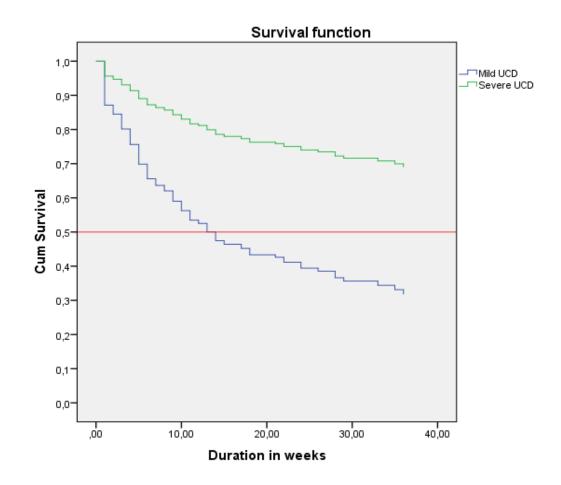
Previous observation Current observation N of transitions observed Chance (%)

 Table 7, Transitions. The chances are calculated per class of the previous observation.

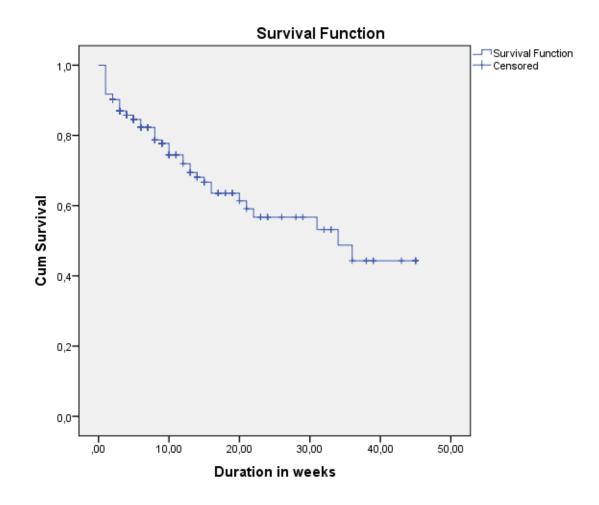




Graph 7, Results of the Cox regression analysis.



Graph 8, Results of the Cox regression analysis, stratified for the mild (blue) and severe (green) form of UCD.



Graph 9, Results for the Kaplan-Meier analysis. The event is transition from mild to severe.