Investigating the genetic background of bovine digital dermatitis using improved definitions of clinical status

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ABSTRACT

Bovine digital dermatitis (DD) is an increasing claw health problem in all cattle production systems worldwide. The objective of this study was to evaluate the use of an improved scoring of the clinical status for DD via M-scores accounting for the dynamics of the disease; that is, the transitions from one stage to another. The newly defined traits were then subjected to a genetic analysis to determine the genetic background for susceptibility to DD. Data consisted of 6,444 clinical observations from 729 Holstein heifers in a commercial dairy herd, collected applying the M-score system. The M-score system is a classification scheme for stages of DD that allows a macroscopic scoring based on clinical inspections of the bovine foot, thus it describes the stages of lesion development. The M-scores were used to define new DD trait definitions with different complexities. Linear mixed models and logistic models were used to identify fixed environmental effects and to estimate variance components. In total, 68% of all observations showed no DD status, whereas 11% were scored as infectious for and affected by DD, and 21% of all observations exhibited an affected but noninfectious status. For all traits, the probability of occurrence and clinical status were associated with age at observation and period of observation. Risk of becoming infected increased with age, and month of observation significantly affected all traits. Identification of the optimal month concerning DD herd status was consistent for all trait definitions; the last month of the trial was identified. In contrast, months exhibiting the highest least squares means of transformed scores differed depending on trait definition. In this respect, traits that can distinguish between healthy, infectious, and noninfectious stages of DD can account for the infectious potential of the herd and can serve as an alert tool. Estimates of heritabilities of traits studied ranged between 0.19 (± 0.11) and 0.52 (± 0.17), revealing a tendency for

higher values for more complex trait definitions. In terms of genetic selection, all trait definitions identified the best (i.e., most resistant) animals, but only the new trait definitions were able to distinguish between animals with average and high predispositions for DD. Considering repeated measurements resulted in heritability estimates ranging between 0.13 (± 0.05) and 0.29 (± 0.10).

Key words: hoof disorder, digital dermatitis, M-score, genetic parameter

INTRODUCTION

Bovine digital dermatitis (DD) is an infectious claw disease (Cheli and Mortellaro, 1974) affecting cattle in all production systems (Rodriguez-Lainz et al., 1999; Wells et al., 1999; Cramer et al., 2009). Herd prevalence levels of DD are wide ranging and associated with multiple risk factors affecting DD incidence (Holzhauer et al., 2006; Cramer et al., 2009; Schöpke et al., 2013). For instance, breed, parity, stage of lactation (Holzhauer et al., 2006), and BCS (Schöpke et al., 2013) influence herd prevalences.

Among all disorders of the bovine hoof, DD is known to generate high costs (Bruijnijis et al., 2010; Gomez et al., 2015) and it impairs animal welfare by causing painful lesions along the coronary band. Key parameters limiting the severity of DD infections are early identification and the efficiency of topical treatment (Döpfer et al., 2012), making both detection and treatment important to achieve a “manageable endemic state of disease” (Döpfer and Bonino Morlán, 2008). Different clinical stages and the transitions between these stages characterize the dynamics of DD in groups of cattle. Döpfer et al. (1997) established a classification system for stages of DD that allows a macroscopic scoring based on clinical inspections of the bovine foot. This so-called M-scale system describes the stages of lesion development. The 5 M-stages for clinical stages of DD are as follows: **M0** = normal skin appearance; **M1** = small focal circumscribed damage of the epithelium at the skin horn border (<2.0 cm in diameter); **M2** = circumscribed ulcerative skin defect with a red or

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greyish surface that can have a white epithelial margin and overlong hair (>2.0 cm in diameter); **M3** = the healing stage of DD, after the M2 lesion has covered itself with a scab; **M4** = chronic stage of DD that is characterized by a thickened epithelium or proliferative growth of the epithelium (heel warts); and **M4.1** = the chronic stage as described under M4, but with an M1 lesion within its perimeter (Döpfer et al., 1997; Berry et al., 2012). Berry et al. (2012), Holzhauer et al. (2008), and Gomez et al. (2014) describe the scoring system for DD in detail and present successful applications of the scoring method. The scoring system also allows the categorization of “DD cow types” with regard to the number of acute clinical DD events (Döpfer et al., 2004; Holzhauer et al., 2008). These DD cow types are precisely defined in Döpfer et al. (2004), Holzhauer et al. (2006), and Gomez et al. (2014). Based on the recurrence of M2 lesions, cows are classified into type I: cows that never develop M2 stages; type II: cows that develop M2 stages once and never again for prolonged period, and type III: cows that develop M2 stages repeatedly; for example, every 14 d. These DD cow types have been shown to differ in their immune response against *Treponema* spp. (Gomez et al., 2014), which are considered to be the most important bacterial agents during the pathogenesis of DD (e.g., Evans et al., 2008; Klitgaard et al., 2008; Yano et al., 2010; Gomez et al., 2012; Zinicola et al., 2015).

Despite knowledge regarding the different stages of DD, estimations of co-variance components have neglected the dynamics of DD and the approaches are predominantly based on simple trait definitions of classifying cows, such as affected or unaffected by DD. The resulting dichotomous response variables have been analyzed using linear, threshold, and recursive models (König et al., 2008; Swalve et al., 2011; Häggman and Juga, 2013). Resulting estimates for the heritability of DD vary between 0.05 and 0.14. This range reflects the variety in the types of models used for analysis, including linear as well as threshold models. The lower estimates (0.05) arise from analyses using recursive models (König et al., 2008). Schöpke et al. (2013) estimated a comparatively high heritability for DD (0.14), possibly attributable to the study design, in which the same person evaluated all animals for the presence of DD. The application of threshold random regression models revealed a varying genetic background during the course of lactation with higher heritabilities for DD directly after calving; for example, 0.28 at DIM 6 and 0.23 at DIM 20 (Gernand and König, 2014). Grouping different diseases into “dermatitis” resulted in slightly varying estimates (Buch et al., 2011; Ødegård et al., 2013; van der Spek et al., 2013). Stoop et al. (2010) and van der Linde et al. (2010) used a categorical trait

definition (4 classes of severity) and obtained heritability estimates for DD of 0.09 applying linear models. Genetic-statistical analyses based on data from the macroscopic scoring system of different clinical stages using the M-scale (Döpfer et al., 1997; Berry et al., 2012) have not been reported in the literature and observations regarding transitions between stages of DD have not been used for genetic-statistical analyses.

The hypothesis of the present study was that application of the more detailed scoring system for DD stages, in addition to records about transitions between clinical stages of DD, would improve the phenotype definition of DD, and consequently allow for better assessment of the genetic background for this infectious disease. The purpose of this study was to define new traits based on clinical inspections of cows’ feet using the M-scale, to identify factors associated with these traits, and to estimate genetic parameters for the DD traits defined during the study.

MATERIALS AND METHODS

Data were collected in a commercial Holstein dairy herd (in Wisconsin, United States) that was endemically affected by DD. The number of pregnant heifers initially included in the study was 729. The total duration of the study was 15 mo, from July 2011 to September 2012, with a mean (SD) individual cow observation time of 175.6 d (20.1), a minimum of 2.6 mo, and a maximum of 7.4 mo. The heifers’ back feet were inspected in a stand-up chute (M-Series; Comfort Hoof Care Inc., Baraboo, WI) on a regular basis starting when the heifer moved into a pregnant-heifer pen. Feet evaluations occurred at least 3 times per heifer during the study. Additional observations between regular evaluations were available for 61.3% of the heifers. Additional observations were usually, but not always, associated with topical treatments and follow-up evaluations to check clinical cure posttreatment. Treatment was the application of 15 mL of dry tetracycline-HCl powder (Tet-Sol 324; Alpharma Inc., Fort Lee, NJ) directly on the cleaned surface of an active DD lesion matching the inclusion criterion of larger than 2 cm in diameter under a light wrap that was removed after 24 and 48 h. Maximum number of observations per cow was 14. A group of 38 heifers had only 2 observations during the observation time. In total, there were 6,444 clinical observations using the 5-point scale as defined by Döpfer et al. (1997) and Gomez et al. (2014). Briefly, lesions were classified as follows: M0 for unaffected animals with no clinical lesions; M1 for infected heifers with early lesions <2 cm in diameter (nonactive); and M2 for infected heifers with a classic active lesion of >2 cm of diameter considered infectious. An M4 stage denotes late and chronic

stages of DD with (M4.1) or without (M4) small (<2 cm diameter) M1 lesions within their perimeter. An M4.1 lesion was considered a “small active DD lesion.” Relative frequencies of the clinical stages were 68.0, 4.7, 9.8, 10.9, and 6.6% for M0, M1, M2, M4, and M4.1. The M3 or healing stage was not observed during the study because time intervals between observations were spaced at least 1 wk apart.

At the time of first observation, heifers had an average (SD) age of 20.6 (2.8) mo and 153.5 (68.1) d of pregnancy. For all heifers, information on the sire and the dam was available. For the paternal path, pedigree information of up to 4 generations was traced. For the maternal path, the identifications of the dams ($n = 725$), of the maternal grandsires, and of the maternal great-grandfather were available. In total, pedigree data contained 2,688 animals. Heifers ($n = 729$) descended from 172 sires resulting in an average number of daughters per sire of 4.24.

Trait Definitions

An overview on the different trait definitions is given in Table 1. The first trait (**TBIN**) denotes a very basic description of clinical DD status as a binary trait and consistently separates unaffected animals throughout the entire observation period compared with all other heifers. Heifers showing scores of M0 throughout all observations received a score of 0, and those with at least one observation different from M0 were coded with 1. For the special consideration of heifers reaching an active stage of lesions, **TBIN** was modified to **TBINA**. For **TBINA**, heifers that had at least one M2 or M4.1 classification were given a score of 1, otherwise 0. Both traits presented so far can also be defined per observation date, resulting in repeated measurements for both traits (**TBIN_R** and **TBINA_R**); **TBIN_R** is very similar to the commonly used way to describe hoof health data with repeated measurements (e.g., Gernand et al., 2012; Häggman and Juga, 2013), and thus, **TBIN_R** can be used as a reference trait representing the conventional yes/no definition for the DD case when repeated measurements are available. When only single measurements per cow exist, a reference scenario can be defined by considering the first evaluation of each heifer as the only information. The term “reference scenario” as used here denotes a single scoring for DD, as has been commonly used in most studies applying genetic-statistical methods. The trait in this case was denoted as **TREF**, where animals scored as affected at first evaluation were coded as 1 and 0 otherwise.

Trait 2 (**TSEVCAT**) was used to describe the severity of DD cases afflicting a heifer in 2 slightly different

versions: **TSEVCAT** consistently compared unaffected heifers (always M0; score = 1) with heifers having at least one M1, M4, or M4.1 but never M2 (score = 2), and cows suffering at least once from classic active ulcers (M2; score = 3). Trait **TSEVCAT41** was very similar to **TSEVCAT** but differed concerning the scoring of M4.1 stages. In **TSEVCAT41**, heifers with at least one M4.1 event received a score of 3 and thus were considered as affected by DD as animals recorded with M2 stages. Both traits, **TSEVCAT** and **TSEVCAT41**, were categorical traits with 3 scoring classes. Identical rules applied when scores were defined per observation date, thus considering repeated measurements. The resulting trait definitions were denoted as **TSEVCAT_R** and **TSEVCAT41_R**.

In the definition of trait 3 (**TCTM2SC**), we attempted to transfer the known differences between different M2-cow types (Gomez et al., 2014). The classification of all heifers based upon the number of active M2 lesions during the observation period is converted into a trait score of 1 (type I heifer: no M2 lesions), a trait score of 2 (type II heifer: exactly one M2 lesion, allowing the presence of other lesions), and a trait score of 3 (type III heifer: multiple M2 lesions). Only cows with at least 3 observations were considered. Because there were 2 possibilities to count the number of lesions, there were also 2 versions of trait 3: **TCTM2SC** counted all M2 events considering every leg separately, whereas **TCTM2** counted per event date, which means that a heifer was scored positive for **TCTM2** if M2 was recorded for one or both legs on a given evaluation date. Additionally, an M2 lesion was not counted as a separate event if it occurred within 2 wk of the previous M2 event. Consequently, the number of M2 events differed with the 2 traits according to the counting methods and thus the distribution of heifers in score classes 2 and 3 was slightly different for **TCTM2SC** and **TCTM2** (Table 1). Because both traits were counts of observations over the entire observation period, the definition of a trait considering repeated measurements was not possible.

For a better description of DD infection dynamics, trait 4 (**TTRANS**) accounted for the changes of the M-stages over successive evaluations. Thus, the transitions between stages were classified, the classes were weighted, and a transition score was derived. The classification of the 4,984 transitions implies 4 different conditions: (1) staying unaffected; (2) healing, improving; (3) staying affected on the same stage or on a comparable stage; and (4) aggravating between evaluations (Table 1). These 4 transition classes are weighted with points from 1 to 4. To compute **TTRANS** for each heifer, all observations were classified for heifer type as explained above, weighted, summarized, and divided

Table 1. Description of trait definitions for digital dermatitis (DD), number of observations in the final data set, means, and standard deviations (SD); category frequencies instead of means for traits with more than 2 categories

Trait	Trait definition	No. of observations (no. of cows)	Mean	SD
TBIN	Binary trait that differentiates between cows consistently not affected by DD (0) and cows with at least one observation with a DD lesion (1)	729 (729)	0.52	0.50
TBINA	Binary trait that differentiates between cows that never (0) and at least once (1) experience an active stage of DD lesion	729 (729)	0.40	0.49
TBIN_R	Binary trait that differentiates every observation into unaffected by DD (0) or affected (1)	6,444 (729)	0.32	0.47
TBINA_R	Binary trait that differentiates every observation into nonactive (0) or active (1)	6,444 (729)	0.16	0.37
TSEVCAT	Categorical trait that differentiates between 3 severity categories of DD lesions: consistently unaffected (1), at least once M1, M4, or M4.1 (2), at least once M2 (3)	729 (729)	(1) 48.3% (2) 15.7% (3) 36.0%	
TSEVCAT41	Categorical trait that differentiates between 3 severity categories of DD lesions: consistently unaffected (1), at least once M1 or M4 (2), at least once active stage M2 or M4.1 (3)	729 (729)	(1) 48.3% (2) 11.9% (3) 39.8%	
TSEVCAT_R	Categorical trait that differentiates every observation into unaffected (1), M1, M4, or M4.1 (2), M2 (3)	6,444 (729)	(1) 67.9% (2) 22.3% (3) 9.8%	
TSEVCAT41_R	Categorical trait that differentiates every observation into unaffected (1), affected but nonactive: M1 or M4 (2), affected and active: M2 or M4.1 (3)	6,444 (729)	(1) 67.9% (2) 15.7% (3) 16.4%	
TCTM2	Categorical trait that differentiates between 3 DD cow types concerning the number of M2 events	691 (691)	1.57	0.79
TCTM2SC	Categorical trait that differentiates between 3 DD cow types concerning the number of M2 events considering legs separately	691 (691)	1.61	0.83
TTRANS	Transition score for the classified and weighted transitions between DD stages	729 (729)	17.90	9.05
TTRANS_R	Classification of the single transitions between DD stages: staying unaffected (1), improving, healing (2), staying affected (3), aggravating (4)	4,984 (691)	1.98	1.22
TTRANS_R	Detailed classification of the single transitions between DD stages: staying unaffected (1), complete curing (2), transition to a better but still affected stage (3), staying affected on the same or on comparable stage (4), aggravating transition (5), staying on an active stage, chronic (6)	4,984 (691)	2.44	1.78
TREF	Binary trait that differentiates the first observation of the cow into unaffected (0) or affected (1)	729 (729)	0.12	0.33

by the number of transitions observed (Equation [1]). If the first observation already denoted an affected stage (i.e., $\neq M0$), another 4 points were added to account for transitions that must have occurred before the first observation. The resulting values for trait TTRANS ranged between 10 and 42. These TTRANS values display the dynamics of a cow's DD infection and they enable the combined evaluation of the cow's ability to stay not affected, the cow's ability to recover, and the cow's ability to gain a degree of resistance:

$$\text{TTRANS} = 10[n_{\text{trans}_{cl1}} + 2(n_{\text{trans}_{cl2}} + 3(n_{\text{trans}_{cl3}}) + 4(n_{\text{trans}_{cl4}})]/n_{\text{trans}_{\text{ges}}}, \quad [1]$$

where $n_{\text{trans}_{cl1...4}}$ is the number of transitions in class (cl) 1 to 4; $n_{\text{trans}_{\text{ges}}}$ is the total number of transitions of the individual. Multiplication by factor 10 serves as a scaling factor.

Considering repeated measurements for trait **TTRANS_R**, every transition of a cow was classi-

fied and weighted as described before, but in contrast to TTRANS, measures were not averaged, so that TTRANS_R was a categorical trait with 4 classes. To define this in an ordinal way, a second, more detailed classification was used. This classification included 6 classes, which were class 1 (scored as 1) for staying unaffected, class 2 (scored as 2) for complete cure, class 3 (scored as 3) for transition to a recovered but still affected stage, class 4 (scored as 4) for staying affected on the same stage or for staying in a comparable stage, class 5 (scored as 5) for an aggravated transition, and class 6 (scored as 6) for a chronic case remaining present and active. The resulting trait was termed **TTRANS_R**.

Statistical Analyses

Analyses of variance of the traits for DD was performed using linear mixed models implemented in the SAS procedure MIXED in addition to logistic models

using the SAS procedure GLIMMIX (version 9.4; SAS Institute Inc., Cary, NC). Models were developed separately for each trait definition by backward step elimination of the nonsignificant ($P > 0.05$) effects. In total, the effects of year, season (in 3-mo periods), month, observation date, age at observation, age at first observation, average age during observation period, pregnancy stage, height, girth circumference, observation time from first to last observation, and number of observations were evaluated in the different models. Effects were checked for significance of association with the outcomes, grouped into classes, as continuous covariates, and as combined effects. In addition, interactions (e.g., between age and stage at pregnancy) were tested. After these checks, the models were chosen based on goodness of fit or simplicity compared with more-complicated models.

Variance components were estimated using a REML animal model and applying the ASReml 3.0 software package (Gilmour et al., 2009).

Because TBIN, TBINA, and TREF were binary traits, residuals were not normally distributed, resulting in a logistic model with mixed effects formulated as

$$\text{logit}(p_{ijk}) = \mu + YM_i + AGE_OT_j + animal_k, \quad [2]$$

where

$$\text{logit}(p_{ijk}) = \ln \left[\frac{p_{ijk}}{1 - p_{ijk}} \right] = \ln \left[\frac{P(Y_{ijk} = 1)}{1 - P(Y_{ijk} = 1)} \right], \quad [3]$$

with $p_{ijk} = P(Y_{ijk} = 1)$ denoting the probability of heifer k having a DD disorder in month-year i ; Y_{ijk} is the binary record for TBIN, TBINA, or TREF. The overall mean is represented by μ , YM_i is the fixed effect of year-month i ($i = 1$ to 15), AGE_OT_j is the fixed effect of the combination of j (9 classes, early-short, early-medium, early-long, medium-short, medium-medium, medium-long, late-short, late-medium, late-long) for age at first observation (3 classes: <570 d, 570 – 660 d, >660 d) and time from first to last observation (<150 d, 150 – 180 d, >180 d), and $animal_k$ is the random animal effect. Because there is no error term in the equation, the residual variance of the binary traits was fixed to the underlying liability to $\sigma_e^2 = 1$. Heritabilities were calculated correcting the residual variance by the variance of the standard logistic distribution; that is, $\pi^2/3$ (Fahrmeir and Tutz, 1994).

Traits TBIN, TBINA, and TREF were also analyzed with linear models for comparison. In this case, and for the estimation of variance components for traits

TSEVCAT, TSEVCAT41, TCTM2SC, TCTM2, and TTRANS, the following linear animal model was used:

$$Y_{ijk} = \mu + YM_i + AGE_OT_j + animal_k + e_{ijk}, \quad [4]$$

where Y_{ijk} is the phenotypic value of the trait, μ is the overall mean, YM_i is the fixed effect of year-month i ($i = 1$ to 15), AGE_OT_j is the fixed effect of combination j for age at first observation and time from first to last observation as defined in equation [2], $animal_k$ is the random animal effect, and e_{ijk} is the random residual effect.

Estimates for traits with repeated measurements were estimated with linear animal models as follows:

$$Y_{ijk} = \mu + YM_i + \beta(AGE) + pe_j + animal_j + e_{ijk}, \quad [5]$$

where Y_{ijk} is the phenotypic value of the trait, μ is the overall mean, YM_i is the fixed effect of year-month i ($j = 1$ to 15), β is the regression coefficient for age at day of observation (468 to 980 d), pe_j is the random animal permanent environmental effect associated with the animal, $animal_j$ is the random animal genetic effect, and e_{ijk} is the random residual effect. For the bivariate analyses, the model described by equation [4] was used for all combinations.

RESULTS

Incidence and Frequencies of Different DD Stages

From 6,444 observations, 68.0% of the records were found to be negative; that is, “healthy” regarding DD. Out of the 32% DD-positive observations, 54.8% showed a chronic stage (M4 or M4.1), of which 37.7% were chronic and active (M4.1). The infectious stages M2 and M4.1 together accounted for 11.3% of all observations, and 48.2% of the heifers were consistently unaffected by DD during the entire observation time. Forty-five cows were permanently suffering from DD, and 3 of them stayed infectious with M2 or M4.1 over the whole period of observation.

Scoring at the heifer level, the resulting 3,222 events included 1,877 events (58.3%) where the legs were unaffected (M0), and 719 events (22.3%) where both legs were affected ($\neq$ M0). Consequently, for the remaining 19.4% of records, one or both legs were affected by DD at the time of observation.

In the course of the observation time, the relative frequencies of the DD stages fluctuated (Figure 1). In August 2011 and May 2012, over 45% of the observations indicated presence of DD; however, during the

Figure 1. Monthly frequencies for clinical status of digital dermatitis; M0 = unaffected animals, M1 = infected heifers with early, small, nonactive lesions, M2 = infected heifers with a classic active lesion, M4 = late and chronic stages without lesion, and M4.1 = late and chronic stages with small M1 lesion.

last 4 mo (July–September 2012), less than 25% of the observations were positive. The herd reached its highest infectious status in July 2011 and August 2011, with nearly 28% of all observations being M2 or M4.1.

Fixed Effects

Environmental effects on DD were examined. Month-year significantly affected all traits. When selecting the top 3 mo with the lowest least squares means for the single traits, mo 13, 14, and 15, the last 3 in the trial, proved concordantly to be the months associated with lowest DD prevalence values in the herd (Figure 2). The month with the highest least squares means in prevalence compared with any other month revealed a large difference between the reference trait and the new defined traits that identified concordantly the first 2 mo with the highest prevalence. In contrast, month 1 ranked with the eighth-highest least squares means by the reference trait (TREF), which in turn revealed July as the month with the highest value.

In the process of developing the final model, age of animal showed a statistically significant association with all traits except for TREF. The direction of the age effect was such that older animals have a higher susceptibility for DD. Combining the age class of first observation and the length of observation time led to the finding that heifers inspected early (i.e., the young-

er ones) had lower least squares means for all traits (except TREF), independently of observation time. For animals that had their first observation at a medium or higher age, a short or a long observation time tended to result in higher least squares means for DD.

Estimates of Heritabilities and Genetic Correlations

The estimates for the heritabilities of traits from univariate linear models (Table 2) ranged between 0.19 (TBIN, TREF) and 0.52 (TCTM2), with standard errors between 0.11 (TBIN) and 0.17 (TCTM2). The results from the univariate logistic models were 0.11 (0.05), 0.12 (0.06), and 0.15 (0.09) for heritability of traits TBIN, TBINA, and TREF. Pooled heritability values resulting from bivariate analyses were slightly lower for most of the traits with 0.20, 0.17, 0.25, 0.21, 0.39, 0.48, 0.38, and 0.07 for TBIN, TBINA, TSEVCAT, TSEVCAT41, TCTM2SC, TCTM2, TTRANS, and TREF, respectively. Traits considering repeated measurements (Table 3) showed estimates between 0.13 (TBINA_R) and 0.29 (TBIN_R).

Estimation of genetic correlations revealed strong associations among DD traits considering different M-stages with values ranging from 0.97 to 1.00; corresponding standard errors were between 0.01 and 0.10. Genetic correlations between all other traits and the reference trait TREF showed lower estimates of

Figure 2. Least squares means for different digital dermatitis (DD) traits in the course of observation months. TTRANS_R = classification of single transitions between DD stages: staying not affected (1), improving, healing (2), staying affected (3), aggravating (4); TTRANS_D_R = detailed classification of the single transitions between DD stages: staying not affected (1), complete curing (2), transition to a better but still affected stage (3), staying affected on the same or on comparable stage (4), aggravating transition (5), staying on an active stage, chronic (6); TSEVCAT_R = categorical trait that differentiates every observation into not affected (1), M1, M4, or M4.1 (2), M2 (3); TSEVCAT41_R = categorical trait that differentiates every observation into not affected (1), affected but nonactive: M1 or M4 (2), affected and active: M2 or M4.1 (3); TREF = binary trait that differentiates the first observation of the cow into not affected (0) or affected (1); TBINA_R = binary trait that differentiates every observation into not affected by DD (0) or affected (1).

0.68, 0.63, 0.69, 0.65, 0.77, 0.82, and 0.80 for the relationship of TREF with TBIN, TBINA, TSEVCAT, TSEVCAT41, TCTM2SC, TCTM2, and TTRANS, respectively. Corresponding standard errors for genetic correlations varied between 0.15 and 0.25.

For bulls with at least 10 daughters ($n = 21$), Spearman rank correlation coefficients were calculated to determine the relationship between the bulls' breeding values resulting from different trait definitions. Among the breeding values of the newly defined traits, the correlation coefficient reached a value of up to 0.99 (TBINA – TSEVCAT41). Coefficients <0.9 resulted for the relationship between TBIN and TCTM2SC (0.86), TBIN and TCTM2 (0.83), TSEVCAT and TTRANS (0.89), TCTM2SC and TTRANS (0.87), and TCTM2 and TTRANS (0.86). All correlations were significantly different from zero. Rank correlation coefficients between the new traits and the reference trait were remarkably lower. Correlations ranged from 0.30 to 0.46, where only the associations between TCTM2SC and TREF (0.46), TCTM2 and TREF (0.44), and TTRANS and TREF (0.43) were significantly different from zero.

The 21 sires with >10 daughters were assigned to a "resistance level" according to their breeding values. Comparing the ranking resulting from breeding values for different traits, the top bulls (upper third) showed a high level of agreement. On the contrary, the bottom bulls (lower third) were nearly the same for the new traits, but differed remarkably for the reference trait.

DISCUSSION

Frequencies and Fixed Effects

The course of the disease in the herd used in this study was described by the relative frequencies of the DD stages over the observation period and reflected by the course of least squares means for the different traits. The changes in frequencies across time reflect the rapid dynamics of DD. The spread of the disease and healing due to topical treatment of animals detected with DD can occur within only a few days. The least squares means show partially different trend lines caused by the individual trait definition and their way of handling M2 and M4.1 observations. Trait TBIN_R distinguishes between positive and negative DD observations and exhibits a very similar trend curve compared with TBINA_R. Despite this, both trait definitions identified different "poorest" months due to the explicit consideration of infectious stages in TBINA_R, which in turn was in close agreement with TSEVCAT_R and TSEVCAT41_R. Traits TTRANS_R and TTRANS_D_R had slightly different trend lines compared with the other 4 traits, which

Table 2. Estimates of heritabilities (h^2) with standard errors (SE), additive (σ_a^2) and residual variance (σ_e^2) for different digital dermatitis traits in the linear univariate model

Trait ¹	No. of observations (no. of cows)	σ_a^2	σ_e^2	h^2 ($\pm$ SE)
TBIN	729 (729)	0.043	0.179	0.194 $\pm$ 0.106
TBINA	729 (729)	0.041	0.162	0.203 $\pm$ 0.108
TSEVCAT	729 (729)	0.187	0.511	0.268 $\pm$ 0.123
TSEVCAT41	729 (729)	0.175	0.574	0.234 $\pm$ 0.115
TCTM2SC	691 (691)	0.269	0.319	0.457 $\pm$ 0.163
TCTM2	691 (691)	0.280	0.258	0.521 $\pm$ 0.171
TTRANS	729 (729)	30.522	41.726	0.423 $\pm$ 0.149
TREF	729 (729)	0.019	0.080	0.193 $\pm$ 0.109

¹Trait definitions are given in Table 1.

shows that these 2 traits score the transitions and thus represent the dynamics of the disease in the individual herd. For management purposes, both trait definitions might be too complex. However, TTRANS_R and TTRANSD_R can be of special interest when considering frequencies and least squares means to account for the direction of the dynamics. In contrast, trait definitions TBINA_R, TSEVCAT_R, and TSEVCAT41_R enable the identification of highly infectious herd states and thus, could act as an alert signal for the farmer. Trait TBIN_R can serve as a warning as well, but it does not account for the infectious level of the herd and displays a general disease state regarding DD. Consequently, using trait TBIN_R can result in a delayed alarm when the total number of affected animals is low to moderate but with a high percentage of cows with active stages (M2 and M4.1).

Incidence rates of DD are known to differ considerably between herds despite similar management conditions, particularly depending on the season (Koenig et al., 2005; Schöpke et al., 2013). A direct comparison of the DD health status of the analyzed herd with values from other studies in the literature is not justified because most studies only present the proportion of affected cows evaluated once during the individual study or evaluate M-stages reflecting severity. If DD severity

were differentiated, a comparison of the clinical appearance of different stages as well as of the transitions between different stages is mostly of limited relevance because, among studies, differences exist concerning treatment of affected animals, total observation time, or timespan between consecutive observations. The timespan between consecutive observations is important because a very dynamic development has been observed for DD (Holzhauer et al., 2008; Nielsen et al., 2012).

Our analyses revealed an association between age of heifer and susceptibility for DD. This might be explained by the fact that the older the animal, the longer its exposure to infection with DD, and thus the higher the risk of becoming infected. This result is in agreement with Capión et al. (2012), who identified age at calving to be an influencing factor for DD infection; those authors found that the higher the age at calving, the greater the odds of being intermittently or consistently infected with DD. Holzhauer et al. (2012) observed increasing DD prevalence with increasing age for grazing and nongrazing cows, which is in agreement with an age factor related to DD prevalence.

In our study, month of observation had a statistically significant effect on clinical stage of DD. This association fluctuated and was assumed to display the indi-

Table 3. Estimates of heritabilities (h^2) with standard errors (SE), additive (σ_a^2), permanent environmental (σ_{pe}^2), and residual (σ_e^2) variance for different dermatitis digitalis traits with repeated measurements in the linear univariate model

Trait ¹	No. of observations (no. of cows)	σ_a^2	σ_{pe}^2	σ_e^2	h^2 ($\pm$ SE)
TBIN_R	6,444 (729)	0.056	0.021	0.117	0.288 $\pm$ 0.101
TBINA_R	6,444 (729)	0.017	0.007	0.105	0.130 $\pm$ 0.051
TSEVCAT_R	6,444 (729)	0.106	0.027	0.266	0.266 $\pm$ 0.091
TSEVCAT41_R	6,444 (729)	0.129	0.057	0.332	0.250 $\pm$ 0.090
TTRANS_R	4,984 (691)	0.295	0.254	0.850	0.211 $\pm$ 0.069
TTRANSD_R	4,984 (691)	0.682	0.548	1.678	0.235 $\pm$ 0.077

¹Trait definitions are given in Table 1.

vidual clinical course of disease for this herd. Statistical significance of seasonal affects could not be identified, which might be due to the short observation period.

Genetic Parameters

Several studies presenting estimates of heritabilities for DD exist in the literature (e.g., van der Linde et al., 2010; Schöpke et al., 2013; Gernand and König, 2014). However, until now, none of the published studies has used M-stage scored records for a genetic-statistical analysis of DD. In the present study, heritability estimates were higher than those reported in the literature. However, it should be emphasized that for the present study, data from only one herd with a limited size was used; hence, standard errors were relatively elevated. The results from the present study should be viewed as a comparison between trait definitions that reach beyond a separation of affected and unaffected animals at a given point in time, and a well-established classification system for clinical stages and their succession over time is the basis for the trait definition. Notably high estimates of heritabilities were found for TCT-M2SC and TCTM2. The definition of these traits is based on the differentiation of heifer types considering the number of M2 events. The 3 types of heifers in question have been found to show different immune responses against *Treponema* spp. (Gomez et al., 2014). Accordingly, it seems that the predisposition of a cow to DD can be divided into the susceptibility to develop DD and the ability to acquire a degree of resistance after having been infected. For practical purposes, the identification of type III heifers is crucial because these animals apparently have a predisposition to chronic DD and consequently incur multiple infectious periods during their life. The painful active lesions can impair milk production (Gomez et al., 2015) and may lead to DD outbreaks if an accumulation of M2 lesions occurs in a herd. Therefore, individual management of type III animals seems to be important in controlling DD in endemically affected herds.

The trait definition of TTRANS resulted in a trait with a comparatively high heritability estimate. The TTRANS trait accounts for transitions between stages of consecutive observations and represents the dynamics of DD. However, TTRANS is sensitive to censoring and thus requires a standardized scheme of repeated scoring over a given time. The lowest estimates of heritability with values of 0.19 were found for TBIN and TREF. These trait definitions are similar to each other and to the traits analyzed in literature, which is reflected by the estimates of genetic parameters (e.g., Häggman and Juga, 2013; Schöpke et al., 2013). Extending the observation period for TBIN, compared

with TREF, did not result in a significant change of description of DD cases, because the traits in general only differed with regards to affected versus unaffected cases. Trait TREF was intended to represent the existing definition for DD similar to a reference trait. At first, the estimate of heritability for TREF appeared to be higher than values found in the literature. However, considering the standard error and the fact that only one person scored all animals, the difference of the estimate for TREF from the known range for DD heritabilities (0.05–0.14) was not significant, although our estimate was at the upper end of the range. The inclusion of repeated measurements for TBIN_R resulted in a noticeably higher estimate of heritability (0.28). This value was also higher than estimates from other studies using repeated measurements on DD (van der Linde et al., 2010; Häggman and Juga, 2013), which might be attributable to the relatively short time interval between the repeated measurements in our study. Although other studies are almost exclusively based on claw trimming data, where the timespan usually varies between 6 and 12 mo or longer, the design of the presented study allows repeated observation of the heifers within a short time span. This might lead to a better capture of the DD dynamics, because the lesion stages are known to be transient (Döpfer et al., 2012; Nielsen et al., 2012). Apparently there is no benefit from repeated measurements for the other traits, which might be explained by the trait definitions that already consider the repeated character of the information and by the relatively short time interval.

As the intention is to improve these traits through genetic selection, the evaluation of clinical stages seems to be very beneficial because a greater proportion of genetic variance can be captured when including this information in the DD trait definition. When focusing on DD, scoring stages of DD requires very little training for staff doing the scoring and it is not time consuming because DD stages may be scored while the animal is standing in the milking parlor. This especially applies to rotary parlors with external milking—a system of consistently increasing importance worldwide. It is recommended to monitor for DD lesions once per week in herds of up to 1,000 cows. In herds larger than 1,000 cows, an evaluation once a month for every pen would be a minimum. Furthermore, the comparative ranking of breeding values demonstrates that traits that include clinical stages can be used to select the most-resistant individuals to DD. The ranking also differentiates between average and undesired individuals, which might be important because little is known about the precise genetic association between disposition for DD stages and milk performance. Research conducted by Gomez et al. (2015) indicates that type III heifers and cows

seem to be high performers for milk yield, but at the same time, they are more likely to suffer from DD and consequently will show a comparatively higher loss in milk within the first lactation days than their herd mates.

The choice of models in the present study was influenced by the comparatively small size of the data set. For categorical variables such as the TSEVCAT traits, linear models had to be used because of convergence problems with categorical models. Analogously, not all traits, or classes of traits, could be analyzed in fully multiple models, and bivariate models had to be used. Overall, it is necessary to validate the results presented with a larger data set. Until then, the results found in this study have to be viewed with caution because they are based on only one herd. In addition, it is important to verify whether the described heritability estimates can be confirmed when using records of adult cows instead of exclusively heifers.

CONCLUSIONS

The novel aspect of our study on the genetic predisposition for DD is the application of the M-scale scoring system. This system has a widespread use in the veterinary field but not in the field of animal breeding. Results from this study showed higher heritability estimates than previously known reported and therefore support the hypothesis that genetic predisposition for DD as an infectious disease is higher than previously assumed. This finding indicates that using the M-scale for classification of DD lesions and the resulting types of animals allows for improved strategies for genetic selection as well as improved management strategies against DD. Traits derived from the knowledge of different DD stages could serve as an alert tool for management purposes. Scoring using the M-scale is not limited to veterinarians but can be performed by trained experts of various backgrounds. In addition, some of the traits not only enable detection of a predisposition for DD itself but also for DD chronicity. Consequently, research efforts in the field of genetic improvement of DD should be of great benefit. In summary, we consider the application of the M-scale scoring system to be a helpful tool for controlling DD in cattle production systems at the management level as well as for breeding purposes.

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