Estimation of genomic breeding values for the susceptibility to digital dermatitis in Holstein dairy cattle using improved methods for phenotyping

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Summary

Bovine Digital Dermatitis (BDD) has become one of the greatest plagues in cattle herds around the world. While the acute phase of this infectious disease is easily identified as lesions at the coronary band of the bovine hoof with the color and shape of strawberries, other stages of the disease, with the infectious agents encapsulated in the skin, are often neglected. In the present study, a total of 6,230 cows were scored repeatedly for disease status in seven large dairy herds in Eastern Germany, differentiating between healthy animals (M0), acute stages (M2), and encapsulated stages (M4). A randomly chosen subset (data set I) of 2,520 animals were genotyped using either a 50-K bead chip or a 10-K bead chip with SNP genotypes imputed to 50-K. Genotypes and phenotypes defined across all observations for each animal were used for single-step genomic best linear unbiased prediction (ssGBLUP). For sires, correlations with official breeding values from the German national system were favorable and significant for EBV for somatic cell score (0.15), longevity (0.20), and the German total merit index RZG (0.14). Genomic EBV for sires were validated in an independent data set (data set II) of 37,021 first, 27,961 second, and 18,293 third lactation disease status scores. However, this data set originated from scores as done by various hoof trimmers who typically only take M2 stages as 'diseased'. Sires were grouped from low to high susceptibility in five classes according to their genomic EBV from data set I. Sires were identified in data set II and their EBV class code was used in a statistical model for analysis of data set II. Accounting for herd-visit-date and days in milk, least-square means of BDD incidence for EBV classes of sires in data set II were 0.196, 0.191, 0.172, 0.171, and 0.147 for first lactations. Hence, a substantial decrease in the disease frequency can be found with increasing EBV for resistance. Results for later lactations were similar. The results show that even a relatively small data set may be used for prediction of meaningful genomic EBV under the condition that phenotyping is highly accurate and the genetic architecture of the trait favors genomic predictions.
Keywords: digital dermatitis, susceptibility, genomic prediction, ssGBLUP, validation

Introduction

Bovine Digital Dermatitis (BDD) is an infectious disease located at the bovine hoof. It can be defined as an infection of the digital and/or interdigital skin with erosion, mostly painful ulcerations and/or chronic hyperkeratosis/proliferation (ICAR, 2015). BDD was first described by Cheli and Mortellaro (1974) in Italy, later reports documented a spreading of

this infectious disease across Europe and also in North America and further parts of the world. Apart from the strong effect on the well-being of the affected animal, economic losses caused by the disease were estimated as 133 US $ per case and, given an incidence of 25 %, and totaling 1.1 Billion Dollar in Europe and the USA (Zinicola et al., 2015).

BDD is caused by an infection with bacteria of the genus *treponema* although participation by other species of bacteria cannot be ruled out (Döpfer et al., 1997). The disease has two main characteristics that are of great importance for housing and management of cattle: a) the infectious agents can be responsible for acute, infectious forms but can also encapsulate in the skin causing non-infectious, 'dormant' forms of the disease, and b) the disease up to now is not easily cured as chemical, systemic, and topical antibiotic or aseptic treatments only lead to partial eradication of the infectious agents. Döpfer et al. (1997) developed a scheme for clinical diagnosis of BDD that comprises five stages, characterized in brief by M0 = healthy skin, M1 = small lesions, not painful, M2 = large ulcerative lesions, strawberry like in color and shape, M3 = healing lesions with dry surface, M4 = chronic stage, *treponema* are encapsulated, often with proliferative or hyperkeratotic appearance of lesions, and M4.1, chronic stage, including an M1 lesion. It is important to note that M4 lesions can undergo a transition to M4.1 as well as M2 and vice versa.

As only M2 lesions are easily identified by their shape and color, it has to be assumed that in most genetic studies, especially studies based on records taken at time of hoof trimming, only M2 lesions are usually coded as 'affected', resulting in a form of censoring as only fractions of affected cattle are identified. Genetic studies applying quantitative genetic statistical methods (e.g. König et al., 2008; van der Linde et al., 2010; Swalve et al., 2011) commonly report low to moderate heritabilities in the range of 0.05 to 0.29, depending on parity and especially depending on the choice of the model, linear or threshold. Hence, it was concluded that genetic selection could improve resistance to BDD. Schöpke et al. (2015) estimated genetic parameters based on phenotypes scored with the M-stage system and found substantially increased heritabilities in the range of 0.19 to 0.52. Genomic studies would be of interest but have been scarce up to now (see Scholey et al., 2012; van der Spek et al., 2015; Wu et al., 2016) and are hampered by limitations in size of the available datasets and/or in the accuracy of phenotyping.

The aim of the present study was to establish a sample of genotyped cows that are phenotyped repeatedly for BDD status based on the M-stage system thus increasing the precision of phenotyping and estimate genomic EBV for the susceptibility to BDD with a validation of the EBV for sires using a second, independent data set.

Material and Methods

The project was established as a sub-project with the project KUH-L (Establishing a female reference for Holsteins in Germany). The KUH-L project consisted of genotyping of 20,000 first lactation cows in 56 large contract herds that had implemented a wide range of recording of phenotypes. Lactations were initiated between 2014 and 2016. Within these herds, seven herds were selected for the BDD project according to feasibility, i.e. mostly according to the existence of an external rotary parlor to allow for easy scoring of cows standing in the milking parlor. Of the seven herds, five had external rotary parlors, one herd had a rotary parlor and an additional herringbone parlor and one herd had a side-by-side parlor. Within the KUH-L project, first lactation cows were genotyped at random within all 56 herds. Within the BDD project, carried out between October 2015 and April 2016, all cows present at milking

were assessed for BDD status repeatedly with the aim of recording scores three times with an interval of three weeks between scoring. A total of 8,148 cows were scored for the stages M0, M2, and M4 along with scoring for chronicity and proliferation. After edits for completeness, merging with calving data and keeping only cows that were scored at least twice thus attempting to cover the dynamics of the disease , 6,230 cows from all parities remained. This data set was merged with the KUH-L genotype data base which yielded 2,520 cows with genotypes and phenotypes (data set I) of which 1,197 cows were in first lactation and 1,073 cows were in their second lactation. A further 250 cows belonged to parities 3 to 5 as these cows had been genotyped as dams of KUH-L animals.

For the present study, traits across repeated observations were defined as TBIN with 0 as the score for M0 (healthy) and 1 otherwise (scores M2 and M4). Scoring as commonly done would have been to score healthy (M0) vs. acute infections (M2). This trait was denoted as TBINA. Raw means for TBIN were 42.7 % (0) and 57.3 % (1) while for TBINA, raw means were 88.7 % (0) and 11.3 % (1). The raw means thus underline the importance of identifying M4 stages. Means for TBIN for all seven herds in were 57.8, 83.0, 59.3, 45.6, 55.7, 41.2, and 60.5 % while for TBINA the means were 10.6, 49.6, 5.8, 3.1, 14.2, 15.4, and 9.8 % which point to an outbreak of BDD in herd #2 as this herd had an increased frequency of acute M2 cases.

As a preparatory step, conventional estimation of heritabilities using a threshold animal model and the ASReml 3.0 software (Gilmour et al., 2009) was performed for all 6,230 cows with repeated phenotypes. As fixed effects, herd, parity, and days in milk were considered. Estimates of heritability were 0.134 and 0.054 for TBIN and TBINA, respectively.

Data set I (2,520 cows) was used for ssGBLUP estimation of breeding values for TBIN. Computations were carried out using the BLUPF90 suite of programs as suggested by Misztal (1999) and for ssGBLUP by Aguilar et al. (2014). A threshold model using Gibbs sampling was applied and comprised of herd, parity and stage of lactation as fixed effects. Genomic information, i.e. SNP genotypes, were used for all cows in the data set. A total of 2,004 cows had been genotyped with the Eurogenomics-10-k array while 516 cows were genotyped with the Illumina 54-K array. All genotypes for 10-k animals were imputed to 54-k. Genotypes not in Hardy-Weinberg equilibrium and with MAF < 0.05 were excluded leaving 41,778 SNP for TBIN. For pedigree relationships, all available pedigree information as supplied by the national computing centre vit were used. Genomic EBVs for sires were estimated in a second step from SNP estimates of the ssGBLUP estimation. This was done to mimic a situation in which SNP estimates later could be used on a national basis for any animal instead of restricting the analysis to animals within the KUH-L project or the BDD-subproject. Genomic EBV were standardized to have a mean = 100 and a standard deviation of 12 and were converted so that high numeric values were associated with a high resistance to BDD. For 720 domestic sires for which genotypes were available within the KUH-L-project, EBVs were correlated to the official national EBV for various traits.

For validation, a second data set (data set II) was established that comprised scoring of BDD at time of hoof trimming in years 2009 to 2016 by various hoof trimmers in 31 contract herds from the same region as in the BDD-subproject. Only contract herds that had supplied at least two trimming events were considered. The total number of herd-visit-dates was 259, thus 8.4 trimming events had been supplied by the herds on average. Differentiated by parity, a total of 37,021 first, 27,961 second, and 18,293 third lactation disease status scores could be used. Genomic EBV of domestic sires were grouped in classes from low to high resistance to BDD. Data were analyzed separately by parity for the influence of sires' EBV class in a mixed model considering herd-visit-date and days in milk as fixed effects along with sires'

EBV for BDD class and also accounting for repeated observations by fitting the cow as a random effect. As incidence rates for TBIN = 1 were high, a linear model was used for simplicity and LSMEANS for sires' EBV class were estimated using HPMIXED of SAS.

Results and Discussion

With ssGBLUP and using data set I, the heritability for TBIN was estimated as 0.33. Correlations between genomic EBV for BDD and official national breeding values for 720 domestic sires only were significantly different from zero for Total Merit (0.14), Somatic Cell Score (0.14), and longevity (0.20). Given an assumed theoretical repeatability of the genomic EBV for BDD resistance (Trait TBIN) of around 0.30 and the repeatability of the national EBV of around 0.70, these correlations between EBV appear to be at the upper limit for strongly correlated traits.

Results from the validation using the independent data set II are in Table 1. Least squares means BDD status (healthy, affected) are shown for classes of genomic breeding values for sires separately for parity. The results reveal a strong decrease in the incidence of BDD with increasing genomic EBV class for resistance.

Genomic EBV for sires were also taken directly from the ssGBLUP solutions instead of deriving them from SNP solutions. The results pertaining to correlations as well as for estimating LSMEANS of EBV classes in data set II were nearly identical with the results reported here.

Table 1. Least Square Means for BDD status for genomic EBV class from low to high resistance for sires as estimated from data set I under precise phenotyping in data set II consisting of hoof trimmers' scores for status of Bovine Digital Dermatitis (0 = healthy, 1 = affected).

		Parity		
Class #	gEBV range	1	2	3
1	< 85	0.196^{a}	0.183^{a}	0.161^{a}
2	86 – 95	0.191^{a}	0.187^{a}	0.149^{ac}
3	96 – 105	0.172^{b}	0.157^{b}	0.129^{bd}
4	106 – 115	0.171^{b}	0.154^{b}	0.136^{bcd}
5	> 115	0.147^{c}	0.153^{b}	0.125^{d}

LSMEANS with differing superscripts are significantly different at $P < 0.01$

Conclusions

The results show that even a relatively small data set may be used for prediction of meaningful genomic EBV under the condition that phenotyping is highly accurate and the genetic architecture of the trait favors genomic predictions.

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