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Genome-wide association study for claw disorders and trimming status in dairy cattle

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ABSTRACT

Performing a genome-wide association study (GWAS) might add to a better understanding of the development of claw disorders and the need for trimming. Therefore, the aim of the current study was to perform a GWAS on claw disorders and trimming status and to validate the results for claw disorders based on an independent data set. Data consisted of 20,474 cows with phenotypes for claw disorders and 50,238 cows with phenotypes for trimming status. Recorded claw disorders used in the current study were double sole (DS), interdigital hyperplasia (IH), sole hemorrhage (SH), sole ulcer (SU), white line separation (WLS), a combination of infectious claw disorders consisting of (inter-)digital dermatitis and heel erosion, and a combination of laminitis-related claw disorders (DS, SH, SU, and WLS). Of the cows with phenotypes for claw disorders, 1,771 cows were genotyped and these cow data were used for the GWAS on claw disorders. A SNP was considered significant when the false discovery rate ≤ 0.05 and suggestive when the false discovery rate ≤ 0.20. An independent data set of 185 genotyped bulls having at least 5 daughters with phenotypes (6,824 daughters in total) for claw disorders was used to validate significant and suggestive SNP detected based on the cow data. To analyze the trait "trimming status" (i.e., the need for claw trimming), a data set with 327 genotyped bulls having at least 5 daughters with phenotypes (18,525 daughters in total) was used. Based on the cow data, in total 10 significant and 45 suggestive SNP were detected for claw disorders. The 10 significant SNP were associated with SU, and mainly located on BTA8. The suggestive SNP were associated with DS, IH, SU, and laminitis-related claw disorders. Three of the suggestive SNP were validated in the data set of 185 bulls, and were located on BTA13, BTA14, and BTA17. For infectious claw disorders, SH, and WLS, no significant or suggestive SNP associations were detected. For trimming status, 1 significant and 1 suggestive SNP were detected, both located close to each other on BTA15. Some significant and suggestive SNP were located close to SNP detected in studies on feet and leg conformation traits. Genes with major effects could not be detected and SNP associations were spread across the genome, indicating that many SNP, each explaining a small proportion of the genetic variance, influence claw disorders. Therefore, to reduce the incidence of claw disorders by breeding, genomic selection is a promising approach.

Key words: association study, hoof lesion, Holstein-Friesian

INTRODUCTION

Breeding goals in dairy cattle focus not only on production traits, but increasing emphasis is also on health and durability traits (Miglior et al., 2005). Claw disorders are common in dairy cattle with a prevalence of more than 70% (e.g., Manske et al., 2002; van der Waaij et al., 2005). Claw disorders are important because of welfare issues (Enting et al., 1997) and economic impact (Bruijnis et al., 2012a,b). A trait currently not considered but of interest is the need for claw trimming. Some cows need more claw trimming than others and van der Spek et al. (2013) showed that the need for trimming, or "trimming status," is a heritable trait. High scores for trimming status reflect that daughters of a bull need more trimming, which is unfavorable and which is positively correlated with increased occurrence of claw disorders (van der Spek et al., 2013).

Genetic selection for reduced claw disorders is difficult because the disorders are not routinely recorded. Indicator traits for claw disorders, which may be more accurate and easier to obtain, are lameness (Laursen et al., 2009; Weber et al., 2013) and feet and leg conformation traits (van der Waaij et al., 2005; van der Linde et al., 2010). Scores for feet and leg conformation are routinely collected in most breeding schemes. Previous studies have detected QTL for lameness and feet and leg conformation (Ashwell et al., 1998a,b; Schrooten et al., 2000; Boichard et al., 2003; Buitenhuis et al., 2007). However, to the best of our knowledge, no link-

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age or GWAS have been reported on claw disorders. The bovine genome sequencing and the emergence of high-throughput genotyping technologies have made it possible to perform genome-wide association studies (**GWAS**, e.g., Tellam et al., 2009). Genome-wide association studies enable the detection of genetic variants associated with a particular trait or disease, using dense genome-wide markers, also known as SNP (Hirschhorn and Daly, 2005; Matukumalli et al., 2009). Performing a GWAS might add to a better understanding of the development of claw disorders and the need for trimming, when the underlying genetic background can be identified. A GWAS is a good method to detect SNP associations, but some of the results can be false positives. False-positive associations occur especially due to population structure (Goddard and Hayes, 2009). Even if population structure is accounted for in the analysis and stringent significance thresholds are used, false-positive results might occur due to the high chance of some unaccounted for data structure in livestock populations given the large number of tested SNP (Hayes, 2013). To eliminate false positives, associations detected in a GWAS study should therefore be validated in an independent population (Chanock et al., 2007; Hayes, 2013). Therefore, the aim of the current study was to perform a GWAS on several claw disorders in dairy cows and to validate the results for claw disorders based on an independent data set. In addition, a GWAS will be performed on the trait trimming status using daughter yield deviations (**DYD**) of bulls.

MATERIALS AND METHODS

Analyses were performed based on 2 data sets: one with genotyped cows and one with genotyped bulls. The data set with cows was based on genotyped cows, which also have phenotypes for claw disorders. These data will be referred to as the cow data. The data set with bulls was based on genotyped bulls that have daughters with phenotypes for claw disorders. Phenotypes of cows adjusted for systematic environmental effects were used to calculate the DYD for bulls. Phenotypes from genotyped cows used in the cow data were dropped from calculating DYD for bulls. In this case, no overlap exists in phenotypes between the 2 data sets. The DYD data of bulls were used to validate significant or suggestive SNP detected for claw disorders using the cow data and will be referred to as the bull validation data. The trait trimming status was analyzed with the bull data without removing phenotypes of genotyped daughters. The DYD were calculated and used as a phenotype for bulls. These data will be referred to as the trimming status data.

Phenotypic Data on Claw Disorders

After removing records of cows with both parents unknown or with 2 different trimming records on the same date (n = 6,374 records), the data set contained 50,238 cows. The cows descended from 3,603 sires with an average of 14 daughters per sire. Phenotypes on claw disorders were collected by 6 professional claw trimmers, from January 2007 through February 2012, during routine visits on 574 dairy farms in France. The farmer decided which cows were to be trimmed, and as a result, not all cows present in a herd were trimmed. Information on parity, stage of lactation, and pedigree was available on all cows present in a herd at the moment of trimming (including the nontrimmed cows). Of the 50,238 cows, 20,474 had one or more claw trimming records and in total 29,994 claw trimming records were available. Trimming records were repeated within and across lactations; 69% of the cows had 1 trimming record, 20% had 2 trimming records, and 11% had 3 or more trimming records. Claw disorders were recorded for the hind legs and scored as a binary trait: 0 = no claw disorder, 1 = claw disorder in at least one hind leg. Recorded claw disorders used in the current study were double sole (**DS**), interdigital hyperplasia (**IH**), sole hemorrhage (**SH**), sole ulcer (**SU**), white line separation (**WLS**), and a combination of infectious lesions (**DER**) consisting of (inter-)digital dermatitis and heel erosion. The trimming status trait indicates whether a cow was trimmed (score 1) or not trimmed (score 0) during a visit by the claw trimmer on a specific date. The claw disorders and the trait trimming status are explained in more detail by van der Spek et al. (2013). van der Spek et al. (2013) showed moderate to high genetic correlations between laminitis-related claw disorders (DS, SH, SU, and WLS). Therefore, 4 laminitis-related claw disorders were combined by adding up the scores for the individual traits, resulting in a trait **LAMIN**, with scores ranging from 0 (no claw disorder) to 4 (all 4 claw disorders present). For trimming status, 50,238 cows with phenotypes were available, and for claw disorders 20,474 cows with phenotypes were available.

Genotypic Data

The DNA was extracted from blood or semen samples. Herds with at least 10% of the cows having claw disorders in previous years were identified and all cows on these herds trimmed in the second half of 2012 or first half of 2013 were sampled. Subsequently, all cows with trimming records available were genotyped. Genotypes of bulls were already available and were included when the bull had daughters with trimming records. In total, 1,771 Holstein-Friesian cows and 506 Holstein-Friesian