Genomic analyses of claw health traits in Holstein cattle

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Summary

Claw lesions are one of the most impactful health issues in dairy cattle. Our objectives were to compare various genetic and genomic evaluation methods, to identify the most suitable one for the evaluation of seven claw lesion traits and to identify QTLs having a strong influence on these traits. 46 787 cows with own performances (including 7 333 genotyped cows) and their ancestors were analyzed with BLUP, GBLUP, BayesC and single-step genomic BLUP (SSGBLUP), in a validation study. QTLs were detected using a BayesC approach. Among all evaluation approaches, SSGBLUP performed best in terms of accuracy and control of bias. However, accuracies of all evaluation approaches were generally low. In total, over all lesion traits, 161 QTLs with strong evidence were found, including 5 with major evidence and 6 overlapping QTL regions for at least two traits. Genomic approaches and the use of QTL seem promising for the genetic evaluation of claw health traits.

Keywords: claw health, genomic evaluation, QTL, validation study

Introduction

Claw lesions are one of the most impactful health issues in dairy cattle, both economically and in terms of welfare. Therefore, improving claw health is of major importance. Claw health traits have low heritabilities and hence their genetic evaluation lacks precision: there is a strong need for genomic evaluation of claw health traits. The objectives of this study were to compare various evaluation methods, to identify the most suitable one for the evaluation of claw health traits and to identify QTLs having a strong influence on these traits.

Material and methods

Data

The phenotypes used were trimming information recorded from April 2014 to February 2017 on French Holstein cows by professional trimmers who followed the same training. Lesions considered were Digital Dermatitis (DD), Heel Horn Erosion (HHE), Interdigital Hyperplasia (IH), Sole Hemorrhage Circumscribed (SHC), Sole Hemorrhage Diffused (SHD), Sole Ulcer (SU) and White Line Fissure (WLF), as described in (Croue *et al.*, 2017). After data editing (as described in Croue *et al.* (2017), with in addition a minimum of 100 recorded trimmings per trimmer x year combination required), 46 787 individual cows remained, each cow having a single phenotype. A cow was given a score of 1 for a lesion if the lesion was observed by the trimmer, 0 if it was not. Pedigree was traced back 3 generations and included 117 916 animals.

Genotypes were extracted from the French genomic database. Animals were genotyped (or their genotype was imputed from their LD genotype) on the Illumina Bovine SNP50 BeadChip. A regular quality control was performed. In the end, 43 801 SNP were used. 7 333 phenotyped cows and 2 360 sires had genotypes available. Among them, 7 122 females and 1 147 sires were genotyped by the EVOLUTION breeding company.

Methods

Four different evaluation approaches were compared: a conventional BLUP, two two-step genomic methods: GBLUP (VanRaden, 2008) and BayesC (Habier *et al.*, 2011), with a proportion π of one percent of the total SNPs considered to have an effect, and single-step genomic BLUP (SSGBLUP), as described by Misztal *et al.* (2009) and Christensen and Lund (2010).

Pre-adjusted performances were calculated using the BLUP evaluation, in a multitrait context, including a supplementary trimming status traits, as described as scenario 3 in (Croue *et al.*, 2017) and transformed into YDs (for genotyped cows) and DYDs (for genotyped sires of non-genotyped cows). Both GBLUP and BayesC used YDs and DYDs as phenotypic records, weighted by their equivalent number of performances. The BLUP and SSGBLUP evaluations were run for genotyped and non-genotyped animals, on phenotypic observations, with the model described in scenario 1 of (Croue *et al.*, 2017), with heterogeneous residual variances depending on a random trimmer*year effect. All four approaches were run in a single-trait context.

All public phenotypes and genotypes were used for BLUP and SSGBLUP and only animals genotyped by the breeding company EVOLUTION were kept in the reference population for GBLUP and BayesC.

QTL detection was run on YDs and DYDs, as described above, weighted according to their equivalent number of performances, for the whole EVOLUTION reference population. We used a BayesC approach, assuming that 1% of the SNPs had an effect at each iteration: i.e. 438 SNPs were select at each iteration. The Bayes Factor (Schurink *et al.*, 2012) was used to assess the degree of association between each SNP and the traits. BF was transformed to logBF (computed as twice the natural logarithm of BF) in order to gain clarity for visual appraisal of QTL.

SNPs were grouped into QTL regions as described in Michenet *et al.* (2016), except that SNPs close to a QTL with strong evidence (logBF>=6) were included in the QTL region if they had logBF>=2, according to the thresholds of significance proposed by Kass and Raftery (1995).

The validation population consisted of the 20% youngest EVOLUTION animals (cows with genotypes and own performances). All cows born after the oldest validation cow had their phenotypes deleted when the validation evaluation was run. There were 1 654 cows in the validation population. Evaluation approaches were compared based on evaluation accuracy (correlation between EBVs and YDs) and evaluation bias (regression coefficient of YDs on EBVs). Standard errors of bias and accuracy were estimated using bootstrap with 1000 samples.

Results and discussion

Comparison between evaluation methods

Table 1. Accuracy (correlation) and bias (slope of the regression), for two of the traits. SE in parenthesis.

	BLUP		GBLUP		BayesC		SSGBLUP	
Lesion[1]	Accuracy	Slope	Accuracy	Slope	Accuracy	Slope	Accuracy	Slope
DD	0.05 (0.02)	0.47 (0.21)	0.08 (0.02)	0.38 (0.11)	0.09 (0.03)	0.53 (0.15)	0.12 (0.02)	0.74 (0.16)
SU	0.07 (0.04)	0.92 (0.35)	0.12 (0.03)	0.53 (0.13)	0.10 (0.03)	0.66 (0.17)	0.12 (0.03)	1.03 (0.24)

[1]DD: Digital Dermatitis; SU: Sole Ulcer

Accuracies were very low for all evaluation approaches. Generally, genomic approaches allowed for slightly higher accuracies than BLUP. Among all the genomic approaches, SSGBLUP had the highest accuracies. Bias was generally higher using GBLUP and BayesC than using BLUP, indicating a higher bias with two-step genomic approaches. SSGBLUP generally had a better control of bias than other genomic approaches and even outperformed BLUP for most of the traits. However, these are only tendencies, as standard errors were high.

QTL detection

QTLs were detected for all of the traits. 40 QTL with strong (logBF>=6) evidence were found for DD, 28 for HHE, 11 for SHC, nine for SHD, 31 for IH, 21 for WLF and 21 for SU. Two of the QTL found for DD and IH and 1 of WLF had major evidence (logBF >= 10), see Table 2.

Table 2. Major evidence (logBF>=10) QTLs detected.

Trait[1]	Chromosome	Region start (Mb)	Region end (Mb)	Peak position (Mb)	Peak logBF
DD	17	33.402	33.496	33.496	10.8
DD	27	39.519	39.612	39.519	10.2
IH	1	90.378	90.562	90.561	10.5
IH	14	11.601	11.601	11.601	10.3
WLF	11	37.261	37.733	37.733	10.1

[1]DD: Digital Dermatitis, IH: Interdigital Hyperplasia, WLF: White Line Fissure

Six QTL regions overlapped for two of the traits (see table 3). On the common QTL region for DD and IH on chromosome 19, nine genes were reported. Two genes were also reported on the strong evidence QTL of IH on chromosome 1, one on the strong evidence QTL of IH on chromosome 14. However none of these genes had functions known to be linked to claw health.

Table 3. Overlapping QTL regions among two claw health traits.

Traits[1]	Chromosome	Overlapping region[2]	Peak position trait 1[2]	Peak position trait 2[2]
SHC-SU	4	28.572-28.622	28.847	28.622
SHD-SU	11	6.508-6.518	7.118	5.290
DD-IH	4	24.150-24.210	24.150	24.210
DD-IH	19	28.546-28.546	28.546	28.546
DD-WLF	10	101.760-101.916	102.211	101.792
HHE-IH	22	42.791-42.791	42.791	43.862

[1]SHC: Sole Hemorrhage Circumscribed, SU: Sole Ulcer, SHD: Sole Hemorrhage Diffused, DD: Digital Dermatitis, IH: Interdigital Hyperplasia, WLF: White Line Fissure, HHE: Heel Horn Erosion

[2]Positions are in MegaBases

An important number of QTL regions were also reported on similar traits in the literature (Cole *et al.*, 2011; Wu *et al.*, 2013; Wu *et al.*, 2016).

Conclusion

QTL detection on claw health traits revealed that 161 QTLs have strong evidence of being associated to these traits. Five of these QTLs have major evidence and 6 of the QTL regions identified impact at least two of the traits. Some of the identified regions were also reported in the literature. Although this detection requires to be confirmed on a larger reference population, considering QTL in the evaluation of health traits seems promising.

Various genetic and genomic evaluation approaches were compared for the evaluation of claw health traits. High standard errors make the interpretation of results difficult, but the validation study suggests that SSGBLUP is the most suitable evaluation approach for these traits.

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