

Evaluating Male Fertility in Brown Swiss Cattle Combining Multiple Sources of Information

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Abstract

Improving reproductive performance remains one of the major goals for the dairy industry worldwide. Bull fertility has been recognized as an important factor influencing reproductive success in dairy cattle. In this study, we investigated bull fertility in the Italian Brown Swiss dairy cattle population based on extensive records. The data set included a total of 397,926 breeding records from 1,228 bulls and 129,858 lactating cows between first and fifth lactation from 2000 to 2019, and all bulls have a genomic analysis on 454k single nucleotide polymorphisms (SNP). We estimated sire conception rate using only factors related to the bulls, our analyses revealed that there is a substantial variation in conception rate among Brown Swiss bulls, with more than 20% conception rate difference between high-fertility and low-fertility bulls and cross-validation analyses achieved predictive correlations equal to 0.30 for sire conception rate. The analysis included alternative whole-genome scans and gene-set analyses identified two genomic regions, located on BTA6 and BTA26 that showed marked non-additive effects. These regions harbor genes, such as *WDR19* and *ADGRA1*, that are directly involved in male fertility, including sperm motility, acrosome reaction, and embryonic development. The analysis to evaluate association between runs of homozygosity (ROH) and male fertility showed four different ROH regions located on chromosomes 6, 10, 11, and 24 were significantly overrepresented in low-fertility bulls. The predictive performance of the linear kernel-based regression models fitting the entire set of SNP markers exhibited predictive correlations around 0.19. Interestingly, the inclusion of two major non-additive markers as fixed effects achieved predictive correlations around 0.32. Moreover, including in the estimation also a new knowledge on the effect of ROH on the male fertility could improve reliability of prediction.

Key words: Bull fertility, Genomic analysis, Genomic Inbreeding, Brown Swiss cattle

Introduction

Fertility is a critical factor for profitable dairy farming, but challenges persist in achieving optimal reproductive performance in dairy herds, leading to economic losses (Abdollahi-Arpanahi et al., 2017). While female reproductive traits have been a focus in breeding programs, male fertility, which also plays a significant role in pregnancy success, has been somewhat overlooked (García-Ruiz et al., 2016; Toledo-Alvarado et al., 2017). Traditional laboratory methods are used to assess bull fertility based on semen characteristics. However, these methods often fall short in accurately predicting a bull's true fertility, which can be better estimated using field records, such as cow insemination and

pregnancy data. Some national evaluations exist for female fertility traits, but male fertility assessments are usually conducted by individual breeding organizations and may not be widely available (Stahlhammar et al., 1994; Kastelic and Thundathil, 2008; Han and Peñagaricano, 2016). The Brown Swiss breed, with a substantial global presence, holds great importance in the dairy industry. This study aims to investigate bull fertility in the Italian Brown Swiss dairy cattle population by examining cow field records and evaluating statistical models for pregnancy success and sire conception rate (SCR), focusing on factors related to the bull (Kuhn and Hutchison, 2008; Kuhn et al., 2008). The study also assesses model predictive ability through cross-validation techniques.

Materials and Methods

We meticulously analyzed a comprehensive dataset, encompassing 397,926 breeding records from 1,228 bulls and 129,858 lactating cows over a two-decade period (2000-2019). This extensive dataset provided a valuable resource for our investigation. Moreover, for all bulls the genotype based on 454k SNPs were available. The fundamental metric we employed to gauge bull fertility was the Sire Conception Rate (SCR).

Sire conception rate was estimated using different factors closely related to the fertility of the bull. These factors included the age of the bull, inbreeding levels, mating inbreeding, the AI company involved, and the year of insemination (Kuhn and Hutchison, 2008a; Kuhn et al., 2008b). Additionally, our model incorporated genetic components, both additive and non-additive, and other influential variables. These variables encompassed the number of lactations, days in milk, AI company-specific effects, and the effects associated with different herd-year-season conditions:

$$SCR = 100 \times \left(\begin{array}{l} \hat{\beta}_5 \times Age_{Bull} + \hat{\beta}_6 \times Age_{Bull}^2 + \hat{\beta}_9 \\ \times Inbreeding_{Bull} + \hat{\beta}_{10} \times Inbreeding_{Bull}^2 \\ + AI_{company_year+Bull} \end{array} \right)$$

The solutions for the linear and quadratic effects for age and inbreeding of the bull, namely $\hat{\beta}_5$, $\hat{\beta}_6$, $\hat{\beta}_9$ and $\hat{\beta}_{10}$, and the solutions for the random effects AI company_year were all obtained from the model used to evaluate cow pregnancy success. The proportion of the total variation in SCR due to additive genetic effects was estimated using a classical animal model with SCR as response variable and the kinship matrix constructed using pedigree information. Finally, male fertility evaluations were assessed using the Spearman's rank correlation coefficient on the cross-validation test (Pacheco et al., 2021).

Whole-genome sequencing for additive and no additive effect were conducted to assess the impact of additive and non-additive effects on

service sire fertility at a genomic level. A two-step mixed-model approach was employed, involving a model with fixed and random effects for SCR records and the evaluation of individual SNP effects for various genetic effects using a regression approach (Nicolini et al., 2018; Pacheco et al., 2022).

We evaluated the feasibility of predicting bull fertility in Brown Swiss using genomic data under different scenarios. To assess the predictive power of the entire high-density SNP dataset, a whole-genome prediction model was employed using two model one with just a polygenic effect and the second including two SNPs (identify with genome scan on the non-additive effect) were coded as 0 or 1, to represent the effect of having at least one or two copies of the B allele and were fitted as fixed effects in an alternative whole-genome prediction models. The predictive ability of two models was assessed by 5-fold cross-validation. Runs of homozygosity (ROH) analysis was conducted using PLINK software (Chang et al., 2015). The genome was scanned for consecutive homozygous SNPs. Various characteristics of ROH segments were calculated, including the total number of segments, average and maximum segment length, and the number of SNPs within each ROH (Pacheco et al., 2023). The bull population was divided into low- and high-fertility groups based on SCR (Sire Conception Rate). The level of homozygosity, measured as total ROH length, was compared between these groups. To explore potential genetic factors related to male fertility, genomic regions with overlapping ROH segments were examined.

Results & Discussion

The study unveiled a myriad of insights into the factors influencing male fertility in Brown Swiss cattle.

Sire Conception Rate

The Sire Conception Rate (SCR) reflects male fertility, with a 1-point difference

representing a 1% change in Conception Rate (CR). SCR values varied significantly among the 1,228 Italian Brown Swiss bulls, with a 20% difference between high and low-fertility bulls. Notably, 20% of this variation was attributed to additive genetic effects. A positive correlation of +0.35 (**P < 0.01) was observed between Italian and American SCR values for 44 bulls evaluated in both countries.

We then assessed the predictive performance of different models for SCR, revealing correlations between SCR and bull's CR ranging from 28.2% to 30%. Variables like milk yield (MY), AI company within a specific year (AI company_year) and inbreeding of the potential embryo (Inbreeding mating) influenced these correlations.

Genomic Non-Additive Effects

Whole-genome scans divulged the presence of two genomic regions on BTA6 and BTA26 with substantial non-additive effects on male fertility. These regions encompassed genes like *WD Repeat Domain 19 (WDR19)* and *Adhesion G protein-coupled receptor A1 (ADGRA1)*, with known direct implications for key aspects of male fertility, such as sperm motility, acrosome reaction, and embryonic development (Figure 1).

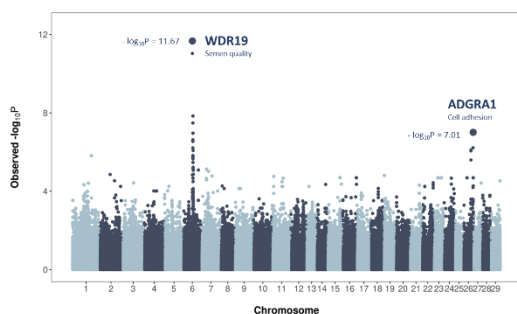


Figure 1. The Manhattan plot illustrates the significance of recessive effects and their relevance to male fertility in Italian Brown Swiss cattle.

Enhancing Genomic Predictive Accuracy

Figure 2 shows the predictive ability of linear kernel-based regression models fitting the whole-genome model, ‘IT: Polygenic’, and the

‘IT: Polygenic + Major Markers’ model that includes two significant recessive SNPs fitted as fixed effects. The ‘IT: Polygenic’ model exhibited an average correlation between observed and predicted SCR values of 0.19, and a mean-squared error of prediction (MSEP) equal to 22.11. The ‘IT: Polygenic + Major Markers’ model delivered an average predictive correlation equal to 0.32 and MSEP equal to 20.34. Notably, the model predictive ability was largely improved by including the two markers with large effect, representing an increase in predictive correlation of about 68%. Pacheco et al. (2022) reported that these significant non-additive markers are near genes directly involved in male fertility, including sperm motility, acrosome reaction, and embryonic development.

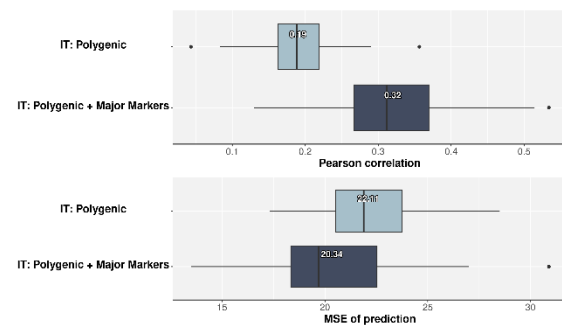


Figure 2. Genomic predictions within the Italian Brown Swiss population using alternative whole-genome predictive models. Predictive correlation (top) and mean squared error of prediction (bottom) were calculated using 5-fold cross-validation with 10 replicates. Light blue boxes represent the ‘IT: Polygenic’ model that includes the whole SNP dataset (481,839 SNPs). Dark blue boxes represent the ‘IT: Polygenic + Major SNPs’ model that includes two major SNP markers fitted as fixed effects.

Runs of Homozygosity

The study highlighted the detrimental impact of inbreeding on male fertility in Brown Swiss cattle. Four regions of homozygosity located on chromosomes 6, 10, 11, and 24 were significantly overrepresented in low-fertility bulls. The results underscored the complexity of factors influencing male fertility and the potential of combining multiple sources of

information to enhance our understanding of this critical aspect of cattle breeding.

Conclusions

This study delves into the male fertility of Italian Brown Swiss dairy bulls using extensive cow field records and genomic data. It uncovers substantial variability in sire conception rates and successfully demonstrates the potential of assessing bull fertility directly from confirmed pregnancy records. The research reveals insights into genetic and genomic factors influencing male fertility, highlighting non-additive genetic effects, relevant genomic regions, and the impact of inbreeding. Ultimately, this study provides a foundation for refining management and selection strategies in the dairy industry and offers valuable contributions to understanding male fertility in Brown Swiss cattle, with potential for future enhancements in this field.

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