Exploring the inclusion of genomic information and metafounders in Latxa dairy sheep genetic evaluations

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ABSTRACT

The availability of genomic marker panels has made possible more precise estimates of breeding values. Sheep breeding programs are implementing genomic selection. In Latxa dairy sheep breed, a previous study using pre-corrected data and a small number of genotyped animals did not show a clear advantage of genomic selection. The objective of the present study was to ascertain the possible benefits of GS for the Latxa breed based on more data than before and using better tools, in particular single-step genomic BLUP using metafounders to model missing pedigree. Goodness of prediction of pedigree and genomic evaluations was analyzed by cross-validation comparing predictions of young rams using whole and partial (truncated) data sets. The results showed that with the current available data, genetic and genomic evaluations have the same accuracy. Contrary to the previous study, predictions were nearly unbiased, which shows the advantage of using single-step genomic BLUP. However, genomic information did not yield more precise evaluations. This could be explained by the small number of sibs in the young rams.

Key words: genomic selection, cross-validation, Latxa breed, dairy sheep

INTRODUCTION

The Latxa is a dairy sheep breed from the Western Pyrenees. Two strains are distinguished, mainly according to the skin color, the black strain Latxa Cara Negra and the red strain Latxa Cara Rubia (**LCR**). Moreover, the black strain is divided in 2 geographic areas with slight morphological differences: Euskadi (**LCNEUS**) and Navarre (**LCNNAF**). Three separate breeding programs exist for the 3 strains. Currently milk yield, milk composition, and udder morphology traits are be-

ing selected. Presently, the breeding program is well implemented and shows consolidated results with an annual genetic gain (**AGG**) between 0.19 and 0.23 standard deviations, depending on the strain.

With the development of genomics, SNP are being used to implement genomic selection (**GS**) in several livestock species. In small ruminants, GS is less frequent and generally gains in accuracy introducing GS are small (Mrode et al., 2018). Regarding dairy sheep, empirical studies to analyze accuracies of genomic predictions in the Lacaune breed showed that genomic estimated breeding value (**GEBV**) for milk yield was 0.15 more accurate than (pedigree-based) EBV (Duchemin et al., 2012; Baloché et al., 2014b). An experiment (selecting rams using either GEBV or EBV) confirmed the gain in AGG (Baloché et al., 2014a).

Because generation interval is already short (4 yr), the implementation of GS in dairy sheep depends critically on the ability to select accurately young rams. Modeling genomic versus classic scheme showed that AGG could increase up to 51.7% with genomic information, with a reference population of at least 1,000 animals (Shumbusho et al., 2013). A performing GS scheme in Lacaune was conceived and implemented (Buisson et al., 2014). This scheme yields extra 10 to 20% of gain in AGG and 20 to 40% reduction of AI rams. The latter is important because in progeny-testing dairy sheep schemes using fresh semen, a large number of rams are waiting (and consuming resources) for first crop after their first use on AI, whereas a genomic scheme could avoid this waiting period based on breeding values estimated with a higher precision. Therefore, by modifying the management toward a GS scheme there could be fewer rams in the AI center, reducing costs and with no loss of genetic diversity.

In Western Pyrenees breeds, the implementation of GS was studied for the first time in 2014. Legarra et al. (2014) carried out a study with 6 breeds of dairy sheep, including the 2 strains of French Manech (which is a breed highly related to Latxa), Spanish Latxa with 3 strains, and Basco-Béarnaise. Results showed a gain in accuracy when genomic information was included [0.11

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for Manech Tête Noire, 0.16 for Manech Tête Rousse (**MTR**), and 0.06 for Basco-Béarnaise]; therefore, GS was started in 2017. However, the studies of Legarra et al. (2014) did not show a clear advantage of GS in Latxa. Increases in accuracy using GEBV were -0.18 (a deterioration) for LCNEUS, 0.30 for LCR and 0.04 for LCNNAF. Genomic predictions were generally less biased than pedigree predictions. However, some results are difficult to understand. For instance, for LCR EBV had almost 0 accuracy, which does not agree with the observed genetic progress of the breeding program. Predictions in some strains were frankly biased. Authors attributed these problems to poor genotyping (e.g., many “holes” across the years) and perhaps to poor modeling (pseudo-single-step GBLUP was used, using daughter yield deviations). Also, a weak relationship was present between genotyped rams in training and validation groups.

Since 2014, the Latxa breeding program has collected more phenotypic and pedigree data and has genotyped all the new males used in the last years in AI. Also, new developments in evaluation, such as single-step GBLUP (**ssGBLUP**), which enables the use of phenotypes of both animals with and without genotypes, yield better predictions (Legarra et al., 2009; Christensen and Lund, 2010). New methods in validation of results (**LR** method; Legarra and Reverter, 2018) may yield more objective measures of predictive ability. Furthermore, the metafounders (**MF**) theory (Legarra et al., 2015) provides a more coherent framework for genomic evaluation theory (Garcia-Baccino et al., 2017; Meyer et al., 2018; Bradford et al., 2019). In essence, the MF theory models missing pedigrees using populations (such as genetic groups), but these populations are of finite size and related according to observed genomic relationships of their descendants.

Thus, the objective of this work is to take a new look, with more data and better tools, into the effect of including genomic information into the genetic evaluations of LCR and LCNEUS strains. The LCNNAF population was not included in this study due to the small increase in number of genotyped rams.

MATERIALS AND METHODS

Phenotypic and Pedigree Data

All data came from the Latxa Breeders' Associations' Confederation (**CONFELAC**). The full data set included in this study comprised 639,517 lactations and 263,308 animals in the LCNEUS pedigree and 392,109 lactations and 150,185 animals in the LCR pedigree. The evaluated trait was 120-d standardized milk yield

Table 1. Description of the pedigree and phenotypic data (milk yield in 120 d of lactation) included in the study for Latxa Cara Negra from Euskadi (LCNEUS) and Latxa Cara Rubia (LCR)

Data (1984–2017)	Breed	
	LCNEUS	LCR
No. of animals in pedigree	263,308	150,185
% animals with data and complete genealogy	22.28	35.30
No. of phenotypic records	639,517	392,109
No. of females in data	235,360	133,230
No. of flocks	456	325
No. of AI males with progeny in data	1,883	1,837

whose heritability is 0.18 and 0.22 for LCNEUS and LCR, respectively. More details about phenotypic and pedigree data are shown in Table 1.

Because of the frequent use of natural mating with several rams, the breeding program only accepts filiations for AI rams. Also, several dams are unknown, mainly in flocks entering the breeding scheme. As a result, based on the average of the full data set, 31% of the ewes with milk records have unknown sire and dam, even though since 2000 this percentage has decreased to 21%. In addition, importation of semen from the French breed MTR to the Spanish LCR scheme has been sporadic since the 1990s and systematic since 2010. The ancestries of those MTR individuals included into LCR pedigree are unknown, and because the French breeding scheme started earlier, they should not be considered genetically equal to Spanish unknown contemporary individuals as was reported by Ugarte et al. (1996).

To palliate for these 2 kinds of missing pedigree, genetic groups (Quaas, 1988) are used for BLUP. However, the use of genetic groups in ssGBLUP is problematic (Misztal et al., 2013) and we decided to use MF (Legarra et al., 2015) to model missing pedigree. The assignment of MF was done looking for a balanced number of individuals in each MF group, considering the year of birth and the Spanish or French origin of the progeny. With this aim, for LCNEUS 11 MF groups were defined, from 1985 to 2015 every 3 yr; and for LCR 14 MF groups, from 1985 to 2015 every 3 yr for Spanish progeny and every 9 yr for French origin.

Genotypic Data

Using stored (for old) and recent DNA samples, AI rams were genotyped with the OvineSNP50 BeadChip (Illumina Inc., San Diego, CA). As quality control, animals with call rate <0.90 and parent-progeny Mendelian conflicts ($<5\%$) were eliminated. For SNP, markers

with heritability estimate of gene content <0.98 were removed (Forneris et al., 2015), as well as those with call rate <0.97 , minor allele frequency <0.05 , monomorphic, or located in sex chromosomes. After quality control 780 rams (353 LCNEUS and 427 LCR) and 39,159 and 38,168 effective SNP for LCNEUS and LCR, respectively, were considered for genomic evaluations. Regarding the previous study (Legarra et al., 2014), this work includes 178 new genotyped individuals (80 LCNEUS and 98 LCR) corresponding to the rams entering the AI center from 2010 to 2014. Genotyping was irregular during the first years, but from 2011 all the rams entering the AI center have been genotyped, which enables a more balanced and stronger data structure. The distribution of genotyped rams by year of birth is shown in Figure 1.

Estimation of (Genomic) Breeding Values

To obtain (G)EBV the Blupf90 family programs (Miszta et al., 2002) were used, using either pedigree-based BLUP or ssGBLUP (Legarra et al., 2009; Christensen and Lund, 2010). In both cases the model for the milk yield included flock-year-season, parity number-age at lambing, number of alive lambs born, and interval between lambing and the first test day as fixed effects, and permanent environmental and additive genetic (Legarra et al., 2005) with MF as random effects. Strains were evaluated separately because they do not interbreed. The MF approach considers relationships within and across base populations. These relationships are summarized in a matrix $\mathbf{\Gamma}$, which was estimated using the generalized least squares method in Garcia-Baccino et al. (2017). Supplemental Tables S1 and S2 (<https://doi.org/10.3168/jds.2019-18033>) show $\mathbf{\Gamma}$ estimates for each breed.

Goodness of Prediction

The goodness of prediction of pedigree and genomic evaluations was analyzed by cross-validation using the LR method (Legarra and Reverter, 2018). This method measures biases and accuracies from global changes in (G)EBV of candidates to selection from a “partial” (1984–2014) to a “whole” (1984–2017) data set. We chose a set of validation individuals, considering genotyped AI rams born into the last 3 cohorts of the partial data set (between 2012 and 2014). The details of rams’ distribution across validation and training group are described in Table 2. These animals were not progeny tested in the partial data set and have at least 10 daughters with lactations in the whole data set. First, GEV were estimated in whole and partial data

sets using ssGBLUP. Second, EBV were estimated in whole and partial data sets using BLUP. Statistics of bias, slope, and correlation $\rho_{w,p}$ for validation individuals were calculated from the linear regression of GEV estimated with whole data on GEV estimated with partial data and from the linear regression of EBV estimated with whole data on EBV estimated with partial data.

Bias defines the capacity to predict average value of candidates to selection and 0 would mean unbiasedness and is measured as the difference of average (G)EBV across whole and partial; slope could be taken as a measure of the dispersion of (G)EBV of candidates to selection, which should be 1, and it was obtained as the slope of the regression of (G)EBV estimated with whole data on (G)EBV estimated with partial data. Finally, we estimated the correlation $\rho_{w,p}$ (G)EBV from partial data with (G)EBV from whole data, which could be understood as the relative increase of accuracy from partial to whole data. For instance, a value of 0.9 means that (G)EBV with partial data (with parent average or genomic information, but not offspring) were almost equal to (G)EBV with whole data (with progeny). In that sense, high values are expected for genomic prediction, and low values for pedigree-based prediction. Due to the small size and selected character of validation groups, a bootstrap procedure with 1,000 iterations was implemented to sample with replacement the validation individuals and calculate the bootstrap distribution of bias, slope, and $\rho_{w,p}$ and their differences (e.g., the distribution of bias in ssGBLUP minus bias in BLUP).

The relationship between and within training and validation group is known to be important for genetic prediction (Pszczola et al., 2012). For both breeds a high proportion of validation individuals have sire and maternal grandsire in the training group. In addition, around half of the validation rams have their sire genotyped, whereas one-third of the maternal grandsires are genotyped. In the case of nongenotyped relatives GS could still work, but with less advantage than with genotyped relatives (Pszczola et al., 2011). The described pedigree relationships (shown in Tables 3 and 4) may not be optimal, but compared with the previous study (Legarra et al., 2014) the reference population is larger and more related to the candidates for selection.

RESULTS AND DISCUSSION

Table 5 shows the main results of the cross-validation using the LR method. The bias of validation individuals was small, not significantly different from 0, and very similar in pedigree and genomic evaluations (the

Figure 1. Rams used in AI by year of birth and the distribution of the genotyped individuals for Latxa Cara Negra from Euskadi (LCNEUS) and Latxa Cara Rubia (LCR).

Table 2. Number of rams distributed across categories, year of birth, and average daughter number with lactations in the whole data set per genotyped ram for Latxa Cara Negra from Euskadi (LCNEUS) and Latxa Cara Rubia (LCR)

Breed	Rams in training group, AI progeny tested				Rams in validation group, AI progeny tested		
	No. of genotyped	No. of nongenotyped	Birth years	Average daughters	No. of genotyped	Birth years	Average daughters
LCNEUS	216	1,401	1984–2011	54.04	59	2012–2014	21.32
LCR	202	1,305	1983–2011	67.53	91	2012–2014	30.54

difference of estimated biases is 4.21 ± 2.63 and 4.08 ± 2.55 , for LCNEUS and LCR, respectively). Note that these differences are expressed in liters, and the genetic standard deviation is 17.52 and 21.31 for LCNEUS and LCR, respectively. Across both breeds, BLUP had slopes closer to 1 than ssGBLUP, and LCR was significantly different from 1. Although the use of selectively genotyped individuals could affect the results (Vitezica et al., 2011), experience in dairy cattle and other dairy sheep breeds (VanRaden et al., 2009; Baloché et al., 2014b) shows that genotyping selected males does not result in bias because these animals will become average animals in the next generation. Moreover, a possible explanation for LCR lower estimates, which is hard to verify, is that imported MTR rams are a selected population and this was not correctly accounted for. Regarding the estimator of accuracies, $\rho_{w,p}$, predictions based on pedigree information had moderate-high $\rho_{w,p}$, 0.55 and 0.50 for LCNEUS and LCR, respectively. When predictions were based also in genomic information, $\rho_{w,p}$ was slightly higher, 0.56 and 0.51 for LCNEUS and LCR, respectively. The comparison of BLUP and ssGBLUP shows that the inclusion of genotypes did not increase or decrease the accuracy of predictions for any of the breeds.

Comparing the current results with the previous ones (Legarra et al., 2014), in general predictions are more consistent, indicating that breeding values are more correctly estimated. Biases are lower and with considerably smaller standard errors, which were remarkably high in the previous study (around 60 for LCNEUS and 100 for LCR). The current slopes of the regression for both methodologies are closer to 1 than previous ones,

which were around 0.30 in both LCNEUS and LCR. Accuracy of estimations is in all cases positive (whereas negative values were observed in the previous work) and with small standard errors, they are higher than the previous estimates and more coherent with the results of the breeding program. The change achieved in the pedigree-based EBV for LCR is especially relevant, whose accuracy was -0.05 ± 0.26 , and the current one is 0.50 ± 0.07 .

These better results may be associated with a stronger data structure (e.g., higher number of genotyped rams, closer relationship between reference and candidates to selection). In addition, the current evaluations were done with ssGBLUP, instead of using pseudo-ssGBLUP, avoiding daughter yield deviations calculation and transmission of inaccuracies to genomic predictions (daughter yield deviations in dairy sheep are not as accurate as in dairy cattle). Moreover, in these evaluations missing pedigree has been modeled using MF (Legarra et al., 2015), which is more consistent with genomic information. We did some analysis using genetic groups instead of MF, and results were not satisfactory because we obtained more biased evaluations and smaller slopes (results not shown).

The lack of increase of accuracy with genomic evaluations is influenced by the characteristics of the genotyped animals. VanRaden (2008) and Hayes et al. (2009) showed that the increase in accuracy from pedigree to genomic predictions can be explained as better relationships. Hayes et al. (2009) considered the case of sibships and showed that extra accuracy is a function of sibship size. In our case, the size of sibships is small (2–3 animals) and thus the expected increase using genomic

Table 3. Considering validation rams, number of validation sires or maternal grandsires genotyped or nongenotyped for Latxa Cara Negra from Euskadi (LCNEUS) and Latxa Cara Rubia (LCR)

Breed	No. of rams in validation group	No. of sires in training group		No. of maternal grandsires in training group	
		Genotyped	Nongenotyped	Genotyped	Nongenotyped
LCNEUS	59	31	25	18	36
LCR	91	43	46	16	67

Table 4. Considering validation rams, number of full-sib rams, number of sires, sires with one or more than one ram, and rate of rams per sire for Latxa Cara Negra from Euskadi (LCNEUS) and Latxa Cara Rubia (LCR)

Breed	No. of rams in validation group	No. of full-sib rams	No. of sires			Rams/sire
			Total	With 1 ram	With >1 ram	
LCNEUS	59	2	20	8	12	2.95
LCR	91	2	36	22	14	2.53

is small. Moreover, only the rams that went through progeny testing have been genotyped, and these rams were selected based on classical pedigree evaluations (parent average). Selection of siblings is typically avoided to handle genetic diversity. Therefore, the set of genotyped rams and of candidates to selection in the validation population is not a representative sample of all of the population. However, this does not hamper GS because in practical GS the breeding scheme would genotype a larger number of half-sib candidates for selection.

Lacaune and MTR reported increases in accuracy using genomic information of 0.15 and 0.16 for milk yield, respectively. These results were based on bigger reference populations with 1,900 and 1,000 genotyped animals (Baloche et al., 2014b; Legarra et al., 2014). In fact, the correlation between gain in accuracy and the reference population size (and the heritability of the trait) is known to be high (Goddard, 2009; Daetwyler et al., 2012; Auvray et al., 2014). Moreover, the constitution of a big reference population based on AI rams could be difficult due to the general low use of AI and the small size of populations. But the decrease in genotyping cost, combining with cheaper low-density chips and imputation methodologies, has brought the possibility of carrying on other strategies to maximize the benefits of genomic information (Rupp et al., 2016) by genotyping natural service rams or genotyping females, for instance. Genotyping other types of animals could be a good strategy and a simulation study is planned in Latxa.

In addition, we performed an extra analysis regarding the effect that genomic evaluations may have into

lamb selection for AI center. Currently around 120 lambs of each breed are considered based on their EBV for progeny testing. These lambs come from the 5% genetically best ewes, which have been inseminated by progeny-tested males (CONFELAC, 2016). Based on this working procedure, the selected lambs based on EBV or GEBV were compared and no dissimilarities were found; the same animals would be selected by both methodologies. The absence of sibships into the genotyped rams and the limited number of genotyped rams each year is hampering the benefit from the use of genomic information. A bigger genotyping population to preselect AI rams based on genomic values will increase the advantages of the methodology (Aguilar et al., 2010). So, a change in the breeding scheme organization would be necessary, like that proposed by Buisson et al. (2014), which provided a 15% increase in AGG in Lacaune breed by genotyping 3 times the number of lambs required to fulfill the needs of AI center. Therefore, the implementation of GS needs to be tailored to the specific requirements of the breeding programs (Jonas and de Koning, 2015; Mrode et al., 2018).

CONCLUSIONS

No clear advantages have been found for GS of Latxa breeds. The characteristics and structure of each breed and breeding scheme are key factors that determine the possible beneficial effect of genomic information in terms of evaluation accuracy and AGG. We perceive that the number of genotyped animals (all of them AI males) is low and the link between genotyped individu-

Table 5. Bias, slope, and accuracy $\pm$ SE (by bootstrap) of pedigree and genomic evaluations and their difference (genomic-pedigree) for Latxa Cara Negra from Euskadi (LCNEUS) and Latxa Cara Rubia (LCR)

Breed	Methodology	Bias	Slope	$\rho_{w,p}^1$
LCNEUS	Pedigree	1.41 $\pm$ 6.41	0.96 $\pm$ 0.20	0.55 $\pm$ 0.09
	Genomic	5.62 $\pm$ 5.52	0.82 $\pm$ 0.17	0.56 $\pm$ 0.08
	Genomic-pedigree	4.21 $\pm$ 2.63	-0.14 $\pm$ 0.08	0.01 $\pm$ 0.04
LCR	Pedigree	7.66 $\pm$ 6.06	0.68 $\pm$ 0.12	0.50 $\pm$ 0.07
	Genomic	11.74 $\pm$ 5.32	0.57 $\pm$ 0.10	0.51 $\pm$ 0.07
	Genomic-pedigree	4.08 $\pm$ 2.55	-0.11 $\pm$ 0.05	0.01 $\pm$ 0.04

¹ $\rho_{w,p}$ = estimator of accuracies.

als with phenotypic data and candidates to selection is not strong enough. Therefore, we have to solve these 2 handicaps before moving toward GS, and to have reliable information about how this change would affect the breeding scheme, further studies are planned in Latxa breeds.

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