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Milk coagulation properties are moderately heritable in dairy cows: a meta-analysis using the random-effects model

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Research Article

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Abstract

This study aimed to conduct a meta-analysis using the random-effects model to merge published genetic parameter estimates for milk coagulation properties (MCP: comprising rennet coagulation time (RCT), curd-firming time (k20), curd firmness 30 min after rennet addition (a30), titrable acidity (TA) and milk acidity or pH) in dairy cows. Overall, 80 heritability estimates and 157 genetic correlations from 23 papers published between 1999 and 2020 were used. The heritability estimates for RCT, a30, k20, TA, and pH were 0.273, 0.303, 0.278, 0.189 and 0.276, respectively. The genetic correlation estimates between RCT-a30, RCT-pH, and RCT-TA were 0.842, 0.549 and −0.565, respectively. Genetic correlation estimates between RCT and production traits were generally low and ranged from −0.142 (between RCT and casein content) to 0.094 (between RCT and somatic cell score). Moderate and significant genetic correlations were observed between a30-pH (−0.396) and a30-TA (0.662). Also, the genetic correlation estimates between a30 and production traits were low to moderate and varied from −0.165 (between a30 and milk yield) to 0.481 (between a30 and casein content). Genetic correlation estimates between pH and production traits were low and varied from −0.190 (between pH and milk protein percentage) to 0.254 (between pH and somatic cell score). The results of this meta-analysis indicated the existence of additive genetic variation for MCP that could be used in genetic selection programs for dairy cows. Because of the moderate heritability of MCP and small genetic correlations with production traits, it could be possible to improve MCP with negligible correlated effects on production traits.

World demand for dairy products is expanding, and further development of trade in dairy products is anticipated. Besides, in recent years, there has been a growing interest in milk components with potential advantages for human health (Toffanin *et al.*, 2015). The significance of milk composition in the production process of dairy products is well accepted (Williams, 2003; Murphy *et al.*, 2016), which implies the importance of including milk composition traits in different dairy cow breeding goals (Miglior *et al.*, 2005). Milk processability, which indicates the possibility of converting milk into different dairy products such as cheese and milk powder, is a major feature of milk composition. Despite this, milk processability is not precisely included in dairy cow breeding goals (Visentin *et al.*, 2017).

Milk processability indicators are generally identified as milk coagulation properties (MCP), and these mainly involve rennet coagulation time (RCT), curd-firming time (k20), curd firmness 30 min after rennet addition (a30), titrable acidity (TA), and milk acidity or pH. Good MCP is required for the process of cheese production. MCP is affected by genetic and non-genetic factors (Bittante *et al.*, 2012) including breed, somatic cell count, milk protein composition, casein composition and stage of lactation (Tyrisevä *et al.*, 2004; Cassandro *et al.*, 2008; Bittante *et al.*, 2012). Ikonen *et al.* (2004) stated that MCP is heritable and could be improved in genetic selection plans. The problem with MCP relates to difficulties in measuring its phenotype in a routine, timely manner and at a low cost on individual cows. This complicates the collection of an adequate number of reliable phenotypes for MCP to warrant genetic selection in dairy herds. Therefore, an alternative method could be the selection and improvement of traits that favourably associate with MCP (Duchemin *et al.*, 2020).

In previous years, genetic parameters have been estimated for MCP in different dairy cattle breeds. However, these estimates have been obtained from studies based on populations of different breeds and lactations, generally with limited sample size and considering various effects in the model, all of which has contributed to large associated standard errors of the estimated (co) variance components. This has led to high variability among genetic parameter estimates. Meta-analysis is a statistical method to systematically evaluate the results of previous research studies to get a comprehensive conclusion on a specific topic. Two well-known statistical models for the meta-analysis are the fixed- and random-effects models. Performing a meta-analysis using the random-effects model is considered a conservative

method because it can supply estimates closest to the actual parameters. The heterogeneity of variance among different studies is accounted for in random-effects meta-analysis models (Borenstein *et al.*, 2009; Ghavi Hossein-Zadeh, 2021), and, therefore, this is generally the recommended approach (Lean *et al.*, 2009). To the author's knowledge, a particular meta-analysis of the genetic parameter estimates for MCP in dairy cows has not been yet reported in the literature. Therefore, this study aimed to perform a meta-analysis based on a random-effects model to merge published heritability estimates for these traits and their genetic correlations with production traits in dairy cows.

Material and methods

Characterizing the scope of the meta-analysis study

A systematic search of the literature using electronic databases of ISI Web of Knowledge (https://apps.webofknowledge.com), Google Scholar (https://scholar.google.com), NCBI (https://www.ncbi.nlm.nih.gov), and ResearchGate (https://www.researchgate.net) was conducted to identify all references reporting genetic parameter estimates for MCP and milk pH in dairy cows. The most exhaustive research query was built, using synonyms and derivatives of the following keywords: 'dairy cow', 'milk coagulation properties', 'milk acidity', 'genetic parameters', 'heritability', 'genetic correlation', 'genetic evaluation' and 'performance traits'. In total, 80 heritability and 157 genetic correlation estimates from 23 peer-reviewed articles were used in the present study. The considered articles were published between 1999 and 2020 (online Supplementary Table S1) and the literature cited in the articles was also checked. The estimates were derived from restricted maximum likelihood (REML) and Bayesian inference estimation methods on a mixed model. Only articles published in indexed journals and the proceedings of scientific conferences were included in this meta-analysis study. The MCP attributes considered in this study were rennet coagulation time (RCT), curd-firming time (k20), curd firmness 30 min after rennet addition (a30), titrable acidity (TA), and milk acidity or pH.

Data recorded and variable transformation

The data sets included information on direct heritability estimates for RCT, k20, a30, TA, and pH as well as genetic correlations between these traits and the performance traits milk yield (MY), milk fat percentage (FP), milk protein percentage (PP), somatic cell score (SCS), casein percentage (CN) and lactose percentage (Lac), and standard errors for these published parameter estimates. Other information recorded was the publication year, journal name, the number of records, breed name, parity, country of origin, years of data collection, phenotypic mean and standard deviation, the estimation method used (REML or Bayesian) and model of analysis (univariate or multivariate). Once an estimate of a genetic parameter that was similar was reported in multiple publications, based on the same data set, the latest estimate was considered in the meta-analysis. Moreover, the analysis was performed exclusively for traits in which the parameter estimates were placed on not less than two distinct data sets.

For articles in which the standard errors for the heritability or correlation estimates were not reported, approximated standard errors were derived by using the combined-variance method (Sutton *et al.*, 2000), which is given by the following formula:

$$SE_{ij} = \sqrt{\left(\frac{\sum_{k=1}^{K} s_{ik}^2 n_{ik}^2}{\sum_{k=1}^{K} n_{ik}/n'_{ij}}\right)}$$

where SE_{ij} is the predicted standard error for the published parameter estimate for the ith trait in the j^{th} article that has not reported the standard error, s_{ik} is the published standard error for the parameter estimate for the i^{th} trait in the k^{th} article that has reported the standard error, n_{ik} is the number of used records to predict the published parameter estimate for the i^{th} trait in the k^{th} article that has reported the standard error, and n'_{ij} is the number of used records to predict the published parameter estimate for the i^{th} trait in the j^{th} article that has not reported the standard error.

Most meta-analyses do not use the published correlation estimate itself because it usually does not have a normal distribution. Rather, the published correlation is converted to the Fisher's Z scale, and all analyses are performed using the transformed values. The results, such as the estimated parameter and its confidence interval, would then be converted back to correlations for presentation (Borenstein *et al.*, 2009). The approximate normal scale based on Fisher's Z transformation (Steel and Torrie, 1960; Borenstein *et al.*, 2009) is as follows:

$$Z_{ij} = 0.5[\ln(1 + r_{g_{ij}}) - \ln(1 - r_{g_{ij}})]$$

where r_{gij} is the published genetic correlation estimate for the i^{th} trait in the j^{th} article. To return to the original scale, the following equation (Borenstein *et al.*, 2009) was used:

$$r^*_{g_{ij}} = \frac{e^{2Z_{ij}} - 1}{e^{2Z_{ij}} + 1}$$

where $r^*_{g_{ij}}$ is the re-transformed genetic correlation for the i^{th} trait in the j^{th} article, and Z_{ij} is the Fisher's Z transformation.

Phenotypic trait

Means and standard deviations were calculated for all traits using the sample sizes as weights. The total number of records for each phenotypic trait was calculated as the sum of the number of records in each article that reported the trait. The coefficient of variation in percentage (CVi(%)) for each i^{th} trait was calculated as follows:

$$CV_i(\%) = \frac{s_i}{\bar{X}_i} \times 100$$

where s_i is the standard deviation for the i^{th} trait and $\bar{X}_i$ is the trait mean.

Heritabilities and genetic correlations

Meta-analysis was performed based on a random-effects model (Borenstein *et al.*, 2009) using the comprehensive meta-analysis (CMA) software version 2.2 (Biostat, USA) to calculate the effect size for genetic parameter estimates. In the random-effects model, observed differences among study results are due to the play of chance in repeated sampling and random changes in real values

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of parameters. The general form of the random-effects model was as follows:

$$\hat{\theta}_j = \bar{\theta} + u_j + e_j$$

where $\hat{\theta}_j$ is the published parameter estimate in the j^{th} article, $\bar{\theta}$ is the weighted population parameter mean, u_j is the among study component of the deviation from the mean, assumed as $u_j \sim N(0, \tau^2)$, where τ^2 is the variance representing the amount of heterogeneity among studies, e_j is the within-study component due to sampling error in the parameter estimate in the j^{th} article, assumed as $e_j \sim N(0, \sigma_e^2)$, where σ_e^2 is the within-study variance. Forest plots were constructed to indicate the effect size for each study. Effect sizes for forest plots were the mean heritability estimates for conformation traits or genetic correlation estimates at a 95% confidence interval using the random-effects model.

Heterogeneity

Chi-square (Q) test and the I^2 statistic were performed to measure heterogeneity. Variation among the study level was assessed using a Q test. The significance level was set at 0.1 because the Q test has relatively low power when a few studies are included (Lean *et al.*, 2009). Although the Q test helps identify heterogeneity, the measure I^2 was used to measure heterogeneity as follows (Lean *et al.*, 2009):

$$I^2(\%) = \frac{Q - (k-1)}{Q} \times 100$$

where Q is the χ^2 heterogeneity statistic and k is the number of studies. Q is the Q statistics given by the following formula:

$$Q = \sum_{j=1}^{k} w_j (\hat{\theta}_j - \bar{\theta})^2$$

where w_j is the parameter estimate weight (assumed as the inverse of published sampling variance for the parameter, $1/s_j^2$) in the j^{th} article; $\hat{\theta}_j$ and $\bar{\theta}$ were defined above in the random-effects model, and k is the number of used articles. The I^2 statistic describes the percentage of variation across studies due to heterogeneity. Negative values of I^2 are set equal to zero; consequently, I^2 lies between 0 and 100% (Lean *et al.*, 2009). Its value might not be important if it falls within the range of 0–40%. However, a value of 40–60% often indicates moderate heterogeneity and a value in the range of 60–100% represents considerable heterogeneity. The 95% lower and upper limits for the estimated parameter would be computed respectively for each trait as follows:

$$LL_{\bar{\theta}} = \bar{\theta} - 1.96 \times SE_{\bar{\theta}} \text{ and } UL_{\bar{\theta}} = \bar{\theta} + 1.96 \times SE_{\bar{\theta}}$$

where $SE_{\bar{\theta}}$ is the predicted standard error for the estimated parameter $\bar{\theta}$, given by:

$$SE_{\bar{\theta}} = \sqrt{\frac{1}{\sum_{j=1}^{k} w_j}}$$

Publication bias

Egger's linear regression asymmetry was used to examine the presence of publication bias. When significant bias was detected ($P < 0.10$) the trim-and-fill method (Duval and Tweedie, 2000) was applied to find the number of missing studies.

Funnel plots were used to present asymmetry. This technique indicates the symmetric distribution of effect sizes around the true effect size. No publication bias suggests that the most extreme results have not been published. Once the number of missing observations is estimated, estimated missing values are included to recalculate a weighted mean effect size and its variance. When heterogeneity (Q test, $P < 0.10$) was detected for the parameters analysed, testing for the occurrence of possible publication bias is not appropriate because it may lead to false-positive claims (Ioannidis and Trikalinos, 2007).

Results

Descriptive statistics

The number of literature estimates, measurement units, the total number of records, weighted mean, standard deviation, and coefficient of variation for MCP of dairy cows are indicated in Table 1. The weighted coefficients of variation for MCP were generally low to moderate and varied from 0.75 (for pH) to 24.86% (for a30).

Heritability estimates

Effect size and heterogeneity of the heritability estimates for MCP obtained from the random-effects model of the meta-analysis are presented in Table 2. The heritability estimates for RCT, a30, k20, TA, and pH were 0.273, 0.303, 0.278, 0.189, and 0.276, respectively. These estimates generally had low standard errors, and their 95% confidence intervals were small. Also, the heritability estimates for MCP were significant ($P < 0.05$). The heterogeneity test of heritability estimates, conducted by Q statistic, indicated that heritability estimates for a30, k20, and pH had high Q values and significant heterogeneity ($P < 0.10$), but heritability estimates for RCT and TA had non-significant heterogeneity ($P > 0.10$). In agreement with the results observed by Q statistic, the I^2 values showed considerable heterogeneity for the heritability estimates of a30, k20, and pH, but negligible heterogeneity for the heritability estimates of RCT and TA (Table 2). The forest plots of individual studies and the overall outcome for heritability estimates of MCP in dairy cows are indicated in online Supplementary Figs S1 to S5. The funnel plot of mean heritability estimates for RCT and TA are shown in Figs 1 and 2. Results from statistical tests to evaluate publication bias and the trim-and-fill method to correct funnel plot asymmetry in heritability estimates of RCT and TA that did not present heterogeneity showed that one and two missing studies were needed at the left side of the funnel plot for RCT and TA to correct funnel plot asymmetry according to the trim-and-fill method, respectively (Table 3). After correcting the funnel plot asymmetry by including the imputed studies, the mean heritability estimates for RCT and TA were 0.272 and 0.173, respectively (Table 3).

Genetic correlation estimates

Effect size and heterogeneity of the genetic correlation estimates between MCP and production traits of dairy cows are shown in Table 4. The genetic correlation estimates between RCT-a30,

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Table 1. Number of literature estimates (N), measurement units (Unit), the total number of records (Records), weighted mean, standard deviation (SD), and coefficient of variation (CV) for MCP of dairy cows

Trait	Unit	N	Records	Mean	SD	CV (%)
RCT	Minute	24	601 476	18.73	4.64	24.77
a30	Millimetre	22	559 501	22.04	5.48	24.86
k20	Minute	8	431 115	6.10	0.68	11.15
TA	Soxhlet Henkel°/50 ml	4	5312	3.31	0.07	2.11
pH	–	19	412 806	6.69	0.05	0.75

RCT, Rennet coagulation time; a30, Curd firmness; k20, Curd firming time; TA, Titrable acidity.

Table 2. Effect size and heterogeneity of the heritability estimates for MCP in dairy cows obtained from the random-effects model of meta-analysis

Trait[a]	*N*	h^2	SE	95% CI	*P*-value	*Q*	*P*-value	I^2
RCT	26	0.273	0.008	0.257–0.290	0.000	30.729	0.198	18.643
a30	22	0.303	0.027	0.249–0.357	0.000	233.280	0.000	90.998
k20	8	0.278	0.063	0.155–0.401	0.000	227.311	0.000	96.921
TA	4	0.189	0.025	0.140–0.237	0.000	1.681	0.641	0.000
pH	20	0.276	0.023	0.230–0.321	0.000	215.261	0.000	91.173

[a]For traits, see Table 1.

RCT-pH, and RCT-TA were −0.842, 0.549 and −0.565, respectively ($P < 0.05$). Genetic correlation estimates between RCT and production traits were generally low and ranged from −0.142 (between RCT and CN) to 0.094 (between RCT and SCS). Except for the genetic correlation estimate between RCT and SCS, the genetic correlations between RCT and other production traits were non-significant ($P > 0.05$). For non-significant genetic correlation estimates, 95% CI included zero. Therefore, these correlation estimates could not be statistically different from zero. Moderate and significant genetic correlations were observed between a30-pH (−0.396) and a30-TA (0.662). Also, the genetic correlation estimates between a30 and production traits were low to moderate and varied from −0.165 (between a30 and MY) to 0.481 (between a30 and CN). Except for the genetic correlations between a30 and MY, SCS and Lac, genetic correlation estimates between a30 and other production traits were significant and statistically different from zero ($P < 0.05$). Genetic correlation estimates between pH-FP and pH-PP were −0.156 and −0.190, respectively ($P < 0.05$). Genetic correlation estimates between pH and MY, SCS, and CN were low and non-significant ($P > 0.05$). Therefore, genetic correlations between pH and MY, pH and SCS, and finally pH and CN could not be statistically different from zero. The heterogeneity test of genetic correlation estimates, conducted by Q statistic, indicated that except for the genetic correlations between RCT and SCS, RCT and Lac, RCT and TA and finally a30 and TA, which had low Q values and non-significant heterogeneity ($P > 0.10$), the genetic correlations between MCT traits with production traits showed significant heterogeneities ($P < 0.10$) with greater Q values (Table 4). Consistent with the Q values, the I^2 values indicated negligible heterogeneities for the genetic correlations between RCT and SCS, RCT and Lac, RCT and TA and finally a30 and TA, but considerable heterogeneities for genetic correlation estimates among other traits (Table 4).

The forest plots of individual studies and the overall outcome for the genetic correlation estimates between MCP are depicted in online Supplementary Figs S6 to S10. The funnel plots of the mean genetic correlation estimates between RCT and SCS, RCT and Lac, RCT and TA and finally a30 and TA are presented in Figs 3–6, respectively. Results of statistical tests to examine publication bias and the trim-and-fill method to adjust funnel plot asymmetry in genetic correlation estimates that did not indicate heterogeneity are presented in Table 5. The results of Egger's test showed non-significant ($P > 0.10$) publication bias for the genetic correlation estimates between RCT and SCS, RCT and Lac and finally RCT and TA (Table 5). Two missing studies were required on the left side of the funnel plot for genetic correlation between RCT and SCS, and one missing study was required on the left side of the funnel plot for genetic correlation between RCT and Lac to obtain funnel plot symmetry based on the trim-and-fill method (Table 5). Also, one missing study was required on the right side of the funnel plot for genetic correlation between RCT and TA to obtain funnel plot symmetry. After correcting the funnel plot asymmetry by including the imputed studies, the genetic correlation estimates of RCT and SCS, RCT and Lac and finally RCT and TA were 0.067, −0.007, −0.541 and 0.662, respectively (Table 5).

Discussion

Interest in the improvement of MCP has increased in recent years. It has been extensively demonstrated that milk with desirable clotting characteristics, namely relatively short clotting time, suitable firming rate and high curd firmness at the cut, leads to higher cheese yield than poorly coagulating milk (Pretto *et al.*, 2013; Tiezzi *et al.*, 2013) resulting in increased profitability for the dairy industry (Formaggioni *et al.*, 2005). The improvement of MCP is strongly recommended to increase dairy sector efficiency, especially in countries where milk is mainly intended for cheese production (Geary *et al.*, 2010; Tiezzi *et al.*, 2013). Assessing genetic variation in MCP parameters and evaluating their genetic associations with production traits will be helpful for the

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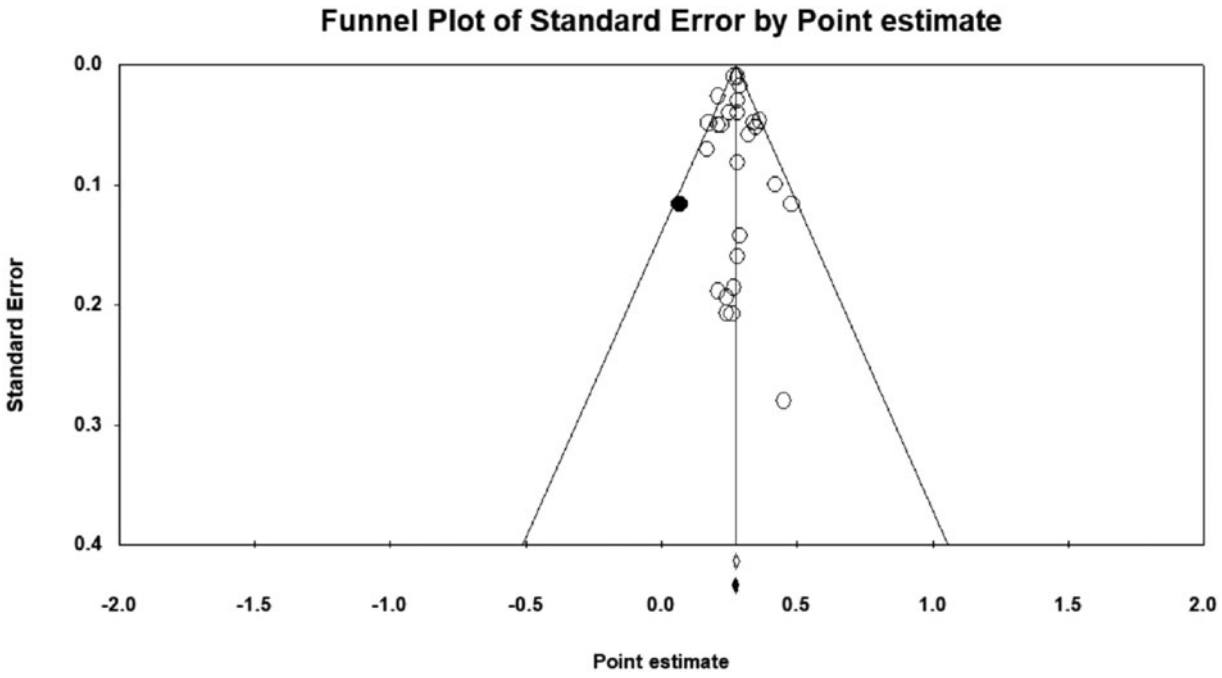

Figure 1. The funnel plot of the heritability estimates for RCT. The solid dots are the potentially missing studies imputed from the trim-and-fill method. The open diamond represents the mean and confidence interval of the existing studies and the solid diamond represents the mean and confidence interval if the theoretically imputed studies were included in the meta-analysis.

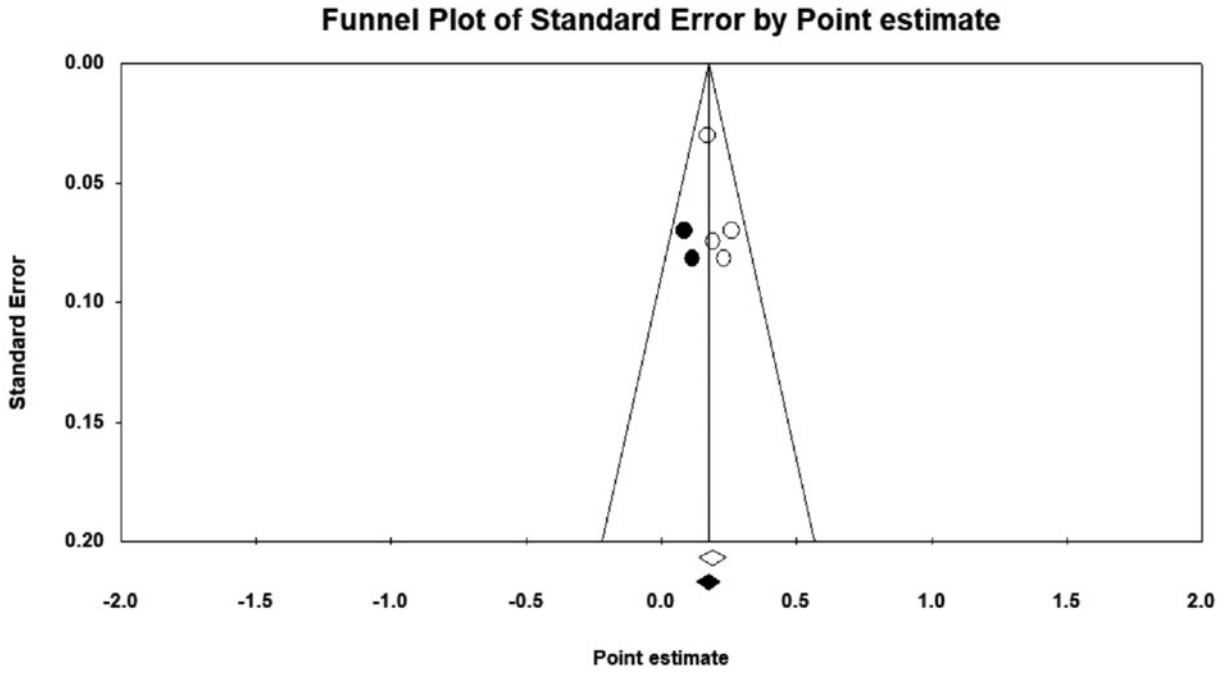

Figure 2. The funnel plot of the heritability estimates for TA. Detailed information is provided in Fig. 1.

development of novel management and breeding programs in dairy cows. In this regard, Wood *et al.* (2003) stated three preconditions would be required. First, MCP must be sufficiently heritable for a relatively rapid and substantial improvement. Second, it is necessary to prove the presence of adequate genetic variability for these traits in dairy cow populations. Third, it is required to know the genetic relationships between MCP and economically important traits in the under-study population. For including MCP in effective genetic evaluation and improvement programs, understanding the genetic parameters for these traits is necessary.

The lowest weighted coefficient of variation was observed for milk pH (0.75%), showing the limited phenotypic variation for

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Table 3. Results from statistical tests to evaluate publication bias and the trim-and-fill method to correct funnel plot asymmetry in mean heritability estimates of MCP that did not present heterogeneity

Trait[a]	Egger's test *P*-value	Trim-and-fill method		
		Missing	Mean	95% CI
RCT	0.782	1	0.272	0.254–0.290
TA	0.183	2	0.173	0.129–0.217

[a]For traits, see Table 1. Missing: Number of missing studies.

this trait from a biological view. Also, this low weighted coefficient of variation indicated a low dispersion around the weighted mean of the trait among studies. This result implied the more accurate weighted mean estimate for milk pH. On the other hand, the greatest weighted coefficient of variation was estimated for a30 (24.86%), indicating greater phenotypic variation in this trait than in other traits.

The standard errors and 95% confidence intervals of the mean heritability estimates of MCP were low, which implies the appropriate precision of mean heritability estimates reported in the current study. In general, the moderate heritability estimates observed for MCP indicated the moderate influence of additive genetic effects on the expression of the studied traits. The moderate heritability estimates for major MCP indicated the existence of an exploitable additive genetic variation for these traits that could be used in genetic selection plans. Although heritability would influence the rate of genetic gain, this rate also depends on other effective factors such as genetic variation, selection intensity and generation interval. Because meta-analysis integrates published genetic parameter estimates reported by different studies, the difference in the actual parameter among the studies could be expected (Ghavi Hossein-Zadeh, 2022). Several factors might explain the inconsistencies among genetic parameter estimates reported in different studies, such as sample size, the investigated breeds, models and methods of estimations as well as variation across laboratories (Cassandro *et al.*, 2008).

As indicated, RCT and a30 were highly correlated because coagulation and firming are consecutive steps of the same process. If milk takes a short time to coagulate, it leaves more time for curd firming and has better coagulation ability, thus, the final curd will be firmer. Conversely, if milk takes a long time to coagulate, the curd will have less time to firm and be weaker (Cassandro *et al.*, 2008). The results of this study showed that desirable MCP (i.e., short coagulation time and high curd firmness) were markedly associated with the acidity of milk, measured both as milk pH and TA. Because milk pH and TA can be measured more easily than MCP, enhancement of MCP could be achieved through indirect selection based on these indicator traits. The

Table 4. Effect size and heterogeneity of the genetic correlation estimates between MCP and production traits in dairy cows obtained from the random-effects model of meta-analysis

Trait 1	Trait 2	*N*	r_g	95% CI	*P*-value	*Q*	*P*-value	I^2
RCT	a30	11	−0.842	−0.934– −0.645	0.000	147.068	0.000	93.200
RCT	MY	9	0.056	−0.095–0.203	0.470	29.374	0.000	72.765
RCT	FP	10	−0.125	−0.305–0.064	0.194	80.747	0.000	88.854
RCT	PP	10	−0.014	−0.290–0.264	0.922	181.728	0.000	95.048
RCT	SCS	9	0.094	0.017–0.170	0.017	7.334	0.501	0.000
RCT	CN	7	−0.142	−0.452–0.198	0.415	146.914	0.000	95.916
RCT	Lac	4	−0.007	−0.075–0.061	0.847	2.852	0.415	0.000
RCT	pH	10	0.549	0.252–0.751	0.001	407.292	0.000	97.790
RCT	TA	3	−0.565	−0.646– −0.473	0.000	1.392	0.499	0.000
a30	MY	9	−0.165	−0.340–0.022	0.083	51.149	0.000	84.360
a30	FP	9	0.268	0.062–0.453	0.011	89.579	0.000	91.069
a30	PP	9	0.381	0.089–0.613	0.012	180.845	0.000	95.576
a30	SCS	9	−0.107	−0.265–0.057	0.200	25.474	0.001	68.595
a30	CN	7	0.481	0.150–0.716	0.006	244.643	0.000	97.547
a30	Lac	3	−0.060	−0.238–0.122	0.522	13.568	0.001	85.260
a30	pH	8	−0.396	−0.576– −0.179	0.001	75.016	0.000	90.669
a30	TA	3	0.662	0.505–0.777	0.000	2.993	0.224	33.181
pH	MY	5	0.047	−0.085–0.177	0.485	10.151	0.038	60.594
pH	FP	6	−0.156	−0.260– −0.048	0.005	13.257	0.021	62.283
pH	PP	6	−0.190	−0.299– −0.076	0.001	25.155	0.000	80.123
pH	SCS	5	0.254	−0.040–0.507	0.090	23.409	0.000	82.913
pH	CN	5	−0.153	−0.344–0.050	0.138	28.045	0.000	85.737

RCT, Rennet coagulation time; a30, Curd firmness; k20, Curd firming time; TA, Titrable acidity; Milk yield (MY), milk fat percentage (FP), milk protein percentage (PP); SCS, Somatic cell score; CN, Casein percentage; Lac, Lactose percentage;r_g, Genetic correlation.

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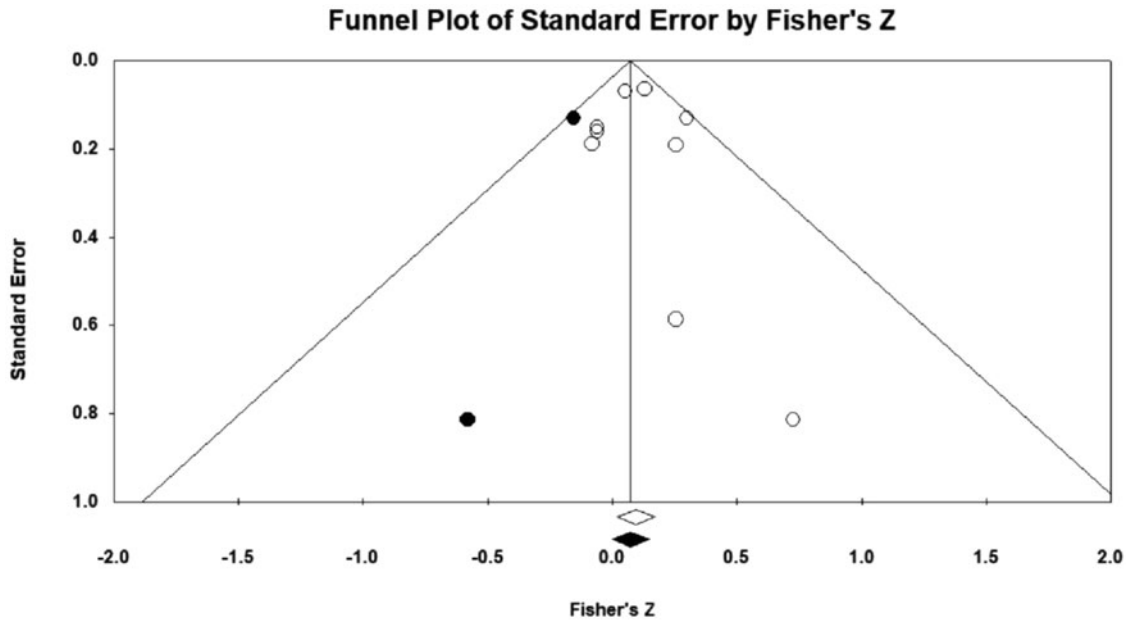

Figure 3. The funnel plot of the genetic correlation estimates between RCT-SCS. Detailed information is provided in Fig. 1.

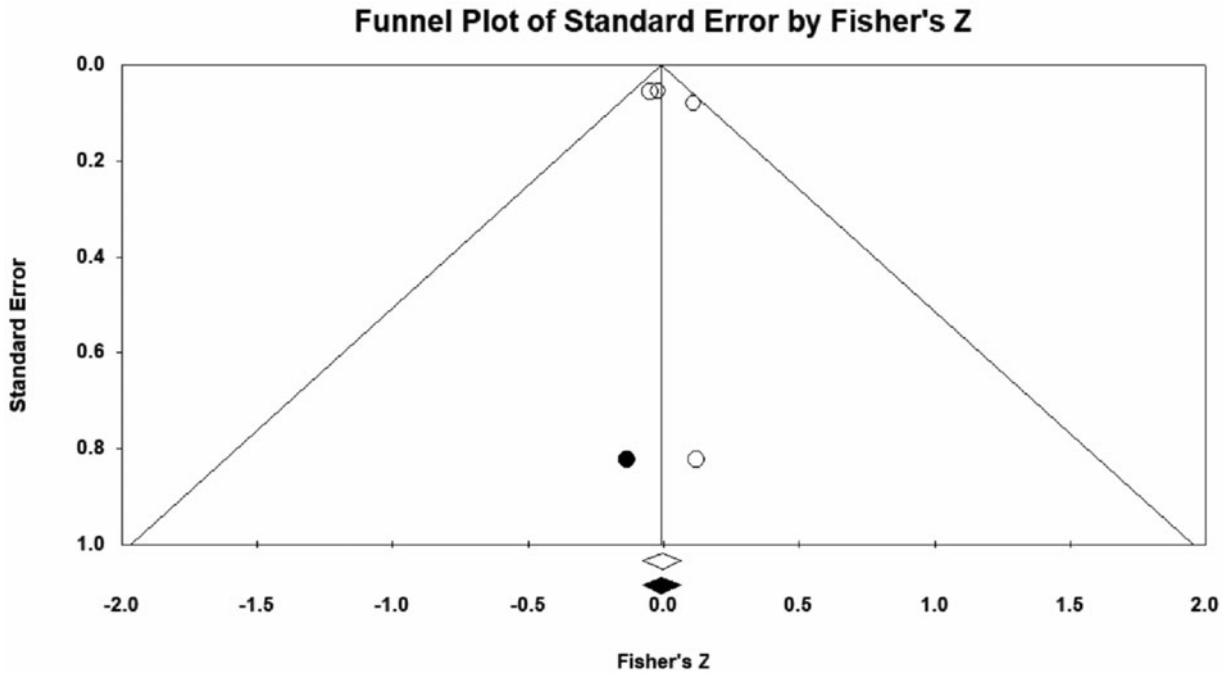

Figure 4. The funnel plot of the genetic correlation estimates between RCT-Lac. Detailed information is provided in Fig. 1.

genetic correlations between MCP and production traits were generally negligible and near zero or non-significant. The non-significant genetic correlation estimates between MCP and production traits had 95% CI which included zero. Thus, these genetic correlations must be interpreted with caution. This lack of genetic association proposes that selection for MCP would not cause a significant change in milk production traits in dairy cows. On the other hand, the selection of production traits is unlikely to influence MCP. The negligible genetic correlations between MCP and production traits indicated distinct genetic and physiological mechanisms controlling these traits. These results show that the correlated response of milk coagulation ability to changes in milk yield and composition, as dictated by current breeding goals of dairy cattle populations, is expected to be restricted. MCP exhibited positive but low genetic correlations with RCT and pH. Because current breeding objectives for dairy cow populations favor low SCS, these correlations are considered desirable. Low milk pH and high TA correlated with short RCT and high a30, which are desirable milk properties for cheese making. This suggests that variation in milk acidity might be used to

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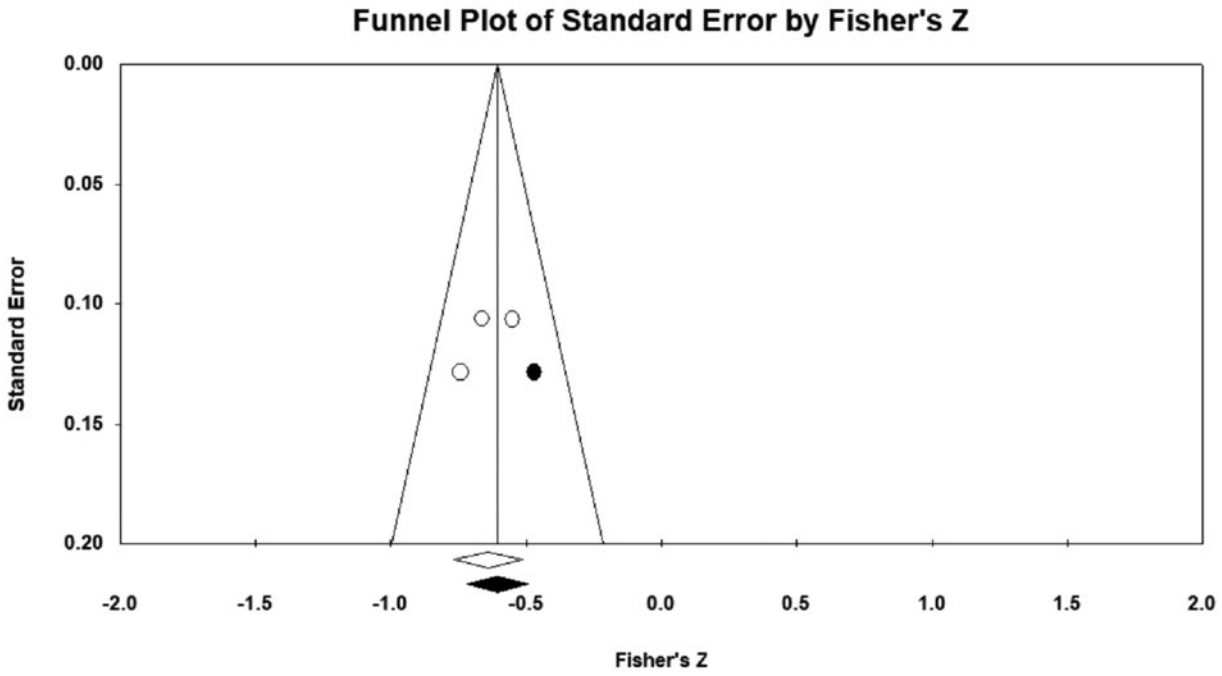

Figure 5. The funnel plot of the genetic correlation estimates between RCT-TA. Detailed information is provided in Fig. 1.

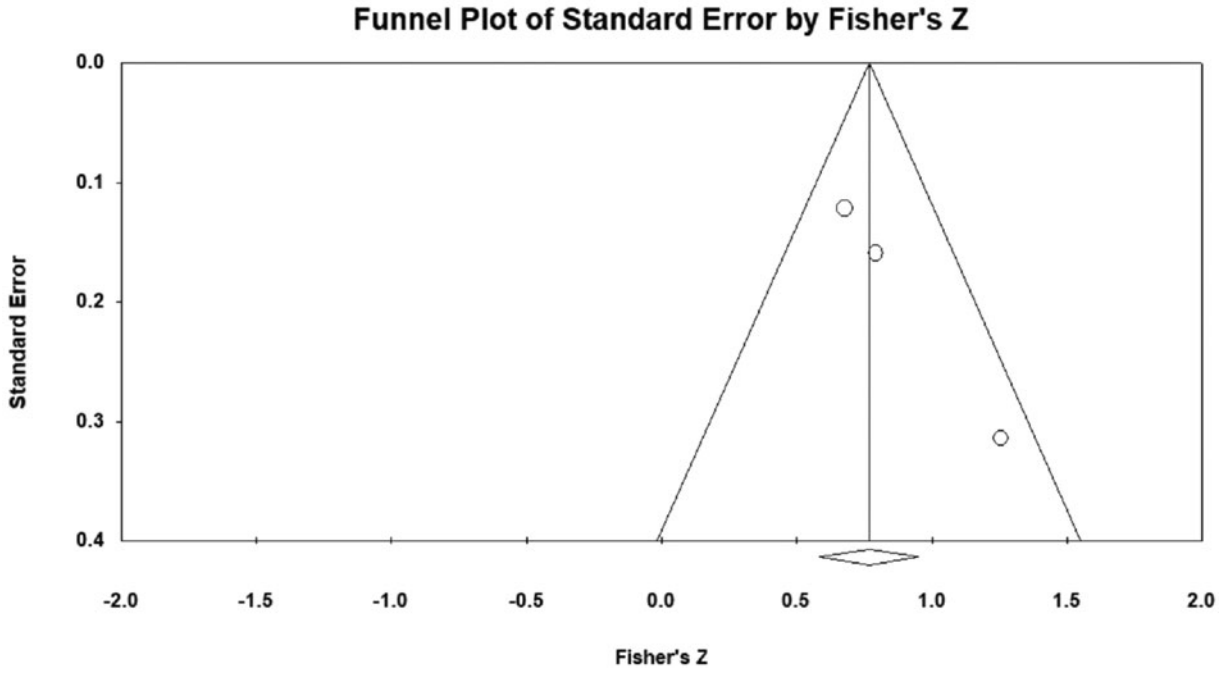

Figure 6. The funnel plot of the genetic correlation estimates between a30-TA. Detailed information is provided in Fig. 1.

increase the coagulation ability of milk (Cecchinato and Carnier, 2011). Low SCS was correlated with high a30, which is desirable for cheese making. A possible explanation is that increased somatic cell count is associated with increased plasmin activity. The accumulation of plasmin degradation products might also affect coagulation because these components interfere with the aggregating micelles responsible for curd formation (Politis and Ng-Kwai-Hang, 1988; Cecchinato and Carnier, 2011). A moderate and positive genetic correlation was observed between a30 and CN. The important role of CN content in determining a30 variation has been reported in previous studies (Summer *et al.*, 1999; Malacarne *et al.*, 2006). The a30 parameter indicated moderate relationships with milk acidity traits (pH and TA). Okigbo *et al.* (1985) reported that a30 decreased when pH increased and, generally, milk samples did not coagulate when pH was greater than 6.85. Ikonen *et al.* (2004) indicate that pH

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Table 5. Results from Egger's test to assess publication bias and implementing the method of trim-and-fill to adjust the asymmetry of funnel plot for genetic correlations of MCP with production traits in dairy cows

			Trim-and-fill method		
Trait 1[a]	Trait 2[a]	Egger's test *P*-value	Missing	Mean	95% CI
RCT	SCS	0.780	2	0.067	−0.018–0.151
RCT	Lact	0.635	1	−0.007	−0.075–0.061
RCT	TA	0.449	1	−0.541	−0.617– −0.456
a30	TA	0.003	0	0.662	0.505–0.777

[a]For traits, see Tables 1 and 3. Missing: Number of missing studies.

modifications exert significant effects on a30. Changes in pH are known to affect enzyme activity (Okigbo *et al*., 1985). The positive and moderate to high genetic correlations between some traits (such as between RCT and TA, a30 and pH and finally a30 and TA) are evidence for common genetic and physiological mechanisms controlling these traits.

In conclusion, because genetic parameter estimates from one animal population cannot be used for other breeds or populations, the combined estimates obtained through meta-analysis can be a reliable alternative. The results of this meta-analysis indicated moderate heritability estimates for MCP. Therefore, an exploitable additive genetic variation for these traits could be used in genetic selection plans for dairy cows. Because of the moderate heritability of MCP and small genetic correlations with production traits, it could be possible to improve MCP with negligible correlated effects on production traits.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0022029923000444.

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