The impact of dietary supplementation of arginine during gestation in a commercial swine herd: II. Offspring performance

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ABSTRACT: Arginine (**Arg**) is an important amino acid of pig fetal development; however, whether Arg improves postnatal performance is ill-defined. Therefore, the influence of Arg supplementation at different gestational stages on offspring performance was evaluated in a commercial swine herd. Sows (n = 548) were allocated into 4, diet by stage of gestation treatments: Control (n = 143; 0% suppl. Arg), or dietary treatments supplemented with 1% L-Arg (free-base; Ajinomoto Animal Nutrition North America, Inc., Chicago, IL): from 15 to 45 d of gestation (n = 138; Early-Arg); 15 d of gestation to farrowing (n = 139; Full-Arg); and from day 85 of gestation to farrowing (n = 128; Late-Arg). All offspring were individually identified and weighed at birth; at weaning, a subset was selected for evaluation of carcass performance at market. All data were analyzed using birth weight (BiWt) and age as covariates. Wean weights (WW) and prewean (PW) ADG tended to increase (P = 0.06) in progeny from sows supplemented with Arg, as compared to progeny from Control sows. Preplanned contrast comparisons revealed an increased (P = 0.03) BiWt for pigs from sows receiving 1% L-Arg prior to day 45 of gestation (Early-Arg and Full-Arg; 1.38 kg/pig), as compared to pigs from sows not supplemented

prior to day 45 of gestation (Control and Late-Arg; 1.34 kg/pig). No difference in BiWt was observed (1.36 kg/pig; P = 0.68) for Arg supplementation after day 85 of gestation (Full-Arg and Late-Arg), as compared to those not receiving Arg supplementation after day 85 (Control and Early-Arg); although WW and PW ADG were greater (P = 0.02), respectively. A 3.6% decrease (P = 0.05) in peak lean accretion ADG occurred when dams received 1% L-Arg prior to day 45 of gestation (Early-Arg and Full-Arg), however, no other significant differences were detected in finishing growth parameters or carcass characteristics ($P \ge 0.1$). Pig mortality rates tended (P = 0.07) to decrease in progeny of dams supplemented Arg after day 85 (3.6%) compared to dams not provided additional Arg during late gestation (4.9%). Collectively, these data suggest that Arg provided during late gestation may improve WW and PW ADG, however, finishing performance was not affected. While Arg supplementation provided some moderate production benefits, further investigation is warranted to comprehensively understand the gestational timing and biological role of Arg supplementation during fetal and postnatal development in commercial production systems.

Key words: arginine, fetal programming, growth, mortality, pig, swine

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INTRODUCTION

Amino acid (AA) supplementation has been extensively studied in weaned and growing pigs; however, similar attention has not been invested in understanding the effects of AA supplementation on the developing fetus via maternal nutrition. Despite this, it is accepted that maternal diet and uterine environment influences offspring metabolism and growth (Armitage et al., 2004; Jahan-Mihan et al., 2015). Currently, sows used in commercial production possess advanced reproductive ability due to genetic advances. Yet, knowledge on the dietary needs of the gestating sow for many AA has not improved with increasing productive capacity (Kraeling and Webel, 2015).

Increased sow litter sizes have resulted in reduced piglet birth weight (BiWt), presumably due to intrauterine growth restriction (IUGR), which is associated with poor growth performance and increased mortality (Foxcroft et al., 2007). Maternal diet may play a role in IUGR, as inadequate quantities of macro- and micro-nutrients can influence offspring development across species (Sankaran and Kyle, 2009). Thus, modifying the maternal diet maybe a useful approach in developing mitigation strategies for IUGR related to increased litter sizes. Arginine in particular has been thought to influence offspring BiWt (Wu et al., 2013). Traditionally considered a dispensable AA for both postpubertal growth and during gestation in pigs (Easter et al., 1974), Arg has recently been reclassified as conditionally essential for gestating sows (NRC, 2012). Additionally, Arg is considered an essential AA for young pigs due to inadequate Arg in sow milk and a lack of capacity for endogenous Arg synthesis (Wu et al., 2004b). Arginine has also been shown to benefit fetal myogenesis (Bérard and Bee, 2010; Garbossa et al., 2015; Madsen et al., 2017). Despite evidence of Arg utility in the developing fetus and young pigs, the long-term benefit to offspring productivity from gestational supplementation has not been investigated in commercial settings. Therefore, the objective of this project tested the hypothesis that supplementing Arg during different stages of gestation would improve offspring growth metrics in a commercial swine production system.

MATERIALS AND METHODS

Animals and Experimental Design

All procedures involving animals were approved by the Iowa State University Institutional Animal Care and Use Committee. Breeding and sow assignment to maternal diets have been previously described (Hines et al., 2019). Briefly, commercial gilts (n = 548; PIC 1050, Hendersonville, TN) were selected for breeding with pooled semen (DNA 600 boars, Columbus, NE) and assigned to 1 of 4, stageof-gestation by diet treatments. A base diet was formulated for all maternal treatments, this base formulation served as the Control diet (0% supplemental L-Arg), supplying 0.65% (approximately 15.9 g/d) Arg. Diets containing additional Arg were created through the addition of 1% L-Arg (free-base; Ajinomoto Animal Nutrition North America, Inc., Chicago, IL), to the control diet. Additional Arg increased the supply of total Arg in treatment diets to 1.28% Arg (approximately 25g/d) in the EarlyArg (1% supplemental L-Arg from day 15 to day 45 of gestation), Full-Arg (1% supplemental L-Arg from day 15 to farrowing), and Late-Arg (1% supplemental L-Arg from day 85 to farrowing) maternal dietary treatments. All diets met or exceeded the requirements for gestating gilts (NRC, 2012). During gestation, all gilts were allotted 2.6 kg/d until day 30 of gestation to address aggression as a result of mixing prior to the establishment of pregnancy; each gilt then received 2.3 kg/d from day 30 to farrowing. The total number of sows that produced a litter at farrowing were as follows: Control, n = 143; Early-Arg, n = 138; Full-Arg, n = 139; Late-Arg, n = 128.

At farrowing, viable offspring were individually identified by maternal dietary treatment: Control (n = 1,454); Early-Arg (n = 1,589); Full-Arg (n = 1,603); and Late-Arg (n = 1,451). Dietary treatments were initiated on day 15 of gestation, as excess levels of energy or protein prior to day 10 of gestation may negatively impact implantation (Bazer et al., 1968; Rehfeldt et al., 2012). Feeding of supplemental Arg in late gestation (after day 85) was selected to observe the potential benefits of capitalizing on late gestation protein accretion and muscle hypertrophy (Regnault et al., 2005; Yates et al., 2014). Management of gilts through gestation and diet treatment administration are described in detail in Hines et al. (2019).

Collection of Prewean Performance Data

Farrowing housing, treatment distribution within farrowing room, feed administration, and litter characteristics are described in Hines et al. (2019). Briefly, litter parameters and individual offspring (pig) characteristics were recorded within 24 h of birth, including number born alive (BA), number stillborn (SB), the number of mummified fetus, and individual birth weight (BiWt) of BA and SB pigs. Individual identification was assigned to each pig when BiWt was collected. Prewean mortality (PWM) was monitored daily. Individual wean weights (WW) were collected 24 to 48 h prior to weaning; age at WW was also recorded for calculation of lactation length and prewean (PW) ADG. A subset of pigs received secondary ear tag identification at weaning to ensure collection of performance data through market weight.

Postwean Performance and Mortality

Piglets were weaned based on inventory needs of the receiving facilities and age (day 17.4 ± 0.2 d). All pigs in the trial were weaned into 1 of 2 nursery facilities before final placement at a common growfinish facility for postwean growth data collection. All housing facilities included automated ventilation controls, ad libitum feed, and water supply, as well as fully slatted concrete floors. Nursery facilities provided exogenous heat, starting at 27 °C and gradually decreasing to around 21 °C as pigs increase in weight and size. Pigs were housed in large group pens, with hospital pens for pigs needing extra attention during the nursery phase. At approximately 18 kg (average weight), pigs were moved to a grower facility. A standard commercial mash diet was provided to offspring from wean to finish in 6 phases, with a focus on adjustment of protein content, energy, and lysine as pigs matured to finishing. Diets were composed predominantly of corn, distillers dried grains (with solubles), and soybean meal and formulated for minimum lysine and energy requirements at or above NRC recommendations (2012).

Whole litters were selected for postwean performance, with selection criteria based on possible limiting factors for in utero growth as well as competitive factors during preweaning growth. These selection criteria included, litter birth weight, number born alive, number of pigs cross-fostered (placed in or taken out of litter), and number weaned. Individual animal weaning weight was utilized as a covariate for individual pig performance but not as a selection criterion for performance, as differences

in weight at weaning may be related to gestation dietary treatment when all other factors have been accounted. Litters selected for postwean performance received a secondary identification at weaning to allow for maintained identification to slaughter. This selected subset included approximately 1,000 offspring. Additional weights were collected on offspring during the postwean growth phase as identification was maintained in available pigs.

Postwean growth performance was evaluated by BW, growth rate, carcass characteristics, and mortality prior to market. Body weights recorded following weaning were collected at specifically planned times representing different stages in growth during the finishing phase of production; these stages represented rapidly increasing rate of lean growth, peak rate of lean growth, and declining rate of lean growth rate (adipose deposition dominates). To achieve this, individual BW were recorded from selected pigs at single time points when the average weight of the group was estimated to be 30 (FIN1), 60 (FIN2), and 100 kg (FIN3). Mortality of all tagged pigs were recorded by individual animal identification and date of death; this continued until the final BW were recorded (FIN3). The number of pigs for each measure can be found in Table 1.

Performance to harvest was obtained from the remaining pigs of the original subset. Harvest data were collected a commercial abattoir in central Iowa. At harvest, hot carcass weight (HCW), loin depth (mm), and fat depth (mm) were collected as carcasses passed the Fat-O-Meater (SFK Ltd., Hvidovre, Denmark). Measurements for lean depth and fat depth were utilized to calculate fat to lean ratio (FLr).

Table 1. Number of pigs for each parameter of growth measured

	Treatments				
	Control	Early-Arg	Full-Arg	Late-Arg	
Parameter	n	n	n	n	
Litters, per diet	143	138	139	128	
Birth weight, kg	1,454	1,589	1,603	1,451	
$WnWt^1$	1,340	1,462	1,473	1,321	
FIN1 ²	473	635	528	424	
FIN2 ³	515	686	518	442	
FIN3 ⁴	192	194	215	211	

¹Wean weight, collected approximately 24 to 48 h prior to weaning.

²Finishing weight 1, recorded when average weight of group was estimated to be 30 kg, representing rapid lean growth.

³Finishing weight 2, recorded when average weight of group was estimated to be 60 kg, representing peak lean growth.

⁴Finishing weight 3, recorded when average weight of group was estimated to be 100 kg, representing adipose accumulation.

Statistical Analysis

Statistical analyses were performed utilizing a mixed linear regression model (Proc Mixed, SAS 9.0, Cary, NC) to evaluate individual pig growth performance and carcass data, with maternal dietary treatment, BiWt, and age-at-wean weight collection as covariates; sow and gestation pen were classified as random effects. Due to a 20-d breeding period for sows, sow breed week was utilized as a fixed blocking effect for offspring analysis. Pigs participating in cross-foster events were removed from all growth performance analysis.

As part of the experimental design, preplanned contrast comparisons were conducted by comparing the following groups: Arg supplementation before day 45 of gestation, represented by combined Early-Arg and Full-Arg maternal treatments, for comparison to no Arg supplementation prior to day 45 of gestation, represented by combining Control and Late-Arg treatment groups. Similarly, to evaluate the effects of Arg supplementation after day 85 of gestation, Full-Arg and Late-Arg were compared to those receiving no Arg supplementation during late gestation represented by the combined Control and Early-Arg treatments.

Mortality data were evaluated on individual pigs born into the trial, utilizing a mixed effect logistical regression model (Proc GLIMMIX, SAS), with sow diet and breed week as fixed effects, and random effect of sow nested within gestation pen. Age at mortality was evaluated utilizing the mixed linear regression model, considering maternal dietary treatment and sow breed week as fixed effects while sow and gestation pen were identified as random effects.

Standard error was estimated with a Satterthwaite adjustment for estimating degrees of freedom under a random effect. All values reported are least square means and maximum estimated standard error of the mean was reported in tables for each main effect comparison. Tukey-Kramer multiple comparison adjustments were made when comparing contrast comparison groups for timing of Arg in maternal gestation diets.

RESULTS

Prewean Growth Performance Improved with Supplementation of Arg During Late Stages of Gestation

Individual piglet BiWt $(1.37 \pm 0.02 \text{ kg})$ was not significantly different (P = 0.20) across maternal dietary treatments (Table 2). Piglet WW tended to

be influenced (P = 0.06) by maternal dietary treatment (5.12, 5.17, 5.25, 5.36, \pm 0.07 kg for Control, Early-Arg, Full-Arg, and Late-Arg, respectively). A tendency (P = 0.06) was also observed in PW ADG in offspring from sows in the Late-Arg dietary treatment compared to Control (0.228 vs. 0.214 \pm 0.004 kg/d, respectively).

Preplanned contrast comparisons were conducted to gain more insight on the impact of timing on arginine supplementation during gestation. These contrast comparisons revealed increased (P = 0.03)BiWt of offspring from sows receiving Arg prior to day 45 of gestation (1.38 kg; Early-Arg and Full-Arg) compared to progeny from sows that did not receive supplemental Arg through day 45 of gestation (1.34 kg; Control and Late-Arg; Table 3). No difference (P = 0.68) in BiWt (1.36 ± 0.01 kg) was observed for offspring from sows receiving additional L-Arg after day 85 of gestation (Full-Arg and Late-Arg maternal dietary treatments), in comparison to offspring from sows without Arg supplementation after day 85 of gestation (Control and Early-Arg maternal diets). Specific contrasts evaluating WW (5.21 vs. 5.25 kg) and PW ADG (0.219 vs. 0.221 kg/d) of piglets from sows supplemented Arg prior to day 45 of gestation (Early-Arg and Full-Arg) did not differ $(P \ge 0.58)$ from sows on the control diet from to day 45 of gestation (Control and Late-Arg; Table 3). However, sows receiving Arg after day 85 of gestation (Full-Arg and Late-Arg) had offspring with increased (P = 0.02) WW (5.31 vs. 5.15 kg) and PW ADG (0.225 vs. 0.215 kg/d) compared to piglets from sows fed the control diet (Control and Early-Arg) after day 85 of gestation (Table 4).

Postwean Growth Performance Was Not Affected by Maternal Diet Treatment

Pig PW ADG was not significantly different among maternal treatments (Table 2). Offspring weight at FIN1 across maternal diets was not significantly different (average 34.7 \pm 1.4 kg; P = 0.82). Similarly, ADG from weaning until FIN1 was not significantly different (P = 0.82) across maternal dietary treatments. This pattern of similar growth $(P \ge 0.17)$ among treatments continued through FIN3 (Table 2). Overall growth performance (ADG from birth to FIN3) was not significantly different (P = 0.67) between maternal diets (Table 2). Contrast comparisons revealed a difference (P = 0.05) in growth rate during the peak lean accretion phase (30 to 60 kg) with an increase in ADG in Control and Late-Arg offspring (0.83 \pm 0.01 kg/d) as compared to Early-Arg and Full-Arg offspring (0.80 ±

Table 2. Effect of maternal dietary supplementation of 1% Arg and timing during gestation on offspring growth performance

		Treatment ¹				
Parameter	Control	Early-Arg	Full-Arg	Late-Arg	SEM^2	P-value
BiWt³, kg	1.35	1.38	1.39	1.35	0.02	0.20
WW Age ⁴ , d	17.7	17.5	17.2	17.4	0.2	0.33
WW ⁵ , kg	5.12	5.17	5.25	5.36	0.07	0.06
PW ADG ⁶ , kg/d	0.214	0.217	0.221	0.228	0.004	0.06
FIN1 ⁷ , kg	33.9	34.5	35.7	34.8	1.4	0.82
Wean to FIN1 ADG8, kg/d	0.43	0.44	0.45	0.44	0.01	0.82
FIN29, kg	63.3	63.8	63.4	64.0	1.3	0.97
FIN1 to FIN2 ADG10, kg/d	0.82	0.79	0.81	0.83	0.02	0.17
FIN3 ¹¹ weight, kg	101.5	98.6	105.3	100.8	6.2	0.75
FIN2 to FIN3 ADG12 kg/d	1.05	1.10	1.08	1.05	0.04	0.42
Birth to FIN3 ADG ¹³ , kg/d	0.67	0.68	0.69	0.66	0.02	0.67

¹Maternal dietary treatments consisted of: Control (0% supplemental L-Arg); Early-Arg (1% supplemental L-Arg 15 to 45 d of gestation); Full-Arg (1% supplemental L-Arg 15 d of gestation until farrowing); and Late-Arg (1% supplemental L-Arg 85 d of gestation until farrowing).

0.01 kg/d), however, no differences were detected ($P \ge 0.1$) in other postweaning parameters or carcass characteristics due to maternal Arg supplementation during early or late gestation (Tables 3 and 4).

Supplementation of Arg During Gestation Did Not Significantly Improve Carcass Characteristics of Offspring

Offspring carcass characteristics were not significantly affected by maternal dietary treatment. Hot carcass weight was similar (85 kg \pm 0.02 kg; P = 0.67) across maternal dietary treatments (Table 5). Carcass characteristics of lean depth and fat depth were also not different ($P \ge 0.94$) by treatment (Table 5). Finally, FLr ratio was similar among treatments (P = 0.97), with an average FLr of 0.32 \pm 0.02 for offspring evaluated at harvest (Table 5).

Offspring Mortality Rate Was Not Significantly Improved by Maternal Dietary Supplementation of Arg

Total PWM was not different (P = 0.64) across maternal dietary treatment (Table 6), with similar

results observed in the 24 h postbirth (P = 0.65) and mortality from 24 h postbirth to weaning (P = 0.73). Overall pig mortality rate, from birth to FIN3, was similar by treatment (P = 0.99). Contrast comparisons showed a tendency for decreased postwean mortality rates in offspring from sows receiving Arg after day 85 (Full-Arg and Late-Arg maternal dietary treatments) of gestation compared to offspring from sows on the control diet after day 85 (Control and Early-Arg maternal dietary treatments) of gestation (3.6 vs. $4.9 \pm 0.6\%$, respectively; P = 0.07; Table 8). No significant treatment differences were observed in any other contrast comparisons for offspring performance (Tables 7 and 8).

DISCUSSION

Recent increases in litter size of commercial sows has been associated with reduced BiWt, presumably due to intrauterine crowding, leading to IUGR and a subsequent reduction in growth performance and survivability (Foxcroft et al., 2006). Pigs experiencing IUGR are at a greater risk for low BiWt, reduced capacity for efficient gain, and increased rates of morbidity and mortality

²Maximum value of standard error of the mean for all treatments.

³Average birth weights (within 24 h postbirth) of all pigs born alive as reported in Hines et al. 2019.

⁴Wean weight age, age of offspring postbirth when wean weights were collected. Weaning occurred approximately 24 to 48 h postwean weight collection.

⁵Wean weight, collected 24 to 48 h prior to weaning.

⁶Prewean average daily gain, wean weight – birth weight/wean weight age.

⁷Finishing weight 1, recorded when average group weight was estimated to be 30 kg, representing rapid lean growth.

⁸Average daily gain from wean to FIN1.

⁹Finishing weight 2, recorded when average group weight was estimated to be 60 kg, representing peak lean growth.

¹⁰Average daily gain from FIN1 to FIN2.

¹¹Finishing weight 3, recorded when average group weight was estimated to be 100 kg, representing adipose accumulation.

¹²Average daily gain from FIN2 to FIN3.

¹³Average daily gain from birth to FIN3.

Table 3. Contrast comparing inclusion of maternal dietary supplementation of 1% Arg prior to day 45 of gestation on offspring growth performance¹

Parameter	Trea	atment		
	Control and Late-Arg ²	g ² Early-Arg and Full-Arg ³		P-value
BiWt ⁵ , kg	1.34	1.38	0.01	0.03
WW ⁶ , kg	5.25	5.21	0.05	0.59
PW ADG ⁷ , kg/d	0.221	0.219	0.003	0.58
FIN1 weight8, kg	34.36	35.08	0.98	0.60
Wean to FIN1 ADG9, kg/d	0.43	0.44	0.01	0.43
FIN2 weight ¹⁰ , kg	63.7	63.7	0.9	0.98
FIN1 to FIN2 ADG11, kg/d	0.83	0.80	0.01	0.05
FIN3 weight ¹² , kg	101.4	102.2	5.2	0.85
FIN2 to FIN3 ADG ¹³ kg/d	1.05	1.09	0.04	0.10
Birth to FIN3 ADG14, kg/d	0.67	0.68	0.02	0.24

¹Parameter estimate contrasts from offspring born to maternal dietary treatments of Control (0% supplemental L-Arg) and Late-Arg (1% supplemental L-Arg 85 d of gestation until farrowing) as compared to offspring born to maternal dietary treatments of Early-Arg (1% supplemental L-Arg 15 to 45 d of gestation) and Full-Arg (1% supplemental L-Arg 15 d of gestation until farrowing).

(Alvarenga et al., 2013; Kraeling and Webel, 2015). This is important as BiWt and WW are correlated with growth capacity later in life (Beaulieu et al., 2010) and maternal diet can impact offspring development across species. Due to the influence of maternal diet on piglet BiWt, subsequent survival, and growth performance, altering the sow's diet represents an opportunity to improve swine industry productivity and minimize mortality.

Arginine has been observed in multiple studies to increase piglet BiWt, as reviewed by Wu et al. (2013); however, the long-term benefits on offspring growth and productivity has not been thoroughly investigated. In this experiment, sows receiving 1% supplemental L-Arg during the late stages of pregnancy (after day 85 of gestation) showed a tendency to influence WW and PW ADG of progeny. Currently, knowledge on metabolic partitioning of specific nutrients from maternal blood towards fetal and placental function is sparse, though it is known that dramatic changes in maternal nutrition during gestation can influence offspring metabolism (De Rooij et al., 2006; Foxcroft et al., 2006). Specifically, changes to tissue formation, such as skeletal muscle

(Waylan et al., 2005; Rehfeldt et al., 2011; Hines et al., 2013) and adipose (Satterfield et al., 2012) have been observed with nutrient specific changes to maternal diets. Maternal supplementation of Arg during early gestation (day 14–28) has been observed to influence muscle fiber number (Bérard and Bee, 2010) or muscle fiber diameter (Garbossa et al., 2015). In the Garbossa et al. (2015) study, offspring had increased birth and nursery weights after Arg supplementation during early gestation (day 25) to 53), although these improvements waned in the grower and finishing phases of production. Like the current experiment, Garbossa et al. (2015) found no differences in postwean growth performance. Garbossa et al. (2015) further observed increases in HCW of male offspring at 142 d of age from Arg supplemented sows; however, this is in contrast to the work presented in this paper. Improvements to WW are generally accepted as influential on postwean growth; however, there are numerous factors in finishing production that might influence pig growth and final carcass performance.

Transportation, dietary restrictions, environmental conditions, competition within pen, and

² Control and Late-Arg treatments representing litters not provided additional L-Arg during gestations days 15 to 45.

³Early-Arg and Full-Arg treatments representing offspring from litters provided 1% additional L-Arg during gestation days 15 to 45.

⁴ Maximum value of standard error of the mean for all treatments.

⁵Average birth weights (within 24 h postbirth) of all pigs born alive as reported in Hines et al., 2019.

⁶Wean weight, collected approximately 24 to 48 h prior to weaning.

⁷Prewean average daily gain, wean weight – birth weight/wean weight age.

⁸Finishing weight 1, recorded when average group weight was estimated to be 30 kg, representing rapid lean growth.

⁹Average daily gain from wean to FIN1.

¹⁰Finishing weight 2, recorded when average group weight was estimated to be 60 kg, representing peak lean growth.

¹¹Average daily gain from FIN1 to FIN2.

¹²Finishing weight 3, recorded when average group weight was estimated to be 100 kg, representing adipose accumulation.

¹³Average daily gain from FIN2 to FIN3.

¹⁴Average daily gain from birth to FIN3.

Table 4. Contrasts of maternal dietary supplementation of 1% Arg after day 85 of gestation on offspring growth performance¹

	Treat	tment		<i>P</i> -value
Parameter	Control and Early-Arg ²	Full-Arg and Late-Arg ³	SEM^4	
BiWt ⁵ , kg	1.36	1.36	0.01	0.68
WW ⁶ , kg	5.15	5.31	0.05	0.02
PW ADG ⁷ , kg/d	0.215	0.225	0.003	0.02
FIN1 weight8, kg	34.1	35.3	1.0	0.44
Wean to FIN1 ADG9, kg/d	0.44	0.44	0.01	0.52
FIN2 weight ¹⁰ , kg	63.6	63.8	0.9	0.89
FIN1 to FIN2 ADG11, kg/d	0.81	0.82	0.01	0.27
FIN3 weight ¹² weight, kg	100.4	103.3	5.3	0.51
FIN2 to FIN3 ADG ¹³ , kg/d	1.08	1.07	0.04	0.59
Birth to FIN3 ADG14, kg/d	0.68	0.67	0.02	0.87

¹Parameter estimate contrasts from offspring born to maternal dietary treatments of Control (0% supplemental L-Arg) and Early-Arg (1% supplemental L-Arg 15 to 45 d of gestation) as compared to offspring born to maternal dietary treatments of Full-Arg (1% supplemental L-Arg 15 d of gestation until farrowing) and Late-Arg (1% supplemental L-Arg 85 d of gestation until farrowing).

Table 5. Effect of maternal dietary supplementation of 1% Arg and timing during gestation on offspring carcass characteristics¹

		Treat	tment	, 	,	'
Parameter	Control	Early-Arg	Full-Arg	Late-Arg	SEM^2	P-value
HCW ³ , kg	84.3	84.5	85.5	84.9	0.00	0.67
Loin depth4, mm	54.2	54.4	53.7	54.0	1.50	0.94
Fat depth ⁵ , mm	16.7	16.7	16.7	16.8	0.70	0.99
FLr ⁶	0.31	0.31	0.32	0.32	0.02	0.97

¹Parameter estimate contrasts from offspring born to maternal dietary treatments of Control (0% supplemental L-Arg) and Early-Arg (1% supplemental L-Arg 15 to 45 d of gestation) as compared to offspring born to maternal dietary treatments of Full-Arg (1% supplemental L-Arg 15 d of gestation until farrowing) and Late-Arg (1% supplemental L-Arg 85 d of gestation until farrowing).

health challenges are all production components that can influence growth performance of postwean pigs. Pigs with heavier WW demonstrate superior development of the digestive system and survival (Wattanakul et al., 2007), both of which may reduce the negative effects of postwean stress experienced

by weanling pigs in transition to new facilities and diet. Pigs that are nutritionally restricted during lactation, or immediately postweaning, also exhibit differences in growth performance (Wattanakul et al., 2007). Additionally, larger BiWt, and subsequently larger WW, pigs have an increased

²Control and Early-Arg treatments representing offspring from litters not provided 1% additional L-Arg during gestation day 85 to farrowing.

³Full-Arg and Late-Arg treatments representing offspring from litters provided 1% additional L-Arg during gestation day 85 to farrowing.

⁴ Maximum value of standard error of the mean for all treatments.

⁵Average birth weights (within 24 h postbirth) of all pigs born alive as reported in Hines et al. 2019.

⁶Wean weight, collected approximately 24 to 48 h prior to weaning.

⁷Prewean average daily gain, wean weight – birth weight/wean weight age.

⁸Finishing weight 1, recorded when average group weight was estimated to be 30 kg, representing rapid lean growth.

⁹Average daily gain from wean to FIN1.

¹⁰Finishing weight 2, recorded when average group weight was estimated to be 60 kg, representing peak lean growth.

¹¹Average daily gain from FIN1 to FIN2.

¹²Finishing weight 3, recorded when average group weight was estimated to be 100 kg, representing adipose accumulation.

¹³Average daily gain from FIN2 to FIN3.

¹⁴Average daily gain from birth to FIN3.

²Maximum value of standard error of the mean for all treatments.

³Hot carcass weight.

⁴Loin depth, mm measured at 10th rib.

⁵Fat depth, mm measured at 10th rib.

⁶Fat to lean ratio, calculated as fat/lean.

Table 6. Effect of maternal dietary supplementation of 1% Arg and timing during supplementation on off-spring mortality¹

	Treatment					
Parameter	Control	Early-Arg	Full-Arg	Late-Arg	SEM^2	P-value
Prewean mortality ³ , %	11.5	10.2	12.4	12.2	1.5	0.64
24 hr. mortality ⁴ , %	5.2	3.7	4.9	4.5	1.0	0.65
PWM, dead post-245, %	6.4	6.7	7.5	7.8	1.1	0.73
Postwean mortality ⁶ , %	4.4	5.4	3.8	3.5	0.9	0.24
Age at mortality, postplacement	72.8	73.0	82.5	70.2	7.1	0.58
All mortality, birth to 100 kg ⁷ , %	15.6	15.1	15.8	15.5	1.7	0.99

¹Parameter estimate contrasts from offspring born to maternal dietary treatments of Control (0% supplemental L-Arg) and Early-Arg (1% supplemental L-Arg 15 to 45 d of gestation) as compared to offspring born to maternal dietary treatments of Full-Arg (1% supplemental L-Arg 15 d of gestation until farrowing) and Late-Arg (1% supplemental L-Arg 85 d of gestation until farrowing).

Table 7. Contrasts of maternal dietary supplementation of 1% Arg prior to day 45 of gestation on mortality rates of offspring, birth through finishing¹

	Trea	Treatment		
Parameter	Control and Late-Arg ²	d Late-Arg ² Early-Arg and Full-Arg ³		P-value
Prewean mortality ⁵ , %	11.9	11.3	1.0	0.67
24 h mortality ⁶ , %	4.8	4.2	0.7	0.51
PWM, dead post-247, %	7.1	7.1	0.7	0.96
Postwean mortality8, %	3.9	4.5	0.5	0.41
Total mortality, birth to 100 kg9, %	15.5	15.4	1.2	0.95

¹Parameter estimate contrasts from offspring born to maternal dietary treatments of Control (0% supplemental L-Arg) and Late-Arg (1% supplemental L-Arg 85 d of gestation until farrowing) as compared to offspring born to maternal dietary treatments of Early-Arg (1% supplemental L-Arg 15 to 45 d of gestation) and Full-Arg (1% supplemental L-Arg 15 d of gestation until farrowing).

likelihood of achieving full value at market (Fix et al., 2010), as compared to smaller counterparts. In the current work, contrast comparisons indicated that offspring receiving late Arg supplementation (after day 85 of gestation) had improved WW and PW ADG. This may indicate that the effect of Arg during late gestation may be more readily observed in enabling the sow to provide improved nutrition to offspring during lactation and not through an improvement in fetal development.

Mammary development and lactation performance, resulting in improved quantity and/ or quality of sow milk, can improve offspring growth during lactation. Specific AA supplementation may influence lactation performance and Arg is readily utilized by mammary gland tissues, although its direct impact on milk quality has been questioned, as Arg levels are not increased in milk when Arg is supplemented during lactation (Rezaei et al., 2016). In support of mammary utilization, Arg has been implicated in improving protein concentration of milk when fed after day 30 of gestation through lactation (Krogh et al., 2015) and weight gain of suckling pigs (Zhu et al., 2017). Interestingly, Krogh et al. (2016) observed improvements to finishing

²Maximum value of standard error of the mean for all treatments.

³Total mortality, from birth to weaning as reported in Hines et al. 2019.

⁴Mortality rate of pigs born alive that died or were euthanized prior to 24 h of life.

⁵Mortality rate of pigs born alive that died or were euthanized post-24 h of life.

⁶Mortality rate of pigs weaned to finishing.

⁷Mortality rate of all offspring, from birth to finishing.

²Control and Late-Arg treatments representing offspring from litters not provided additional L-Arg during gestations days 15 to 45.

³Early-Arg and Full-Arg treatments representing offspring from litters provided 1% additional L-Arg during gestation days 15 to 45.

⁴Maximum value of standard error of the mean for all treatments.

⁵Total mortality, from birth to weaning.

⁶Mortality rate of pigs born alive that died or were euthanized prior to 24 h of life.

⁷Mortality rate of pigs born alive that died or were euthanized post-24 h of life.

⁸Mortality rate of pigs weaned to finishing.

⁹Mortality rate of all offspring, from birth to finishing.

Table 8. Contrasts of maternal dietary supplementation of 1% Arg after day 85 of gestation on mortality rates of offspring, birth through finishing¹

	Treat	Treatment		
Parameter	Control and Early-Arg ²	Full-Arg and Late-Arg ³	SEM^4	P-value
Prewean mortality ⁵ , %	10.9	12.3	1.0	0.28
24 hr. mortality ⁶ , %	4.3	4.7	0.7	0.71
PWM, dead post-24 ⁷ , %	0.6	0.7	0.8	0.27
Postwean mort8, %	4.9	3.6	0.6	0.07
All mortality, birth to 100 kg9, %	0.6	0.5	1.2	0.84

¹Parameter estimate contrasts from offspring born to maternal dietary treatments of Control (0% supplemental L-Arg) and Early-Arg (1% supplemental L-Arg 15 to 45 d of gestation) as compared to offspring born to maternal dietary treatments of Full-Arg (1% supplemental L-Arg 15 d of gestation until farrowing) and Late-Arg (1% supplemental L-Arg 85 d of gestation until farrowing).

performance in offspring due to supplementation of Arg after day 30 of gestation through lactation. In combination with previous work, the results of the current experiment may indicate that starting supplementation at day 85 of gestation may improve lactation performance in the sow, however, without providing lasting effects on the offspring.

Results of this study suggest that Arg during gestation may influence offspring performance as an extension of lactation performance. Additional hypothesis should be tested to better understand the AA requirements of the sow and the developing offspring prior to or during gestation to understand the effects of maternal nutrition on prenatal programming that provides lasting effects on postweaning growth performance.

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LITERATURE CITED

Alvarenga, A. L., H. Chiarini-Garcia, P. C. Cardeal, L. P. Moreira, G. R. Foxcroft, D. O. Fontes, and F. R. Almeida. 2013. Intra-uterine growth retardation affects birthweight and postnatal development in pigs, impairing muscle accretion, duodenal mucosa

morphology and carcass traits. Reprod. Fertil. Dev. 25:387–395. doi:10.1071/RD12021

Armitage, J. A., I. Y. Khan, P. D. Taylor, P. W. Nathanielsz, and L. Poston. 2004. Developmental programming of the metabolic syndrome by maternal nutritional imbalance: How strong is the evidence from experimental models in mammals? J. Physiol. 561:355–377. doi:10.1113/jphysiol.2004.072009

Bazer, F. W., A. J. Clawson, O. W. Robison, C. K. Vincent, and L. C. Ulberg. 1968. Explanation for embryo death in gilts fed a high energy intake. J. Anim. Sci. 27:1021–1026. doi:10.2527/jas1968.2741021x

Beaulieu, A. D., J. L. Aalhus, N. H. Williams, and J. F. Patience. 2010. Impact of piglet birth weight, birth order, and litter size on subsequent growth performance, carcass quality, muscle composition, and eating quality of pork. J. Anim. Sci. 88:2767–2778. doi:10.2527/jas.2009-2222

Bérard, J., and G. Bee. 2010. Effects of dietary l-arginine supplementation to gilts during early gestation on foetal survival, growth and myofiber formation. Animal. 4:1680–1687. doi:10.1017/S1751731110000881

Easter, R. A., R. S. Katz, and D. H. Baker. 1974. Arginine: A dispensable amino acid for postpubertal growth and pregnancy of swine. J. Anim. Sci. 39:1123–1128. doi:10.2527/jas1974.3961123x

Fix, J. S., J. P. Cassady, J. W. Holl, W. O. Herring, M. S. Culbertson, and M. T. See. 2010. Effect of piglet birth weight on survival and quality of commercial market swine. Livest. Sci. 132:98–106. doi:10.1016/j. livsci.2010.05.007

Foxcroft, G. R., W. T. Dixon, S. Novak, C. T. Putman, S. C. Town, and M. D. Vinsky. 2006. The biological basis for prenatal programming of postnatal performance in pigs. J. Anim. Sci. 84 Suppl:E105–E112. doi:10.2527/2006.8413_supple105x

Foxcroft, G., G. Bee, W. Dixon, M. Hahn, J. Harding,
J. Patterson, T. Putman, S. Sarmento, M. Smit,
T. WaiYue, et al. 2007. In: J. Wiseman, M. A. Varley,
S. McOrist, and B. Kemp, editors. Paradigms in pig

²Control and Early-Arg treatments representing offspring from litters not provided additional L-Arg during gestation days 85 to farrowing.

 $^{^3}$ Full-Arg and Late-Arg treatments representing offspring from litters provided 1% additional L-Arg during gestation days 85 to farrowing.

⁴Maximum value of standard error of the mean for all treatments.

⁵Total mortality, from birth to weaning.

⁶Mortality rate of pigs born alive that died or were euthanized prior to 24 h of life.

⁷Mortality rate of pigs born alive that died or were euthanized post-24 h of life.

⁸Mortality rate of pigs weaned to finishing.

⁹Mortality rate of all offspring, from birth to finishing.

- science: Consequences of selection for litter size on piglet development. 62nd ed. Nottingham University Press, Nottingham. p. 207–229.
- Garbossa, C. A. P., F. M. Carvalho Júnior, H. Silveira, P. B. Faria, A. P. Schinckel, M. L. T. Abreu, and V. S. Cantarelli. 2015. Effects of ractopamine and arginine dietary supplementation for sows on growth performance and carcass quality of their progenies. J. Anim. Sci. 93:2872–2884. doi:10.2527/jas2014-8824
- Hines, E. A., J. D. Coffey, C. W. Starkey, T. K. Chung, and J. D. Starkey. 2013. Improvement of maternal vitamin D status with 25-hydroxycholecalciferol positively impacts porcine fetal skeletal muscle development and myoblast activity. J. Anim. Sci. 91:4116–4122. doi:10.2527/ jas.2013-6565
- Hines, E. A., M. R. Romoser, Z. E. Keifer, A. F. Keating,
 L. H. Baumgard, J. Niemi, N. K. Gabler, J. F. Patience,
 B. Haberl, N. H. Williams, et al. 2019. The impact of dietary supplementation of arginine during gestation in a commercial swine herd: I. Gilt reproductive performance.
 J. Anim. Sci.
- Jahan-Mihan, A., J. Rodriguez, C. Christie, M. Sadeghi, and T. Zerbe. 2015. The role of maternal dietary proteins in development of metabolic syndrome in offspring. Nutrients. 7:9185–9217. doi:10.3390/nu7115460
- Kraeling, R. R., and S. K. Webel. 2015. Current strategies for reproductive management of gilts and sows in north America. J. Anim. Sci. Biotechnol. 6:3. doi:10.1186/2049-1891-6-3
- Krogh, U., N. Oksbjerg, P. Ramaekers, and P. K. Theil. 2015. Colostrum and milk production in sows fed supplementary arginine during gestation and lactation. In: 13th Digestive Physiology of Pigs, May 19–21, 2015, Kliczkow, Poland. p. 1–12.
- Krogh, U., N. Oksbjerg, P. Ramaekers, and P. K. Theil. 2016. Long-term effects of maternal arginine supplementation and colostrum intake on pre- and postweaning growth in pigs. J. Anim. Sci. 94:117–120. doi:10.2527/jas2015-9492
- Madsen, J. G., C. Pardo, M. Kreuzer, and G. Bee. 2017. Impact of dietary l-arginine supply during early gestation on myofiber development in newborn pigs exposed to intra-uterine crowding. J. Anim. Sci. Biotechnol. 8:58. doi:10.1186/s40104-017-0188-y
- NRC. 2012. Nutrient requirements of swine. 11th Revised Edition. The National Academies Press, Washington, DC.
- Regnault, T. R. H., J. E. Friedmann, R. B. Wilkening, R. V. Anthony, and W. W. Hay. 2005. Fetoplacental transport and utilization of amino acids in IUGR--a review. Placenta. 26(Suppl A): S52–62. doi:10.1016/j. placenta.2005.01.003
- Rehfeldt, C., I. S. Lang, S. Görs, U. Hennig, C. Kalbe, B. Stabenow, K. P. Brüssow, R. Pfuhl, O. Bellmann, G. Nürnberg, et al. 2011. Limited and excess dietary protein during gestation affects growth and compositional traits in gilts and impairs offspring fetal growth. J. Anim. Sci. 89:329–341. doi:10.2527/jas.2010-2970

- Rehfeldt, C., L. Lefaucheur, J. Block, B. Stabenow, R. Pfuhl, W. Otten, C. C. Metges, and C. Kalbe. 2012. Limited and excess protein intake of pregnant gilts differently affects body composition and cellularity of skeletal muscle and subcutaneous adipose tissue of newborn and weanling piglets. Eur. J. Nutr. 51:151–165. doi:10.1007/ s00394-011-0201-8
- Rezaei, R., Z. Wu, Y. Hou, F. W. Bazer, and G. Wu. 2016. Amino acids and mammary gland development: Nutritional implications for milk production and neonatal growth. J. Anim. Sci. Biotechnol. 7:20. doi:10.1186/s40104-016-0078-8
- de Rooij, S. R., R. C. Painter, D. I. Phillips, C. Osmond, R. P. Michels, I. F. Godsland, P. M. Bossuyt, O. P. Bleker, and T. J. Roseboom. 2006. Impaired insulin secretion after prenatal exposure to the Dutch famine. Diabetes Care. 29:1897–1901. doi:10.2337/dc06-0460
- Sankaran, S., and P. M. Kyle. 2009. Aetiology and Pathogenesis of IUGR. Best Pract. Res. Clin. Obstet. Gynaecol. 23:765–777. doi:10.1016/j.bpobgyn.2009.05.003.
- Satterfield, C. M., K. A. Dunlap, D. H. Keisler, F. W. Bazer, and G. Wu. 2012. Arginine nutrition and fetal brown adipose tissue development in diet-induced obese sheep. Amino Acids. 43:1593–1603. doi:10.1007/s00726-012-1235-9
- Wattanakul, W., J. A. Rooke, A. H. Stewart, P. R. English, and S. A. Edwards. 2007. Effect of milk deprivation during the lactation period on performance and digestive enzyme activities of the piglets following weaning. Animal. 1:381–387. doi:10.1017/S1751731107684997
- Waylan, A. T., J. P. Kayser, D. P. Gnad, J. J. Higgins, J. D. Starkey, E. K. Sissom, J. C. Woodworth, and B. J. Johnson. 2005. Effects of L-carnitine on fetal growth and the IGF system in pigs. J. Anim. Sci. 83:1824–1831. doi:10.2527/2005.8381824x
- Wu, G., F. W. Bazer, T. A. Cudd, C. J. Meininger, and T. E. Spencer. 2004a. Maternal nutrition and fetal development. J. Nutr. 134:2169–2172. doi:10.1093/jn/134.9.2169
- Wu, G., F. W. Bazer, M. C. Satterfield, X. Li, X. Wang, G. A. Johnson, R. C. Burghardt, Z. Dai, J. Wang, and Z. Wu. 2013. Impacts of arginine nutrition on embryonic and fetal development in mammals. Amino Acids. 45:241– 256. doi:10.1007/s00726-013-1515-z
- Wu, G., D. A. Knabe, and S. W. Kim. 2004b. Arginine nutrition in neonatal pigs. J. Nutr. 134:2783S–2790S. doi:10.1093/ jn/134.10.2783S
- Yates, D. T., D. S. Clarke, A. R. Macko, M. J. Anderson, L. A. Shelton, M. Nearing, R. E. Allen, R. P. Rhoads, and S. W. Limesand. 2014. Myoblasts from intrauterine growth-restricted sheep fetuses exhibit intrinsic deficiencies in proliferation that contribute to smaller semitendinosus myofibres. J. Physiol. 592:3113–3125. doi:10.1113/jphysiol.2014.272591
- Zhu, C., C. Yi Guo, K. Guo Gao, L. Wang, Z. Chen, X. Yong Ma, and Z. Yong Jiang. 2017. Dietary arginine supplementation in multiparous sows during lactation improves the weight gain of suckling piglets. J. Integr. Agric. 16:648–655. doi:10.1016/S2095-3119(16)61426-0