scientific reports

OPEN

Evaluation of organ and skeletal physiological characteristics for improved classification of growth-restricted newborn piglets

Pau Salgado-López[1], Eudald Llauradó-Calero[1]✉, Sílvia García-Vilana[2], David Sánchez-Molina[3], Albert Brun[4], Maria Font-i-Furnols[4], Josep Gasa[1] & David Solà-Oriol[1]

The identification of potentially slow-growing pigs at birth, using both external and internal traits, would enable the early implementation of targeted management and feeding strategies to optimize herd management and improve production efficiency. Twenty-four piglets from six hyperprolific sows were classified into four categories based on birth body weight (BW), body mass index (BMI), and crow-to-rump length (CRL): severe intrauterine growth restriction (sIUGR), low birth weight (LBW), moderate birth weight (MBW), and high birth weight (HBW). Organ weights, computed tomography (CT) measurements, bending tests to assess tibial mechanical and geometric properties, and tibial mineral content analysis were performed to evaluate organ and skeletal physiological characteristics. Severe IUGR piglets exhibited higher brain-to-organ ratios and relative brain weights, which decreased linearly across categories. High birth BW piglets demonstrated 70% more bone volume and a greater proportion of high-density bones than sIUGR piglets, along with the largest cortical area and thickness in tibia measurements. On the other hand, sIUGR showed higher maximum stress, stiffness values, and manganese content in their tibiae compared to other categories. These findings reveal that piglets with varying degrees of IUGR prioritize brain development, exhibit asymmetrical organ growth, and experience impaired ossification and longitudinal bone growth. This study underscores the need to incorporate complementary birth indicators to refine the classification of newborn piglets with different degrees of restriction.

Keywords Bending tests, Computed tomography, Intrauterine growth restriction, Mineral content, Organ and skeletal physiological characteristics, Swine

One of the primary economic drivers in pig production is the reproductive efficiency, which is typically defined as the number of piglets produced per sow per year. Optimizing this factor is crucial for the sustainability and productivity of the global pork industry. In recent decades, continuous genetic advancements have focused on increasing sow prolificacy, aiming to raise the number of slaughtered pigs produced per sow per year[1]. However, this increase in prolificacy has led to a significant reduction in average birth body weight (BW), resulting in a higher number of lightweight piglets at birth[2,3]. Piglets born small may experience varying degrees of intrauterine growth restriction (IUGR)[4–7] and are likely to struggle to catch up with their heavier counterparts throughout the production cycle[2,3,8].

It is estimated that approximately 10–15% of pigs in any given batch exhibit slow growth[9]. Recent studies have highlighted the identification of this subset of pigs at different production stages by applying different machine learning algorithms to robust and powerful databases[10,11]. These pigs are at a higher risk of mortality throughout the production cycle[9,12]. Those that survive present significant management challenges in modern swine production systems, which aim to group contemporary pigs within the same batch to ensure optimal animal health and performance[13]. In addition, it is also reported that as pigs near the end of the production

[1]Animal Nutrition and Welfare Service (SNIBA), Department of Animal and Food Science, Autonomous University of Barcelona, Bellaterra 08193, Spain. [2]Polytechnic School of Engineering of Vilanova i la Geltrú (EPSEVG), Polytechnic University of Catalonia, Av. Víctor Balaguer, 1, Barcelona 08800, Spain. [3]Barcelona East School of Engineering (EEBE), Polytechnic University of Catalonia, Av. Eduard Maristany, 14, Barcelona 08019, Spain. [4]IRTA-Food Quality and Technology, Finca Camps i Armet, Monells, Girona 17121, Spain. ✉email: eudald.llaurado@uab.cat

cycle, the likelihood of lighter pigs being sent to the slaughterhouse at a later stage increase[14]. Therefore, early identification of slow-growing pigs and the implementation of effective preventive measures are essential to enhance their performance and reduce variability. This is further supported by studies emphasizing that changes in pigs' BW category are more frequent during the lactation period[15,16].

Potentially slow-growing pigs can be easily identified at birth if they exhibit severe IUGR and display a distinctive head morphology previously described[17]. However, identifying piglets that lack these traits at birth but experience poor subsequent growth performance, persistently remaining in the lower quartile of the birth weight population distribution, becomes a greater challenge. Birth BW is widely recognized as one of the most critical determinants of lifetime growth performance[18] and survivability[19] in pigs. However, extensive scientific literature research has also explored other individual traits influencing pre-weaning mortality and growth. These include morphometric attributes[6,7,20] physiological characteristics[21–23] and behavioral features[24]. In addition, risk factors related to the sow, the environment, and BW variability[14,25,26] among others, have also been examined highlighting their collective impact on piglet growth and survival.

The identification of slow-growing pigs at birth would facilitate the implementation of targeted management and feeding strategies during early life, allowing farmers to optimize herd management and enhance overall farm production efficiency[15]. Within these strategies, particular attention should be given to those focusing on piglet care during their first days of life. A common practice in pig production, particularly for supporting low-birth weight piglets, is colostrum supplementation. For example[27], reported that orally supplementing weaker piglets with freshly milked colostrum from sows within the same herd helped stabilize their body temperature and enhanced litter performance within the first 24 h. Another strategy is split suckling prior to cross-fostering, which has been shown to improve daily weight gain and litter uniformity at weaning[28]. Equally important is the feeding management of piglets during the early stages. One widely used strategy is creep feeding, which stimulates feed intake and promotes post-weaning growth. This practice has been associated with increased total weight gain in eater pigs[29,30] reduced weight variability at weaning[31] and improved growth during the early post-weaning period[29,32,33]. Although less common than creep feeding, milk replacer supplementation has also demonstrated significant benefits, including higher weaning weights, increased total litter weight[34,35] and enhanced weight gain after weaning[16].

Among the performance criteria described in the literature for identifying these growth-restricted piglets, birth BW, along with other indicators of body conformation, such as body mass index (BMI)[6] and crown-to-rump length (CRL; the piglet's supine length measured from the crown of the head to the base of the tail), stand out as the most widely studied. Despite extensive investigation, little is known about their correlation with internal measurements, such as those related to the physiological status of organs and bones, which are key factors in postnatal growth. The interest in assessing bone characteristics in piglets at birth lies in finding a more specific indicator of skeletal development than birth weight alone. This could help identify neonates at greater risk of compromised postnatal growth trajectories. In humans, several studies have demonstrated that neonates with IUGR exhibit altered biochemical markers of bone formation, such as lower circulating osteocalcin and 1.25-dihydroxyvitamin D concentrations, relative to appropriate-for-gestational-age infants[36]. These alterations arise in part from impaired endochondral ossification under conditions of placental insufficiency and maternal metabolic dysfunction, which limit the availability of substrates necessary for normal skeletogenesis[36,37]. Importantly, bone physiological status has been linked to growth and bone mass accretion during infancy. For example[38], showed that IUGR-associated reductions in endochondral ossification correlate with impaired postnatal growth velocity and lower bone strength in early childhood.

We hypothesized that piglets with low body metrics at birth exhibit impaired organ and bone physiological status compared to their heavier counterparts. Identifying strong correlations between external and internal measures is essential for reliably identifying potentially slow-growing piglets at an early stage. This early identification would enable the timely implementation of effective intervention strategies for this subset of pigs. In this context, the objectives of this study were to (1) characterize piglets at the level of organ and bone physiological status at birth, and (2) investigate whether these characteristics correlate with individual external physical metrics currently used as indicators of survivability and growth performance in suckling piglets.

Results
Descriptive results
Average birth BW of severe intrauterine growth restricted (sIUGR), low birth weight (LBW), moderate birth weight (MBW) and high birth weight (HBW) piglets were 0.49 ± 0.037 kg, 0.97 ± 0.042 kg, 1.18 ± 0.027 kg, and 1.69 ± 0.121 kg, respectively. Significant differences in birth BW between these four categories of piglets were also reflected in BMI and CRL measurements, likely due to the strong correlation among these variables. Pearson's correlation coefficient analysis showed that birth BW was significantly positively correlated with BMI ($R = 0.870$; $P \leq 0.001$) and CRL ($R = 0.935$; $P \leq 0.001$). The HBW piglets exhibited the highest BMI and CRL values, while the MBW and LBW piglets had intermediate values that did not differ significantly from each other. The sIUGR piglets showed the lowest values for both BMI and CRL.

Organ weights
Relative organ weights and the different organ ratios calculated are shown in Table 1. The relative brain weight was higher in sIUGR piglets ($P < 0.001$) and progressively decreased across categories, reaching the lowest values in HBW piglets. The brain: heart, brain: liver, and brain: lungs ratios were also significantly higher in sIUGR piglets compared to all other categories ($P \leq 0.009$), which showed no significant differences among themselves. These differences revealed that sIUGR piglets had a significantly larger relative brain size compared to the other categories. The spleen was significantly larger ($P = 0.027$) in the lowest weight categories (sIUGR and LBW)

Items[1]	Piglet type[2]				SEM	P-value[3]
	sIUGR	LBW	MBW	HBW		
n	6	6	6	6		
ROW (g/kg BW)						
Brain	54.13[a]	32.10[b]	27.23[c]	20.65[d]	1.401	< 0.001
Heart	11.35	11.80	8.56	8.05	1.573	0.170
Liver	23.72	26.50	21.24	21.86	2.866	0.451
Lungs	26.51	29.14	23.34	23.75	2.209	0.157
Kidneys	9.39	10.13	7.85	8.58	1.547	0.626
Stomach	7.34	7.75	5.33	6.60	0.724	0.068
Spleen	1.45[ab]	1.82[a]	0.98[b]	1.05[ab]	0.206	0.027
Intestine	44.05	59.43	50.14	48.70	7.657	0.493
Organ ratios						
Brain: heart	5.19[a]	2.82[b]	3.27[b]	2.58[b]	0.596	0.009
Brain: liver	2.37[a]	1.25[b]	1.32[b]	0.96[b]	0.210	< 0.001
Brain: lungs	2.06[a]	1.11[b]	1.22[b]	0.88[b]	0.130	< 0.001

Table 1. Effect of piglet type (sIUGR, LBW, MBW, or HBW) on organ weights at birth. [1]ROW = Relative organ weights. [2]sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. [3]*P*-value obtained from ANOVA test. [a, b,c, d]Different superscripts within row indicate significant differences ($P \leq 0.05$).

Items[1]	Piglet type[3]				SEM	P-value[4]
	sIUGR	LBW	MBW	HBW		
n	6	6	6	6		
EBV (cm^3)	57.13[c]	105.97[b]	122.07[b]	182.79[a]	4.932	< 0.001
REBV (cm^3/kg BW)	114.99	109.11	103.87	108.43	6.189	0.558
(%) of bones between						
HU[2] 140 and HU 499	92.85[a]	90.88[b]	90.19[c]	88.29[d]	0.041	< 0.001
HU 500 and HU 999	6.95[d]	8.73[c]	9.35[b]	11.18[a]	0.040	< 0.001
HU 1000 and HU 1499	0.20[d]	0.39[c]	0.45[b]	0.52[a]	0.009	< 0.001
HU 1500 and HU 1700	0.00[b]	0.00[b]	0.01[ab]	0.01[a]	0.001	< 0.001
Left tibia measures						
Cortical area (mm^2)	13.40[c]	20.25[b]	26.40[b]	35.67[a]	1.920	< 0.001
Mean HU	578.98	573.00	661.16	680.44	33.348	0.041
Thickness (mm)	1.50[b]	1.48[b]	2.19[ab]	2.66[a]	0.237	0.004

Table 2. Effect of piglet type (sIUGR, LBW, MBW, or HBW) on computed tomography measurements at birth. [1]EBV = Entire bone volume, REBV = Relative entire bone volume, HU = Hounsfield unit. [2]Hounsfield units are a standardized, dimensionless unit used in computed tomography scans to quantify the density of tissues and fluids. [3]sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. [4]*P*-value obtained from ANOVA test. [a, b,c, d]Different superscripts within row indicate significant differences ($P \leq 0.05$).

compared to MBW and HBW piglets, while the relative stomach weight showed only a tendency ($P = 0.068$) to be greater in the lowest weight categories (sIUGR and LBW).

Computed tomography (CT) measurements

Results of the CT measurements are presented in Table 2. As expected, there was a significant difference in the total bone volume at birth among the four categories of piglets ($P < 0.001$). The HBW piglets exhibited the largest bone volume, with values ranging from 173.25 to 193.34 cm^3while the sIUGR piglets had approximately 70% lower volumes. No significant differences were detected between the LBW and MBW piglets, which had intermediate bone volumes. No differences were observed in the relative total bone volume across the four piglet categories. Furthermore, the proportion of bones with different densities also differed significantly depending on the piglet category ($P < 0.001$). Specifically, piglets with lower bone volume had a higher percentage of low dense bones (low Hounsfield unit (HU) values), whereas piglets with higher bone volume had a higher percentage of high dense bones (high HU values).

Specific measurements of the left tibiae revealed that HBW piglets had a higher cortical area ($P < 0.001$) compared to the other categories, with an average value of 35.67 mm^2. The cortical area of the left tibia was

Items[1]	Piglet type[3]				SEM	P-value[4]
	sIUGR	LBW	MBW	HBW		
n	6	6	6	6		
$\sigma_{C,\max}$ (MPa)[2]	113.1^{a}	77.7^{b}	67.5^{b}	74.9^{b}	8.436	0.002
$\sigma_{T,\max}$ (MPa)	104.6^{a}	69.8^{b}	61.1^{b}	66.7^{b}	7.970	0.001
E (MPa)	7886^{a}	5279^{ab}	4378^{b}	5053^{b}	747.25	0.006
ε_u (%)	1.80	2.03	2.04	2.00	0.166	0.611
W_e (J/m^3)	53.15	49.35	41.08	38.86	10.608	0.699
W_u (J/m^3)	105.28	92.43	76.74	77.65	15.979	0.453
ρ (g/cm^3)	1.32	1.33	1.32	1.29	0.028	0.670
A (mm^2)	9.33^{c}	18.32^{b}	21.24^{ab}	25.88^{a}	1.510	< 0.001
I_z (mm^4)	11.20^{b}	42.47^{ab}	51.49^{a}	72.34^{a}	9.480	< 0.001

Table 3. Effect of piglet type (sIUGR, LBW, MBW, or HBW) on mechanical and geometric properties of piglet tibiae at birth. [1]$\sigma_{C,\max}$ = Maximum compression stress, $\sigma_{T,\max}$ = Maximum tensile stress, E = Young's modulus, εu = Ultimate strain, W_e = Proof resilience, W_u = Toughness, ρ = Density, A = Area of the cross-section, I_z = Area moment of inertia for the cross-section. [2]MPa = Megapascal. [3]sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. [4]P-value obtained from ANOVA test. [a, b,c]Different superscripts within row indicate significant differences ($P \le 0.05$).

Items[1]	Piglet type[2]				SEM	P-value[3]
	sIUGR	LBW	MBW	HBW		
n	6	6	6	6		
Mineral content (mg/g)						
P	186.2	184.9	186.8	185.3	1.940	0.887
Ca	392.4	388.7	390.4	391.1	2.766	0.723
Mn	16.41^{a}	12.30^{ab}	12.22^{ab}	10.90^{b}	1.386	0.028
Cu	2.89	3.07	3.37	2.76	0.283	0.370
Zn	213.5	201.6	185.1	170.2	12.17	0.067

Table 4. Effect of piglet type (sIUGR, LBW, MBW, or HBW) on the mineral content of piglet tibiae at birth. [1]P = Phosphorus, Ca = Calcium, Mn = Manganese, Cu = Copper, Zn = Zinc. [2]sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. [3]P-value obtained from ANOVA test. [a, b]Different superscripts within row indicate significant differences ($P \le 0.05$).

reduced by approximately 60% in sIUGR piglets ($P < 0.001$), while LBW and MBW piglets exhibited intermediate values, showing a tendency to differ from each other ($P = 0.069$). HBW piglets also showed greater tibial thickness ($P = 0.01$) compared to the lower weight categories (sIUGR and LBW), with an average value of 2.66 mm. Both sIUGR and LBW piglets had the lowest left tibial thickness, whereas MBW piglets exhibited values not different from other piglets. Similarly, the mean HU values differed significantly among categories ($P = 0.041$), although no differences were observed between individual categories. The mean HU values for sIUGR and LBW piglets, as well as for MBW and HBW piglets, were numerically similar.

Mechanical and geometric magnitudes of piglet tibiae

The results of the mechanical and geometric properties of piglet tibiae are presented in Table 3. The maximum stress values ($\sigma_{C,\max}$ and $\sigma_{T,\max}$) were significantly higher ($P = 0.002$ and $P = 0.001$, respectively) in the tibiae of sIUGR piglets compared to those of the other piglet categories. The Young's modulus values also differed significantly ($P = 0.006$) among the piglet categories, with sIUGR piglets exhibiting higher values than both MBW and HBW piglets ($P < 0.05$) (differences reaching up to 7281.40 MPa). In contrast, significant differences ($P < 0.001$) in the area moment of inertia (I_z) and cross-section (A) of the tibiae were observed in the opposite direction, with HBW piglets showing the highest values for both variables.

Mineral content in piglet tibiae

The mineral content of piglet tibiae is shown in Table 4. The phosphorus (P), calcium (Ca), and copper (Cu) content in the tibiae of piglets did not differ among the four categories studied. However, the manganese (Mn) content varied depending on the piglet category ($P = 0.028$), with sIUGR piglets exhibiting the highest levels and HBW piglets the lowest, showing differences of up to 15.4 mg/g ($P = 0.031$). The Mn content in LBW and MBW piglets was intermediate, not different from that of either sIUGR or HBW piglets. Additionally, there was a tendency toward decreasing zinc (Zn) content ($P = 0.067$) from sIUGR piglets to HBW piglets, although the differences among the piglet categories were not statistically significant.

Correlations between external physical characteristics (birth BW, BMI, CRL) and internal parameters

The correlations between the three external physical characteristics used to classify piglets at birth (birth BW, BMI, and CRL) and the internal parameters analyzed post-mortem are presented in Table 5. Four correlations involving various organ weight measures and external parameters had strong negative correlation coefficients below − 0.63 ($P < 0.01$). Among these, the relative brain weight exhibited the strongest negative correlations with external parameters (–0.93 for birth BW, − 0.88 for BMI, and − 0.93 for CRL), followed by the organ weight ratios of brain: lungs, brain: liver, and brain: heart. Similarly, the mechanical properties of maximum compression stress, maximum tensile stress, and Young's modulus also showed negative correlations with external parameters, with coefficients ranging from − 0.62 to − 0.47 ($P < 0.05$). The Mn and Zn content in the piglet tibiae also demonstrated negative correlations with external parameters, with coefficients ranging from − 0.56 to − 0.48 ($P < 0.05$).

Conversely, the parameters mainly related to skeletal development were positively correlated with the external parameters. Specifically, the entire bone volume (EBV) showed the strongest positive correlation with birth BW (0.98, $P < 0.001$), CRL (0.92, $P < 0.001$), and BMI (0.84, $P < 0.001$). Bone density was also correlated with external parameters, with the proportion of high and very high-density bones exhibiting positive correlation coefficients ranging from 0.50 to 0.77 ($P < 0.05$). Furthermore, regarding piglet tibiae measures and geometric magnitudes, the cortical area (0.74 for BMI to 0.91 for birth BW), area (0.74 for BMI to 0.88 for birth BW), and inertia of the Sect. (0.64 for CRL to 0.74 for BMI) were also positively correlated with external parameters ($P < 0.001$).

Discussion

Birth BW is a critical indicator of postnatal performance, as piglets born small often remain stunted and are unable to catch up to their larger counterparts throughout the entire production cycle[8,39,40]. Some studies have defined pigs with a birth BW of less than 1.0–1.25 kg and without organ growth restriction as low birth BW pigs[15,18,41,42]. Accordingly, in the current study, piglets were selected within the lower and upper thresholds of these established cut-off points to identify differences among those considered small at birth. Piglets within the lower threshold had a mean birth BW of 0.97 ± 0.037 kg and were considered LBW, while those within the upper threshold had a mean birth BW of 1.18 ± 0.027 kg and were considered MBW. As some studies suggest that pigs born small may have the potential to compensate during suckling[2,15,16] and subsequent growth stages[25,43,44] it is important to evaluate and differentiate their characteristics at birth. To encompass the entire birth BW distribution of the population, piglets with the characteristic head morphology of severe IUGR[17] along with those with a birth BW exceeding 1.25 kg, were also evaluated.

While the link between birth BW and survivability is well established[19] additional measures of body conformation, such as BMI and CRL, also serve as important indicators of survivability[6,45,46]. Furthermore, body shape at birth has been identified as a reliable predictor of postnatal growth in piglets born with low birth BW[25]. In this context, it is suggested that not all light pigs are similar and that their performance is more strongly influenced by body shape than by birth BW[20]. In this study, we found high correlation coefficients between BMI

Traits[1]	Organ ratios			Relative organ weights							
	Brain: heart	Brain: lungs	Brain: liver	Liver	Heart	Lungs	Brain	Kidneys	Intestine	Spleen	Stomach
Birth BW[2]	**− 0.64**	**− 0.83**	**− 0.79**	− 0.17	*− 0.47*	− 0.29	**− 0.93**	− 0.21	0.14	− 0.41	*− 0.48*
CRL[3]	**− 0.63**	**− 0.82**	**− 0.78**	− 0.18	*− 0.46*	− 0.31	**− 0.93**	− 0.14	0.19	− 0.41	*− 0.44*
BMI[4]	**− 0.65**	**− 0.85**	**− 0.82**	− 0.08	− 0.40	− 0.13	**− 0.88**	− 0.34	0.12	− 0.37	*− 0.47*

Traits	EBV	REBV	(%) of bones between				Left tibia measures			Mechanical properties	
			HU 140 and HU 499	HU 500 and HU 999	HU 1000 and HU 1499	HU 1500 and HU 1700	Cortical area	Mean HU	Thickness	$\sigma_{C,\max}$	$\sigma_{T,\max}$
Birth BW	**0.98**	−0.21	**−0.50**	**0.47**	**0.76**	**0.60**	**0.91**	**0.55**	**0.69**	**−0.57**	**−0.60**
CRL	**0.92**	−0.20	**−0.56**	**0.54**	**0.77**	**0.50**	**0.92**	**0.58**	**0.69**	**−0.56**	**−0.59**
BMI	**0.84**	−0.21	−0.28	0.25	**0.67**	**0.68**	**0.74**	0.33	*0.49*	**−0.59**	**−0.62**

Traits	Mechanical properties					Geometric magnitudes		Mineral content				
	E	ε_u	W_e	W_u	ρ	A	I_z	P	Ca	Mn	Cu	Zn
Birth BW	**−0.52**	0.47	−0.24	−0.28	−0.16	**0.88**	**0.72**	−0.06	−0.11	**−0.60**	−0.02	**−0.55**
CRL	**−0.56**	0.29	−0.19	**0.50**	−0.12	**0.88**	**0.64**	−0.08	−0.09	**−0.59**	0.03	**−0.51**
BMI	**−0.47**	0.25	−0.26	−0.32	−0.16	**0.74**	**0.74**	−0.01	−0.16	**−0.62**	0.01	**−0.48**

Table 5. Correlation coefficients between birth body weight, crown-to-rump length, body mass index, and internal body variables. [1]EBV = Entire bone volume, REBV = Relative entire bone volume, HU = Hounsfield unit, $\sigma_{C,\max}$ = Maximum compression stress, $\sigma_{T,\max}$ = Maximum tensile stress, E = Young's modulus, εu = Ultimate strain, W_e = Proof resilience, W_u = Toughness, ρ = Density, A = Area of the cross-section, I_z = Area moment of inertia for the cross-section, P = Phosphorus, Ca = Calcium, Mn = Manganese, Cu = Copper, Zn = Zinc. [2]BW = Body weight. [3]CRL = Crown-to-rump length. [4]BMI = Body mass index. Note: bold $P \leq 0.05$ and italic $0.05 < P \leq 0.10$.

and CRL and birth BW (0.870 and 0.935, respectively). However, no significant differences in these body shape metrics were observed between LBW and MBW piglets. These findings suggest that differentiating light piglets at birth based just on morphometric characteristics is challenging, and that internal physiological status likely may play a critical role in their subsequent growth performance.

Despite the strong interest in extensively studying the internal physiological status of newborn piglets, these traits are difficult to estimate non-invasively, often requiring euthanasia and expensive analytical techniques. The main limitation of this study is the relatively small sample size, with only 6 piglets per category. Consequently, the findings should be regarded as a preliminary step toward understanding the physiological status of organs and bones in newborn piglets based on their birth characteristics, which may significantly impact their future growth performance. Further research involving a larger sample size is crucial to improve the reliability and generalizability of these results. Assessing organ and bone characteristics at birth could aid in identifying neonates at greater risk of compromised postnatal growth trajectories. Similarly, other traits, such as the number and size of muscle fibers, have been extensively studied as critical factors influencing postnatal growth potential. Low birth weight piglets tend to have fewer muscle fibers due to a reduced ratio of secondary to primary fibers[47,48]. Notably, since muscle fiber hyperplasia is completed by day 90 of gestation, the alterations in fiber number observed at birth are permanent[49]. These effects directly affect the concept of fetal programming, which may significantly influence neonatal survival, as well as subsequent growth and efficiency in pigs[50].

The increased litter size in pigs over the past decades has led to uterine crowding. This, in turn, limits nutrient availability to the embryos during critical periods of development, compromising placental development in surviving fetuses and increasing the likelihood of having runt fetuses[451,52] demonstrated that intrauterine crowding becomes a limiting factor when the number of embryos exceeds 14. In this way, piglets affected by IUGR experience asymmetrical organ growth during gestation as part of a fetal adaptative response to placental insufficiency[5,53,54]. The brain and heart are identified as the organs most protected from growth restriction compared to others. Consistent with these studies, the relative brain weight was significantly greater in sIUGR piglets at birth, showing a significant linear decrease as the piglets exhibited better external physical metrics. However, these differences among piglet categories were not reflected in organ ratios, where significant differences were observed only between the sIUGR group and the other categories[23,55]. This was most likely due to what has been described as the “brain-sparing effect”[54] which primarily affects piglets with the most severe degree of IUGR. Another study revealed that the preferential growth of the nervous and cardiovascular systems in small fetuses can be detected as early as day 45 of gestation[56]. Interestingly, most relative organ weights were comparable between sIUGR and LBW piglets but differed numerically from those of MBW and HBW piglets, which were also similar to each other.

Differences in bone growth and development were also observed among the 4 categories of piglets. The growth in bone length is stated that depends on body size and, consequently, on nutritional status[57]. Restricted and undernourished fetuses are smaller than normal and possess bones that are anatomically less developed compared to well-nourished fetuses of the same age[57]. In agreement with that, HBW piglets exhibited the highest EBV at birth, which was approximately 70% greater than that of the sIUGR piglets. In humans was described that skeletal ossification is more advanced than normal in large fetuses and delayed in those small for their gestational age[58]. This observation could be related to differences in the proportions of bones with higher or lower densities identified in our study. In this context, sIUGR piglets exhibited a higher percentage of low-density bones and a lower percentage of high-density bones compared to their heavier counterparts. Regarding LBW and MBW piglets, differences in bone density were observed between these two categories, indicating that not all light piglets at birth (< 1.25 kg) exhibit the same physiological status. The proportions of bones with different densities were determined using the HU value cut-off ranges originally described for adult pigs[59,60] where higher HU values indicate greater bone density[61]. Despite this, these ranges successfully differentiated between bones of varying densities in newborn piglets, demonstrating the sensitivity of this method and its applicability to small piglets.

These findings on organ development, ossification, and bone growth in newborn piglets support the statement that the lower preweaning growth observed in runt pigs cannot be fully explained by their lower birth BW. This suggests that IUGR exerts a more complex influence on development potential[62]. This influence likely originates during gestation, where growth-retarded pig fetuses are associated with smaller placentas characterized by slower blood flow[63] and fewer, less dense areolae[45] compared to their littermates. The placenta plays a pivotal role in fetal growth and development as it facilitates the transport of nutrients and respiratory gases between maternal and fetal circulation[64]. Consequently, fetuses associated with smaller placentas exhibit alterations in fetal organ development, changes in the number and type of muscle fibers[4] and impaired endochondral ossification[36,37] thereby compromising their future developmental potential. Within-litter variation in fetal weight is reported to be detectable as early as day 28 of gestation and increases as gestation progresses and fetuses grow[56]. This finding suggests that small fetuses identified early in gestation are likely to maintain a reduced growth rate, may experience further compromise in later gestation, and are ultimately born as low-weight or IUGR piglets. The differences we observed, primarily in brain weight, EBV, and bone density among the various categories of piglets, may help identify varying degrees of restriction likely established during gestation. These intrauterine growth restrictions seem to have a direct impact on the piglets’ postnatal growth and development.

To gain a deeper understanding of the differences among these growth-restricted piglets at birth, we also analyzed various parameters related to their tibiae. The tibia was selected as the optimal long bone for analysis for several reasons. First, it allows for the most precise measurements using CT, facilitating the calculation of specific metrics previously described in the literature[60]. Additionally, the tibia is well-known as a significant mineral reservoir, particularly for Ca and P. Its mineral content and mechanical properties have been studied in pigs in previous research[65,66]. Proper bone growth, along with normal joint structure and function, is essential for the overall development of the organism[67]. Therefore, piglets with a larger cortical area and greater tibial thickness are likely to exhibit better development at birth compared to their littermates, as demonstrated in our study. High birth BW piglets had the largest cortical area, approximately 60% greater than that of sIUGR piglets. Similarly, HBW piglets exhibited greater tibial thickness compared to the lower weight categories (sIUGR and LBW). These two measures are influenced by the process of bone growth, which is regulated by a complex system of endocrine signals. It is described that the growth of long bones is influenced by growth factors, dietary factors, and other cellular signals that are essential for chondrocyte differentiation[68–70]. Among those factors that can damage the growth plate, IUGR piglets are being associated with impaired plasma IGF-1 levels[71]. Since insulin/IGF-1 signaling plays a pivotal role in early development and fetal growth, IUGR pigs are more prone to skeletal disorders caused by disruptions in the endocrine regulation of the growth plate[67]. Indeed, IGF-1 not only stimulates longitudinal bone growth but also has demonstrated direct effects on bone modeling, supported by both in vivo[72] and in vitro[73] evidence.

Although our results suggest that piglets born light are more likely to experience impaired ossification, the mechanical properties of the tibiae, including maximum stress in compression and tension, as well as rigidity, were highest in the sIUGR group compared to the other categories. This could be supported by the following: (1) these mechanical properties are intrinsic to the bone itself and, therefore, remain independent of both its size and the piglet's birth BW, and (2) as part of a fetal adaptive response to placental insufficiency and limited access to nutrients from the sow, similar to the "brain-sparing effect", piglets affected by IUGR may prioritize intrinsic bone quality over longitudinal bone growth. Although this specific physiological phenomenon has not been extensively studied in the literature[57], described that full-term runts had bones and epiphyses with a chemical composition more aligned with their age than their size. This implies that, regardless of weight, piglets can achieve chemical maturation of their bones as a function of age. Moreover, this study identified differences in the mineral content of the tibiae, which correlate with the observed variations in mechanical properties. Greater bone mineralization is associated with improved intrinsic bone quality. Ca and P, both essential for optimal bone formation and mineralization[66] displayed similar levels in both sIUGR and HBW piglets. Hydroxyapatite ($Ca_5(PO_4)_3(OH)$), a mineral form of Ca and P that provides bones with their rigidity and strength, is the primary and essential component of bones in animals[74,75]. Differences were observed in the Mn and Zn content, both of which play crucial roles in bone and cartilage development[76–78]. The highest Mn and Zn levels were found in sIUGR piglets, with a linear decrease observed toward the HBW piglets. Given that Ca and P levels were consistent across piglet categories, and sIUGR exhibited higher Mn and Zn content in their bones, the impaired ossification identified in these sIUGR piglets did not lead to changes in intrinsic bone properties, such as rigidity and strength. Mn plays a role in bone and cartilage matrix formation through its involvement with proteoglycans[76] while Zn influences bone mass and is critical for matrix quality[77,78]. Regarding the mechanical properties and mineralization of the bone, it is important to note that no differences were found between LBW and MBW piglets. Since piglets were euthanized immediately after birth without having access to colostrum, this suggests the existence of an anticipated fetal adaptive response in bone quality that appears to be evident only in piglets with a severe degree of IUGR.

This characterization of piglets at organ and skeletal development levels will enable a more precise assessment of their susceptibility and subsequent risk of mortality due to their IUGR status at birth. Previous studies[5,79] noted that some small piglets can still achieve their genetic growth potential, exhibiting normal growth, whereas piglets affected by IUGR do not. These differences in genetic growth potential and survivability among low birth BW may be attributed to the asymmetrical organ and skeletal growth experienced by IUGR piglets during gestation. In the present study, the most pronounced differences were observed between HBW and sIUGR piglets, while less significant differences were noted between LBW and MBW piglets. LBW piglets exhibited greater similarity to sIUGR piglets, whereas MBW piglets were more comparable to HBW piglets. This suggests that although light piglets at birth (LBW and MBW piglets) may be affected to varying degrees by a "mild-moderate" form of IUGR, distinguishing them clearly across different categories remains challenging. These two categories of light piglets studied align with the findings of[15] which identified two distinct populations among piglets born with low BW based on their future growth performance. The authors further propose that incorporating additional variables measured at birth, especially in population with high birth BW variability, could allow for the identification and study of additional piglet categories. Other easily measurable on-farm indicators, such as the piglet's relative birth BW within its litter[6] the difference between the piglet's birth BW and the average litter weight at birth or after cross-fostering[10,11] and colostrum intake[5] among others, should be used as complementary indicators alongside those employed in this study. Incorporating these measures would enable a more precise and robust classification of light piglets at birth.

Identifying piglets with some degree of IUGR at birth using easily measurable on-farm indicators offers farmers a quick and practical method to determine which piglets require additional support to optimize neonatal survival and growth performance. Our study demonstrates that birth BW, BMI, and CRL are strongly correlated with most of the internal characteristics analyzed, confirming their reliability as indicators of survivability and growth potential. Specifically, these morphological traits showed strong negative correlations with relative brain weight and organ ratios, and strong positive correlations with total bone volume and the longitudinal growth of the tibia. The results of the present study indicate that these external indicators can explain the organ and skeletal physiological status of piglets at birth but are not precise or accurate enough to distinguish between light piglets at birth (LBW and MBW piglets). The interest in this pig population lies in their varying growth performance potential and their ability to transition between categories of weight during the early stages of life. Some authors have highlighted the potential benefits of prediction methods using large data sets to identify pigs at risk of growth retardation[10,11]. Further research is needed to improve the early identification of piglets affected by varying degrees of IUGR.

This study provides a deeper understanding of organ and bone physiological status in newborn piglets classified by birth weight, body mass index, and crown-to-rump length. Piglets experiencing some degree of

IUGR exhibit asymmetrical organ growth favoring brain development, along with impaired ossification and longitudinal bone growth. Furthermore, these piglets show enhanced mechanical properties of the tibia, attributed to increased manganese and zinc content. The findings of this study reveal that the strong correlation between morphological characteristics at birth and organ and skeletal physiological characteristics is insufficient to accurately identify piglets classified as LBW or MBW, which are small at birth and with a "mild-moderate" degree of IUGR. Improving this classification criterion by incorporating complementary indicators at birth could enable pig farmers to design specific management and nutritional strategies targeted at this vulnerable population, ultimately enhancing their performance and survivability.

Methods

All animal experimentation procedures were approved by the Ethics Committee of the Universitat Autònoma de Barcelona (CEEAH2788M2) in accordance with the European Union guidelines for the care and use of animals in research[80]. This study is reported in accordance with ARRIVE guidelines.

Animals and experimental design

This study was conducted with 24 piglets (*Pietrain* x [*Danish Landrace* x *Danish Yorkshire*]) from 6 multiparous sows of the same batch, sourced from a commercial farm in Lleida, Spain. The average total litter size was 20.2 ± 1.20 piglets, and the average total litter weight was 26.8 ± 2.00 kg. On the day of parturition (day 0), before litter equalization, piglets were individually weighed, and the BMI and CRL were measured. The degree of IUGR was determined based on the head morphology criteria described by[17]. Four piglets per sow were selected according to the previously described measures to generate four different groups ($n = 6$ piglets/group): sIUGR, LBW, MBW, and HBW. Piglets classified as sIUGR exhibited a steep, dolphin-like forehead, bulging eyes, and wrinkles perpendicular to the mouth. Piglets with a birth BW between 0.75 and 1.0 kg, without morphological signs of sIUGR, were categorized as LBW, while those with a birth BW between 1.0 and 1.25 kg were considered MBW. Piglets with a birth BW exceeding 1.25 kg were classified as HBW. All descriptive statistics by group are provided in Table 6. After classifying the piglets, they were euthanized with an intramuscular injection of azaperone (Sediron 40 mg/ml; Livisto Int'l, S.L.) and ketamine (Ketamidor 100 mg/ml; VetViva Richter GmbH), followed by an intravenous injection of sodium pentobarbital (Euthasol 400 mg/ml; Dechra Pharmaceuticals PLC).

Computed tomography, post-mortem examination, and organ and tibiae sampling

Piglets were fully scanned post-mortem after birth with a Philips Brilliance 16 scanner (Philips Healthcare, Madrid, ES). The CT scanner undergoes daily internal calibration prior to use. The acquisition conditions were as follows: 120 kV, 200 mA, field of view (FOV) 150 mm, 512 × 512 matrix, collimation 16 × 1.5, helical 3 mm-thick images every 3 mm (pitch 0.938). The reconstruction algorithm used was the standard.

Image analysis was performed with software Matlab 2008b (The MathWorks Inc., Natick, MA, USA) using a customized script. From all the images of each piglet, frequency of voxels (3D pixels) associated with each HU value, were obtained and transformed into volume using the image thickness, matrix size and FOV values[81]. The volume corresponding to HU values between + 140 and + 1,700 was classified as bone tissue[82] and this range was used to calculate the total volume of bones. Moreover, four bone density ranges were defined in order to obtain volume measurements of bones with different densities: low dense bones between HU values + 140 and + 499, medium dense bones between HU values + 500 and + 999, high dense bones between HU values + 1,000 and + 1,499, and very high dense bones between HU values + 1,500 and + 1,700, following[60] but including an additional range. Based on the volume of each range and the total bone volume, the proportion corresponding to each density range was determined.

Measurements were taken axially in the central part of the left tibia using VisualPork software[83]. External and internal cortical bone areas were manually selected as regions-of-interest (ROI), and the area of the cortical bone was obtained as a difference between the two areas. Moreover, the average HU value of the cortical area and the thickness of the cortical bone were also determined (Fig. 1).

Afterwards, the brain, heart, liver, lungs, kidneys, and spleen were harvested and blotted dry before these were weighed on a precision scale (Sartorius AG, Model ED224S, Germany). The intestine and stomach were carefully removed intact, rinsed thoroughly and weighed. The hind legs of each piglet were separated from the rest of the body and individually frozen for subsequent tibiae analyses (mechanical and geometric properties and mineral determination).

	sIUGR		LBW		MBW		HBW		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*-value[1]
Birth BW (kg)	0.49^{d}	0.037	0.97^{c}	0.042	1.18^{b}	0.027	1.69^{a}	0.121	< 0.001
BMI (kg/m^2)	14.35^{c}	1.368	18.00^{b}	2.806	18.48^{b}	1.107	22.71^{a}	1.771	< 0.001
CRL (cm)	18.57^{c}	0.673	23.40^{b}	1.817	25.25^{ab}	0.880	27.30^{a}	1.397	< 0.001

Table 6. Descriptive statistics for birth body weight (BW), body mass index (BMI), and crown-to-rump length (CRL) [Mean ± Standard deviation (SD)] for piglets ($n = 6$ piglets per group) classified as severe intrauterine growth restricted (sIUGR), low birth weight (LBW), moderate birth weight (MBW), and high birth weight (HBW). [1]*P*-value obtained from ANOVA test. [a, b,c, d]Different superscripts within row indicate significant differences ($P \leq 0.05$).

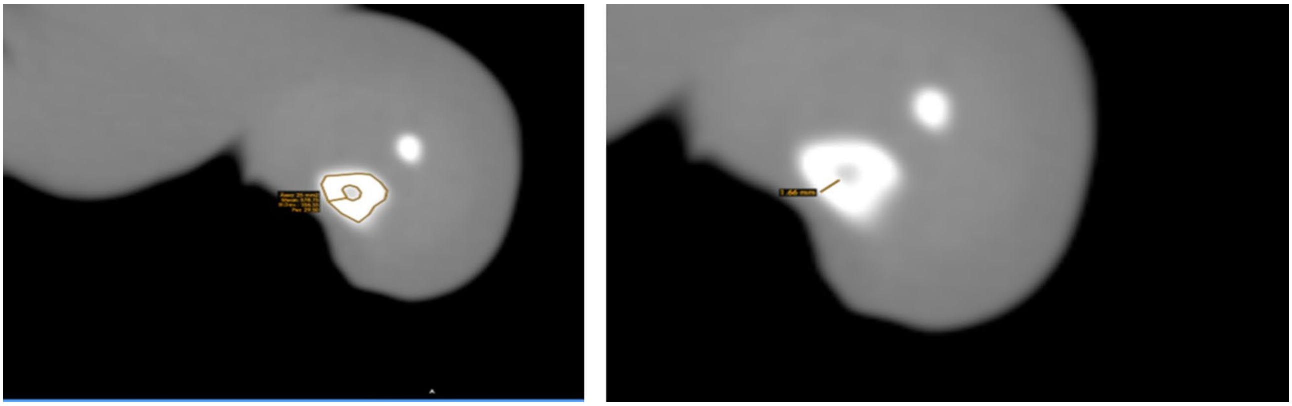

Fig. 1. The area of the cortical bone (left) and thickness of the cortical bone (right) measured in tibia bone.

Bending tests for mechanical properties of piglet tibiae determination

The left hind leg of each piglet was thawed and placed in the autoclave at 121 °C for 30 min. Then, the flesh was removed from those hind legs to obtain only the clean left tibiae. The tibia density (ρ) of each specimen was determined from two measurements, the unsubmerged weight (P_{air}) and the weight of the same sample submerged (P_{sum}, the latter measurement being equal to the weight in air plus the buoyant force of the fluid). The geometric magnitudes, including the cross-sectional area and moment of inertia, were calculated and subsequently used to determine the following properties. The mechanical properties of porcine bone (left piglet tibiae) were determined from three point bending tests using a Universal Test Machine (UTM) Zwick All-around table-top 5 kN (ZwickRoell S.L., Ulm, Germany), equipped with a load cell of 500 N. The real values of A and I_z of the fractured cross-section were computed for each specimen from an image using ImageJ® software. Specifically, the mechanical properties calculated were the following: stiffness (Young's modulus) (E), maximum stress (σ_{max}), ultimate strain (ε_u), proof resilience (W_e), and toughness (W_u). The mechanical properties E, σ_{max}, W_e, and W_u were determined through analytical approximations from the final stress-strain curves. The ε_u was calculated from the maximum displacement.

All tibia specimens were tested at the same displacement rate (v = 0.5 mm/min). This rate was controlled by the UTM, which simultaneously recorded both displacement and applied force. Due to differences in specimen size and strength, displacement at failure consistently ranged between 0.4 and 1.0 mm, resulting in total test durations of 75 to 125 s. Both the strain rate (dε/dt) and the loading rate (dF/dt) increased linearly with the imposed displacement rate (v), although they were also influenced by the cross-sectional dimensions and strength of each tibia. The calculated strain rate values ranged from 2.0 × 10^(−4) to 1.0 × 10^(−5) s^{-1}, depending on the specimen geometry. These values fall within the quasi-static regime, ensuring that the mechanical behavior corresponds to a rigid-elastic model with brittle failure. Higher testing speeds would induce viscoelastic effects, which would hinder meaningful comparisons between specimens. The loading rate, in turn, was affected not only by the displacement rate but also by the stiffness and strength of the individual tibiae. In all cases, the loading rate ranged from 1.0 to 4.0 N/s.

Inductively coupled plasma mass spectrometry (ICP-MS) for piglet tibiae mineral determination

For the right hind legs, as with the left, they were thawed and placed in an autoclave at 121 °C for 30 min to obtain clean right tibiae. Tibiae bones were then dried at 103 °C for 12 h, followed by immersion in acetone for 48 h to remove any remaining fat residues. Finally, to obtain the tibiae ash, they were heated again at 103 °C for 12 h and then placed in a muffle furnace at 550 °C for 12 h.

Concentrations of P, Ca, Zn, Cu, and Mn were determined in the ash obtained from the right tibiae samples according to the AOAC 984.27 method, using a mass spectrometer ICP-MS 7900 (Agilent Technologies, Santa Clara, California, USA).

To validate the accuracy of the analytical method, a standard was added to the samples (spiked samples). The recovery percentages for these spiked samples were 98% for P, 97% for Ca, 105% for Mn, 101% for Cu, and 93% for Zn. Furthermore, the minimum concentrations quantifiable in the sample using the described methodology were 8 mg/g for P, 10 mg/g for Ca, 0.2 mg/g for Mn, 2 mg/g for Cu, and 2 mg/g for Zn.

Statistical analysis

All calculations and statistical analyses were performed with open-source software R v.4.4.0[84]. Pig was used as the experimental unit in all data analyses. Residuals were tested for normality using the Shapiro-Wilk test (*ols_test_normality* function, *olsrr* package) and assessed with normal probability plots. Birth BW, BMI, and CRL measures were analyzed using a linear mixed-effect model (*lmer* function, *lme4* package), with piglet category as a fixed effect and sow as a random effect. All other examined variables, except those related to the proportion of bones with different densities, were similarly analyzed using a linear mixed-effect model (*lmer* function, *lme4* package), including category of piglet as fixed effect and sow as random effect. The variables related to the proportion of bones with different densities were analyzed using a generalized linear mixed-effect model (*glmer* function, *lme4* package) with a binomial family, also including piglet category as fixed effect and sow as random effect. Multiple means comparisons were done using Tukey-Kramer's correction. Results for the fixed effects are presented as least squares means with the standard error of the mean (SEM). Results were considered significant at $P \leq 0.05$ and a tendency when $0.05 < P \leq 0.10$. Pearson correlations were calculated using the *cor.test* function.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Received: 31 March 2025; Accepted: 18 August 2025
Published online: 02 October 2025

References

1. Rutherford, K. M. D. et al. The welfare implications of large litter size in the domestic pig I: biologica factors. *Anim Welf.* **22**, 199–218 (2013).
2. Quiniou, N., Dagorn, J. & Gaudré, D. Variation of piglets' birth weight and consequences on subsequent performance. *Livest. Prod. Sci.* **78**, 63–70 (2002).
3. Beaulieu, A. D., Aalhus, J. L., Williams, N. H. & Patience, J. F. 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 (2010).
4. Foxcroft, G. R. et al. The biological basis for prenatal programming of postnatal performance in pigs. *J. Anim. Sci.* **84**, 105–112 (2014).
5. Amdi, C. et al. Intrauterine growth restricted piglets defined by their head shape ingest insufficient amounts of colostrum. *J. Anim. Sci.* **91**, 5605–5613 (2013).
6. Hales, J., Moustsen, V. A., Nielsen, M. B. F. & Hansen, C. F. Individual physical characteristics of neonatal piglets affect preweaning survival of piglets born in a noncrated system. *J. Anim. Sci.* **91**, 4991–5003 (2013).
7. Hansen, C. F., Hales, J., Amdi, C. & Moustsen, V. A. Intrauterine growth-restricted piglets defined by their head shape have impaired survival and growth during the suckling period. *Anim. Prod. Sci.* **59**, 1056–1062 (2019).
8. Fix, J. S. et al. Effect of piglet birth weight on survival and quality of commercial market swine. *Livest. Sci.* **132**, 98–106 (2010).
9. Calderón Díaz, J. A. et al. Early life indicators predict mortality, illness, reduced welfare and carcass characteristics in finisher pigs. *Prev. Vet. Med.* **146**, 94–102 (2017).
10. Casellas, J. et al. Classification of light Yorkshire pigs at different production stages using ordinary least squares and machine learning methods. *Animal* **18**, 88 (2024).
11. Salgado-López, P. et al. Applicability of machine learning methods for classifying lightweight pigs in commercial conditions. *Transl Anim. Sci* **8**, 97 (2024).
12. Larriestra, A. J. et al. Pig characteristics associated with mortality and light exit weight for the nursery phase. *Can. Vet. J.* **47**, 560–566 (2006).
13. Maes, D. G. D. et al. Risk factors for mortality in Grow-finishing pigs in Belgium. *J. Vet. Med.* **51**, 321–326 (2004).
14. López-Vergé, S. et al. Potential risk factors related to pig body weight variability from birth to slaughter in commercial conditions. *Transl Anim. Sci.* **2**, 383–395 (2018).
15. Montoro, J. C. et al. Predicting productive performance in grow-finisher pigs using birth and weaning body weight. *Animals* **10**, 1–14 (2020).
16. Blavi, L. et al. Management and feeding strategies in early life to increase piglet performance and welfare around weaning: A review. *Animals* https://doi.org/10.3390/ani11020302 (2021).
17. Chevaux, E., Sacy, A., Le Treut, Y. & Martineau, G. P. O.175 IntraUterine Growth Retardation (IUGR): morphological and behavioral description. in *Proceedings of the 21st IPVS Congress*Vancouver, Canada, (2010).
18. Douglas, S. L., Szyszka, O., Stoddart, K. & Edwards, S. A. Kyriazakis, I. A meta-analysis to identify animal and management factors influencing gestating Sow efficiency. *J. Anim. Sci.* **92**, 5716–5726 (2014).
19. Roehe, R. & Kalm, E. Estimation of genetic and environmental risk factors associated with pre-weaning mortality in piglets using generalized linear mixed models. *Anim. Sci.* **70**, 227–240 (2000).
20. Huting, A. M. S., Sakkas, P., Wellock, I., Almond, K. & Kyriazakis, I. Once small always small? To what extent morphometric characteristics and postweaning starter regime affect pig lifetime growth performance. *Porcine Health Manag* **4**, 36 (2018).
21. Amdi, C., Klarlund, M. V., Hales, J., Thymann, T. & Hansen, C. F. Intrauterine growth-restricted piglets have similar gastric emptying rates but lower rectal temperatures and altered blood values when compared with normal-weight piglets at birth. *J. Anim. Sci.* **94**, 4583–4590 (2016).
22. Vanden Hole, C. et al. Glucose and glycogen levels in piglets that differ in birth weight and vitality. *Heliyon* **5**, e02510 (2019).
23. Lynegaard, J. C., Hansen, C. F., Kristensen, A. R. & Amdi, C. Body composition and organ development of intra-uterine growth restricted pigs at weaning. *Animal* **14**, 322–329 (2020).
24. Muns, R., Manzanilla, E. G., Sol, C., Manteca, X. & Gasa, J. Piglet behavior as a measure of vitality and its influence on piglet survival and growth during lactation. *J. Anim. Sci.* **91**, 1838–1843 (2013).
25. Douglas, S. L., Edwards, S. A., Sutcliffe, E., Knap, P. W. & Kyriazakis, I. Identification of risk factors associated with poor lifetime growth performance in pigs 1. *J. Anim. Sci.* **91**, 4123–4132 (2013).
26. Riddersholm, K. V., Bahnsen, I., Bruun, T. S., de Knegt, L. V. & Amdi, C. Identifying risk factors for low piglet birth weight, high within-litter variation and occurrence of intrauterine growth-restricted piglets in hyperprolific sows. *Animals* **11**, 1–17 (2021).
27. Muns, R., Silva, C., Manteca, X. & Gasa, J. Effect of cross-fostering and oral supplementation with colostrums on performance of newborn piglets. *J. Anim. Sci.* **92**, 1193–1199 (2014).
28. Donovan, T. S. & Dritz, S. S. Effects of split-nursing management on growth performance in nursing pigs. *Kans. Agricultural Exp. Stn. Res. Rep.* https://doi.org/10.4148/2378-5977.6550 (1996).
29. Sulabo, R. C. et al. Effects of varying creep feeding duration on the proportion of pigs consuming creep feed and neonatal pig performance. *J. Anim. Sci.* **88**, 3154–3162 (2010).
30. Kuller, W. I. et al. Effects of intermittent suckling and creep feed intake on pig performance from birth to slaughter. *J. Anim. Sci.* **85**, 1295–1301 (2007).
31. Sola-Oriol, D. & Gasa, J. Feeding strategies in pig production: sows and their piglets. *Anim. Feed Sci. Technol.* **233**, 34–52 (2017).
32. Bruininx, E. M. A. M. et al. Effect of creep feed consumption on individual feed intake characteristics and performance of group-housed weanling pigs. *J. Anim. Sci.* **80**, 1413–1418 (2002).
33. Bruininx, E. M. A. M. et al. Individually assessed creep food consumption by suckled piglets: influence on post-weaning food intake characteristics and indicators of gut structure and hind-gut fermentation. *Anim. Sci.* **78**, 67–75 (2004).
34. Zijlstra, R. T., Whang, K. Y., Easter, R. A. & Odle, J. Effect of feeding a milk replacer to Early-Weaned pigs on growth, body composition, and small intestinal morphology, compared with suckled littermates. *J. Anim. Sci.* **74**, 2948–2959 (1996).

35. Dunshea, F. R., Kerton, D. J., Eason, P. J. & King, R. H. Supplemental skim milk before and after weaning improves growth performance of pigs. *Aust J. Agric. Res.* **50**, 1165–1170 (1999).
36. Briana, D. D. & Malamitsi-Puchner, A. Bone Biomarkers in Intrauterine Growth Restriction. in *Biomarkers in Bone Disease* (ed. Preedy, V. R.) 1–12 (2016). https://doi.org/10.1007/978-94-007-7745-3_30-1
37. Pastor, F. M., de Melo Ocarino, N., Silva, J. F., Reis, A. M. S. & Serakides, R. Bone development in fetuses with intrauterine growth restriction caused by maternal endocrine-metabolic dysfunctions. *Bone* **186**, Preprintathttpsdoiorg101016jbone2024117169 (2024).
38. Chen, H., Miller, S. & Lane, R. Moyer-Mileur, L. Intrauterine growth restriction decreases endochondral ossification and bone strength in female rats. *Am. J. Perinatol.* **30**, 261–266 (2013).
39. Gondret, F. et al. Influence of piglet birth weight on postnatal growth performance, tissue lipogenic capacity and muscle histological traits at market weight. *Livest. Prod. Sci.* **93**, 137–146 (2005).
40. Rehfeldt, C., Tuchscherer, A., Hartung, M. & Kuhn, G. A second look at the influence of birth weight on carcass and meat quality in pigs. *Meat Sci.* **78**, 170–175 (2008).
41. Milligan, B. N., Fraser, D. & Kramer, D. L. Birth weight variation in the domestic pig: effects on offspring survival, weight gain and suckling behaviour. *Appl. Anim. Behav. Sci.* **73**, 179–191 (2001).
42. Milligan, B. N., Fraser, D. & Kramer, D. L. The effect of littermate weight on survival, weight gain, and suckling behavior of Low-Birth-Weight piglets in Cross-Fostered litters. *J. Swine Health Prod.* **9**, 161–168 (2001).
43. Paredes, S. P. et al. Analysis of factors to predict piglet body weight at the end of the nursery phase 1. (2012). https://doi.org/10.2527/jas2011-4574
44. He, Y. et al. Identifying factors contributing to slow growth in pigs. *J. Anim. Sci.* **94**, 2103–2116 (2016).
45. Baxter, E. M. et al. Investigating the behavioural and physiological indicators of neonatal survival in pigs. *Theriogenology* **69**, 773–783 (2008).
46. Baxter, E. M. et al. Indicators of piglet survival in an outdoor farrowing system. *Livest. Sci.* **124**, 266–276 (2009).
47. Handel, S. E. & Stickland, N. C. Muscle cellularity and birth weight. *Anim. Prod.* **44**, 311–317 (1987).
48. Cerisuelo, A. et al. Increased Sow nutrition during midgestation affects muscle fiber development and meat quality, with no consequences on growth performance. *J. Anim. Sci.* **87**, 729–739 (2009).
49. Dwyer, C. M., Stickland, N. C. & Fletcher, J. M. The influence of maternal nutrition on muscle fiber number development in the Porcine fetus and on subsequent postnatal growth'. *J. Anim. Sci.* **72**, 911–917 (1994).
50. Ji, Y. et al. Fetal and neonatal programming of postnatal growth and feed efficiency in swine. *J. Anim. Sci. Biotechnol.* **8**, 55 (2017).
51. Bazer, F. W., Clawson, A. J. & Robison, O. W. Ulberg, L. C. UTERINE CAPACITY IN GILTS. *J. Reprod. Fert*. **18**, 121–124 (1969).
52. Vallet, J. L. Fetal erythropoiesis and other factors which influence uterine capacity in swine. *J. Appl. Anim. Res.* **17**, 26 (2000).
53. Wang, T., Yong, J. H., Shi, F., Ruo, J. X. & Hutz, R. J. Effects of intrauterine growth retardation on development of the Gastrointestinal tract in neonatal pigs. *Biol. Neonate*. **88**, 66–72 (2005).
54. Roza, S. J. et al. What is spared by fetal brain-sparing? Fetal circulatory redistribution and behavioral problems in the general population. *Am. J. Epidemiol.* **168**, 1145–1152 (2008).
55. Bauer, R., Walter, B., Brust, P., Füchtner, F. & Zwiener, U. Impact of asymmetric intrauterine growth restriction on organ function in newborn piglets. *Eur. J. Obstet. Gynecol. Reproductive Biology*. **110**, 40–49 (2003).
56. Lyderik, K. K., Østrup, E., Bruun, T. S., Amdi, C. & Strathe, A. V. Fetal and placental development in early gestation of hyper-prolific sows. *Theriogenology* **197**, 259–266 (2023).
57. Adams, P. H. Intra-Uterine growth retardation in the pig. *Biol. Neonate*. **19**, 341–353 (1971).
58. Berridge, F. R. & Bruce Eton, F. F. R. The accuracy of radiological estimation of foetal maturity. *J Obstet. Gynaecol. (Lahore)* **33**, 625–630 (1958).
59. Gaundré, D., Lebas, N. & Monziols, M. Effects d'une séquence déplétion-réplétion En phosphore En Engraissement. *Journées Recherche Porcine*. **46**, 119–120 (2014).
60. Faba, L., Sola-Oriol, D., Balfagon, A., Coma, J. & Gasa, J. Assessing the effect of ingredients variability on the composition of the final complete feed for swine. *Can. J. Anim. Sci.* **99**, 7–14 (2019).
61. Batawil, N. & Sabiq, S. Hounsfield unit for the diagnosis of bone mineral density disease: A proof of concept study. *Radiography* **22**, e93–e98 (2016).
62. Van der Lende, T. & De Jager, D. Death risk and preweaning growth rate of piglets in relation to the within-litter weight distribution at birth. *Livest. Prod. Sci.* **28**, 73–84 (1991).
63. Wootron, R., Mcfadyen, I. R. & Cooper, J. E. Measurement of placental blood flow in the pig and its relation to placental and fetal weight. *Biol. Neonate*. **31**, 333–339 (1977).
64. Godfrey, K. M. The role of the placenta in fetal programming—A review. *Placenta* **23**, 37 (2002).
65. Vanderschueren, D. et al. Bone and mineral metabolism in the adult guinea pig: long-term effects of estrogen and androgen deficiency. *Journal bone mineral. research* **7**, 45 (1992).
66. Pointillart, A., Colin, C., Lacroix, H. C. & Guéguen, L. Mineral bioavailability and bone mineral contents in pigs given calcium carbonate postprandially. *Bone* **17**, 357–362 (1995).
67. Tomaszewska, E., Dobrowolski, P. & Wydrych, J. Postnatal administration of 2-oxoglutaric acid improves articular and growth plate cartilages and bone tissue morphology in pigs prenatally treated with dexamethasone. *J. Physiol. Pharmacol.* **63**, 547–554 (2012).
68. Orth, M. W. The regulation of growth plate cartilage turnover. *J. Anim. Sci.* **77**, 183–189 (1999).
69. Ytrehus, B., Carlson, C. S. & Ekman, S. Etiology and pathogenesis of osteochondrosis. *Vet. Pathol.* **44**, 429–448 (2007).
70. Athanasiou, K. A., Darling, E. M. & Hu, J. C. *Articular Cartilage Tissue Engineering* (Morgan & Claypool, 2009).
71. Chriett, S., Huërou-Luron, L., Vidal, I., Pirola, L. & H. & Dysregulation of sirtuins and key metabolic genes in skeletal muscle of pigs with spontaneous intrauterine growth restriction is associated with alterations of Circulating IGF-1. *Gen. Comp. Endocrinol.* **232**, 76–85 (2016).
72. Spencer, E. M., Liu, C. C., Si, E. C. C. & Howard, G. A. In vivo actions of Insulin-Like growth Factor-I (IGF-I) on bone formation and resorption in rats. *Bone* **12**, 21–26 (1991).
73. Mccarthy, T. L., Centrella, M. & Canalis, E. Regulatory effects of Insulin-Like growth factors I and II on bone collagen synthesis in rat calvarial cultures**. *Endocrinology* **124**, 301–309 (1989).
74. Zhao, L., Li, M. & Sun, H. Effects of dietary calcium to available phosphorus ratios on bone metabolism and osteoclast activity of the OPG /RANK/RANKL signalling pathway in piglets. *J. Anim. Physiol. Anim. Nutr. (Berl)*. **103**, 1224–1232 (2019).
75. Siris, E. S. et al. Predictive value of low BMD for 1-year fracture outcomes is similar for postmenopausal women ages 50–64 and 65 and older: results from the National osteoporosis risk assessment (NORA). *J. Bone Miner. Res.* **19**, 1215–1220 (2004).
76. Van Riet, M. M. J., Millet, J., Aluwé, M. & Janssens, G. P. J. Impact of nutrition on lameness and claw health in sows. *Livest. Sci.* **156**, 24–35 (2013).
77. Veum, T. L., Ledoux, D. R., Shannon, M. C. & Raboy, V. Effect of graded levels of iron, zinc, and copper supplementation in diets with low-phytate or normal barley on growth performance, bone characteristics, hematocrit volume, and zinc and copper balance of young swine. *J. Anim. Sci.* **87**, 2625–2634 (2009).
78. Skiba, G. et al. Influence of the Zinc and Fibre Addition in the Diet on Biomechanical Bone Properties in Weaned Piglets. *Animals* **12**, 33 (2022).

79. Bauer, R. et al. Body weight distribution and organ size in newborn swine (sus scrofa domestica) - A study describing an animal model for asymmetrical intrauterine growth retardation. *Exp. Toxicol. Pathol.* **50**, 59–65 (1998).
80. European Parliament. Directive 2010/63/EU of the European Parliament and of the Council of 22 of September 2010 on the Protection of Animals Used for Scientific Purposes. Official Journal 33–79. (2010).
81. Font i Furnols, M., Teran, M. F. & Gispert, M. Estimation of lean meat content in pig carcasses using X-ray computed tomography and PLS regression. *Chemometr. Intell. Lab. Syst.* **98**, 31–37 (2009).
82. Font-I-Furnols, M., Carabús, A., Pomar, C. & Gispert, M. Estimation of carcass composition and cut composition from computed tomography images of live growing pigs of different genotypes. *Animal* **9**, 166–178 (2015).
83. Bardera, A., Martínez, R., Boada, I., Font-i-Furnols, M. & Gispert, M. Towards the simulation of a virtual butcher. in *Farm Animal Imaging (FAIM) conference*Dublin, Ireland, (2012).
84. R Core Team. R: A Language and Environment for Statistical Computing. Preprint at. (2024).

Acknowledgements
This work was funded by the Ministerio de Ciencia, Innovación y Universidades, Gobierno de España (PID2019-103915GB-100). P.S.-L. was granted an FI grant (2023 FI-2 00080) from the Departament de Recerca i Universitats, Generalitat de Catalunya. E.L.-C. was granted with a Programa Investigo postdoctoral grant (2023 INV-2 00076) founded by NextGenerationEU.

Author contributions
P.S.-L. (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing—original draft), E.L.-C. (Conceptualization, Investigation, Methodology, Supervision, Writing—review & editing), S.G.-V. (Resources, Writing—review & editing), D.S.-M. (Resources, Writing – review & editing), A.B. (Resources, Writing—review & editing), M. F.-i-F. (Resources, Writing—review & editing), J.G. (Conceptualization, Supervision, Writing – review & editing), and D.S.-O (Conceptualization, Funding acquisition, Project administration, Supervision, Writing – review & editing).

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Correspondence and requests for materials should be addressed to E.L.-C.