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Intrauterine growth restriction defined by increased brain-to-liver weight ratio affects postnatal growth and protein efficiency in pigs

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ABSTRACT

Intrauterine growth restriction (**IUGR**) refers to impaired foetal growth during gestation, resulting in permanent stunting effects on the offspring. This study aimed to investigate the effects of IUGR on growth performance, body composition, blood metabolites, and meat quality of pigs from birth (n = 268) to slaughter (n = 93). IUGR piglets have prioritised brain development as a foetal adaptive reaction to placental insufficiency. This survival mechanism results in a higher brain-to-liver weight ratio (**BrW/LW**). One day (±1) after birth, computed tomography (**CT**) was performed on each piglet to assess their brain and liver weights. A threshold value of 0.78 (mean + SD) was chosen to divide the piglets into two categories – NORM (BrW/LW < 0.78) and IUGR (BrW/LW > 0.78). Moreover, each piglet was classified as either normal (score 1), mild IUGR (score 2), or severe IUGR (score 3) based on the head morphology. BW was recorded weekly, and average daily gain (**ADG**) was calculated for lactation, starter, grower, and finisher periods. Body composition was assessed after weaning (29.6 ± 0.7 d), at 20 kg (64 ± 7.2 d), 100 kg (165 ± 12.3 d), and on the carcasses using Dual-energy X-ray absorptiometry (**DXA**). Content and deposition rates of single nutrients, as well as energy and CP efficiency, were measured at 20 and 100 kg. Feed intake was recorded from 20 kg to slaughter. Meat quality was assessed on the carcasses. A total of 70% of the piglets assigned a score of 3 were NORM according to their BrW/LW. The IUGR category showed a lower ADG in the lactation ($P < 0.01$), starter ($P = 0.07$), and grower phases ($P < 0.05$) and a reduced CP efficiency in the grower–finisher period ($P < 0.01$) compared to the NORM group. IUGR pigs had a lower gain-to-feed ratio in the finisher period ($P = 0.01$) despite similar average daily feed intake, and they required more days ($P < 0.01$) to reach the slaughter weight. Additionally, their meat was darker ($P = 0.01$) than that of NORM pigs. The BrW/LW was inversely proportional to the ADG from birth to slaughter and negatively correlated with the CP deposition rate and efficiency in the grower–finisher period ($P < 0.01$). Furthermore, the higher the BrW/LW, the longer it took the pigs to reach the slaughter weight ($P < 0.01$). In conclusion, the identification of IUGR piglets based on the head morphology does not always agree with an increased BrW/LW. IUGR affects growth performance from birth to slaughter, CP efficiency in the grower–finisher period and meat quality.

Implications

Modern pig breeds show an increased percentage of piglets born undersized and exposed to intrauterine growth restriction. This condition is characterised by relative brain-sparing, while the liver is primarily affected by oxygen and nutrient deprivation. Employing the brain-to-liver weight ratio for the identification of the affected piglets provides an objective approach as it directly reflects the brain-sparing effect. Our study showed that the identification of growth-restricted piglets based on head shape or birth weight is not always consistent with a high ratio. Affected pigs exhibited reduced average daily gain, CP efficiency, and required more days to reach the targeted slaughter weight.

Introduction

The number of pigs produced per sow per year is a fundamental economic driver in the pig industry. One of the first objectives of the modern pig production system is to increase the number of weaned piglets per litter (Hansen et al., 2018). The increase in litter sizes has led to markedly lower birth weight (**BtW**) and an increased percentage of piglets born undersized and exposed to

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different degrees of growth restriction in the uterus (Amdi et al., 2013; Hansen et al., 2018). Intrauterine growth restriction (**IUGR**) is defined as the impaired growth of the mammalian foetus during gestation (Wu et al., 2006). The principal cause behind this condition is an insufficiency of the placenta, which does not allow for an appropriate distribution of oxygen and nutrients to the foetus (Cohen et al., 2015). In the modern pig industry, 15–20% of newborn piglets are affected by IUGR, and they usually show high morbidity and mortality, impaired metabolism, stunted growth and muscle development, reduced feed conversion efficiency (Krueger et al., 2014) and poor carcass quality (Wang et al., 2013; Wu et al., 2006). In order to develop effective management interventions to treat this condition, reliable tools are needed to identify IUGR-affected piglets (Amdi et al., 2013). Accurate diagnosis of piglets affected by IUGR holds the potential to provide physiological characterisation and valuable insights into the condition. This could facilitate the development of targeted and innovative strategies aimed at effectively treating them.

Different authors have characterised IUGR piglets based on their head morphology (Chevaux et al., 2010; Hales et al., 2013; Hansen et al., 2018). Compared to non-IUGR pigs, those suffering from growth restriction in the uterus show a dolphin-like head shape, bulging eyes, and wrinkles perpendicular to the mouth. Apart from these phenotypic traits, IUGR piglets prioritise brain development as part of a foetal adaptive reaction to placental insufficiency (Amdi et al., 2013). This survival mechanism is defined as "brain-sparing effect" and results in a relatively larger brain compared to other organs, such as the liver (Cohen et al., 2015; Matheson et al., 2018). For this reason, the optimal metric for identifying the degree of IUGR considers the ratio between the weight of the brain and other organs (Felicioni et al., 2019). Nevertheless, to assess this ratio, newborn piglets must be euthanised. Consequently, this approach is feasible only in research contexts. The lack of more accurate and non-invasive methods to diagnose IUGR still makes this condition a major challenge in both human and animal health (Felicioni et al., 2019), as the development of management interventions is limited by poor diagnosis.

Our first hypothesis was that an increased brain-to-liver weight ratio (**BrW/LW**) does not always align with morphological alterations of the head shape or with a low BW at birth. The second hypothesis was that IUGR, defined by a high BrW/LW, has a long-lasting detrimental effect on the development of the progeny. To test the first hypothesis, this descriptive study used computed tomography (**CT**) scan imaging as a non-invasive method to assess the BrW/LW in newborn piglets. As for the second hypothesis, a comprehensive investigation was conducted into how IUGR affects growth performance, body composition, blood metabolite traits, and meat quality in pigs from birth to slaughter.

Material and methods

Animal selection and classification

This experiment was performed at the Agroscope swine research facility in Posieux, Switzerland. In this study, 268 Swiss Large White piglets (females = 134 and males = 134) originating from 26 litters from two farrowing series (first farrowing series = 14 litters, second farrowing series = 12 litters) were included. On the day of farrowing (day 0), the BtW of each piglet was recorded. Piglets with a BtW < 1.1 kg were assigned to the low-BtW category (Low BtW), whereas those with a BtW > 1.1 kg were assigned to the normal-BtW category (Normal BtW). On day 1 (±1) after birth, piglets were visually classified as either normal (score 1), mild IUGR (score 2), or severe IUGR (score 3) based on the morphological characteristics of the head (Chevaux et al., 2010; Hales et al., 2013; Hansen et al., 2018). The morphological characteristics of the head of an IUGR piglet are described as follows – dolphin-like head shape, bulging eyes, hair with no direction of growth, and wrinkles perpendicular to the mouth. If none of the IUGR characteristics were applied, the piglet was defined as normal and assigned a score of 1. The piglet was classified with a score of 2 when one of the characteristics was present. Finally, a score of 3 was assigned when two, three or all the characteristics were present.

In addition to visual scoring, CT scan imaging (64-channel multislice scanner Siemens Emotion Duo CT, Siemens, Erlangen, Germany) was performed on all piglets on day 1 (±1) after birth to non-invasively assess the volume of the brain and liver. For the CT measurements, all the animals were anaesthetised by isoflurane inhalation and positioned in sternal recumbency. CT images of the head and thoracic regions were obtained. The raw image sequences were semi-automatically segmented to obtain the volume of the two organs (Turtleseg software 1.2.1). After the CT scan, 30 piglets were euthanised with an intra-cardiac injection of pentobarbital solution (Esconarkon, volume to effect). Three BtW categories (category 1 < 1.1 kg; category 2 ≥ 1.1 and < 1.8 kg; category 3 ≥ 1.8 kg), were defined to cover the full range of BtWs present in the actual population. From each BtW category, 10 piglets were euthanised paying attention to keep a balanced female-to-male ratio (Supplementary Table S1). After euthanasia, the brain and the blood-filled liver were excised. The brain and liver weights were assessed with a scale, and the volume was determined using the water displacement method. The density of the organs was determined by calculating the ratio of their mass to volume using the equation: d = m (g)/V (mL), where d represents the organ density, m represents the mass in g, and V the volume of the organ in mL. The average brain and liver density, together with the brain and liver volumes obtained from the CT scan images, were used to determine the brain and liver weights and the BrW/LW. The average BrW/LW determined in 217 piglets was 0.63 ± 0.15 [mean ± SD]. Piglets with a BrW/LW ≥ 0.78, which correspond to the mean + one SD, were assigned to the IUGR category (IUGR; n = 32), whereas those with a BrW/LW < 0.78 were assigned to the "normal" category (NORM; n = 185). The threshold was calculated on the population surviving after weaning, considering the high preweaning mortality rate of severe IUGR until weaning (Farmer and Edwards, 2022). Indeed, piglets that were euthanised (n = 30) or died before weaning (n = 21), as well as stillborn piglets (n = 43) were excluded when determining the BrW/LW threshold. A threshold calculated on the surviving population includes moderately severe IUGR cases, allowing to investigate the long-term effects of the condition.

The pigs (n = 217) were weaned at 25.2 ± 1.2 days of age. Two piglets (IUGR = 1, NORM = 1) died in the postweaning phase and were not included in the statistical analysis of the starter period.

On day 73 ± 6.4 of age (24 ± 5.3 kg BW), a group of 96 piglets were selected for the grower–finisher phase. As at the time of selection, the CT scan results were not available, the selection relied on traditional traits, namely IUGR score and BtW. The group consisted of 48 castrated males and 48 females. For the selection, all the weaned piglets were first split into two groups according to their sex, castrated males and females. Within each sex, piglets were ranked by decreasing score and then by increasing BtW. The first 24 piglets with the highest IUGR score and lowest BtW were selected for fattening. Similarly, the last 24 pigs with the lowest IUGR score and highest BtW were also selected. The selection process was repeated for each sex (see Supplementary Table S2). Three pigs (NORM = 3) died before the end of the grower period and were not included in the statistical analysis of the grower–finisher period.

Rearing conditions during lactation, starter, grower, and finisher periods

During the whole experiment, *ad libitum* access to water was ensured through nipple drinkers or drinking troughs. Straws were always placed in pens to enrich the environment. The pigs were monitored daily for their health status by trained personnel.

The sows were housed in individual farrowing crates, starting 10 days before the expected farrowing time. During the entire lactation period, the sows were left free in the pen. Each farrowing crate was provided with a heated and covered nest for the piglets. Within the first 14 hours after birth, all the piglets were ear-tagged and treated with an iron injection (Ferridex® 10%, AMAG Pharmaceuticals, Inc., Waltham, USA). Male piglets were castrated under general anaesthesia 48 hours after birth and treated with ketofen (3 mg/kg, Rifen®, Streuli Tiergesundheit AG, Uznach, Switzerland) for pain control. The temperature in the nest was 40 °C immediately after birth and then gradually decreased daily by 0.5 °C to reach a temperature of 32 °C on day 16.

The temperature in the farrowing rooms was set to 24 °C, and artificial lights were kept on from 8 am to 5 pm. Parturition was induced when gestation time exceeded 116 days by an intramuscular injection of 1 mL (0.25 g/mL) of cloprostenol (Estrumate®, MSD Animal Health GmbH, Luzern, Switzerland). The piglets were kept in their dam until day 25.2 ± 1.2 days of age.

All the pigs were housed by litter until 39.2 ± 1.3 days of age (approximately two weeks after weaning), then kept in groups of 12 piglets per pen until they reached an average BW of 24 ± 5.3 k g. The 96 pigs selected for the fattening period were housed in two large connected pens (17.35 m^2).

Growth performance and feeding

Piglets had *ad libitum* access to a standard pre-/early postweaning diet from day 16 after birth to 14 days postweaning (39.2 ± 1.3 days of age, 7.5 ± 1.5 kg BW [mean ± SD]). Subsequently, they were offered *ad libitum* access to a starter diet until the start of the grower period (73 ± 6.4 days of age, 24 ± 5.3 kg BW [mean ± SD]). Piglets were switched to the grower diet when their BW was $\geq$20 kg at the day of the weekly weighing. The pre-/early postweaning feed, as well as the starter diet, was available through feeding troughs. Fresh pre-/early postweaning feed was provided at least once a day, and leftovers were removed every day from day 16 to 39.2 ± 1.3 days of age. However, it was not possible to determine feed intake during this period.

In the grower and finisher periods, each pen was equipped with four automatic feeders and an individual pig recognition system (Schauer Maschinenfabrik GmbH & Co. KG, Prambachkirchen, Austria). The feeder allowed monitoring the individual daily feed intake and the average daily feed intake (**ADFI**). The grower and finisher diets were offered from 24 ± 5.3 to 63.3 ± 2.1 kg and from 63.3 ± 2.1 to 108.3 ± 4.2 kg (mean ± SD), respectively. The ingredients used to formulate the pre-/early postweaning, starter, grower, and finisher diets and the nutrient composition are presented in the supplementary material (Supplementary Table S3). Starting from week 2 after birth, the pigs were weighed individually once a week until slaughter. The average daily gain (**ADG**) was measured for each period (lactation, starter, grower, and finisher). Moreover, the feed intake was recorded from 20 kg until slaughter, and the gain-to-feed ratio was calculated for each pig.

Body composition

A GE lunar dual-energy X-ray absorptiometry (**DXA**; i-DXA, GE Healthcare Switzerland, Glattbrugg, Switzerland) with a narrow-angle fan beam (Collimator Model 42129) was used to scan live pigs right after weaning (n = 217; 29.6 ± 0.7 days, [mean ± SD]) at the start of the grower period (n = 90; BW $\geq$ 20 kg at the day of the weekly weighing; 64 ± 7.2 days [mean ± SD]) and before slaughter (n = 90; BW $\geq$ 100 kg at the day of the weekly weighing. 165 ± 12.3 days [mean ± SD]) as well as the carcasses (n = 88). The procedures to handle the pigs and the carcasses and to analyse the DXA scan images have been described in detail by Kasper et al. (2021). Briefly, on the day of the scan, the pigs were anaesthetised with isoflurane inhalation and then DXA scanned in sternal recumbency, with both the fore legs and the hind legs extended and pointed caudally. The window chosen for the analysis was the entire body scan in thick mode.

The half carcasses (left side) were scanned the day after slaughter. The pigs were slaughtered after 16 h of feed withdrawal at the Agroscope abattoir by exsanguination after CO2 stunning. Immediately after exsanguination, the hair was removed and the animals were eviscerated. The carcass and head were sawed into two halves and chilled at 2 °C. The scanned images from live animals and carcasses were processed to remove artefacts and position the regions of interest. The DXA output variables total mass, total lean mass, total fat mass, total bone mineral content and total bone mineral density were exported from the enCORE software and assessed at weaning, at the start of the grower period, before slaughter and in the carcass halves. Using the equations developed by Kasper et al. (2021), the total mass, total lean mass, total fat mass, and total bone mineral content were used to determine the water, ash, CP, lipid, and energy content of the empty body of the live animals at the start of the grower period, at the end of the finisher period, and of the carcasses. The energy, CP, and fat daily deposition rates, as well as the energy and CP efficiency, were assessed for the grower–finisher period. The equations published by Kasper et al. (2021) were validated within a range of 20–100 kg and on the carcasses. Therefore, it was not possible to assess the content of the single nutrients at weaning.

Blood metabolite traits and blood cell count

The pigs were slaughtered 16 h after feed withdrawal. Blood was sampled from the pigs (n = 91) at the slaughterhouse during bleeding. However, the time at which each pig consumed its last meal before the feed withdrawal was not standardised. Blood was collected using Vacuette blood collection tubes with a serum clot activator for serum or ethylenediaminetetraacetic acid (**EDTA**) for native blood sampling (Greiner Bio-One GmbH, Kremsmünster, Austria). Serum tubes were stored upside down at room temperature for 1 h prior to centrifugation for 15 min at 3 000*g* and subsequently for 2 min at 4 000*g*. Two aliquots of serum were stored at −20° in Eppendorf tubes. The EDTA tubes were kept on ice until analysis and processed within 2 hours after collection with a Vetscan HM5 haematology analyser (Abaxis Inc., Union City, USA). The serum samples were assayed using commercially available kits according to the manufacturer's instructions on a BT1500 autoanalyzer (Biotecnica Instruments Ltd., Roma, Italy) to determine urea (Greiner Diagnostic GmbH, Langenthal, Switzerland) and non-esterified fatty acid (Randox Laboratories Ltd., Crumlin, UK) concentrations. Moreover, from the EDTA samples, the levels of glucose, haemoglobin, haematocrit, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, mean corpuscular volume, and the count of granulocytes, lymphocytes, monocytes, platelets, red blood cells, and white blood cells were assessed. Serum insulin concentration was measured using a Porcine Insulin Kit (Mercodia, Uppsala, Sweden) following manufacturer instructions adapted to the use of a Crocodile 4-in-one assay mini workstation (Berthold GmbH, Bad Wildbad, Germany). Absorbance was read with an Asys UVM340 microplate reader in combination with the MikroWin 2000 software (Biochrom Ltd., Cambridge, UK).

Meat quality

After slaughter, temperature and pH were monitored at 45 min and 24 h *postmortem* in the *longissimus thoracis* (**LT**; at the 10th rib level; n = 91) using a Testo 205 pH meter (Testo Inc., Lenzkirch, Germany). One day after slaughter, the LT was excised from the left carcass side at the 8th to 10th rib level, and 5 $\times$ 1.5 cm thick chops were cut for further analysis. The first chop was immediately vacuum-packaged and stored at −20 °C for chemical analysis. Two chops were used to assess the quantity of purge generated during storage at 4 °C for 48 h, expressed as a percentage of the initial sample weight (Honikel 1998). The colour was assessed after a 20-min bloom period on the two other chops using a CM-700d Chroma Meter (Konica, Minolta, Tokyo, Japan) in the CIE lightness, redness, and yellowness colour space. Three replicated measurements were performed on each sample. Afterwards, the chops were blotted-dry weighted, vacuum-packaged, and then stored for 24 h at 2 °C. At the end of this ageing period, the meat slices were frozen and stored at −20 °C. Within one month after slaughter, these chops were thawed for 24 h at 2–4 °C in vacuum plastic bags, blotted dry, and weighed to assess the thaw loss. The chops were then cooked for 5 min on a preheated (170 °C) Indu-Griddle grill (SH/GR 3500, Schöhbühl, Switzerland) to a core temperature of 69 ± 2 °C and reweighted to determine cooking loss. After being kept at room temperature for 2 h, the Warner-Bratzler shear force was measured in cooked chops using a Texture Analyzer TA.HDplus (Stable Micro Systems, Goldaming, UK) equipped with a 2.5-mm-thick Warner-Bratzler shear blade.

Statistical analysis

All calculations and statistical analyses were performed using R (version 4.0.2). The data were analysed with linear mixed-effect models using the "lmer" function of the lme4 package. For the BW analysis during lactation, starter, grower, and finisher phases, the IUGR category (IUGR, NORM) or BrW/LW, sex (female, castrate), and age and their two- and three-way interactions were considered fixed effects. The interactions were tested and removed if not significant. Age and piglet ID nested into the litter of origin were considered random effects using piglet ID nested into the litter of origin as the grouping factor. The lmer models were routinely checked for the normality of the residuals and the homoscedasticity. If the fixed factors were significant, multiple comparisons were performed using the modified Tukey test from the emmeans package. For the rest of the data, the IUGR category (IUGR, NORM) or the BrW/LW and sex (female, castrate) were considered fixed effects and the litter of origin as a random effect. The two-way interaction between the two fixed effects was always tested and removed if not significant. The pig was considered the experimental unit.

Data on ADG were analysed separately for the lactation, starter, grower, and finisher periods, and those on daily feed intake, and gain-to-feed ratio were analysed for the grower and finisher periods. The DXA results at weaning, at the start of the grower period, before slaughter, and of the carcasses were analysed separately. For the pigs whose DXA results were available at the start of the grower period and at slaughter, nutrient and energy content, deposition rates as well as energy and CP efficiency were calculated. The content of nutrient and energy in the empty body was calculated from the DXA output variables total mass, total lean mass, total fat mass, and total bone mineral content. The rates of nutrient and energy deposition were determined by dividing the difference in nutrient and energy content in the empty body at 100 and 20 kg of BW by the total nutrient and energy intake between the two DXA scans. The daily nutrient deposition rates were calculated by dividing the deposition by the number of days on feed between the two DXA scans. Energy and CP efficiency were calculated by dividing the energy and CP deposition between 20 and 100 kg of BW by the total energy and CP intake between the two DXA scans. For the haematological data, the value of the lower limit of quantification was considered for measurements that were quantifiable but below the value itself. Values below the lower limit of detection were assigned a value of 0. In addition, for the statistical analysis of meat quality, the day of slaughter was set as a random effect together with the litter of origin. The results are presented as least square means and pooled SEM. The IUGR category, BrW/LW and sex effects were considered different at $P \leq 0.05$.

Results

Intrauterine growth restriction classification

On average, IUGR piglets had 55% greater BrW/LW ($P < 0.01$) and 29% lower BtW ($P < 0.01$) compared to NORM pigs (Table 1). In total, 114, 83, and 20 piglets were assigned scores 1, 2, and 3, respectively. Of the NORM pigs, 91% and 81% had scores of 1 and 2, respectively. The remaining pigs were IUGR pigs. Interestingly, 70% of the piglets with a score of 3 were NORM pigs, as they had a BrW/LW < 0.78 (Fig. 1). Out of the 217 pigs, 12 piglets had a BtW < 1.1 kg; however, three were NORM pigs, which led to a misclassification of 25% of the IUGR piglets using the BtW classification.

Growth performance traits from birth to slaughter

Compared to the NORM pigs, the IUGR pigs weighed, on average, 1.1 kg less at weaning ($P < 0.01$), as their ADG during lactation was 37 g/d lower ($P < 0.01$, Table 2). Likewise, from weaning to the start of the grower period, the IUGR pigs grew slower than the NORM pigs, as they displayed a 27 g/d lower ADG ($P = 0.07$, Table 2). At the end of the starter period, IUGR females weighed 3.4 kg less ($P < 0.01$) than their NORM counterparts. By contrast, IUGR castrates were 2.7 kg lighter ($P = 0.01$) than the NORM castrates, which explains the significant interaction ($P = 0.03$) between category (IUGR and NORM) and sex. Similarly, the BrW/LW was inversely proportional ($P < 0.01$) to the ADG in both the lactation and starter periods (Fig. 2).

At the start of the grower period (23.5 ± 1.41 kg BW [least square mean ± SEM]), the IUGR pigs were 4.1 days older ($P = 0.03$) than the NORM pigs. As the study progressed, the age difference between the groups continued to increase, reaching an additional 4 days by the start of the finisher period (63.5 ± 2.53 kg BW [least square mean ± SEM]). However, the age difference did not further increase during finisher period, where the IUGR pigs at slaughter were 8 days older ($P < 0.01$) than the NORM pigs. Accordingly, from the start of the grower period to slaughter, the IUGR pigs grew 4.7% slower ($P = 0.04$) than the NORM pigs (Table 2), which was mainly due to slower ($P = 0.04$) growth in the grower but not in the finisher period. Apart from being less efficient ($P = 0.01$) in the finisher period, ADFI and total feed intake did not differ between the two groups. When considering the BrW/LW instead of the category, pigs with a higher ratio grew slower ($P < 0.01$, Fig. 2) and displayed a lower ADFI ($P = 0.05$, Supplementary Fig. S1) from the start of the grower period to slaughter. This was mainly due to slower ($P < 0.01$) growth and daily feed intake ($P = 0.04$) in the grower but not in the finisher period ($P = 0.10$, Supplementary Fig. S1). Accordingly, as the BrW/LW increased, the gain-to-feed ratio decreased ($P = 0.01$) in the grower–finisher period (Fig. 2). The higher the BrW/LW, the longer ($P < 0.01$) it took for the pigs to reach slaughter weight. At the start of the grower,

Table 1
Effect of classifying the pigs based on the brain-to-liver weight ratio (BrW/LW), head shape, birth weight (BtW), and sex on the BrW/LW and the BtW.

	BrW/LW[1]			Sex			P-value[2]	
Item	IUGR	NORM		Female	Castrate	SEM[3]	BrW/LW	Sex
Number of pigs	32	185		115	102			
BrW/LW	0.90	0.58		0.74	0.73	0.018	<0.001	0.45
BtW	1.23	1.59		1.39	1.42	0.043	<0.001	0.37
	Head shape[4]			Sex			P-value[5]	
	Score 1	Score 2	Score 3	Female	Castrate	SEM	Head shape	Sex
Number of pigs	114	83	20	115	102			
BrW/LW	0.58	0.66	0.76	0.67	0.66	0.032	<0.001	0.82
BtW	1.63	1.47	1.28	1.45	1.47	0.057	<0.001	0.50
	Birth weight[6]			Sex			P-value[7]	
	Low BtW	Normal BtW		Female	Castrate	SEM	BtW	Sex
Number of pigs	12	205		115	102			
BrW/LW	0.87	0.61		0.74	0.74	0.041	<0.001	0.93
BtW	1.01	1.57		1.28	1.30	0.071	<0.001	0.62

[1] BrW/LW: IUGR: piglets with a BrW/LW ≥ 0.78; NORM: piglets with BrW/LW < 0.78.
[2] *P*-value for the main effect of the BrW/LW and sex.
[3] Pooled SEM.
[4] Head shape based on the morphological characteristics of the head (Chevaux et al., 2010; Hales et al., 2013; Hansen et al., 2018): score 1: "normal" piglet, score 2: mild intrauterine growth restriction (IUGR); score 3: severe IUGR.
[5] *P*-value for the main effect of head shape classification and sex.
[6] Birth weight: low BtW: piglets with BtW < 1.1 kg; normal BtW: piglets with a BtW ≥ 1.1 kg.
[7] *P*-value for the main effect of BtW and sex.

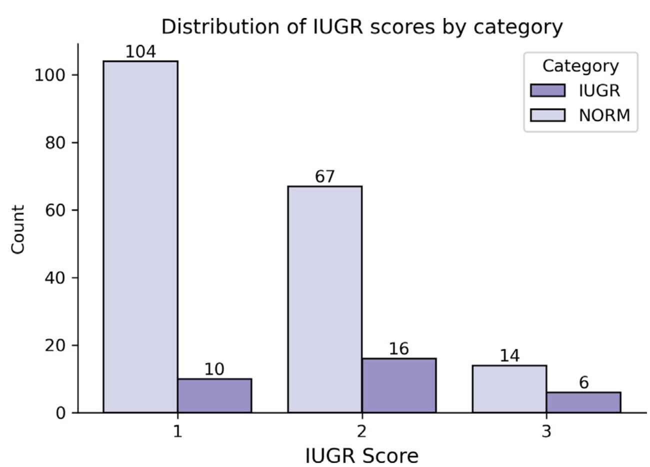

Fig. 1. Comparison between the classification of intrauterine growth restriction (IUGR) based on the head shape of the piglets (score 1, 2 and 3) and the classification based on the brain-to-liver weight ratio (BrW/LW; IUGR and NORM). X-axis: IUGR: piglets with a BrW/LW ≥ 0.78; NORM: piglets with BrW/LW < 0.78; head shape based on the morphological characteristics of the head (Chevaux et al., 2010; Hales et al., 2013; Hansen et al., 2018): score 1: "normal" piglet, score 2: mild IUGR; score 3: severe IUGR. Y-axis: number of pigs (count).

finisher period, and slaughter, the age of the pigs was positively correlated ($P < 0.01$) with the BrW/LW (Fig. 3).

Empty body composition

Regardless of sex, the total bone mineral density, the total bone mineral content, the total lean and fat mass in the empty body were lower at weaning ($P < 0.01$) in the IUGR pigs compared to the NORM pigs (Table 3). However, when these variables were expressed as percentages of the BW, only the total bone mineral density differed between the two groups, showing a higher ($P < 0.01$) value in the IUGR pigs. Similarly, the total bone mineral density, the total bone mineral content, the total lean and fat mass in the empty body decreased ($P < 0.01$) as the BrW/LW increased. However, when these variables were expressed as a percentage of the BW, only the total bone mineral density was affected by the BrW/LW, showing a positive correlation ($P < 0.01$) with the ratio (Fig. 4). The ash content ($P = 0.06$, Table 4) in the empty body tended to be lower in the IUGR pigs than in the NORM pigs at 20 kg but not at 100 kg. In contrast, neither at 20 kg nor at 100 kg BW did empty BW, energy, water, CP, and lipid content differ between IUGR and NORM pigs (Table 4). Except for the daily CP deposition rate that tended ($P = 0.08$) to be lower in the IUGR pigs than in the NORM pigs, the daily energy and fat deposition rates were similar between the two groups. Due to the numerically greater CP intake ($P = 0.15$) and the numerically lower CP content ($P = 0.10$) in the empty body at 100 kg BW, the CP efficiency of IUGR pigs was lower ($P < 0.01$) than that of the NORM pigs. Regarding the BrW/LW, the ash content in the empty body decreased ($P < 0.01$) with an increase in the ratio at 20 kg but not at 100 kg of BW (Fig. 4). In the grower–finisher period, except for the daily CP deposition rate, which was inversely proportional ($P < 0.01$) to the BrW/LW (Fig. 5), the daily energy and fat deposition rate were not affected by the ratio. The CP intake tended to increase ($P = 0.07$) and the CP content in the empty body decreased ($P < 0.01$) with a higher BrW/LW (Fig. 5). As a consequence, the CP efficiency was negatively correlated ($P < 0.01$) with the BrW/LW (Fig. 5).

Blood metabolite traits and blood cell count

At slaughter, the lymphocyte count tended to increase ($P = 0.09$) and the monocyte counts were higher ($P < 0.01$) for the IUGR category compared to the NORM group (Table 5). For the glucose and haemoglobin concentration in the serum and the red blood cell count, despite the significant interaction ($P \leq 0.02$) between the category and the sex, the multiple mean comparisons between IUGR and NORM females and castrates were not significant (Table 6). The other parameters, including urea concentration, non-esterified fatty acids, haematocrit, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, mean corpuscular volume, granulocytes count, and platelets count, showed similar values between the IUGR and NORM categories (Table 5).

Table 2
Effect of classifying the pigs based on the brain-to-liver weight ratio (BrW/LW) and sex on growth performance traits from birth to slaughter.

	BrW/LW[1]		Sex			*P*-value[2]	
Item[3]	IUGR	NORM	Female	Castrate	SEM[4]	BrW/LW	Sex
From birth to the start of the grower period[5]							
Number of pigs	32	185	115	102			
BW, kg							
At weaning	6.2	7.3	6.7	6.7	0.31	<0.001	0.35
At the end of the starter period[6]	20.3	23.4	21.6	22.1	0.84	-	-
ADG, kg/d							
Lactation	0.19	0.23	0.21	0.21	0.012	<0.001	0.14
Starter	0.33	0.36	0.35	0.34	0.016	0.07	0.16
Age, d							
At weaning	25.2	25.2	25.2	25.1	0.25	0.98	0.11
At the end of the starter period	74.2	72.3	72.8	73.7	0.90	<0.01	0.06
From the grower period to slaughter							
Number of pigs[7]	22	71	47	46			
BW, kg							
At the start of the grower period	21.4	25.5	26.4	20.5	1.41	0.73	<0.01
At the start of the finisher period	59.7	67.2	66.1	60.8	2.53	<0.01	<0.01
At slaughter	106	114	112	107	3.5	<0.01	<0.01
ADG, g/d							
Grower period	0.81	0.85	0.79	0.87	0.028	0.04	<0.001
Finisher period	0.91	0.95	0.89	0.97	0.025	0.19	<0.001
Overall	0.86	0.90	0.84	0.92	0.024	0.04	<0.001
Total feed intake, kg							
Grower period	85.8	84.7	84.4	86.0	1.25	0.41	0.15
Finisher period	129.3	129.8	126.9	132.2	3.09	0.88	0.05
Total	215.1	214.4	211.4	218.2	3.11	0.84	0.01
ADFI, kg/d							
Grower period	1.7	1.7	1.6	1.8	0.04	0.22	<0.001
Finisher period	2.7	2.7	2.5	2.8	0.06	0.51	<0.001
Overall	2.1	2.2	2.1	2.3	0.05	0.21	<0.001
Gain-to-feed							
Grower period	0.47	0.48	0.48	0.48	0.005	0.31	0.34
Finisher period	0.34	0.35	0.35	0.34	0.004	0.01	0.08
Overall	0.40	0.41	0.41	0.40	0.006	0.08	0.28
Day on feed, d							
Grower period	52.2	47.9	52.9	49.0	1.53	0.07	<0.001
Finisher period	48.5	48.7	50.4	46.8	1.46	0.87	<0.001
Overall	100.4	98.1	102.9	95.6	2.33	0.24	<0.001
Age, d							
At the start of the grower period	75	71	74	75	1.5	0.03	0.21
At the start of the finisher period	127	119	124	122	2.4	<0.001	0.19
At slaughter	175	167	174	168	2.9	<0.001	<0.001

[1] BrW/LW: IUGR: piglets with a BrW/LW $\geq$ 0.78; NORM: piglets with BrW/LW < 0.78.
[2] *P*-value for the main effect of the BrW/LW and sex.
[3] ADG = average daily gain, ADFI = average daily feed intake.
[4] Pooled SEM.
[5] From birth to weaning, the growth performance traits were determined in 217 piglets. From weaning to the start of the grower period, growth performance traits were determined in 215 out of 217 pigs.
[6] Significant interaction between the category (IUGR, NORM) and the sex (*P* = 0.03). IUGR females and castrates were lighter than their NORM counterparts (*P* < 0.01). Average BW of the IUGR females: 19.9 kg; average BW of the NORM females: 23.3 kg; average BW of the IUGR castrates: 20.8 kg; average BW of the NORM castrates: 23.5 kg.
[7] In the grower and finisher period, the growth performance traits were determined in 93 of the 217 pigs.

When considering the BrW/LW, the serum urea tended to increase (*P* = 0.09) as the BrW/LW increased at slaughter (Fig. 5). The monocyte count was positively correlated (*P* < 0.01) with the ratio (Fig. 6). For the castrated pigs, as the BrW/LW increased, the haemoglobin concentration in the blood (*P* = 0.05) and the red blood cell count (*P* < 0.01) increased (Fig. 6). For high values of the BrW/LW, females displayed a lower haematocrit (*P* = 0.02) compared to the castrates (Fig. 6). Serum insulin was detectable in just 67 out of 90 pigs (in 76% of the IUGR and 73% of the NORM category). For these animals, the insulin concentration did not differ between IUGR and NORM pigs (Table 5). However, the insulin concentration in the serum tended to be positively correlated (*P* = 0.08) with the BrW/LW (Fig. 7).

Carcass composition and meat quality

Carcass weight, energy, water, ash, CP, and lipid content did not differ between the IUGR and NORM pigs (Supplementary Table S4). Likewise, no significant differences were detected when testing the effect of the BrW/LW on the composition of the carcasses.

In the IUGR category, the lightness of the LT muscle was lower (*P* = 0.01) while the shear force was increased (*P* < 0.01) compared to the NORM group (Supplementary Table S4). The other traits did not show significant differences between the two groups. Likewise, the BrW/LW was inversely proportional (*P* < 0.01) to the lightness of the LT muscle (Supplementary Fig. S2). In addition, the cooking loss tended to be negatively correlated (P = 0.09) with the BrW/LW (Supplementary Fig. S2).

Discussion

Intrauterine growth restriction identification

In this study, we considered the BrW/LW, BtW, and head morphology at birth as traits to identify IUGR piglets. Our results

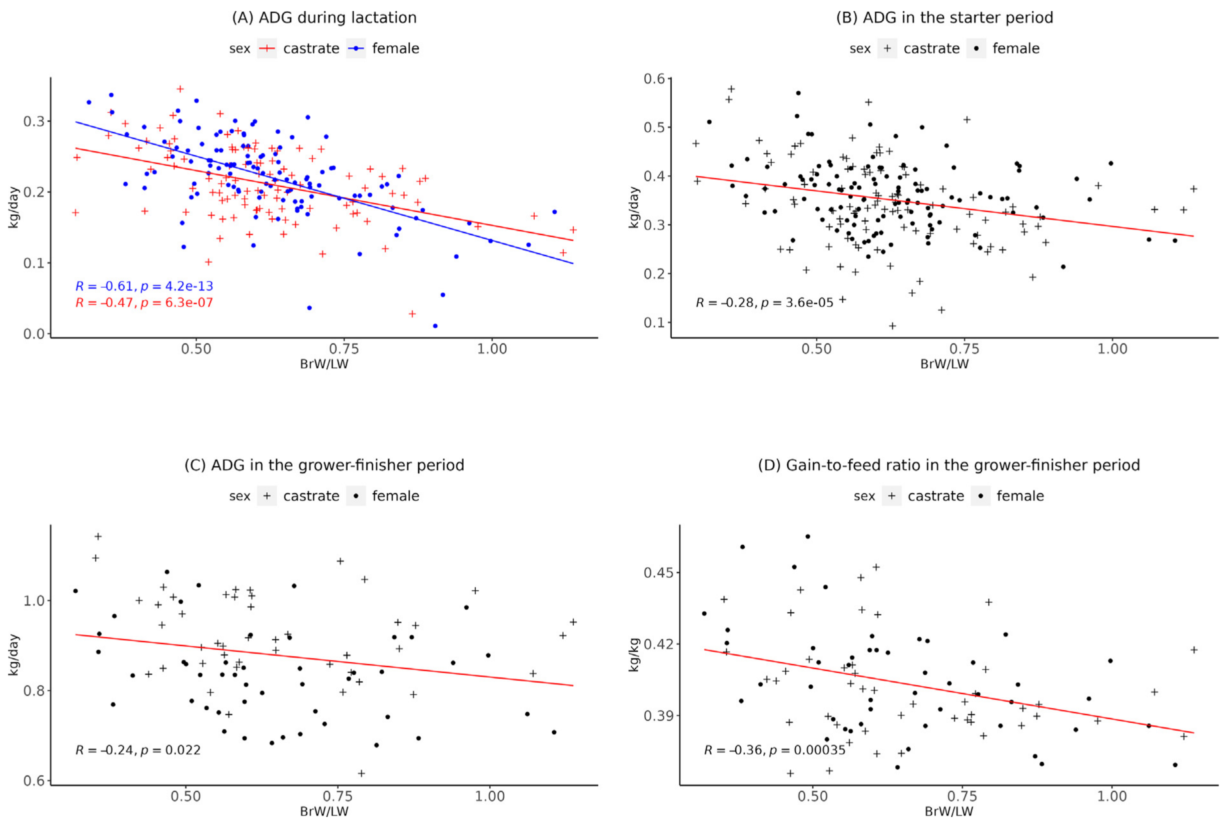

Fig. 2. Effect of the brain-to-liver weight ratio (BrW/LW) and sex on the average daily gain (ADG, g/day) of the pigs from birth to slaughter and the gain-to-feed (kg/kg) ratio in the grower–finisher period. X-axis: BrW/LW; y-axis: ADG of the lactation (A), starter (B), and grower–finisher period (C) and gain-to-feed ratio of the grower–finisher period (D). R: Pearson correlation coefficient; p: *P*-value of the linear correlation. Regression equations: ADG lactation = (BrW/LW × (−0.20)) + 0.34; ADG starter = (BrW/LW × (−0.15)) + 0.44; ADG grower–finisher = (BrW/LW × (−0.14)) + 0.97; gain-to-feed ratio grower–finisher = (BrW/LW × (−0.04)) + 0.43.

showed a discrepancy between the three methods. Based on our assumption that a piglet with a BrW/LW > 0.78 is IUGR, some piglets were classified differently using the phenotypic scoring systems. If BrW/LW is thought to be the optimal measure to identify IUGR, these findings support the hypothesis that the identification of IUGR piglets only based on the head morphology and/or BtW does not always agree with an increased BrW/LW. Indeed, a low BtW does not necessarily imply an IUGR condition, even if the IUGR condition is generally associated with a low BtW (Gupta et al., 2008; De Vos et al., 2014). The classification of IUGR based on head shape can be subjective and may depend on the observer. There is a greater probability of variance in observations when the judgement is subjective. In addition, the head morphology of piglets can be correlated to their parents' features or specific breed traits. There are natural variations in facial characteristics, unrelated to pathology, arise as a result of domestication and subsequent selective pressures (Chakraborty et al., 2021; Wilkinson et al., 2013). In contrast, the identification of IUGR piglets based on increased BrW/LW may be considered as objective, as it is the direct consequence of the brain-sparing effect.

To our knowledge, this is the first study to identify IUGR piglets based on BrW/LW. Therefore, it is challenging to compare the present results with those obtained with other IUGR classifications, either head shape or low BtW. As mentioned before, constituting groups based on head shape or BtW may result in groups containing a mix of IUGR and normal piglets. In the following discussion, the method of determining the IUGR condition will be reported when comparing the characteristics and effects of IUGR between studies. In addition, the two categories used in the present study (IUGR and NORM) were defined based on a threshold set according to the distribution of the population studied. Nevertheless, this binary classification is a simpler model of a condition that has varying degrees of severity. One could argue for a lower or higher threshold for BrW/LW, and changing the threshold may have an impact on the final results. The present discussion will, therefore, not only cover the effects of the IUGR category on the different parameters but will also present the general trend reflected by the correlation between the parameters and the BrW/LW.

Effect of intrauterine growth restriction on growth and average daily gain

In this study, the IUGR pigs showed a lower ADG in the lactation, starter (P = 0.07), and grower phases, even though the feed intake was similar between the two groups in the grower period. In addition, the BrW/LW was negatively correlated with the ADG from birth to slaughter, with a decreasing effect with time. Similarly, in the study of Alvarenga et al. (2013), the IUGR pigs, defined by their low BtW, displayed a lower ADG from birth to the grower phase compared to their normal littermates. In the finishing period, despite a lower gain-to-feed ratio in the IUGR category, the ADG was similar between the IUGR pigs and the NORM pigs. Our results complied with those of Alvarenga et al. (2013) who described a similar ADG on day 150 between IUGR and normal pigs. Moreover, the study of Gondret et al. (2005) showed a decreasing effect of BtW on ADG over time. Santos et al. (2022), on the contrary, observed a reduction in both the BW and the ADG in the IUGR group, defined by a low BtW, from birth to slaughter. However, the differences observed in the studies may be attributed to the different techniques used to define IUGR piglets (BtW, head shape, and brain-to-organ weight ratio). In this study, the IUGR pigs were 8 days older than the NORM pigs at slaughter.

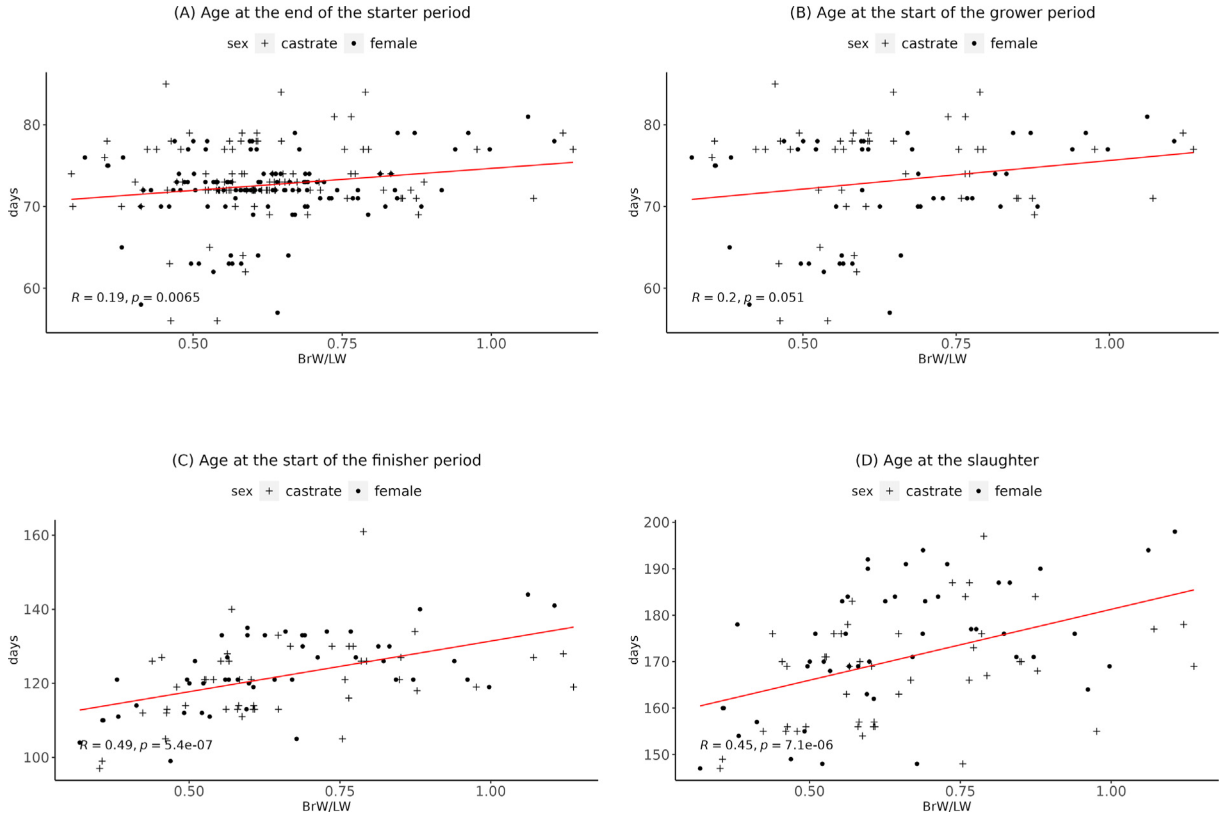

Fig. 3. Effect of the brain-to-liver weight ratio (BrW/LW) and sex on the age (days) of the pigs from the starter period to slaughter. X-axis: BrW/LW; y-axis: age at the end of the starter period (A), at the start of the grower period (B), at the start of the finisher period (C), at slaughter (D). R: Pearson correlation coefficient; p: *P*-value of the linear correlation. Regression equations: age at the end of the starter period = (BrW/LW × 5.39) + 69.3; age at the start of the grower period = (BrW/LW × 7) + 68.6; age at the start of the finisher period = (BrW/LW × 27.4) + 104.1; age at slaughter = (BrW/LW × 30.5) + 150.7.

Table 3
Effect of classifying the pigs based on the brain-to-liver weight ratio (BrW/LW) and sex on total and relative bone mineral density, bone mineral content, lean, and fat mass at weaning.

Item	BrW/LW[1]		Sex		SEM[3]	*P*-value[2]	
	IUGR	NORM	Female	Castrate		BrW/LW	Sex
Number of pigs	32	185	115	102			
BW, g	6 233	7 345	6 877	6 701	285.0	<0.001	0.20
Bone mineral density, g/cm[3]	0.35	0.37	0.36	0.36	0.007	<0.001	0.70
Bone mineral content, g	137	161	150	147	6.0	<0.001	0.19
Lean mass, g	5 385	6 350	5 947	5 788	244.0	<0.001	0.17
Fat mass, g	710	835	780	766	45.9	<0.001	0.53
Expressed as % of total body mass							
Total bone mineral density, %	0.006	0.005	0.006	0.006	0.0002	<0.001	0.53
Bone mineral content, %	2.22	2.22	2.21	2.21	0.036	0.34	0.90
Lean mass, %	86.5	86.5	86.6	86.5	0.39	0.90	0.57
Fat mass, %	11.2	11.3	11.2	11.3	0.40	0.82	0.56

1 BrW/LW: IUGR: piglets with a BrW/LW ≥ 0.78; NORM: piglets with BrW/LW < 0.78.
2 *P*-value for the main effect of the BrW/LW and sex.
3 Pooled SEM.

Moreover, as the BrW/LW increased, the age at which the pigs reached the targeted slaughter weight increased. Our findings comply with the results of previous studies (Gondret et al., 2005) showing that IUGR pigs require more days to reach the slaughter weight compared to their normal littermates. This prolonged time results in an increase in the management costs and a reduction in the production efficiency (Díaz et al., 2017).

Effect of intrauterine growth restriction on body composition

In the current experiment, there was no difference between IUGR and NORM pigs in the bone, lean, and fat tissue when expressed as a percentage of the BW. Similarly, the BrW/LW did not affect the body composition at weaning. This complies with the study of Lynegaard et al. (2020), in which no differences in fat or muscle percentage were found in relation to BW at 24 days of age between the IUGR group (defined by their head shape) and the NORM group. On the contrary, using BtW as a classification criterion, Amdi (2012) showed an increased percentage of fat tissue in low BtW (1.1 kg) piglets compared to medium-BtW (1.5 kg) and high-BtW (1.8 kg) piglets at 28 days of age. Neither the absolute nor the relative (expressed per empty BW) CP and lipid mass and energy content of the empty body differed at 20 and 100 kg BW and in the carcasses between the IUGR and NORM

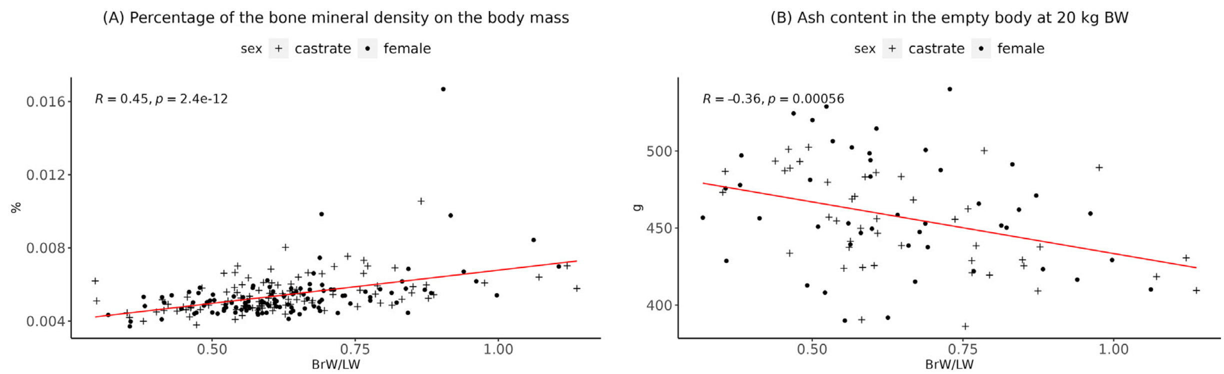

Fig. 4. Effect of the brain-to-liver weight ratio (BrW/LW) and sex on the body composition of the pigs at weaning and at 20 kg of BW. X-axis: BrW/LW; y-axis: percentage (%) of the total bone mineral density (g/cm^2) on the BW at weaning (A); ash content (kg) in the empty body at 20 kg BW (B). R: Pearson correlation coefficient; p: *P*-value of the linear correlation. Regression equations: percentage of the total bone mineral density = (BrW/LW × 3.630e−05) + 3.152e−05; ash = (BrW/LW × (−67)) + 500.5.

Table 4
Effect of classifying the pigs based on the brain-to-liver weight ratio (BrW/LW) and sex on the content of single nutrients in the empty body at 20 and 100 kg.

	BrW/LW[1]		Sex			*P*-value[2]	
Item[3]	IUGR	NORM	Female	Castrate	SEM[4]	BrW/LW	Sex
Number of pigs[5]	20	70	46	44			
Total intake							
Feed, kg	205.0	200.9	199.2	206.8	2.71	0.16	<0.01
CP, kg	30.3	29.7	29.4	30.5	0.39	0.15	<0.01
DE, MJ	2 809	2 752	2 728	2 833	37.1	0.16	<0.01
NE, MJ	2 052	2 010	1 993	2 069	27.2	0.16	<0.01
Empty body, kg							
At 20 kg	18.6	18.4	18.6	18.5	0.36	0.72	0.75
At 100 kg	107.9	108.7	107.3	109.3	0.10	0.51	0.03
Gross energy, MJ/pig							
At 20 kg	140	139	140	139	3.9	0.65	0.64
At 100 kg	1 324	1 303	1 370	1 434	22.1	0.34	<0.001
Water, kg/pig							
At 20 kg	12.7	12.6	12.7	12.6	0.21	0.73	0.79
At 100 kg	59.6	60.7	60.5	59.8	0.64	0.10	0.19
Ash, kg/pig							
At 20 kg	0.46	0.46	0.46	0.45	0.008	0.06	0.13
At 100 kg	2.96	3.03	3.06	2.93	0.073	0.31	<0.01
CP, kg/pig							
At 20 kg	2.6	2.5	2.6	2.5	0.06	0.73	0.79
At 100 kg	16.3	16.7	16.6	16.4	0.19	0.10	0.19
Lipids, kg/pig							
At 20 kg	1.9	1.9	1.9	1.9	0.06	0.61	0.58
At 100 kg	23.0	22.3	21.1	24.2	0.57	0.21	<0.001
Daily nutrient and energy deposition							
Fat g/d	210	208	186	231	8.6	0.79	<0.001
CP, g/d	136	141	134	144	3.3	0.08	<0.001
Gross energy, MJ/d	12	12	11	13	0.4	0.84	<0.001
Nutrient and energy efficiency[6]							
CP_{eff}	0.46	0.48	0.48	0.46	0.007	<0.01	<0.001
DE_{eff}	0.42	0.43	0.41	0.44	0.007	0.63	<0.001
NE_{eff}	0.58	0.58	0.56	0.60	0.010	0.63	<0.001

[1] BrW/LW: IUGR: piglets with a BrW/LW ≥ 0.78; NORM: piglets with BrW/LW < 0.78.
[2] *P*-value for the main effect of the BrW/LW and sex.
[3] DE = digestible energy; NE = net energy.
[4] Pooled SEM.
[5] At 100 kg of BW, the Dual-energy X-ray absorptiometry (DXA) scan was not available for three of the 93 pigs. The content of single nutrients, nutrients deposition rate and efficiency were determined for the 90 pigs scanned with DXA at both 20 and 100 kg of BW.
[6] CP_{eff} = expressed as deposited CP between the two DXA scans divided by total CP intake in the same period; DE_{eff} = expressed as deposited gross energy between the two DXA scans divided by total DE intake in the same period; NE_{eff} = expressed as deposited gross energy between the two DXA scans divided by total NE intake in the same period.

groups. However, the ash content in the empty body tended to be lower in the IUGR group at 20 kg BW. Despite a similar energy, fat, and CP deposition rate in the grower–finisher period, the IUGR category showed a lower CP efficiency. When considering the effect of the BrW/LW, the latter was negatively correlated to both the CP deposition rate and CP efficiency in the grower–finisher period. The results regarding body composition in IUGR pigs are not consistent. Several studies have reported that pigs with a low BtW had a decreased percentage of muscle and an increased percentage of body fat than their heavier littermates at slaughter (Gondret et al., 2006; Krueger et al., 2014; Zhang et al., 2022). On the contrary, no effect of BtW on fat deposition was observed in other studies of low- and high-birth BW pigs (Gondret et al., 2005; Nissen and Oksbjerg, 2011).

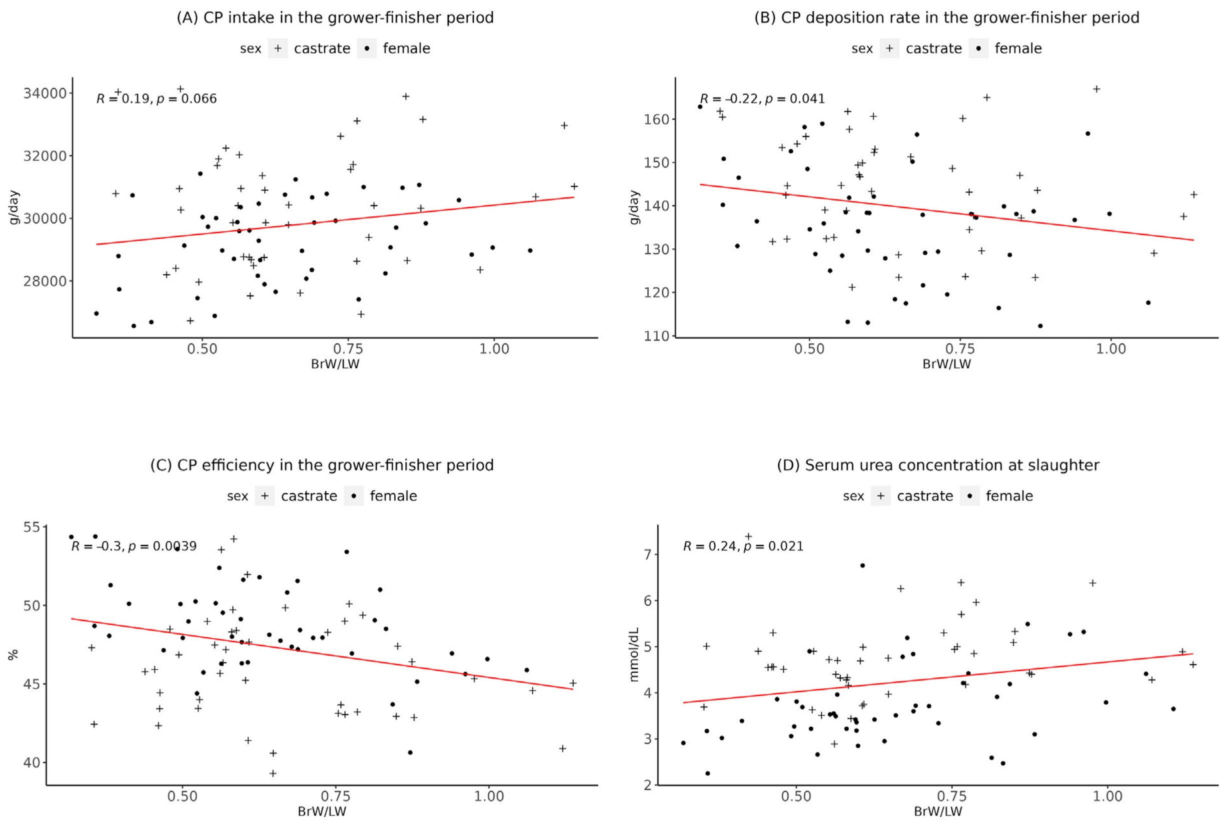

Fig. 5. Effect of the brain-to-liver weight ratio (BrW/LW) and sex on the CP intake (kg/day), deposition rate (g/day), and efficiency (%) in the grower–finisher period and serum urea concentration (mmol/dL) of the pigs at slaughter. X-axis: BrW/LW; y-axis: CP intake (A), deposition rate (B), and efficiency (C) in the grower–finisher period and serum urea concentration at slaughter (D). R: Pearson correlation coefficient; p: *P*-value of the linear correlation. Regression equations: CP intake = (BrW/LW × 1 843) + 28 578; CP deposition rate = (BrW/LW × (−15.7)) + 149.9; CP efficiency = (BrW/LW × (−0.05)) + 0.51; serum urea concentration = (BrW/LW × 1.29) + 3.37.

Table 5
Effect of classifying the pigs based on the brain-to-liver weight ratio (BrW/LW) and sex on the blood metabolites traits, blood cell count, and insulin concentration at slaughter.

	BrW/LW[1]		Sex			*P*-value[2]	
Item	IUGR	NORM	Female	Castrate	SEM[3]	BrW/LW	Sex
Number of pigs[4]	21	70	47	44			
Urea, mmol/L	4.33	4.19	3.77	4.75	0.221	0.50	<0.001
Non-Esterified Fatty Acids, mmol/L	0.184	0.167	0.177	0.175	0.0364	0.62	0.95
Haematocrit, %	49.1	48.9	48.5	49.4	0.91	0.81	0.15
Mean corpuscular haemoglobin, p/g	16.8	16.7	16.6	16.8	0.21	0.62	0.22
Mean corpuscular haemoglobin concentration, g/dL	30.9	30.9	31.1	30.7	0.17	0.60	0.01
Mean corpuscular volume, fL	54.4	54.2	53.6	54.9	0.72	0.72	0.01
Granulocytes, 10^9 cells/L	5.69	5.09	5.15	5.63	0.449	0.16	0.16
Lymphocytes, 10^9 cells/L	16.0	14.5	15.4	15.0	0.81	0.09	0.59
Monocytes, 10^9 cells/L	0.205	0.139	0.173	0.170	0.0164	<0.001	0.86
Platelets, 10^9 cells/L	388	398	397	389	30.1	0.72	0.72
White blood cells, 10^9 cells/L	18.9	18.4	18.5	18.7	0.57	0.40	0.75
Number of pigs[5]	22	68	45	45			
Insulin, mU/L	7.98	5.36	6.57	6.77	1.63	0.13	0.89

[1] BrW/LW: IUGR: piglets with a BrW/LW ≥ 0.78; NORM: piglets with BrW/LW < 0.78.
[2] *P*-value for the main effect of the BrW/LW and sex.
[3] Pooled SEM.
[4] For two of the 93 pigs, it was not possible to collect the blood at slaughter and to perform the blood metabolites traits and blood cell count analysis.
[5] For one of the 91 pigs from which the blood was collected at slaughter, it was not possible to perform the insulin concentration analysis. For 23 of the 90 samples analysed, the insulin concentration was not detectable in the serum and was assigned a value of 0.

Effect of intrauterine growth restriction on blood biochemistry and blood cell count

The urea concentration in the serum is negatively correlated with the efficiency of nutrient utilisation and the deposition of lean tissue (Whang and Easter, 2000). For this reason, it can be used as a marker of CP efficiency in pig production. In the present study, the IUGR pigs were less CP-efficient in the grower–finisher period. In addition, the BrW/LW was negatively correlated to the CP deposition rate in the grower–finisher period, and the urea concentration at slaughter (P = 0.08) tended to get higher as the BrW/LW increased. Using the BtW as a classification criterion,

Table 6
Effect of classifying the pigs based on the brain-to-liver weight ratio (BrW/LW) and sex on the blood glucose, haemoglobin, and red blood cell count at slaughter.

	BrW/LW[1]					P-value[2]		
	Females		Castrates					
Item	IUGR	NORM	IUGR	NORM	SEM	BrW/LW	Sex	BrW/LW × Sex[3]
Number of pigs	11	36	10	34				
Glucose, mmol/L	7.59	8.39	9.43	7.65	0.794	0.32	0.06	0.02
Haemoglobin, g/dL	14.7	15.1	15.6	14.9	0.33	0.19	0.02	0.02
Red blood cells, 10^{12} cells/L	8.85	9.14	9.31	8.92	0.175	0.11	0.04	<0.01

[1] BrW/LW: IUGR: piglets with a BrW/LW ≥ 0.78; NORM: piglets with BrW/LW < 0.78.
[2] *P*-value for the main effect of the BrW/LW, sex, and the two-way interaction (BrW/LW × Sex).
[3] Significant interaction between the category (IUGR, NORM) and the sex ($P < 0.05$) but not significant multiple mean comparisons between IUGR and NORM females and castrates for glucose, haemoglobin, and red blood cell count.

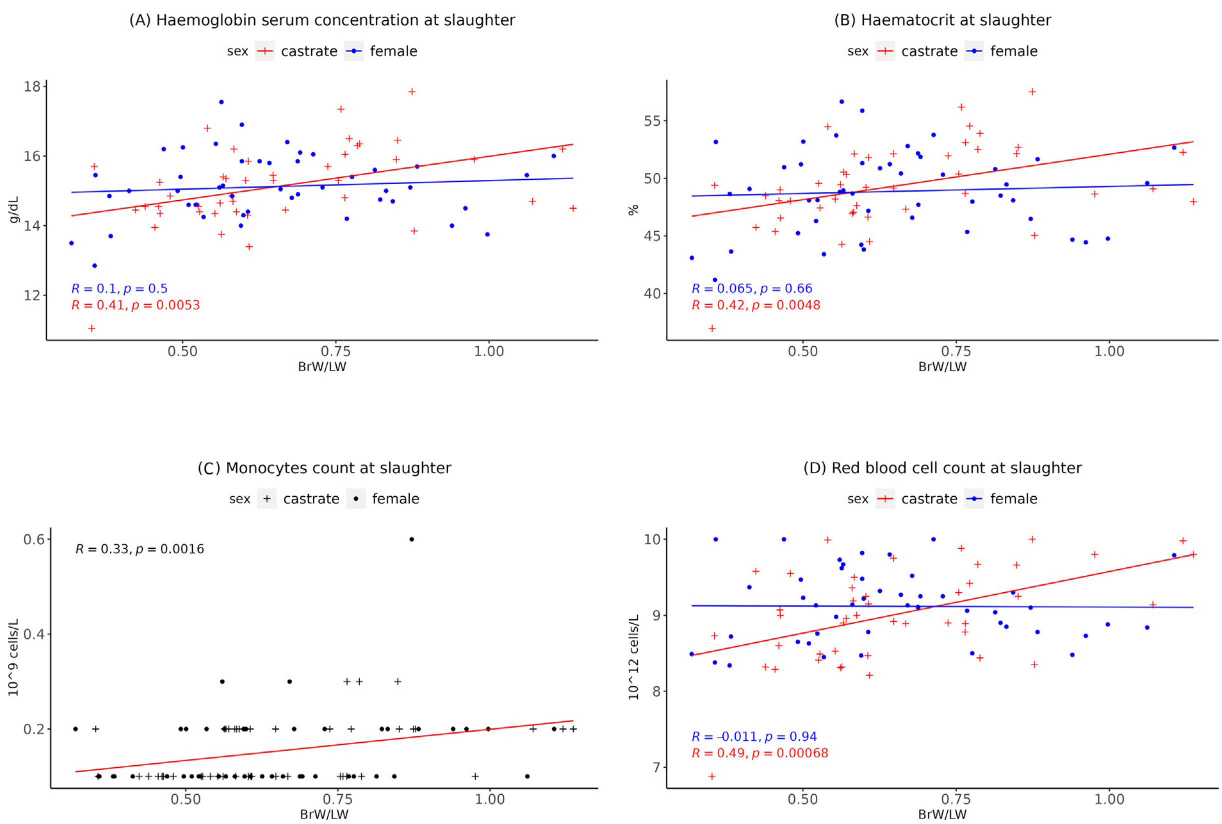

Fig. 6. Effect of the brain-to-liver weight ratio (BrW/LW) and sex on the haemoglobin serum concentration (g/dL), haematocrit value (%), monocytes (10^9 cells/L) and red blood cell (10^{12} cells/L) counts of the pigs at slaughter. X-axis: BrW/LW; y-axis: haemoglobin serum concentration (A), haematocrit value (B), monocytes (C), and red blood cell counts in the serum (D). R: Pearson correlation coefficient; p: *P*-value of the linear correlation. Regression equations: serum haemoglobin concentration = (BrW/LW × 1.48) + 14.2; haematocrit = (BrW/LW × 4.51) + 46.2; monocytes count = (BrW/LW × 0.13) + 0.07; red blood cell count = (BrW/LW × 0.77) + 8.57.

Zhang et al. (2018) showed significantly increased levels of urea nitrogen in IUGR pigs at 160 days of age. Similarly, Li et al. (2021) detected a high plasma urea concentration in the portal vein of IUGR pigs, defined by a low BtW, compared to normal pigs at 85 days of age.

In this study, the serum insulin concentration tended to be positively correlated with the BrW/LW. This complies with the study of Yan et al. (2017) in which the IUGR pigs, identified by a low BtW, showed increased fasting plasma insulin level at 178 days of age, independent of postnatal nutrition. Nevertheless, the pigs were slaughtered after 16 h of feed withdrawal in this study, and the insulin concentration was not detectable and consequently assigned with a value of 0 in the serum of 23 animals, perhaps as a consequence of their fastened status. For these reasons, our results regarding serum insulin concentration at slaughter must be interpreted with caution.

Effect of intrauterine growth restriction on meat quality

The results regarding the colour of the LT muscle are not consistent. Our findings agree with those of Matyba et al. (2021), in which the LT was darker in the IUGR group. IUGR pigs, identified according to their low BtW, show a higher number of type I compared to type II fibres in the skeletal muscle (Felicioni et al., 2020). Type I fibres contain more myoglobin (Yu et al., 2017), and this could explain the darker colour of the meat in the IUGR group. Indeed, the BrW/LW was negatively correlated with the lightness of the LT muscle in this study. The reduced lightness resulting from IUGR may have a negative effect on consumer perception, although it remains unclear whether the different colour is indeed perceived by the consumer. In contrast, in the study by Li et al. (2015), the muscle of the IUGR pigs was lighter. The differences observed among studies may be attributed not just to the different

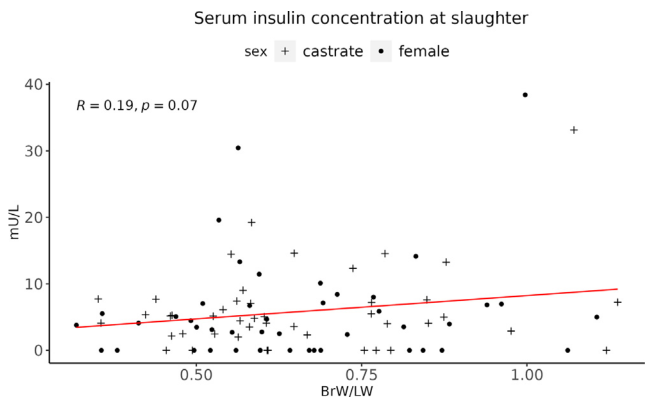

Fig. 7. Effect of the brain-to-liver weight ratio (BrW/LW) and sex on serum insulin (mu/L) of the pigs at slaughter. X-axis: BrW/LW; y-axis: serum insulin concentration: Pearson correlation coefficient; p: *P*-value of the linear correlation. Regression equations: serum insulin = (BrW/LW × 7.02)) + 1.23.

techniques used to define IUGR piglets but also to the different ages at which the animals were slaughtered (day 170 days in our study and 200 and 188 in the studies of Li et al. and Matyba et al., respectively). Latorre et al. (2003) showed that pigs slaughtered at 160 days had a lower redness score and intensity of the colour of the LT muscle compared to pigs slaughtered at 175 days. This result is in line with the study of Virgili et al. (2003), who found that older pigs produced a redder and darker *semimembranosus* muscle.

In conclusion, our study used the BrW/LW to characterise the physiological traits of IUGR piglets. Our results showed that IUGR identification based on head shape or BtW may lead to inaccurate classification, as these characteristics are not always consistent with an increased BrW/LW. Moreover, this study demonstrated that the BrW/LW is inversely proportional to ADG from birth to slaughter and the gain-to-feed ratio in the grower–finisher period. From the start of the grower period to slaughter, the BrW/LW was negatively correlated with the CP deposition rate and CP efficiency and positively correlated with the urea and insulin ($P = 0.08$) concentration in the serum at slaughter. In general, the higher the BrW/LW, the longer it took for the pigs to reach the targeted slaughter weight of 110 kg. The BrW/LW did not affect the proportion of lean, fat, and bone mineral content, but the meat was darker and lost less water during maturation as the BrW/LW increased. For these reasons, the IUGR pigs represent a great economic loss for swine producers, and the development of breeding and management strategies to reduce the frequency of IUGR will be of great importance in pig production.

Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.animal.2023.101044.

Ethics approval

This experiment was performed at the Agroscope research institute, Posieux (Switzerland). All the experimental procedures complied with the Swiss animal welfare guidelines and were approved (experimental approval number 32751) by the Cantonal Veterinary Office of Fribourg (Switzerland).

Data and model availability statement

The data that support the findings of this study were not deposited in an official repository but are available upon reasonable request from the corresponding author [CO].

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors did not use any artificial intelligence-assisted technologies in the writing process.

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Declaration of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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