Is the rabbit a natural model of fetal growth restriction? Morphological and functional characterization study using diffusion-weighted MRI and stereology

Matthieu Dap, Théo Albert, Ikrame Ramdhani, Anne Couturier-Tarrade, Olivier Morel, Pascale Chavatte-Palmer, Marine Beaumont, Charline Bertholdt

Placenta 154 (2024) 74–79

Contents lists available at ScienceDirect

Placenta

journal homepage: www.elsevier.com/locate/placenta

Is the rabbit a natural model of fetal growth restriction? Morphological and functional characterization study using diffusion-weighted MRI and stereology

Matthieu Dap [a,b,c,*], Théo Albert [b], Ikrame Ramdhani [b], Anne Couturier-Tarrade [d,e], Olivier Morel [a,b], Pascale Chavatte-Palmer [d,e], Marine Beaumont [b,f], Charline Bertholdt [a,b]

[a] Université de Lorraine, CHRU-NANCY, Pôle de la Femme, F-54000, Nancy, France
[b] Université de Lorraine, Inserm, IADI, F-54000, Nancy, France
[c] Université de Lorraine, Pôle Laboratoire, F-54000, Nancy, France
[d] Université Paris-Saclay, UVSQ, INRAE, BREED, 78350, Jouy-en-Josas, France
[e] Ecole Nationale Vétérinaire d'Alfort, BREED, 94700, Maisons-Alfort, France
[f] CHRU-NANCY, Inserm, Université de Lorraine, CIC, Innovation Technologique, F-54000, Nancy, France

ARTICLE INFO

Keywords:
Rabbit
Placenta
Intrauterine growth restriction
MRI
DW-MRI
Animal model

ABSTRACT

Introduction: Rabbits are routinely used as a natural model of fetal growth restriction (FGR); however, no studies have confirmed that rabbits have FGR. This study aimed to characterize the fetoplacental unit (FPU) in healthy pregnant rabbits using diffusion-weighted MRI and stereology. A secondary objective of the study was to describe the associations among findings from diffusion-weighted MRI (DW-MRI), fetal weight measurement and histological analysis of the placenta.

Methods: Pregnant rabbits underwent DW-MRI under general anesthesia on embryonic day 28 of pregnancy. MR imaging was performed at 3.0 T. The apparent diffusion coefficient (ADC) values were calculated for the fetal brain, liver, and placenta. The placenta was analyzed by stereology (volume density of trophoblasts, the maternal blood space and fetal vessels). Each fetus and placenta were weighed. Two groups of fetuses were defined according to the position in the uterine horn (Cervix group versus Ovary group).

Results: We analyzed 20 FPUs from 5 pregnant rabbits. Fetuses and placentas were significantly lighter in the Cervix group than in the Ovary group (34.7 ± 3.7 g vs. 40.2 ± 5.4 g; $p = 0.02$). Volume density analysis revealed that the percentage of fetal vessels, the maternal blood space and trophoblasts was not significantly affected by the position of the fetus in the uterine horn. There was no difference in ADC values according to the position of the fetus in the uterine horn, and there was no correlation between ADC values and fetal weight.

Discussion: The findings of a multimodal evaluation of the placenta in a rabbit model of FGR suggested is not a natural model of fetal growth restriction.

1. Introduction

The diagnosis of fetal growth restriction (FGR) is challenging because placental insufficiency remains strongly difficult to characterize during pregnancy in women due to the lack of understanding of the mechanisms underlying FGR [1–3]. Animal experiments are still necessary because of the evolution of the uteroplacental circulation and fetal development, which can be examined with a flexibility in animals that is unavailable in human investigations [4,5]. The rabbit seems to be a relevant model animal for placental studies [5–10]. Finally, FGR can be induced in rabbits by ligating the uterine artery of the bicornuate uterus, which allows case–control studies to be performed [11].

The rabbit model is often described as a natural model of FGR due to the difference in fetal weight according to the position of the fetus in the uterine horn, a well-known phenomenon first described in 1936 [12,13]. However, these statements are based only on observations showing differences in fetal and placental weights between fetuses without morphological or functional evaluations of the placenta.

Thus, we propose a multimodal evaluation of the rabbit model with morphological characterization using placental stereology, which can

* Corresponding author. Université de Lorraine, Inserm, IADI, F-54000, Nancy, France.
E-mail address: m.dap@chru-nancy.fr (M. Dap).

https://doi.org/10.1016/j.placenta.2024.06.014
Received 9 February 2024; Received in revised form 3 June 2024; Accepted 18 June 2024
Available online 19 June 2024

quantify the proportion of trophoblasts, maternal blood space and fetal vessels, and functional characterization using diffusion-weighted magnetic resonance imaging (DW-MRI), which can detect placental vascular changes [10,14]. Indeed, the apparent diffusion coefficient (ADC) obtained through DW-MRI can decrease in response to ischemic conditions, making DW-MRI a complementary tool for detecting placental insufficiency associated with FGR [14]. These two modalities, morphological and functional, were compared between two groups defined according to the position of the fetus in the uterine horn to test the hypothesis that the rabbit model is a natural model of FGR associated with placental insufficiency.

The main objective of this study was to characterize the fetoplacental unit in healthy pregnant rabbits, a natural model of FGR, using diffusion-weighted MRI and stereology. As a secondary objective, we aimed to determine the associations among findings from diffusion-weighted MRI, fetal weight measurement and histological analysis of the placenta.

2. Methods

2.1. Ethics

Experiments were performed at Nancy CHRU in 2017 (research agreement B-54-547-29 valid until December 01, 2017). The protocol was approved by the local animal care and the regional ethical committees ("CELMEA", approved under Number 66 in the National Registry of French Ethical Committees for Animal Experimentation) under protocol number APAFIS#7207 version 1. All experiments were carried out in accordance with the recommendations of the International Guiding Principles for Biomedical Research involving Animals and in accordance with the European Union Directive 2010/63EU. The authors complied with the ARRIVE guidelines (Animal Research: Reporting of the In Vivo Experiments available on htts://arriveguidelines.org/).

2.2. Animals

Five pregnant New Zealand white rabbits in physiological condition at 28 days of gestation (embryonic day ED-28) were used. In rabbits, the mean length of pregnancy is 31 days. We chose ED-28 for the experiment because the difference in fetal weight depending on the position of the fetus in the uterine horn increases as gestational age increases, as described by Flake et al. [13]. Imaging procedures were performed under general anesthesia induced by intramuscular injections of ketamine (0.11 mg/kg, Imalgène1000, Merial®, France), xylazine (0.05 ml/kg, Rompun®, Bayer, France) and butorphanol (0.05 ml/kg, Torbugesic®, Zoetis, France) and maintained by gas anesthesia with isoflurane (5% for induction and 2.5% for infusion and 100% oxygen). An IV line was placed in the marginal ear vein, and the animals were monitored via pulse oximetry during all the experiments.

Dams and fetuses were euthanized directly after MRI using an intravenous bolus of barbiturate (5 ml Dolethal®, Vetoquinol, France). The number of fetuses in each horn was confirmed by an immediate postmortem examination of each rabbit. The placentas and fetuses were weighed. In the literature, the fetuses nearest to the cervix are described as the smallest compared to the fetuses close to the ovary [12]. Thus, two groups of fetuses were defined according to their position in the uterine horn: for each rabbit, the fetus nearest to the cervix was assigned to the "Cervix group", and the fetus nearest to the ovary was assigned to the "Ovary group".

2.3. MR imaging and postprocessing

MR imaging was performed at 3 T (Magnetom Prisma, Siemens Healthineers, Erlangen, Germany) using a knee coil. The MR protocol included two sequences to enable slice positioning and fetal identification. Two sets of images were acquired with good spatial resolution (40 2 mm-thick coronal slices, pixel size = 0.625 × 0.625 mm^2, matrix = 320*250). T2-weighted images were acquired with a turbo spin–echo sequence (TE/TR = 73/3940 ms), and T1-weighted post-Gadolinium injection images were acquired 15 min after contrast agent IV injection (Gd 0.1 mmol/kg, Dotarem®, Guerbet, France), with a 3D flash sequence with fat saturation (TE/TR = 7.5/766 ms). Diffusion weighted imaging (DWI) was performed with a RESOLVE sequence (TE/TR = 53/5600 ms, 6 directions, b-value = 1000, 2 mm-thick coronal slices, pixel size = 1.38*1.38 mm^2, matrix = 174*174). The total acquisition time for these MRI sequences was 1 h.

To perform an accurate analysis, it was crucial to properly identify the position of each fetus in the uterine horn (Fig. 1). The first step was the localization of the two uterine cervixes and the two ovaries, each of which represented the extremities of the uterine horns (Fig. 1A and B). Then, the continuity of the uterine horn between the fetuses from the cervix to the ovary was confirmed by following the uterine wall on individual MR slices, and all the fetuses that were nearest to the ovary were included in the "Ovary group" (Fig. 1C).

Postprocessing was performed using ORS Visual® software (Montreal, Quebec), with a plug-in developed to perform quantitative analysis of diffusion data obtained with DW-MRI. For each fetus, T2-weighted MR images were used to localize the fetoplacental units. Then, a region of interest (ROI) was manually drawn for each placenta, liver and brain on the DWI-MR sequence. For each ROI, the mean and the standard deviation (SD) of the ADC pixel values (× 10^{-3} mm^2/s) were computed.

2.4. Immunohistochemistry and stereological analysis

After fixation in 10% buffered formalin, the placentas were dehydrated in ethanol solutions, cleared in xylene, embedded in paraffin and then cut into 5 μm thick sections. Placental sections were immunostained with a monoclonal mouse anti-vimentin antibody (IgG1, Clone V9, Millipore France) to label fetal capillaries, and a biotinylated donkey anti-mouse secondary antibody (Biotin-SP-conjugated AffiniPure Donkey IgG, Jackson ImmunoResearch, France) was used as described by Lecarpentier et al. [9] (Fig. 2). To amplify the stain, the sections were incubated with an avidin–peroxidase complex (Elite-Vectastain HRPO kit, Vector France). A black precipitate was developed at the site of the anti-vimentin antibody through incubation with diaminobenzidine (Sigma, France) and 2% ammonium nickel sulfate (Sigma, France). The sections were counterstained with 1% toluidine blue alone [9].

All placental sections were scanned using a NanoZoomer Digital Pathology System (NDP Scan U10074-01, Hamamatsu, Japan). Volume fractions of all the components of the labyrinth area, i.e., fetal vessels, labyrinthine trophoblasts, and maternal blood compartments, were quantified by one-stop stereology using Mercator® software [15]. The intersection of each category of cells with the probe estimator was evaluated. In addition, the volume density was automatically calculated by the software as described by Favaron et al. [16].

The person performing the analysis (I.R.) was blinded to the animal group.

2.5. Statistics

Statistical analysis was performed using Stata software version 17.0 (Stata Corporation, College Station, TX). Continuous variables were compared with a nonparametric Wilcoxon test, and each fetus was considered independent of the dam. Quantitative data are expressed as the mean ± SD, and $p < 0.05$ was considered to indicate statistical significance. Student's t tests were used to compare continuous variables, and chi-square or Fisher's exact tests were used, as appropriate, to compare categorical variables. $P < 0.05$ was considered to indicate statistical significance. Spearman correlations were used to analyze correlations between fetal weight and stereological parameters.

The data are represented as box plots: in this representation, the rectangle indicates the distribution, and the median is the line that

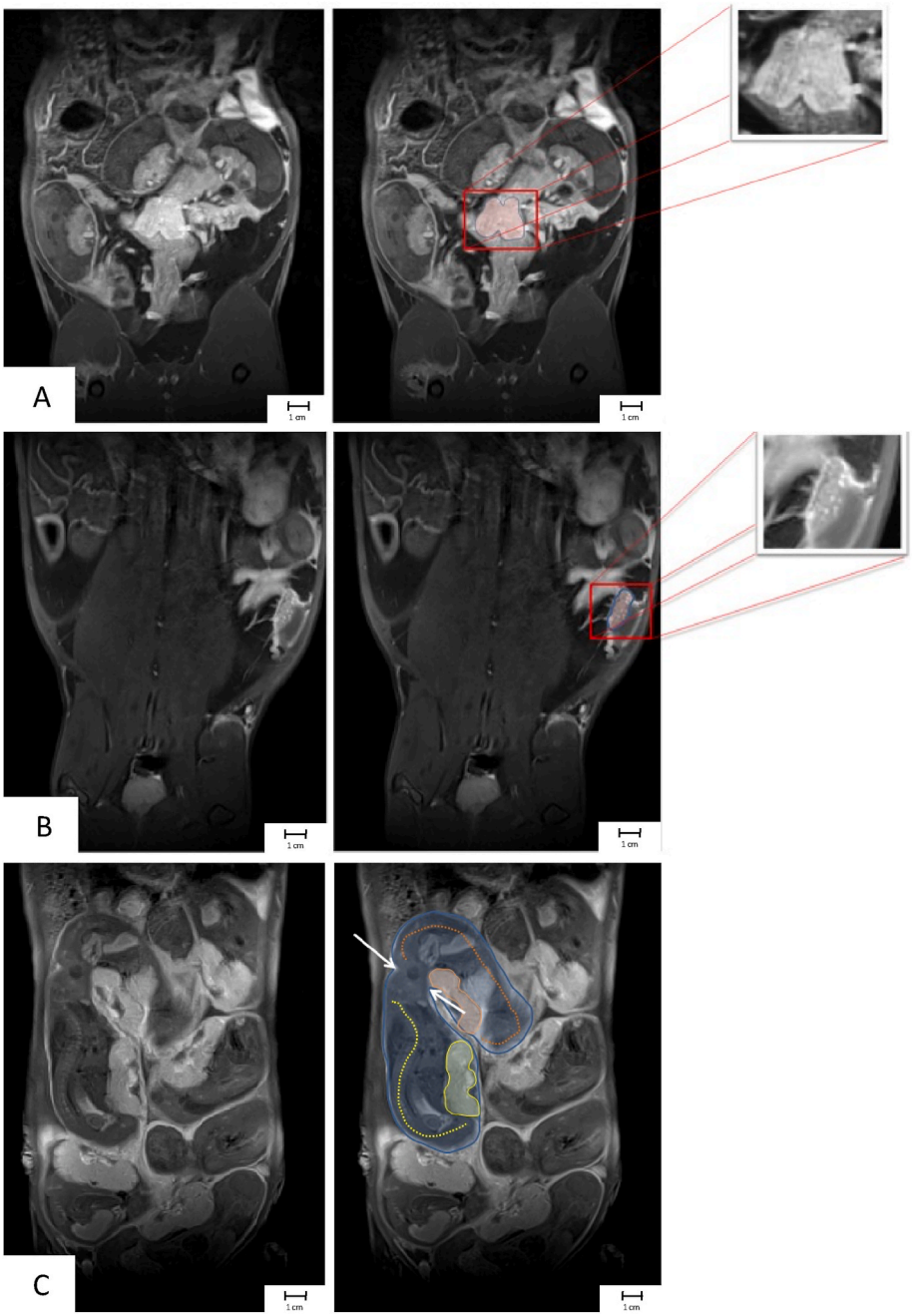

Fig. 1. Identification of the fetuses. Anatomical localization of the rabbit cervix on T1-weighted fat-saturated MRI with gadolinium injection coronal slices (1 A). Anatomical localization of the rabbit's left ovary on T1-weighted fat-saturated MR image with gadolinium injection on coronal slices (1 B). Anatomical confirmation of horn continuity in a pregnant rabbit on T1-weighted fat-saturated MRI with gadolinium injection. Yellow and orange dotted lines are fetal spines, and yellow and orange areas are their respective placentas. The area in blue is the uterine horn. The area between the two white arrows shows the continuity of the uterine horn (1C).

divides the box into two parts. The first quartile (Q1) and the third quartile (Q3) correspond to twenty-five and seventy-five percent of the scores.

3. Results

Five rabbits were imaged, and since each rabbit bore multiple feto-placental units (FPUs), we were able to analyze 20 FPUs (10 in the "Ovary group" and 10 in the "Cervix group"). The mean fetal weight was 37.5 ± 4.5 g. Fetuses were significantly lighter in the Cervix group than in the Ovary group (34.7 ± 3.7 g vs. 40.2 ± 5.4 g; $p = 0.02$) (Fig. 3). The mean placental weight was 6.2 ± 0.24 g. Placental weight was significantly lower in the Cervix group than in the Ovary group (5.6 ± 0.3 g vs. 6.6 ± 0.3 g; $p = 0.05$) (Fig. 4). Spearman's correlation revealed a positive correlation between placental weight and fetal weight (rho = 0.55, $p = 0.04$). The placental/fetal weight ratio (P/F ratio) was similar in the groups (6.3 ± 0.9 for the Cervix group vs. 6.1 ± 0.7 for the Ovary group; $p = 0.5$).

Volume density analysis revealed that the percentage of fetal vessels, maternal blood space and trophoblasts was not significantly affected by the position of the fetus in the uterine horn (Fig. 5).

The mean ADC value was 1044.6 ± 176.9 × 10^{-3} mm^2/s for the placenta, 1170.2 ± 99.4 × 10^{-3} mm^2/s for the fetal brain and 908.9 ± 243.7 × 10^{-3} mm^2/s for the fetal liver. There was no difference in ADC values according to the position of the fetus in the uterine horn (Fig. 6).

Spearman's correlations demonstrated a positive correlation

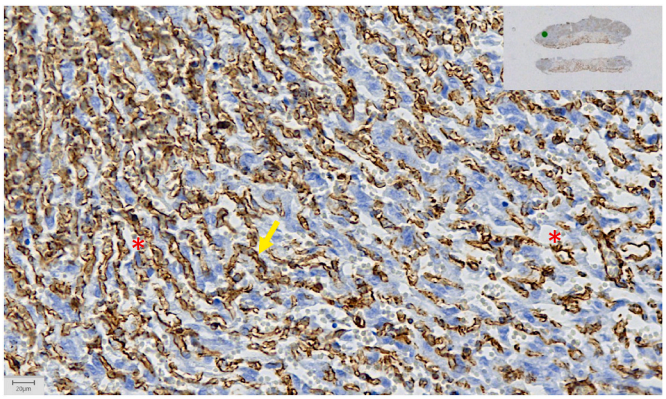

Fig. 2. Immunodetection of vimentin in rabbit placenta: a black precipitate is located on fetal capillaries, counterstained with 1% toluidine blue. The yellow arrow indicates the fetal vessels, and the red star indicates the maternal blood space.

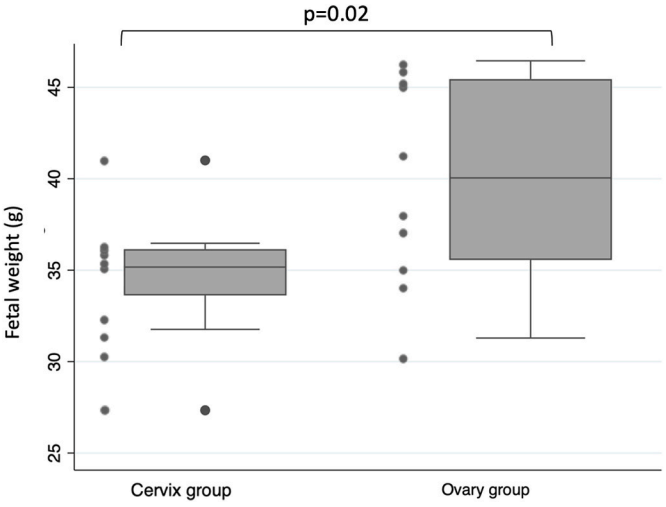

Fig. 3. Weight (in grams) of fetuses according to their position in the uterine horn.

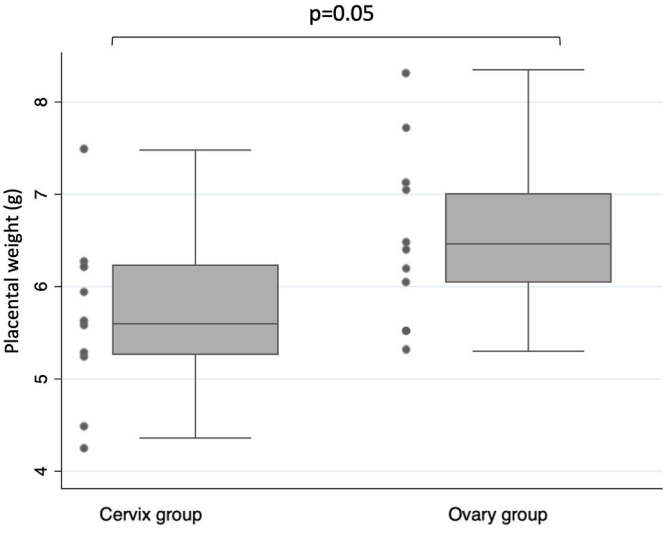

Fig. 4. Placental weight (in grams) according to the position of the fetus in the uterine horn.

between the volume density of fetal vessels and fetal weight (rho = 0.82, p = 0.003) but not between the volume density of the trophoblastic layer and fetal weight (rho = −0.43, p = 0.11) or between the volume of the maternal blood space and fetal weight (rho = −0.31, p = 0.27).

There was no correlation between the volume density of fetal vessels and the placental ADC (rh = 0.23, p = 0.40) or between the volume density of trophoblasts and the placental ADC (rho = 0.21, p = 0.45). A negative correlation between the volume of the maternal blood space and the placental ADC value (rho = - 0.59, p = 0.02) was found. There was no correlation between the fetal weight and the placental ADC value (rho = 0.04, p = 0.89).

4. Discussion

In the present study, advanced FPU characterization was performed in pregnant rabbits using MRI and stereology. The results confirmed previous data demonstrating a significant difference in fetal weight according to the position of the fetus in the uterine horn, with fetuses nearest the ovary having a higher weight than fetuses closest to the cervix in litters with more than three fetuses [1,2]. These results suggest that the rabbit model could be a natural model of FGR. Unfortunately, there was no correlation between fetal weight and placental ADC values or stereology except for fetal weight and the density of fetal vessels.

The placental weight is known to be a surrogate for placental function. The fetoplacental weight ratio has been suggested as a possible indicator of the adequacy of placental reserve capacity in FGR [17]. The present study revealed no difference between groups regarding the P/F ratio, suggesting a similar placental reserve capacity.

There was no significant difference in placental morphology between groups. Moreover, the histological analysis findings did not match the findings obtained for human placentas from FGR fetuses. Indeed, in humans, the placentas of FGR fetuses is known to exhibit maternal vascular underperfusion with larger maternal blood spaces, which is not found in the placentas of the smallest rabbit fetuses [18].

In terms of functional analysis using DW-MRI, there was no significant difference between groups for placental, brain or liver perfusion. These results challenge the hypothesis that the rabbit model is a natural model of FGR since there is no characterized placental vascular insufficiency. Indeed, several studies have shown that placental ADC values are significantly lower in FGR pregnancies than in healthy human pregnancies, which was not found in the present model (8,22). This could be explained by the fact that placentation differs between humans and rabbits. In rabbits, the exchange area is the labyrinthine placenta rather than the villous tree [3]. Additionally, there is no remodeling of spiral arteries, as observed in women.

Moreover, DW-MRI has been used in several studies to assess cerebral changes in fetuses with FGR fetuses showing lower ADC in several cerebral regions than healthy fetuses [19–21]. This difference was also not observed in our study. The ADC is based on water diffusion on a cellular scale, and we found a negative correlation between the volume of the maternal blood space and the placental ADC value. This could be due to the difference in the maternal space volume between placentas.

All these findings suggest that the rabbit model is not a natural model of FGR and that small fetuses cannot be considered victims of placental insufficiency but rather are simply small for gestational age SGA fetuses, as described in humans [22]. The mechanism underlying this weight difference between fetuses is not comparable to that of human FGR and better corresponds to constitutionally healthy fetuses because of the absence of histological and diffusion MRI differences. A similar relationship between fetal weight and the position of the fetus in the uterine horn has been noted in pigs and guinea pigs [13]. The cause of this finding is unclear, but it seems to have an anatomical origin that can be explained by the vascularization supply, which may be different at the two ends of the uterine horns: both the ovarian and uterine supply near the ovary and only the vaginal supply near the cervix. This could correspond to a lower collection upstream of the placenta without

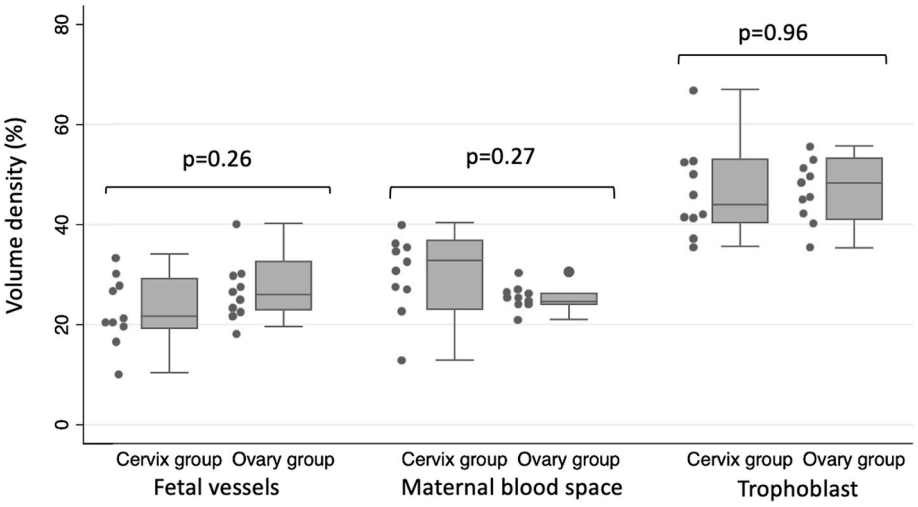

Fig. 5. Volume density (Vv) of trophoblasts, fetal vessels and the maternal blood space in the placenta according to the position of the fetus in the uterine horn (Cervix group and Ovary group) and expressed in %.

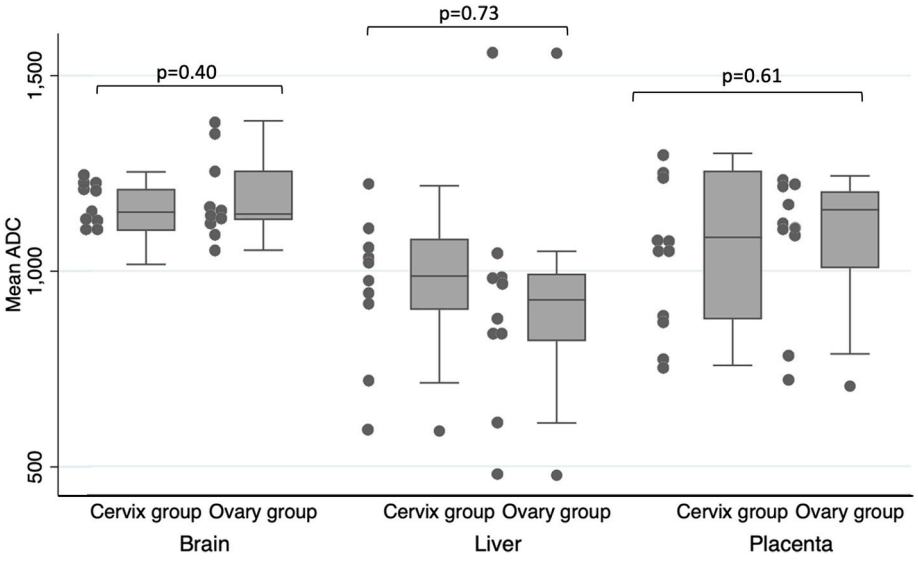

Fig. 6. Box plots of ADC values (10^{-3} mm^2/s) in the placenta, fetal brain and liver according to the position of the fetus in the uterine horn.

causing morphological or functional placental dysfunction.

The limitations of this study are the small sample size and the absence of longitudinal data collected during pregnancy to analyze the evolution of the parameters.

The strength of our study is its originality because to our knowledge, this is the first study to characterize the fetoplacental unit both morphologically and functionally to test the hypothesis that the rabbit model is a natural model of FGR. Moreover, MRI data were based on precise and reliable identification of the position of the fetus in the uterine horn to make *in vivo* (MRI) and *ex vivo* (histology and fetal weight) comparisons. This point is a real added value compared to other studies on MRI in rabbits or rats where the mode of fetal identification probably does not reflect the anatomical reality (the fetus seen on the right is considered to be part of the right horn, which is not observed in fact) [23].

In conclusion, DW-MRI and stereology are adapted tools that permit the evaluation of the functional and morphological aspects of the placenta in animal models. Using these tools, we suggest that the rabbit model is not a natural model of fetal growth restriction because the origin of FGR is more anatomical than functional and is unrelated to a characterizable placental insufficiency.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Matthieu Dap: Writing – original draft, Investigation, Formal analysis, Data curation. **Théo Albert:** Writing – review & editing, Investigation, Formal analysis. **Ikrame Ramdhani:** Writing – review & editing, Investigation, Formal analysis. **Anne Couturier-Tarrade:** Writing – review & editing, Methodology, Conceptualization. **Olivier Morel:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Pascale Chavatte-Palmer:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Marine Beaumont:** Writing – review & editing, Validation, Resources, Project administration, Conceptualization. **Charline Bertholdt:** Writing – review & editing, Methodology, Investigation, Conceptualization.

Declaration of competing interest

None.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.placenta.2024.06.014.

References

[1] C. Sun, K.M. Groom, C. Oyston, L.W. Chamley, A.R. Clark, J.L. James, The placenta in fetal growth restriction: what is going wrong? Placenta 96 (2020) 10–18.
[2] C. Lees, N. Marlow, B. Arabin, C.M. Bilardo, C. Brezinka, J.B. Derks, et al., Perinatal morbidity and mortality in early-onset fetal growth restriction: cohort outcomes of the trial of randomized umbilical and fetal flow in Europe (TRUFFLE), Ultrasound Obstet. Gynecol. 42 (2013) 400–408.
[3] C.M. Bilardo, K. Hecher, G.H.A. Visser, A.T. Papageorghiou, N. Marlow, B. Thilaganathan, et al., Severe fetal growth restriction at 26-32 weeks: key messages from the TRUFFLE study, Ultrasound Obstet. Gynecol. 50 (2017) 285–290.
[4] I. Valenzuela, M. Kinoshita, J. van der Merwe, K. Maršál, J. Deprest, Prenatal interventions for fetal growth restriction in animal models: a systematic review, Placenta 126 (2022) 90–113.
[5] A.M. Swanson, A.L. David, Animal models of fetal growth restriction: Considerations for translational medicine, Placenta 36 (2015) 623–630.
[6] C. Bertholdt, M. Dap, R. Pillot, P. Chavatte-Palmer, O. Morel, M. Beaumont, Assessment of placental perfusion using contrast-enhanced ultrasound: a longitudinal study in pregnant rabbit, Theriogenology 187 (2022) 135–140.
[7] J. Lopez-Tello, M. Arias-Alvarez, A. Gonzalez-Bulnes, A.N. Sferuzzi-Perri, Models of Intrauterine growth restriction and fetal programming in rabbits, Mol. Reprod. Dev. 86 (2019) 1781–1809.
[8] B. Fischer, P. Chavatte-Palmer, C. Viebahn, A. Navarrete Santos, V. Duranthon, Rabbit as a reproductive model for human health, Reprod Camb Engl 144 (2012) 1–10.
[9] E. Lecarpentier, O. Morel, A. Tarrade, M. Dahirel, M. Bonneau, E. Gayat, et al., Quantification of utero-placental vascularization in a rabbit model of IUGR with three-dimensional power Doppler angiography, Placenta 33 (2012) 769–775.
[10] A. Tarrade, E. Lecarpentier, S. Gil, O. Morel, N. Zahr, M. Dahirel, et al., Analysis of placental vascularization in a pharmacological rabbit model of IUGR induced by L-NAME, a nitric oxide synthase inhibitor, Placenta 35 (2014) 254–259.
[11] I. Valenzuela, D. Basurto, Y. Regin, A. Gie, L. van der Veeken, S. Vergote, et al., Placental vascular alterations are associated with early neurodevelopmental and pulmonary impairment in the rabbit fetal growth restriction model, Sci. Rep. 12 (2022) 19720.
[12] P.D. Rosahn, H.S.N. Greene, The influence of intrauterine factors on the fetal weight of rabbits, J. Exp. Med. 63 (1936) 901–921.
[13] A.W. Flake, R.L. Villa, N.S. Adzick, M.R. Harrison, Transamniotic fetal feeding. II. A model of intrauterine growth retardation using the relationship of "natural runting" to uterine position, J. Pediatr. Surg. 22 (1987) 816–819.
[14] S.B. Görkem, A. Coşkun, M. Eşlik, M.S. Kütük, A. Öztürk, Diffusion-weighted imaging of placenta in intrauterine growth restriction with worsening Doppler US findings, Diagn Interv Radiol Ank Turk 25 (2019) 280–284.
[15] M.G. Reed, C.V. Howard, G.S. DE Yanés, One-stop stereology: the estimation of 3D parameters using isotropic rulers, J Microsc 239 (1) (2010) 54–65.
[16] P.O. Favaron, A.M. Mess, M.F. de Oliveira, A. Gabory, M.A. Miglino, P. Chavatte-Palmer, A. Tarrade, Morphometric analysis of the placenta in the New World mouse Necromys lasiurus (Rodentia, Cricetidae): a comparison of placental development in cricetids and murids, Reprod. Biol. Endocrinol. 21 (11) (2013) 10.
[17] T.Y. Khong, E.E. Mooney, I. Ariel, N.C.M. Balmus, T.K. Boyd, M.-A. Brundler, et al., Sampling and Definitions of placental Lesions: Amsterdam placental Workshop group Consensus statement, Arch. Pathol. Lab Med. 140 (2016) 698–713.
[18] G.J. Burton, E. Jauniaux, Pathophysiology of placental-derived fetal growth restriction, Am. J. Obstet. Gynecol. 218 (2018) S745–S761.
[19] J.M. Jouannic, E. Blondiaux, M.V. Senat, S. Friszer, C. Adamsbaum, J. Rousseau, et al., Prognostic value of diffusion-weighted magnetic resonance imaging of brain in fetal growth restriction: results of prospective multicenter study, Ultrasound Obstet. Gynecol. 56 (2020) 893–900.
[20] O.J. Arthurs, A. Rega, F. Guimiot, N. Belarbi, J. Rosenblatt, V. Biran, et al., Diffusion-weighted magnetic resonance imaging of the fetal brain in intrauterine growth restriction, Ultrasound Obstet. Gynecol. 50 (2017) 79–87.
[21] W. Zheng, G. Yan, Y. Jiang, Z. Bao, K. Li, M. Deng, et al., Diffusion-weighted MRI of the fetal brain in fetal growth restriction with maternal Preeclampsia or gestational Hypertension, J. Magn. Reson. Imag. (2023).
[22] N. Melamed, A. Baschat, Y. Yinon, A. Athanasiadis, F. Mecacci, F. Figueras, et al., FIGO (International Federation of Gynecology and Obstetrics) initiative on fetal growth: Best practice advice for screening, diagnosis, and management of fetal growth restriction, Int. J. Gynecol. Obstet. 152 (2021) 3–57.
[23] C.-J. Arthuis, V. Mendes, S. Même, W. Même, C. Rousselot, N. Winer, et al., Comparative determination of placental perfusion by magnetic resonance imaging and contrast-enhanced ultrasound in a murine model of intrauterine growth restriction, Placenta 69 (2018) 74–81.