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Effects of Underfeeding and Overfeeding on Growth and Multi-Organ Metabolic Alterations in Wistar Rats

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Abstract **Original Research Article**

Background: Early-life nutritional imbalance is increasingly recognized as a key determinant of long-term cardiometabolic health. Both undernutrition and overnutrition during critical developmental periods can induce persistent alterations in growth, adiposity, endocrine regulation, and organ function, predisposing individuals to metabolic disorders later in life.

Objective: This study evaluated the long-term metabolic consequences of early-life nutritional imbalance in Wistar rats by comparing growth patterns, organ morphometry, metabolic biomarkers, and cardiometabolic risk indices following underfeeding and overfeeding.

Methods: A controlled experimental study was conducted using male Wistar rats randomly assigned to three groups: underfed, normal-fed, and overfed. Somatic growth parameters (weight, height, length, and circumference gain) were monitored. After the experimental period, major organs were harvested for morphometric analysis. Serum biochemical markers including liver and renal function indices, glucose, lipid profile, inflammatory markers, and oxidative stress indicators were measured. Cardiometabolic risk indices such as the atherogenic index of plasma, Castelli risk indices, and TG/HDL ratio were calculated. Data were analyzed using one-way ANOVA and multiple regression.

Results: Overfeeding significantly increased weight gain and promoted multi-organ hypertrophy, particularly in the liver, heart, spleen, kidneys, and brain, whereas underfeeding restricted somatic growth and reduced organ weights. Underfed animals exhibited lower glucose, triglycerides, cholesterol, inflammatory markers, and oxidative stress, alongside higher HDL and antioxidant activity. Regression analyses revealed that organ morphometry strongly predicted lipid-related cardiometabolic indices.

Conclusion: Early-life nutritional imbalance significantly alters growth, organ development, and cardiometabolic risk profiles. Organ morphometric changes appear closely linked to metabolic regulation and may serve as potential indicators of cardiometabolic risk.

Keywords: Early-life nutrition, Undernutrition, Overnutrition, Wistar rats, Organ morphometry, Cardiometabolic risk, Lipid profile, Oxidative stress, Developmental programming.

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Introduction

Early-life nutritional imbalance is increasingly recognized as a critical determinant of long-term cardiometabolic health. Evidence from experimental studies using Wistar rat models demonstrates that nutritional perturbations during sensitive developmental windows produce enduring effects on growth trajectories, adiposity, endocrine signaling, and organ function. In particular, large-litter rearing models of postnatal undernutrition consistently result in reduced somatic growth and diminished adiposity without complete catch-up growth. Conversely, small-litter–induced early overnutrition accelerates weight gain and is associated with persistent hyperleptinemia and early metabolic dysregulation (Velkoska et al., 2008a, 2008b). When animals exposed to these early nutritional extremes subsequently encounter hypercaloric diets, the metabolic consequences are further amplified, leading to increased visceral adiposity, hepatic dysfunction, and insulin resistance. These findings support the developmental programming hypothesis, which proposes that nutritional conditions during early life shape long-term physiological and metabolic outcomes (Galhardi et al., 2025; Kagios et al., 2025).

Despite growing evidence linking early nutritional imbalance to later cardiometabolic risk, important knowledge gaps remain. Most experimental studies investigate either early undernutrition or overnutrition in isolation, limiting understanding of how these contrasting nutritional environments may converge to produce similar metabolic vulnerabilities. Moreover, many investigations focus on single metabolic endpoints, leaving the integrated effects on growth dynamics, hepatic function, glucose–lipid metabolism, and endocrine regulation insufficiently characterized. The interaction between early-life nutritional programming and subsequent dietary exposure also remains incompletely understood. Consequently, comprehensive multi-system experimental investigations are required to clarify the mechanisms through which early nutritional imbalance predisposes individuals to later cardiometabolic dysfunction.

Research Aim and Objectives

This study aimed to evaluate the long-term metabolic consequences of early-life nutritional imbalance in Wistar rats. It specifically: (1) compared growth and adiposity following early underfeeding and overfeeding; (2) assessed hepatic and cardiometabolic biomarkers; and (3) examined antioxidant capacity changes following underfeeding and overfeeding.

Methodology

This study adopted a controlled experimental animal design to examine the physiological and metabolic consequences of differential nutritional exposure during early life. The primary objective was to evaluate how contrasting nutritional states; undernutrition, normal nutrition, and overnutrition affect somatic growth, organ development, metabolic biomarkers, and cardiometabolic risk indices in Wistar rats. By implementing clearly defined feeding regimens under controlled laboratory conditions, the design enabled a systematic comparison of growth trajectories, organ morphometry, biochemical alterations, and lipid-derived cardiovascular risk indicators across nutritionally distinct groups.

Healthy male Wistar rats (*Rattus norvegicus*) were obtained from the animal facility of the Faculty of Basic Medical Sciences and acclimatized to laboratory conditions prior to experimentation. Animals were housed in standard polypropylene cages under controlled environmental conditions, including a temperature range of 22 - 25 °C, relative humidity of 50 - 60%, and a 12-hour light-dark cycle. Standard laboratory chow and clean drinking water were provided ad libitum except where experimental dietary manipulation was required. All experimental procedures adhered to internationally accepted ethical guidelines for the care and use of laboratory animals.

Following a 10-day acclimatization period, animals were randomly assigned to three experimental groups representing different nutritional exposures. The underfed group was subjected to controlled caloric restriction in order to simulate early-life undernutrition. The normal-fed group received standard laboratory chow and served as the physiological reference group for normal nutritional intake. The overfed group was provided increased caloric intake to model early-life overnutrition. These feeding regimens were maintained throughout the experimental period to induce distinct metabolic and developmental responses associated with each nutritional condition.

Somatic growth was monitored using standardized anthropometric measurements recorded at baseline and at regular intervals during the experimental period. Growth indices included body weight gain, height gain, body length gain, and body circumference gain. Measurements were obtained using calibrated digital scales and precision measuring instruments to ensure accuracy and reproducibility. These parameters were used to characterize developmental responses to differential nutritional exposure and to evaluate how nutritional imbalance influences growth trajectories.

At the conclusion of the experimental period, animals were euthanized under appropriate anesthesia for organ harvesting and morphometric analysis. Major organs were carefully excised, cleared of surrounding connective tissue, and weighed using a calibrated digital analytical balance. Organs examined included the heart, liver, spleen, kidneys, lungs, brain, and pancreas. Both absolute organ weights and relative organ weights were determined to assess organ development in relation to body mass. Relative organ weight was calculated as:

Relative organ weight = (organ weight / body weight) * 100

In addition, organ-to-brain ratios were computed to evaluate proportional organ development relative to neural mass, providing an index of organ growth independent of overall body size.

For biochemical and metabolic analyses, blood samples were collected via the carotid vein and centrifuged to obtain serum. Standard enzymatic and spectrophotometric methods were used to quantify key biochemical markers. Liver function was assessed using alanine aminotransferase (ALT), aspartate aminotransferase (AST), and the AST/ALT ratio. Renal function was evaluated using serum urea and creatinine concentrations. Inflammatory and oxidative stress status were assessed using C-reactive protein (CRP), malondialdehyde (MDA), and superoxide dismutase (SOD). Metabolic status was further evaluated through fasting blood glucose measurements and a comprehensive lipid profile that included total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG).

To obtain an integrated assessment of cardiovascular risk, several lipid-derived cardiometabolic indices were calculated. The atherogenic index of plasma (AIP) was determined using the following relationship:

AIP = log10(TG / HDL)

Additional indices, including Castelli Risk Index I (TC/HDL), Castelli Risk Index II (LDL/HDL), the atherogenic coefficient, and the TG/HDL ratio were also calculated to provide sensitive indicators of lipid imbalance and cardiovascular risk.

All statistical analyses were conducted using IBM Statistical Package for Social Sciences (SPSS) version 27. Data were expressed as mean ± standard error of the mean (SEM). Differences among the three feeding groups were evaluated using one-way analysis of variance (ANOVA). When the overall ANOVA test indicated statistically significant differences, post hoc pairwise comparisons were performed using appropriate multiple comparison procedures to identify specific intergroup differences.

To further explore relationships between growth parameters, organ morphometry, and metabolic outcomes, multiple linear regression analyses were performed. Predictor variables included somatic growth measures (weight, height, length, and circumference gains), absolute organ

weights, relative organ weights, and organ-to-brain ratios. Outcome variables included the AST/ALT ratio, LDL concentration, atherogenic index of plasma, TC/LDL ratio, and TG/HDL ratio. Model performance was evaluated using the correlation coefficient (R), coefficient of determination (R^2), adjusted R^2, standard error of estimate, and ANOVA F-statistics for overall model significance. Regression outputs were reported as both unstandardized coefficients (B) and standardized beta coefficients (β) to facilitate interpretation of the relative strength of predictors.

Given the relatively large number of predictors compared with sample size, additional attention was devoted to model diagnostics to minimize the risk of overfitting and multicollinearity. Differences between R^2 and adjusted R^2 values were examined to assess model stability and generalizability. Statistical significance for all analyses was defined using a two-tailed p-value threshold of less than 0.05.

RESULTS

Tables 1a and 1b present the effects of differential feeding regimens on somatic growth and organ morphometry in Wistar rats. Nutritional status significantly influenced growth outcomes and organ development across the experimental groups. Overfed rats demonstrated significantly greater weight gain compared with normal-fed controls, whereas underfed rats exhibited pronounced weight loss. Height gain was also significantly higher in the overfed group, while circumference gain was markedly reduced among underfed animals. In contrast, body length gain did not differ significantly among the feeding groups, suggesting that longitudinal growth was less sensitive to nutritional variation than other anthropometric parameters.

Analysis of absolute organ weights revealed substantial organ hypertrophy in overfed animals. Significant increases were observed in the heart, liver, spleen, kidneys, and brain, with the liver demonstrating the most pronounced enlargement. Lung weight also differed significantly among groups, with relatively lower values recorded in the overfed rats, whereas pancreatic weight remained comparable across all feeding conditions. Evaluation of relative organ weights indicated that only relative lung weight varied significantly among groups.

Assessment of organ-to-brain ratios further revealed significant alterations in lung/brain, liver/brain, and spleen/brain ratios, indicating disproportionate organ development under extreme nutritional states. Post hoc comparisons showed that underfed animals had significantly lower weight gain than both normal-fed and overfed groups and also exhibited reduced height and circumference gains relative to overfed animals. Undernutrition was additionally associated with significantly lower heart, liver, spleen, kidney, and brain weights. Overall, these findings indicate that undernutrition restricts somatic growth and organ development, whereas overfeeding promotes multi-organ enlargement and altered organ proportionality.

Tables 2a and 2b summarize the biochemical consequences of differential feeding regimens in Wistar rats, demonstrating that nutritional status significantly influenced multiple metabolic, inflammatory, and cardiovascular risk markers. Liver function parameters varied markedly across groups, with alanine aminotransferase (ALT) and aspartate aminotransferase (AST) showing highly significant differences. Normal-fed animals exhibited the highest ALT and AST concentrations, whereas underfed rats displayed significantly lower enzyme levels compared with both normal-fed and overfed groups. Although the AST/ALT ratio differed across feeding conditions, post hoc analyses did not reveal significant pairwise differences.

Renal function markers were also significantly affected by nutritional status. Creatinine concentrations were markedly lower in underfed rats compared with both normal-fed and overfed groups, while serum urea levels were significantly reduced in underfed animals relative to the overfed group. Inflammatory and oxidative stress markers demonstrated similar trends. C-reactive protein (CRP) and malondialdehyde (MDA) were highest in the normal-fed group but significantly reduced in

underfed animals, suggesting a lower inflammatory and oxidative burden under caloric restriction. Conversely, superoxide dismutase (SOD) activity was significantly elevated in underfed rats, indicating enhanced antioxidant defense.

Metabolic parameters followed a consistent pattern. Underfed animals exhibited significantly lower fasting glucose, total cholesterol, and triglyceride levels compared with both normal-fed and overfed groups, while high-density lipoprotein (HDL) levels were higher relative to normal-fed controls. Several lipid-derived cardiovascular risk indices including the TC/HDL ratio, atherogenic coefficient, atherogenic index of plasma, Castelli's risk index I, and TG/HDL ratio were also significantly lower in underfed animals. Collectively, these findings suggest that caloric restriction was associated with reduced cardiometabolic risk markers, lower inflammation and oxidative stress, improved antioxidant status, and more favorable lipid and glycemic profiles.

Tables 3a - 3c present the results of multiple regression analyses evaluating the relationships between somatic growth parameters, organ morphometry, and the AST/ALT ratio. The overall regression model demonstrated an exceptionally strong association between the predictor variables and the outcome measure ($R = 0.998$). The model accounted for nearly all the observed variation in the AST/ALT ratio, explaining 99.5% of the total variance ($R^2 = 0.995$). After adjusting for the relatively large number of predictors included in the model, the adjusted coefficient of determination remained high (adjusted $R^2 = 0.94$), indicating substantial explanatory power. In addition, the standard error of the estimate was very low (0.03), suggesting minimal deviation between predicted and observed AST/ALT values and indicating a highly precise model fit.

Analysis of variance for the regression model indicated borderline statistical significance ($F = 19.17$, $p = 0.05$), suggesting that the combined set of 21 predictor variables collectively explained variation in the AST/ALT ratio at the threshold of statistical significance. However, the small number of residual degrees of freedom relative to the number of predictors indicates that the model may be overly complex and potentially susceptible to overfitting.

Evaluation of individual regression coefficients revealed that only a limited subset of predictors independently contributed to variation in the AST/ALT ratio. Specifically, length gain, relative lung weight, and relative spleen weight emerged as significant positive predictors. Several additional variables including heart, lung, pancreas, and kidney weights, as well as selected relative organ weights and organ-to-brain ratios showed borderline associations. Overall, while the model explained substantial variability, only a small number of predictors demonstrated independent effects on AST/ALT variation.

Tables 4a - 4c present the results of multiple regression analyses evaluating the relationships between somatic growth parameters, organ morphometry, and circulating low-density lipoprotein (LDL) levels in Wistar rats. The overall regression model demonstrated exceptionally strong predictive performance. The correlation coefficient was extremely high ($R = 0.999$), indicating an almost perfect association between the combined predictor variables and LDL concentrations. The model explained 99.8% of the total variance in LDL levels ($R^2 = 0.998$), and the adjusted R^2 remained very high (0.98) after accounting for the number of predictors included in the model. Furthermore, the standard error of the estimate was low (0.07), suggesting a high level of precision in the prediction of LDL values.

Analysis of variance confirmed that the overall regression model significantly predicted LDL concentrations ($F = 47.22$, $p = 0.02$). The regression sum of squares accounted for nearly all the total variation in LDL levels, while residual variance was minimal, indicating that the combined effects of growth and organ-related variables strongly influenced circulating LDL concentrations. Examination of individual regression coefficients identified several significant predictors. Absolute heart weight and relative heart weight were both significantly associated with LDL levels. Specifically, greater

absolute heart mass was linked to increased LDL concentrations, whereas higher relative heart weight demonstrated an inverse relationship. In addition, relative lung weight and the lung-to-brain ratio emerged as significant predictors. These findings suggest that cardiovascular and pulmonary growth characteristics, particularly when normalized to body or brain size, may play important roles in determining circulating LDL concentrations.

Tables 5a - 5c present the results of multiple regression analyses assessing the relationships between somatic growth parameters, organ morphometry, and the atherogenic index of plasma (AIP). The overall regression model demonstrated exceptionally strong predictive performance. The correlation coefficient was extremely high (R = 0.999), indicating a near-perfect association between the predictor variables and AIP. The model accounted for 99.7% of the total variance in AIP (R^2 = 0.997), and the adjusted coefficient of determination remained high (adjusted R^2 = 0.97), suggesting that the included predictors retained substantial explanatory power even after adjustment for model complexity. The standard error of the estimate was very low (0.02), indicating minimal deviation between observed and predicted values and reflecting high predictive precision. Nevertheless, the very high R^2 in combination with the large number of predictors relative to the sample size suggests a potential risk of model overfitting.

Analysis of variance further indicated that the regression model significantly predicted AIP (F = 34.92, p = 0.028). The regression sum of squares accounted for nearly all observed variability in AIP, while residual variance was minimal, demonstrating an excellent model fit. However, the limited residual degrees of freedom relative to the number of predictors suggests that the model may be highly saturated.

Evaluation of individual regression coefficients identified several significant predictors. Circumference gain showed a significant negative association with AIP, whereas absolute heart and spleen weights were positive predictors. In contrast, relative heart weight, relative lung weight, and the spleen-to-brain ratio were negatively associated with AIP, while relative brain weight demonstrated a strong positive relationship, highlighting the influence of both absolute and proportional organ growth on cardiometabolic risk.

Tables 6a - 6c present the results of multiple regression analyses evaluating the associations between somatic growth parameters, organ morphometry, and the cholesterol-to–low-density lipoprotein (CHOL/LDL) ratio. The regression model demonstrated extremely strong predictive performance. The correlation coefficient was essentially perfect (R = 1.00), indicating a near-complete linear relationship between the predictors and the CHOL/LDL ratio. The model explained 99.9% of the total variance in the outcome variable (R^2 = 0.999), while the adjusted coefficient of determination remained very high (adjusted R^2 = 0.991) after accounting for the number of predictors. The standard error of the estimate was minimal (0.0275), indicating very small deviations between observed and predicted values and reflecting high predictive precision. However, the extremely high R^2 combined with the large number of predictors relative to the sample size suggests a potential risk of model overfitting. Analysis of variance confirmed that the overall regression model significantly predicted the CHOL/LDL ratio (F = 117.21, p = 0.008). The regression sum of squares accounted for nearly all the variability in the lipid ratio, leaving only a negligible residual variance and indicating a very strong model fit. Nevertheless, the limited residual degrees of freedom relative to the number of predictors indicates that the model is highly saturated and should be interpreted cautiously. Evaluation of individual regression coefficients identified several significant organ-related predictors. Absolute heart weight showed a negative association with the CHOL/LDL ratio, whereas lung, liver, spleen, and pancreas weights were positively associated. Relative heart weight demonstrated a positive association, while relative liver weight, relative pancreas weight, and the lung-to-brain ratio were negatively associated. In contrast, growth parameters including weight, length, height, and circumference gain were not significant predictors, suggesting that organ development

rather than somatic growth primarily influenced variation in the CHOL/LDL ratio.

Tables 7a - 7c present the results of multiple regression analyses examining the relationships between somatic growth parameters, organ morphometry, and the triglyceride-to-HDL (TG/HDL) ratio in Wistar rats. The overall regression model demonstrated a very strong association between the combined predictors and TG/HDL levels, with a correlation coefficient of 0.997. The model explained 99.4% of the total variance in TG/HDL (R^2 = 0.994), while the adjusted R^2 remained high at 0.927, indicating that approximately 92.7% of the variability was accounted for after adjusting for the number of predictors. The low standard error of the estimate (0.067) further reflected high predictive precision. However, the difference between R^2 and adjusted R^2 suggests potential overfitting due to the relatively large number of predictors relative to sample size.

Analysis of variance indicated that the model accounted for the majority of variance in TG/HDL, but it did not reach conventional statistical significance (F = 14.81, p = 0.065), likely reflecting limited statistical power and the small residual degrees of freedom.

Examination of individual regression coefficients revealed several significant predictors. Circumference gain was negatively associated with TG/HDL, whereas absolute heart and spleen weights were positively associated. Relative heart weight and relative lung weight showed significant negative associations with the ratio. Other variables, including relative brain weight and spleen-to-brain ratio, demonstrated borderline effects. Most general growth parameters and several organ metrics were not significant. Overall, these findings suggest that organ-specific growth and proportional organ development contribute more substantially to TG/HDL variation than general somatic growth measures.

Table 1a. Effects of underfeeding and overfeeding on growth indices, absolute organ weights, relative organ weights, and organ-to-brain ratios in Wistar rats (mean ± SEM).

	Underfed Mean (sem)	Normal fed Mean (sem)	Overfed Mean (sem)	Total	F	p-value
Weight gain (gm)	-58.50 (5.78)	23.25 (19.08)	57.00 (28.64)	7.25 (18.01)	8.69	0.008
length gain (cm)	18.38 (0.85)	18.38 (0.69)	21.25 (1.25)	19.33 (0.65)	2.99	0.10
height gain (cm)	0.03 (0.03)	0.05 (0.05)	0.80 (0.15)	0.29 (0.12)	23.47	<0.0001
circumference gain (cm)	-5.25 (0.25)	-5.13 (0.13)	-3.10 (0.76)	-4.49 (0.38)	6.67	0.02
Heart (gm)	0.49 (0.01)	0.51 (0.01)	0.57 (0.01)	0.52 (0.01)	16.96	0.001
Lungs (gm)	1.86 (0.26)	2.10 (0.04)	1.33 (0.01)	1.77 (0.12)	6.83	0.02

Liver (gm)	3.34 (0.05)	3.46 (0.05)	4.36 (0.13)	3.72 (0.14)	42.79	<0.0001
Spleen (gm)	0.55 (0.10)	0.87 (0.03)	1.10 (0.03)	0.84 (0.07)	20.11	<0.0001
Pancreas (gm)	0.41 (0.02)	0.38 (0.02)	0.44 (0.04)	0.41 (0.02)	1.10	0.37
Kidneys (gm)	1.03 (0.01)	1.03 (0.01)	1.17 (0.03)	1.08 (0.02)	17.42	0.001
Brain (gm)	1.59 (0.01)	1.56 (0.01)	1.73 (0.04)	1.63 (0.03)	10.17	0.005
Relative Heart Weight	0.41 (0.01)	0.33 (0.03)	0.35 (0.04)	0.36 (0.02)	2.14	0.17
Relative Lung Weight	1.53 (0.22)	1.39 (0.19)	0.81 (0.09)	1.24 (0.13)	4.78	0.04
Relative Liver Weight	2.74 (0.05)	2.27 (0.27)	2.62 (0.22)	2.54 (0.12)	1.42	0.29
Relative Spleen Weight	0.45 (.08)	0.56 (0.05)	0.66 (0.06)	0.56 (0.04)	2.65	0.13
Relative Pancreas Weight	0.33 (0.02)	0.25 (0.03)	0.26 (0.01)	0.28 (0.02)	4.06	0.06
Relative Kidney Weight	0.84 (.01)	0.67 (0.07)	0.70 (0.06)	0.74 (0.04)	2.54	0.13
Relative Brain Weight	1.30 (0.01)	1.03 (0.13)	1.04 (0.09)	1.13 (0.06)	3.09	0.09
Heart/ Brain	0.31 (.01)	0.32 (0.01)	0.33 (0.01)	0.32 (0.01)	1.04	0.39
Lung/ Brain	1.17 (0.16)	1.35 (0.02)	0.77 (0.02)	1.10 (0.09)	9.29	0.006
Liver/ Brain	2.10 (.05)	2.22 (0.04)	2.52 (0.04)	2.28 (0.06)	24.36	<0.0001
Spleen/ Brain	0.35 (0.06)	0.56 (0.02)	0.63 (0.01)	0.51 (0.04)	14.57	0.002
Pancreas/ Brain	0.25 (0.01)	0.24 (0.01)	0.25 (0.02)	0.25 (0.01)	0.15	0.87
Kidney/ Brain	0.64 (0.01)	0.66 (0.01)	0.68 (0.01)	0.66 (0.01)	2.39	0.15

Table 1b. Post hoc multiple comparisons of growth parameters, absolute organ weights, relative organ weights, and organ-to-brain ratios among underfed, normal fed, and overfed groups. Values represent mean differences (I–J), standard error, and significance level following one-way ANOVA with pairwise comparisons.

Dependent Variable	(I) feeding type	(J) feeding type	Mean Difference (I-J)	Std. Error	Sig.
Weight gain (gm)	underfed	normal fed	-81.75	28.49	0.02
		overfed	-115.50*	28.49	0.003
length gain (cm)	underfed	normal fed	0.00	1.36	1.00
		overfed	-2.88	1.36	0.06
height gain (cm)	underfed	normal fed	-0.03	0.13	0.85
		overfed	-0.78*	0.13	<0.0001
circumference gain (cm)	underfed	normal fed	-0.13	0.66	0.85
		overfed	-2.15*	0.66	0.01
Heart (gm)	underfed	normal fed	-0.01	0.01	0.59
		overfed	-0.07*	0.01	<0.0001
Lungs (gm)	underfed	normal fed	-0.24	0.21	0.28
		overfed	0.53*	0.21	0.04
Liver (gm)	underfed	normal fed	-0.12	0.12	0.33
		overfed	-1.02*	0.12	<0.0001
Spleen (gm)	underfed	normal fed	-0.32*	0.09	0.005
		overfed	-0.54*	0.09	<0.0001
Pancreas (gm)	underfed	normal fed	0.02	0.04	0.58
		overfed	-0.04	0.04	0.39
Kidneys (gm)	underfed	normal fed	-0.01	0.03	0.79
		overfed	-0.15*	0.03	0.001
Brain (gm)	underfed	normal fed	0.03	0.04	0.42
		overfed	-0.13	0.04	0.008
Relative Heart Weight	underfed	normal fed	0.08	0.04	0.08
		overfed	0.06	0.04	0.16
Relative Lung Weight	underfed	normal fed	0.15	0.25	0.57
		overfed	0.72*	0.25	0.02
Relative Liver Weight	underfed	normal fed	0.47	0.29	0.14
		overfed	0.13	0.29	0.67
Relative Spleen Weight	underfed	normal fed	-0.11	0.09	0.24
		overfed	-0.21	0.09	0.05

Relative Pancreas Weight	underfed	normal fed	0.08	0.03	0.03
		overfed	0.07*	0.03	0.04
Relative Kidney Weight	underfed	normal fed	0.17	0.08	0.06
		overfed	0.14	0.08	0.12
Relative Brain Weight	underfed	normal fed	0.28	0.13	0.06
		overfed	0.27	0.13	0.07
Heart/Brain	underfed	normal fed	-0.01	0.01	0.40
		overfed	-0.02	0.01	0.19
Lung/Brain	underfed	normal fed	-0.18	0.14	0.22
		overfed	0.39	0.14	0.02
Liver/Brain	underfed	normal fed	-0.12	0.06	0.09
		overfed	-0.43*	0.06	<0.0001
Spleen/Brain	underfed	normal fed	-0.21	0.06	0.004
		overfed	-0.29*	0.06	0.001
Pancreas/Brain	underfed	normal fed	0.01	0.02	0.65
		overfed	0.0002	0.02	0.99
Kidney/Brain	underfed	normal fed	-0.02	0.02	0.28
		overfed	-0.04	0.02	0.06

Table 2a. Effects of feeding type (underfed, normal fed, and overfed) on liver enzymes, renal function markers, inflammatory and oxidative stress indices, glucose levels, lipid profile, and calculated atherogenic risk indices. Values are presented as mean (SEM). Statistical analysis was performed using one-way ANOVA.

	Underfed	**normal**	**Overfed**	**Total**	**F**	**p-value**
ALT (iu/L)	50.95 (1.46)	56.96 (0.93)	47.81 (0.42)	51.91 (1.26)	20.39	<0.0001
AST (iu/L)	51.91 (1.26)	94.99 (0.98)	85.74 (0.56)	89.67 (1.23)	44.21	<0.0001
AST/ALT	1.74 (0.05)	1.67 (0.01)	1.79 (0.02)	1.73 (0.02)	4.57	0.04
Urea (mmol/L)	13.51 (0.18)	13.74 (0.19)	14.18 (0.08)	13.81 (0.12)	4.80	0.04
Creatinine (umol/L)	77.17 (0.86)	90.25 (0.39)	80.98 (0.45)	82.80 (1.69)	124.22	<0.0001

C-Reactive Protein	2.72 (0.02)	3.45 (0.17)	2.82 (0.03)	2.99 (0.11)	16.37	0.001
Malondiadehyde (nmol/L	2.39 (0.16)	4.28 (0.03)	2.69 (0.04)	3.12 (0.26)	111.25	<0.0001
Superoxide Dismutase	109.99 (0.70)	98.84 (0.27)	103.51 (1.32)	104.11 (1.45)	40.86	<0.0001
Glucose (mmol/L)	4.80 (0.05)	5.84 (0.07)	5.77 (0.05)	5.47 (0.15)	111.57	<0.0001
Cholesterol (mmol/L)	3.36 (0.05)	4.45 (0.08)	4.23 (0.03)	4.01 (0.15)	105.86	<0.0001
HDL-Cholesterol (mmol/L)	1.43 (0.02)	1.06 (0.06)	1.20 (0.11)	1.23 (0.06)	6.21	0.02
LDL-Cholesterol (mmol/L)	1.93 (0.11)	2.51 (0.42)	2.85 (0.11)	2.43 (0.18)	3.26	0.09
Triglyceride (mmol/L)	1.13 (0.08)	1.45 (0.04)	1.41 (0.08)	1.33 (0.06)	6.28	0.02
TG/GLUCOSE	0.24 (0.02)	0.25 (0.004)	0.24 (0.01)	0.24 (0.01)	0.31	0.74
TC-HDL	1.93 (0.06)	3.39 (0.13)	3.03 (0.09)	2.78 (0.19)	62.62	<0.0001
Atherogenic Coefficient	1.35 (0.06)	3.24 (0.27)	2.60 (0.32)	2.40 (0.27)	15.20	0.001
Atherogenic index of plasma	-0.11 (0.03)	0.14 (0.03)	0.07 (0.05)	0.03 (0.04)	10.68	0.004
CHOL/TG	3.01 (0.17)	3.07 (0.05)	3.02 (0.16)	3.03 (0.07)	0.05	0.96
Castelli's risk index 1	2.35 (0.06)	4.24 (0.27)	3.60 (0.32)	3.39 (0.27)	15.20	0.001
CHOL/LDL	1.75 (0.08)	1.91 (0.29)	1.49 (0.06)	1.72 (0.11)	1.43	0.29
LDL/TG	1.72 (0.07)	1.71 (0.25)	2.03 (0.08)	1.82 (0.09)	1.36	0.31
Castelli's risk index 2	1.35 (0.06)	2.43 (0.48)	2.45 (0.31)	2.08 (0.23)	3.53	0.07
TG/HDL	0.79 (0.05)	1.38 (0.09)	1.21 (0.16)	1.13 (0.09)	7.89	0.01
TG/LDL	0.58 (0.02)	0.62 (0.09)	0.50 (0.02)	0.57 (0.03)	1.46	0.28

Table 2b. Post hoc pairwise comparisons of biochemical, oxidative stress, lipid, and atherogenic indices among underfed, normal fed, and overfed groups. Values are expressed as mean difference (I–J), standard error, and significance level following one-way ANOVA.

Dependent Variable	(I) feeding type	(J) feeding type	Mean Difference (I-J)	Std. Error	p-value
ALT (iu/L)	underfed	normal	-6.00	1.46	0.003
		overfed	3.15	1.46	0.06
AST (iu/L)	underfed	normal	-6.69	1.02	<0.0001
		overfed	2.56	1.02	0.03
AST/ALT	underfed	normal	0.07	0.04	0.13
		overfed	-0.06	0.04	0.20
Urea (mmol/L)	underfed	normal	-0.23	0.22	0.32
		overfed	-0.67	0.22	0.01
Creatinine (umol/L)	underfed	normal	-13.08	0.85	<0.0001
		overfed	-3.80	0.85	0.002
C-Reactive Protein	underfed	normal	-0.73	0.14	0.001
		overfed	-0.09	0.14	0.51
Malondialdehyde (nmol/L)	underfed	normal	-1.89	0.14	<0.0001
		overfed	-0.29	0.14	0.06
Superoxide Dismutase	underfed	normal	11.15	1.24	<0.0001
		overfed	6.47	1.24	0.001
Glucose (mmol/L)	underfed	normal	-1.04	0.08	<0.0001
		overfed	-0.97	0.08	<0.0001
Cholesterol (mmol/L)	underfed	normal	-1.09	0.08	<0.0001
		overfed	-0.87	0.08	<0.0001
HDL-Cholesterol (mmol/L)	underfed	normal	0.37	0.11	0.007
		overfed	0.23	0.11	0.06
LDL-Cholesterol (mmol/L)	underfed	normal	-0.58	0.36	0.14
		overfed	-0.92	0.36	0.03
Triglycerides (mmol/L)	underfed	normal	-0.32	0.10	0.01
		overfed	-0.28	0.10	0.02
Triglycerides/Glucose	underfed	normal	-0.01	0.02	0.46
		overfed	-0.009	0.02	0.61
TC-HDL	underfed	normal	-1.46	0.14	<0.0001
		overfed	-1.10	0.14	<0.0001

Atherogenic Coefficient	underfed	normal	-1.89	0.35	<0.0001
		overfed	-1.25	0.35	0.006
Atherogenic index of plasma	underfed	normal	-0.24	0.05	0.002
		overfed	-0.18	0.05	0.01
Cholesterol/Triglyceride	underfed	normal	-0.06	0.19	0.78
		overfed	-0.01	0.19	0.94
Castelli's risk index 1	underfed	normal	-1.89	0.35	<0.0001
		Overfed	-1.25	0.35	0.006
Cholesterol/LDL-Cholesterol	underfed	normal	-0.16	0.25	0.53
		overfed	0.26	0.25	0.53
LDL-Cholesterol/Triglyceride	underfed	normal	0.008	0.22	0.97
		overfed	-0.31	0.22	0.19
Castelli's risk index 2	underfed	normal	-1.08	0.47	0.05
		Overfed	-1.09	0.47	0.05
Triglyceride/HDL	underfed	normal	-0.59	0.15	0.004
		overfed	-0.42	0.15	0.02
Triglyceride/LDL	underfed	normal	-0.04	0.08	0.62
		overfed	0.09	0.08	0.28

Table 3a. Model summary of the multiple linear regression analysis assessing the combined contribution of growth indices, absolute organ weights, relative organ weights, and organ-to-brain ratios as predictors of the dependent variable.

R	R Square	Adjusted R Square	Std. Error of the Estimate
0.998[a]	0.995	0.94	0.03

Table 3b. Analysis of variance (ANOVA) for the multiple linear regression model examining the association between growth parameters, absolute and relative organ weights, organ-to-brain ratios, and the dependent variable (AST/ALT).

	Sum of Squares	df	Mean Square	F	p-value
Regression	.284	21	.014	19.17	0.05[b]
Residual	.001	2	.001		
Total	.285	23			

a. Dependent Variable: AST/ALT

b. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative liver weight, Pancreas, Spleen/ Brain, Circumference gain, heart, length gain, brain, Relative Kidney weight, Weight gain, Relative Spleen weight, Relative Pancreas Weight, Relative Lung Weight, kidneys, Relative Heart Weight, liver, Lung/Brain, Relative Brain Weight, spleen

Table 3c. Multiple linear regression coefficients showing the association between growth parameters, absolute organ weights, relative organ weights, organ-to-brain ratios, and the dependent variable (AST/ALT ratio). Values are presented as unstandardized coefficients (B), standard error (SE), standardized beta (β), *t*-values, and significance levels.

Model	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	p-value
(Constant)	15.80	5.07		3.11	0.09
Weight gain (gm)	0.004	0.001	1.56	2.77	0.11
length gain (cm)	0.038	0.007	0.67	5.04	0.04
height gain (cm)	-0.20	0.12	-0.57	1.61	0.25
Circumference gain (cm)	-0.01	0.01	-0.23	0.87	0.48
Heart (gm)	11.75	3.22	8.52	3.65	0.07
Lungs (gm)	-2.86	0.77	-12.40	3.70	0.07
Liver (gm)	0.01	0.31	0.04	0.02	0.99
Spleen (gm)	-1.59	1.94	-3.77	0.82	0.49
Pancreas (gm)	-14.59	3.68	-15.75	3.97	0.06
Kidneys (gm)	9.94	2.69	9.65	3.70	0.07
Brain (gm)	-3.10	2.07	-2.96	1.50	0.27
Relative Heart Weight	-16.07	4.31	-9.92	3.73	0.07
Relative Lung Weight	1.89	0.39	7.14	4.81	0.04
Relative Liver Weight	-0.22	0.43	-0.77	0.52	0.66
Relative Spleen Weight	6.53	0.93	10.25	6.99	**0.02**
Relative Pancreas Weight	18.38	5.12	9.39	3.59	0.07
Relative Kidney Weight	3.78	2.09	3.74	1.81	0.21
Relative Brain weight	-6.66	2.23	-11.26	2.99	0.09
Lung/Brain	1.86	0.95	5.22	1.95	0.19
Spleen/Brain	-6.29	3.47	-8.49	1.81	0.21
Kidney/Brain	-19.98	5.56	-11.93	3.59	0.07

a. Dependent Variable: AST/ALT

Table 4a. Model Summary for Regression Predicting LDL Levels

R	R Square	Adjusted R Square	Std. Error of the Estimate
0.999[a]	0.998	0.98	0.07

a. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 4b. ANOVA Summary for Regression Model Predicting LDL Levels

	Sum of Squares	df	Mean Square	F	Sig.
Regression	4.81	21	0.23	47.22	0.02[b]
Residual	0.01	2	0.005		
Total	4.82	23			

a. Dependent Variable: LDL

b. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 4c. Regression Coefficients Predicting LDL Levels

Model	**Unstandardized Coefficients**		**Standardized Coefficients**		
	B	**Std. Error**	**Beta**	**t**	**p-value**
(Constant)	-12.07	13.31		0.91	0.46
Weight gain (gm)	0.008	0.003	0.87	2.42	0.14
length gain (cm)	-0.05	0.02	-0.19	2.35	0.14
height gain (cm)	1.15	0.32	0.81	3.56	0.07
Circumference gain (cm)	-0.05	0.04	-0.24	1.44	0.29
Heart (gm)	44.04	8.46	7.76	5.21	0.04
Lungs (gm)	-4.96	2.03	-5.23	2.45	0.13
Liver (gm)	-0.42	0.81	-0.67	0.51	0.66
Spleen (gm)	3.63	5.08	2.09	0.72	0.55
Pancreas (gm)	-22.03	9.64	-5.78	2.28	0.15
Kidneys (gm)	-13.58	7.05	-3.20	1.93	0.19
Brain (gm)	0.97	5.42	0.23	0.18	0.88
Relative Heart Weight	-60.76	11.31	-9.12	5.37	**0.03**
Relative Lung Weight	-5.97	1.03	-5.49	5.79	**0.03**
Relative Liver Weight	1.59	1.13	1.34	1.41	0.29

Relative Spleen Weight	-4.35	2.45	-1.66	1.78	0.22
Relative Pancreas Weight	25.82	13.43	3.21	1.92	0.19
Relative Kidney Weight	5.22	5.48	1.26	0.95	0.44
Relative Brain weight	14.27	5.85	5.87	2.44	0.14
Lung/Brain	13.42	2.50	9.18	5.37	**0.03**
Spleen/Brain	-4.09	9.11	-1.35	0.45	0.69
Kidney/Brain	13.53	14.59	1.97	0.93	0.45

a. Dependent Variable: LDL

Table 5a. Model Summary for Regression Analysis of the Dependent Variable

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0.999[a]	0.997	0.97	0.02

a. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 5b. ANOVA Summary for Regression Model Predicting Atherogenic Index of Plasma

Model		Sum of Squares	df	Mean Square	F	p-value
1	Regression	0.22	21	0.01	34.92	0.03[b]
	Residual	0.001	2	0.00		
	Total	0.22	23			

a. Dependent Variable: atherogenic index of plasma

b. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 5c. Regression Coefficients for Predictors of Atherogenic Index of Plasma

Model	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	p-value
(Constant)	-3.51	3.28		1.07	0.39
Weight gain (gm)	0.003	0.001	1.46	3.49	0.07
length gain (cm)	0.005	0.005	0.11	1.14	0.37
height gain (cm)	0.13	0.08	0.43	1.63	0.25
Circumference gain (cm)	-0.06	0.009	-1.33	6.88	0.02
Heart (gm)	12.83	2.09	10.65	6.15	0.03
Lungs (gm)	0.70	0.50	3.48	1.40	0.29
Liver (gm)	0.68	0.20	5.18	3.39	0.08
Spleen (gm)	8.40	1.25	22.83	6.70	0.02
Pancreas (gm)	-4.81	2.38	-5.95	2.02	0.18
Kidneys (gm)	-6.14	1.74	-6.83	3.53	0.07
Brain (gm)	-5.66	1.34	-6.19	4.23	0.05
Relative Heart Weight	-16.99	2.79	-12.01	6.09	0.03
Relative Lung Weight	-2.41	0.26	-10.45	9.48	0.01
Relative Liver Weight	-1.04	0.28	-4.12	3.73	0.07
Relative Spleen Weight	-0.63	0.60	-1.13	1.04	0.41
Relative Pancreas Weight	8.57	3.31	5.02	2.59	0.12
Relative Kidney Weight	0.26	1.35	0.30	0.19	0.86
Relative Brain weight	9.42	1.44	18.27	6.53	0.02
Lung/Brain	1.79	0.62	5.77	2.90	0.10
Spleen/Brain	-11.73	2.25	-18.16	5.22	0.04
Kidney/Brain	9.54	3.60	6.53	2.65	0.12

a. Dependent Variable: Atherogenic index of plasma

Table 6a. Model Summary for Multiple Regression Analysis of the Dependent Variable

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	1.000[a]	.999	.991	.02746

a. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 6b. ANOVA Summary for Regression Model Predicting CHOL/LDL Ratio

Model		Sum of Squares	Df	Mean Square	F	p-value
1	**Regression**	1.856	21	0.088	117.207	0.008[b]
	Residual	0.002	2	0.001		
	Total	1.857	23			

a. Dependent Variable: CHOL/LDL

b. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 6c. Multiple Linear Regression Coefficients for Predictors of CHOL/LDL Ratio

Model	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	p-value
(Constant)	-2.72	5.25		0.52	0.66
Weight gain (gm)	-0.003	0.001	-0.59	2.57	0.12
length gain (cm)	0.02	0.008	0.15	2.72	0.11
height gain (cm)	-0.07	0.13	-0.08	0.57	0.63
Circumference gain (cm)	-0.006	0.02	-0.04	0.39	0.73
Heart (gm)	-24.30	3.33	-6.89	7.29	0.02
Lungs (gm)	7.45	0.80	12.65	9.32	0.01
Liver (gm)	1.53	0.32	3.97	4.76	0.04
Spleen (gm)	8.54	2.00	7.94	4.27	0.05
Pancreas (gm)	25.31	3.80	10.70	6.66	0.02
Kidneys (gm)	-9.39	2.78	-3.57	3.38	0.08
Brain (gm)	-6.35	2.14	-2.38	2.97	0.09
Relative Heart Weight	33.86	4.46	8.18	7.59	0.02
Relative Lung Weight	-0.62	0.41	-0.91	1.51	0.27
Relative Liver Weight	-3.23	0.45	-4.38	7.26	0.02
Relative Spleen Weight	1.69	0.97	1.04	1.75	0.22
Relative Pancreas Weight	-27.30	5.30	-5.46	5.15	0.04
Relative Kidney Weight	-4.22	2.16	-1.64	1.96	0.19
Relative Brain weight	7.49	2.31	4.96	3.25	0.08
Lung/Brain	-9.23	0.99	-10.16	9.36	0.01
Spleen/Brain	-10.83	3.59	-5.73	3.01	0.09
Kidney/Brain	22.29	5.76	5.21	3.87	0.06

a. Dependent Variable: CHOL/LDL

Table 7a. Model Summary for Multiple Regression Analysis

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.997[a]	0.994	0.93	0.07

a. Predictors: (Constant), (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 7b. ANOVA Summary for Regression Model Predicting TG/HDL Ratio

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	1.403	21	.067	14.810	0.07
	Residual	.009	2	.005		
	Total	1.412	23			

a. Dependent Variable: TG/HDL

b. Predictors: (Constant), Kidney/Brain, lungs, height gain, Relative Liver weight, Pancreas, Spleen/Brain, circumference gain, heart, length gain, brain, Relative Kidney Weight, weight gain, Relative Spleen Weight, Relative Pancreas weight, Relative Lung weight, kidneys, Relative Heart weight, liver, Lung/Brain, Relative Brain weight, spleen

Table 7c. Multiple Linear Regression Coefficients for Predictors of TG/HDL Ratio

Model	**Unstandardized Coefficients**		**Standardized Coefficients**		
	B	**Std. Error**	**Beta**	**t**	**Sig.**
(Constant)	-2.119	12.845		0.165	0.88
Weight gain (gm)	.007	.003	1.474	2.296	0.15
length gain (cm)	.000	.019	.003	0.022	0.99
height gain (cm)	.282	.312	.365	0.904	0.46
Circumference gain (cm)	-.166	.036	-1.378	4.638	**0.04**
Heart (gm)	37.574	8.157	12.231	4.606	**0.04**
Lungs (gm)	.922	1.956	1.796	0.471	0.68
Liver (gm)	2.097	.785	6.234	2.670	0.12
Spleen (gm)	23.839	4.899	25.402	4.866	**0.04**
Pancreas (gm)	-18.430	9.303	-8.932	1.981	0.19
Kidneys (gm)	-13.811	6.799	-6.020	2.031	0.18
Brain (gm)	-16.605	5.227	-7.127	3.177	0.09
Relative Heart Weight	-50.145	10.914	-13.899	4.595	0.04

Relative Lung Weight	-6.286	.996	-10.664	6.313	0.02
Relative Liver Weight	-3.113	1.089	-4.843	2.859	0.10
Relative Spleen Weight	-1.042	2.363	-.735	0.441	0.70
Relative Pancreas Weight	30.163	12.961	6.921	2.327	0.15
Relative Kidney Weight	4.267	5.284	1.900	0.808	0.50
Relative Brain weight	22.520	5.645	17.106	3.989	0.06
Lung/Brain	5.988	2.411	7.561	2.483	0.13
Spleen/Brain	-34.762	8.790	-21.087	3.955	0.06
Kidney/Brain	17.207	14.080	4.615	1.222	0.35

a. Dependent Variable: TG/HDL

DISCUSSION

Early-life nutritional imbalance has profound effects on growth, organ structure, and metabolic regulation in experimental models. Evidence from Wistar rat studies shows that early or diet-induced overnutrition consistently promotes obesity, organ hypertrophy, vascular remodeling, and adverse cardiometabolic biomarkers. Postnatal overfeeding—often induced through litter-size reduction or high-fat and high-sucrose diets—leads to increased body weight and adiposity, accompanied by elevations in triglycerides, insulin levels, and blood pressure, as well as structural alterations in vascular tissues such as the aorta (Sánchez-García et al., 2018; Zhao, 2023). These findings support the view that excessive early nutrient exposure disrupts systemic metabolic regulation and contributes to organ-level remodeling.

Organ-specific effects are particularly evident in the liver, heart, and vascular system. Overnutrition has been associated with hepatic steatosis and progressive liver pathology, reflecting the close relationship between obesity and hepatic metabolic dysfunction (Araújo et al., 2024). Similarly, experimental studies demonstrate that postnatal overfeeding and maternal high-fat exposure can induce cardiac hypertrophy, interstitial fibrosis, and sex-dependent impairments in cardiac function in offspring (Ferreira et al., 2022; Cavalet et al., 2020). Vascular remodeling is also commonly observed, with structural and functional abnormalities in the aortic wall reflecting systemic metabolic disturbances associated with early overnutrition (Sánchez-García et al., 2018). At the molecular level, myocardial proteomic analyses reveal alterations in proteins involved in metabolism, antioxidant defense, and structural integrity in obese hearts, suggesting that subclinical cardiac remodeling may occur even before overt functional decline becomes evident (Vileigas et al., 2019).

In contrast, early undernutrition or caloric restriction typically produces growth restriction and reduced organ mass, but its metabolic consequences are less consistent. Perinatal hypocaloric exposure has been shown to reduce birth weight and produce persistent growth deficits in Wistar offspring (Araújo et al., 2024). However, severe caloric restriction during critical developmental periods can also induce adverse cardiac remodeling, including cardiomyocyte hypertrophy, fibrosis, and alterations in signaling pathways such as angiotensin receptor and ERK signaling (Cavalet et al., 2020). Moreover, restricted animals may exhibit increased vulnerability to metabolic dysfunction when later exposed to obesogenic diets, supporting the developmental programming hypothesis (Araújo et al., 2024).

Several studies further suggest that structural or molecular changes in specific organs may reflect broader metabolic disturbances. For example,

aortic morphology and function have been linked to systemic vascular and metabolic dysfunction following postnatal overfeeding (Sánchez-García et al., 2018). Similarly, hepatic steatosis frequently parallels elevations in triglycerides, insulin, and other metabolic syndrome markers, indicating that liver pathology mirrors systemic metabolic status (Araújo et al., 2024). Proteomic alterations in cardiac tissue during obesity progression further highlight how early organ-level molecular remodeling may serve as an early indicator of metabolic stress (Vileigas et al., 2019). Nevertheless, current evidence primarily demonstrates organ-specific associations rather than a unified morphometric framework capable of predicting metabolic outcomes across multiple organs. Consequently, further research integrating multi-organ morphometry with metabolic biomarkers is needed to clarify how developmental organ remodeling contributes to long-term cardiometabolic risk.

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