



## “Differences between small resistance arteries ( mesenteric and pancreatic) on vascular remodeling in protein restriction diet”.

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### Abstract

Protein malnutrition during early stages of development can result in cardiometabolic disorders in adulthood such as insulin resistance, diabetes, and hypertension. Vascular remodeling is a common feature of several cardiovascular diseases. The resistance arteries control the blood flow in different tissues, and are a blood pressure modulator. Vascular remodeling on small arteries by restricted- protein- diet might result in different modulation of regional vascular resistance and blood flow. However, whether or not a protein restriction diet in the early stages of development is associated with a remodeling of resistance arteries is still not known. In this context, the present study evaluate the morphology and structural parameters of resistance arteries from the mesenteric and pancreatic vascular beds of mice fed a post-weaning protein-restricted diet.

### Key words:

*Protein restriction, resistance arteries, vascular remodeling.*

### Introduction

Protein malnutrition during early life stages is an important risk factor for the development of cardiometabolic diseases such as hypertension and type 2 diabetes in adulthood. Vascular remodeling is a common feature of several cardiovascular diseases. In essential hypertension, peripheral resistance arteries present an increase of wall/lumen ratio. The inward hypertrophic remodeling contributes to increase peripheral vascular resistance and to raise blood pressure. However, whether or not a protein restriction diet in the early stages of development is associated with a remodeling of resistance arteries is still not known.

### Results and Discussion

**Objective:** To evaluate the morphology and structural parameters of resistance arteries from the mesenteric and pancreatic vascular beds of mice fed a post-weaning protein-restricted diet.

**Methods:** (Ethics Committee Approval # 4533-1) Male C57Bl/6J mice (28 day- old; n= 9-11 animals per group) were fed with a normal- (14% protein, NP) or a low-protein (6% protein, LP) diet for 90 days. Small mesenteric and pancreatic arteries (internal diameter < 300µm) were isolated and frozen (-80°C) in tissue-tek OCT. Transverse 10 µm thick slices were obtained in a cryostat and then stained with hematoxylin and eosin. Images were obtained with a microscope (DFC300FX) coupled to a camera. Morphometrical analysis was performed using Image J software to obtain the vessel internal and external perimeter and area. Then, internal and external radii (Ri and Re) were calculated according to the formula  $perimeter = 2 \cdot \pi \cdot R$ ; internal diameter (ID) was obtained by  $2 \cdot R_i$ ; wall thickness as  $Re - R_i$ ; and the media cross-sectional area (CSA) as  $\pi (R_e^2 - R_i^2)$ . Statistical analysis: One-way ANOVA, followed by the Newman-Keuls test (\*P<0.05).

**Results:** In resistance mesenteric arteries, there was an increase in ID and in internal and external perimeter and area, while CSA and wall thickness did not significantly change in RP group compared with NP group. The wall thickness/ID ratio was decreased by low-protein diet in mesenteric arteries (NP=0.206 ± 0.02 vs. RP=0.137 ± 0.01\*). In contrast to mesenteric arteries, resistance pancreatic arteries exhibited a reduction in ID and in internal and external perimeter and area in RP group compared with NP group. In addition, wall thickness (NP=12.3 ± 0.55 vs. RP=17.3 ± 1.91\* µm) and the wall thickness/ID ratio (NP=0.141 ± 0.01 vs. RP=0.234 ± 0.02\*) were both significantly increased by low-protein diet in pancreatic resistance arteries.

### Conclusions

In conclusion, the data suggest that post-weaning protein-restricted diet differently affect structure and morphology of mouse small vessels. While induced an outward eutrophic remodeling of mesenteric arteries, protein restriction induced an inward hypertrophic remodeling in pancreatic arteries. Therefore, protein restriction might result in different modulation of regional vascular resistance and blood flow.

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