A Novel Physiological Application of an Extracorporeal Circulation System: Hepatic Arterial Circulation during Hypothermia

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Abstract — The liver is essential to life, not only due to its complex functions, but also due its vital role as the blood volume reservoir. A large body of experimental data point to the relationship between arterial pressure and hepatic arterial blood flow. However, there is still some disagreement on the subject. The present study aimed to evaluate the regulation of the hepatic artery vasculature, under an extreme physiological condition, hypothermia. Our findings show a general decrease of flow, pressure and resistance, as a physiological adaptation to hypothermia.

Keywords: Hypothermia, Liver, Melrose Apparatus, Hepatic Circulation, Physiological Adaptation

I. INTRODUCTION

The interest in the liver dates back to the ancient times of medicine, not only due to its complex functions in biosynthesis, metabolism and clearance, but also due to its unique dual blood supply from the portal vein and the hepatic artery. Indeed, the liver has the most complex circulation of any organ [5]. To distinguish the individual importance of each of these inflows in normal and extreme physiological states is still a challenging task. A few studies showed that dogs were able to survive severe hepatic ischemia for one hour, whilst under induced hypothermia [1]. Hence we intended to evaluate the ability of hypothermia to affect multiple hepatic processes. Particularly, how the hepatic artery, which supplies the liver with arterial blood in a high pressure/high resistance system, adapts to such conditions.

II. METHODS

All the experimental procedures were approved by the Institutional Animal Care and Ethics Committee of the Faculty of Medicine of University of Lisbon and carried out according to the Portuguese and European laws on animal welfare. All experiments were conducted by physiologists licensed to perform animal surgery, in the Cardiovascular Autonomic Function Laboratory, Lisbon.

A. Animals

Eight healthy dogs of both genders (weights 17,2 ± 7 Kg; means ± SD) were anesthetized with sodium pentobarbitone (0.5 cc/Kg; IP), and supplemented as necessary with an IV 20% solution of the same drug. The animals were divided in two separate groups, according to the following methodology.

B. Ice Immersion

The anesthetized animals (n=3) were laid down on a bath tin and covered with small ice blocks. Rectal temperature was measured every minute and hypothermia considered when body temperature reached 24ºC.

C. Melrose Apparatus

In this second group (n=5), a median laparotomy was preformed, and two plastic catheters were inserted in the abdominal aorta, which had previously been tied up, immediately below the renal arteries, with two surgical insertions, one upstream and one downstream. The tubes were consequently connected to the Melrose refrigeration module (NEP-Series No. 585/103 type nº 919), and replenished with saline solution (120 cc). Before insertion of the catheters, the animals were heparinized with a dose of 1ml (5000 UI of Heparine Chouay). Rectal temperature was measured every minute, and hypothermia reached at 24ºC.

D. Hemodynamic Variables

In the present study we evaluated three variables as follows:

- Hepatic Arterial Inflow (ml/min): Inflow was measured with an electromagnetic flow meter (Nihon Kodhen).
- Hepatic Artery Pressure (mmHg): A catheter probe was inserted through the gastroduodenal artery, until it reached the hepatic artery, and connected to a pressure transducer (Statham P23 AA), and the signal registered by a polygraph (Polígrafo RM – 150; Nihon Kodhen).
- Hepatic Arterial Resistance (cm^{-5}/seg): Resistance was calculated according to the Poiseuille Law.

$$\text{Resistance} = \frac{\text{Pma} \times 1332}{\text{Deb/Sec}} \quad (1)$$

E. Statistics

Statistical analysis was made using Student's unpaired t-test and differences were considered significant where P <

0.05 (GraphPad Software Inc.). All variables are expressed as mean +/- standard deviation.

III. RESULTS

Besides the factor "time to induce hypothermia", which was significantly faster with the Melrose system than with ice immersion, with a $p<0.0001$, favorably to our expectations, there were no significant changes in the different hemodynamic variables considered. Indeed, the final results were extremely similar. As such, we present our findings as a whole.

A. Hepatic Arterial Inflow

During hypothermia (from 37ºC to 24ºC), our results show an accentuated decrease in hepatic arterial inflow (fig. 1). Flow values varied from an average of 96.6±29.8 ml/min before hypothermia, to 65±17.6 ml/min at the end of the experiments ($p<0.0005$).

B. Hepatic Arterial Pressure

Alongside the results for inflow, hepatic pressure decreases as a physiological adaptation to hypothermia. Our present findings, determined an extremely significant decrease of 62% in pressure values, during the experiments (figure 2).

C. Hepatic Arterial Resistance

Finally, as showed in figure 3, the hepatic arterial resistance has also significantly decreased, with a $p<0.0025$, during the induction of hypothermia (from 79.708±23.966 to 47.103±33.378 cm^{-5}/seg).

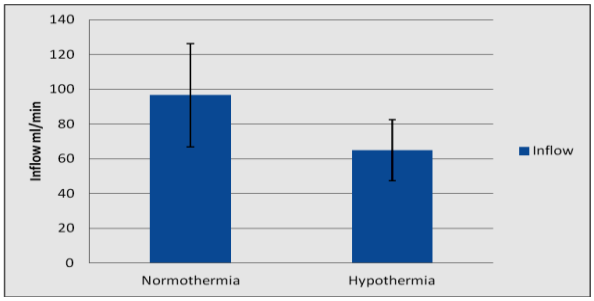

Fig. 1. Hepatic Arterial Inflow. Differences of inflow (ml/min) between normothermia (37ºC) and hypothermia (24ºC); mean ± SD

IV. CONCLUSION

In conclusion, the liver seems to protect itself from severe hypothermia, by adapting its vascular bed, in particular the hepatic artery vasculature, to the new extreme physiological condition.

All hemodynamic variables considered, decreased consistently and proportionally throughout the experiments, regardless of the methodology applied to induce hypothermia (ice immersion vs. Melrose system). These adaptations, may be related to the general decrease in cardiac output in response to hypothermia, as previously suggested [3; 4].

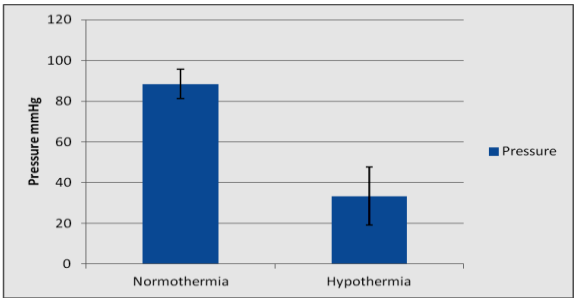

Fig. 2. Hepatic Arterial Pressure. Differences of pressure (mmHg) between normothermia (37ºC) and hypothermia (24ºC); mean ± SD

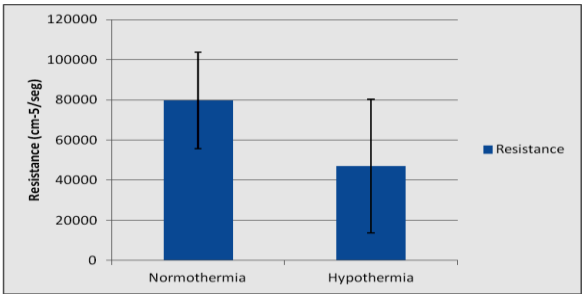

Fig. 3. Hepatic Arterial Resistance. Differences of resistance (cm^{-5}/seg) between normothermia and hypothermia (24ºC); mean ± SD

However, for a better and more sustained understanding underlying the different hepatic adaptations to hypothermia, further investigations should be carried out. From the present results, one can also confirm the application of the Melrose apparatus, for physiological studies during hypothermia.

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