Abstract #96 | Poster

Assessment of porcine liver metabolism after alanine infusion using hyperpolarized [1-^{13}C]pyruvate MRI

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Introduction

In the fasted state, amino acids (e.g. alanine and glutamate) serve as precursors for the synthesis of glucose in the liver through gluconeogenesis, which is tightly regulated by hormones and substrate availability[1]. Hyperpolarized (HP) MRI can quantify metabolic fluxes of pyruvate to its metabolites, lactate, alanine and bicarbonate. Liver injury, fibrosis and hepatic gluconeogenesis can be assessed by HP MRI in animal models[2,3]. Here we investigate if HP MRI can be used to assess metabolic liver function following an alanine infusion with a clinical setup in a large animal model.

Methods

To increase hepatic gluconeogenesis, cold alanine[4] (1.48 mmol/ml) was infused intravenously into pigs (30 kg, n=3) for an hour. The first 15 min was at a rate of 8 ml/min and hereafter for 2 ml/min. T1 proton imaging was obtained in the oblique plane consisting of 5-6 slices to ensure full coverage over the liver, these images were used for the slice selection for the subsequent ^{13}C imaging. Injection of hyperpolarized [1-^{13}C]pyruvate was done before and after alanine infusion. In the liver, signal to noise ratio (SNR) for pyruvate and lactate was calculated for each slice and the three slices yielding the highest SNR (for pyruvate) for each animal was chosen for calculation of ratio maps. Ratios in the liver was calculated as AUC for metabolites over AUC pyruvate.

Results/Discussion

HP MRI images are shown in Figure 1. Alanine infusion resulted in an increase of the raw signal in the liver of pyruvate, lactate and alanine (Figure 2, C-E) and was significant for alanine (P=0.005). The tendency of increase in the raw signals is supported by the simultaneous increase of lactate to pyruvate and pyruvate to alanine (Figure 2, A-B), however not significantly (P=0.071 and P=0.124, respectively). These results suggest that changes in hepatic gluconeogenesis indirectly can be assessed by hyperpolarized [1-^{13}C] pyruvate MRI. These findings are obviously limited by the small sample size in healthy and anesthetized animals. Even though hyperpolarization increases the signal of [1-^{13}C]pyruvate the method is still SNR limited. The tendency we present here needs to be followed up by future studies with respect to sample size but also optimization of SNR. It would be interesting to assess gluconeogenesis in models of hepatic impairment with HP MRI.

Conclusions

Using hyperpolarized [1-^{13}C] pyruvate MRI, the raw signal of alanine in the liver increased with a similar trend found for lactate, consistent with increased hepatic gluconeogenesis following intravenously infusion of alanine. The findings of increased hepatic metabolism in this study shows the potential and feasibility of HP liver MRI that are easily transferable to human trials in a clinical setup.

Acknowledgement

Disclosure

I or one of my co-authors have **no financial interest** or **relationship** to disclose regarding the subject matter of this presentation.

Affix

References

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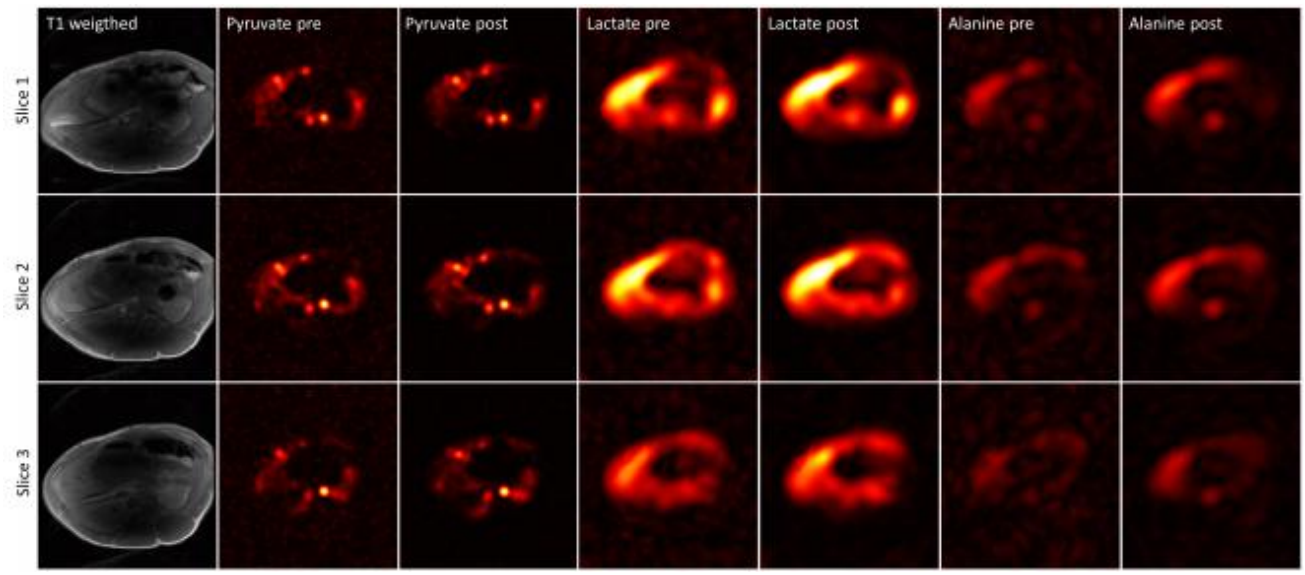

Figure 1
Proton and HP MRI images showing three slices of one animal. Raw intensity maps summed over the whole acquisition time = 60 s, for pyruvate, lactate and alanine. Lactate and alanine images are scaled 10 times to their respective pyruvate images.

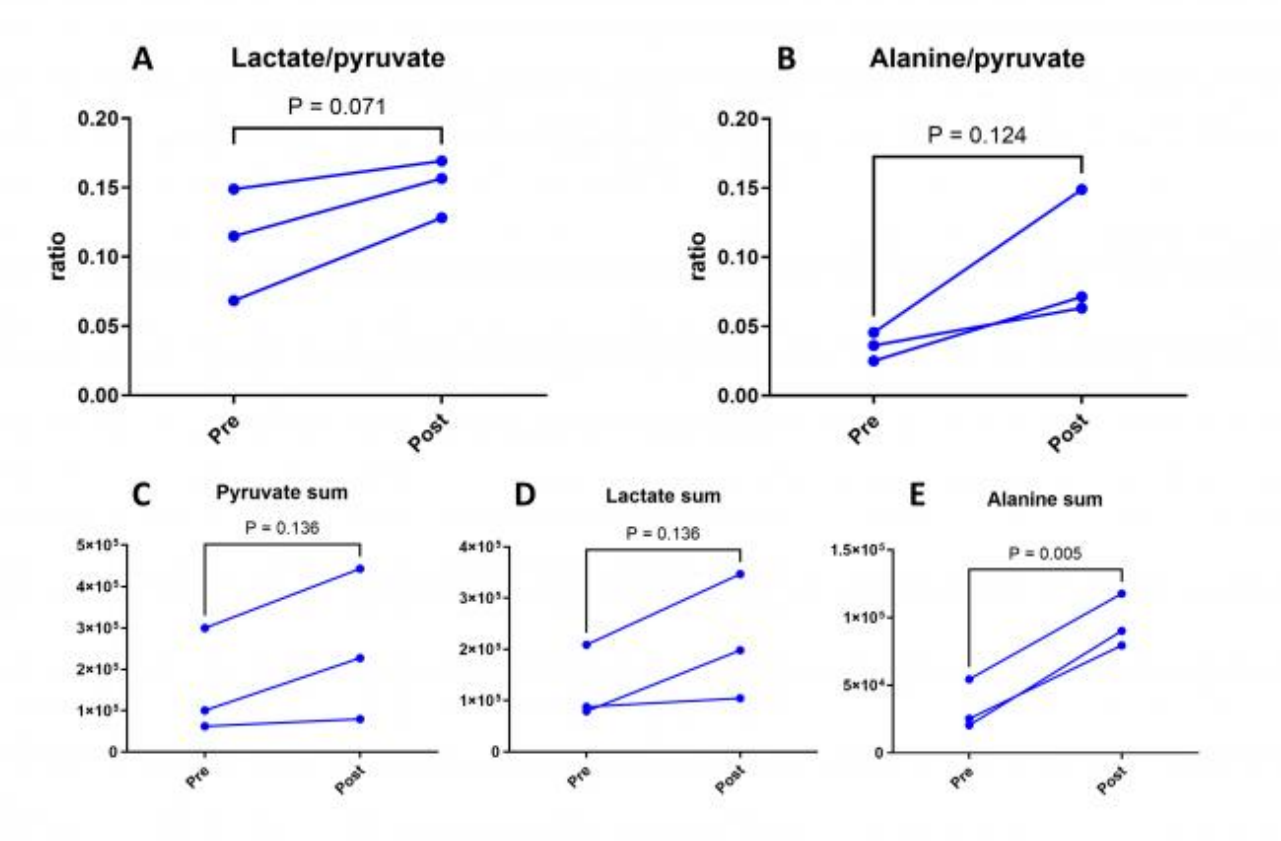

Figure 2

Hyperpolarized measurements (A) lactate to pyruvate ratio (P = 0.071) and (B) alanine to pyruvate ratio (P = 0.124) following alanine infusion. Raw signal summed of pyruvate, lactate and alanine (C-E), respectively. Tested with paired t-test. Sample size N = 3. Data presented as individual means.