

# Plasma Citrulline level during and following critical illness

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## Background:

Citrulline (Cit) has been suggested as a biomarker for intestinal absorption function, also during critical illness, because of its unique metabolism. Citrulline mainly comes from conversion of glutamine via glutamate, glutamate semi-aldehyde, and ornithine in the enterocytes. However, little information on actual citrulline levels during critical illness is available.

## The aims/research questions of the project were:

1. To measure Cit levels at ICU admission in relation to controls
2. Does Cit change during ICU stay?
3. Does Cit change after ICU stay?
4. Does liver failure affect Cit levels?

## Methods:

Four studies previously performed at Karolinska University Hospital Huddinge have been selected for this project. These studies enrolled around 420 ICU patients with different inclusion criteria. At the time of studies, the routine in the unit was early full feeding, usually started within 48 h with a combination of enteral and parenteral nutrition. Blood samples in study 1 were taken within 24h after ICU admittance. In study 2, the initial sample was taken within 24 h of ICU admission, then daily for 5 days. In study 3 the initial sample was taken last 24 h at the ICU and then followed by every 5-7 days after ICU discharge until hospital discharge. In study 4, patients with, chronic liver failure, acute on chronic liver failure, acute liver failure and patients after liver resection were studied.

Samples were previously analyzed for all amino acids by HPLC. Citrulline level from these four studies were compared to controls (healthy volunteers included in different studies between 2000-2012 n=40) and in relation to glutamine (Gln) and arginine (Arg) level from same amino acid analysis. The results were analyzed statistically using Student's t-test, ANOVA, and regression analyses (Excel + Statistica).

## Result:

Plasma Cit level are significantly lower at ICU admission in comparison to healthy volunteers but do not change during and after ICU stay (Fig 1). Several patients (both during and after ICU stay) had Cit levels lower than the control range and in general they stayed low (Fig 1). Patients with liver failure (either acute or chronic) have significantly higher Cit levels, whereas liver resection had no effect (Fig 1). Cit levels correlated positively to Arg and Gln levels (Fig 2 and 3) which is most likely reflecting the metabolism of Cit. No relation to mortality (studies 1 and 3) and Child-Pugh Score (study 4) were observed, but a weak correlation to MELD (study 4) was observed ( $R^2=0.01016$ ,  $P<0.05$ ).

## Conclusion:

Citrulline levels are low at ICU admission and in a subgroup of patients during and after ICU stay. Liver failure increases citrulline levels. The clinical significance of these differences and the possible relation to intestinal function and/or enteral nutrition of these findings needs to be investigated in directly designed studies.

