

Recent haemodialysis induces fasting state during haemodialysis in patients with diabetes mellitus

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OBJECTIVES

<Backgrounds> Haemodialysis (HD) offers a unique means of altering plasma metabolites in an HD patient in the span of a few hours. Wathen *et al.* reported¹⁾ 40 years ago that glucose-free dialysis caused a fasting state, unlike glucose dialysis. It showed a marked decrease in blood levels of glucose, lactate and pyruvate along with profound increases in 3-hydroxybutyrate (3-HB). However, little has been investigated on the metabolic responses in HD patients to recent HD, in Japan. The recent HD uses glucose dialysate and high-performance membrane which removes not only small uremic toxins but also larger molecules, e.g. insulin, vitamins, hormones etc. In such situation, patients with diabetes mellitus (DM) having metabolic disorder are conceived to have special and unstable responses.
 <Aim> The aim was to investigate the metabolic responses to recent HD in DM patients compared with non-DM patients.

METHODS

<HD patients>	n	Age	HD duration y	HbA _{1c} (NSGP)	Kt/V	dialysate Ac /Cit	dialysate glucose mg/dl	membrane type IV / V	intra HD meal insulin
DM	9	74	8 (4 - 13)	5.8	1.7	6 / 3	150	8 / 1	no no
non-DM	9	65	21 (4 - 31)	-	1.7	4 / 5		9 / 0	n2/y7 no

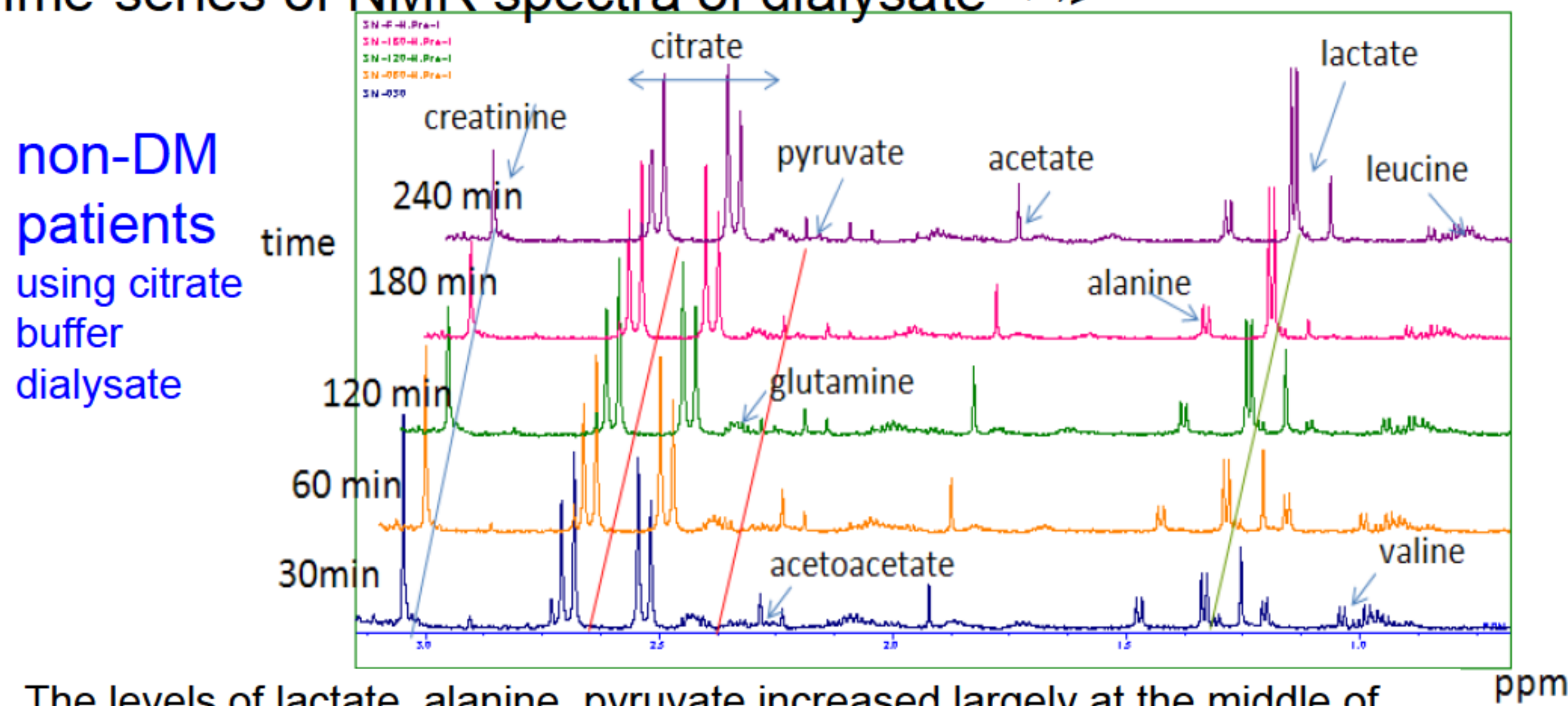
The flow rates of blood and dialysate were 200 and 500 mL/min, respectively. Written informed consent was obtained from the patients.

<Time-course measurements of metabolites>

Spent dialysate samples were collected at 6 points; at 15, 30 min, 1, 2, 3, and 4 h from the initiation of HD for each patient in 5 HD sessions during 4 hrs, and measured by proton magnetic resonance (¹H NMR) spectroscopy (600 MHz, ECA, JEOL Ltd.). The concentrations of main metabolites in plasma were determined on the NMR spectra of dialysate⁴⁾.

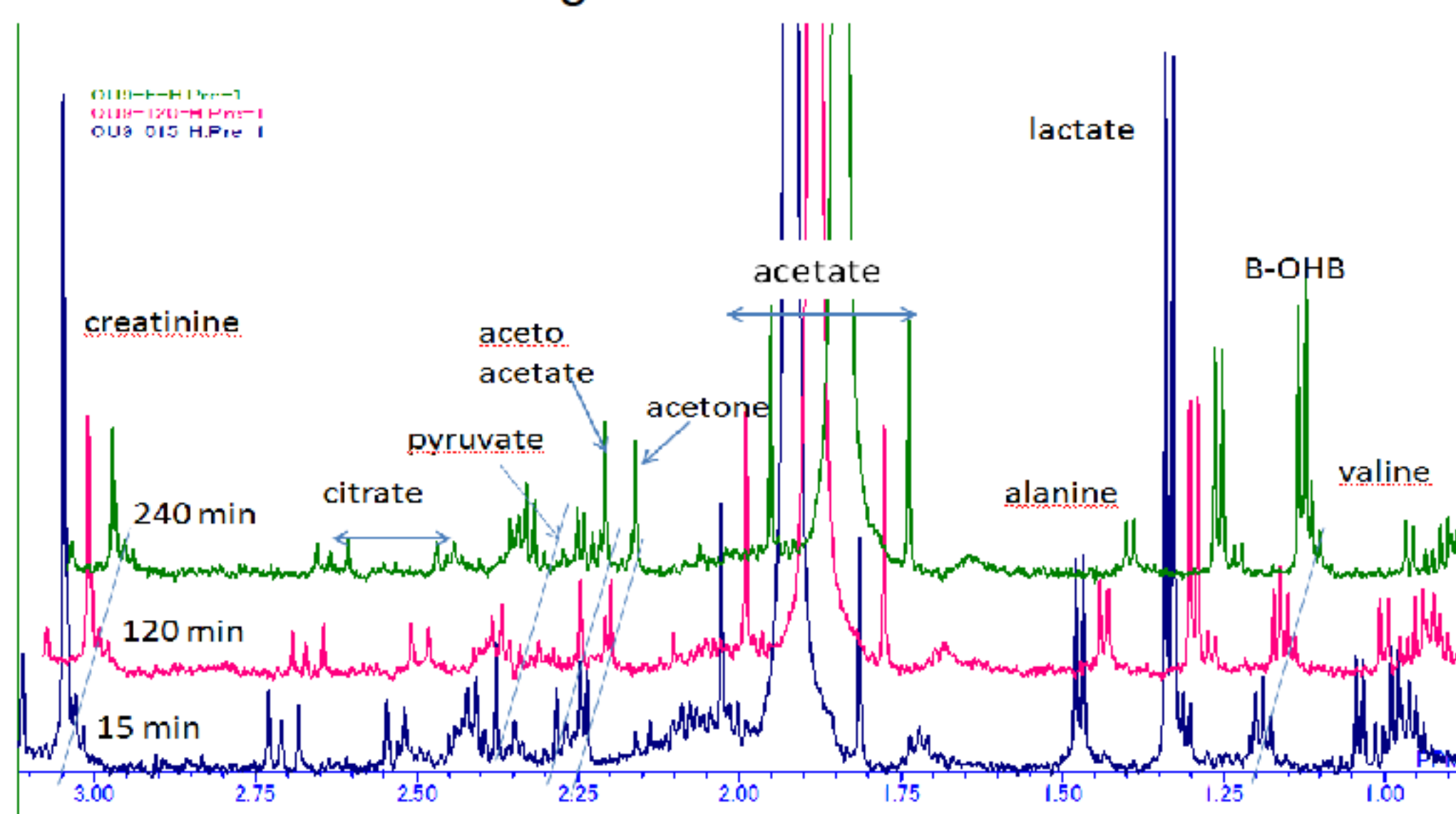
RESULTS

< Time-series of NMR spectra of dialysate ^{2,4)}>



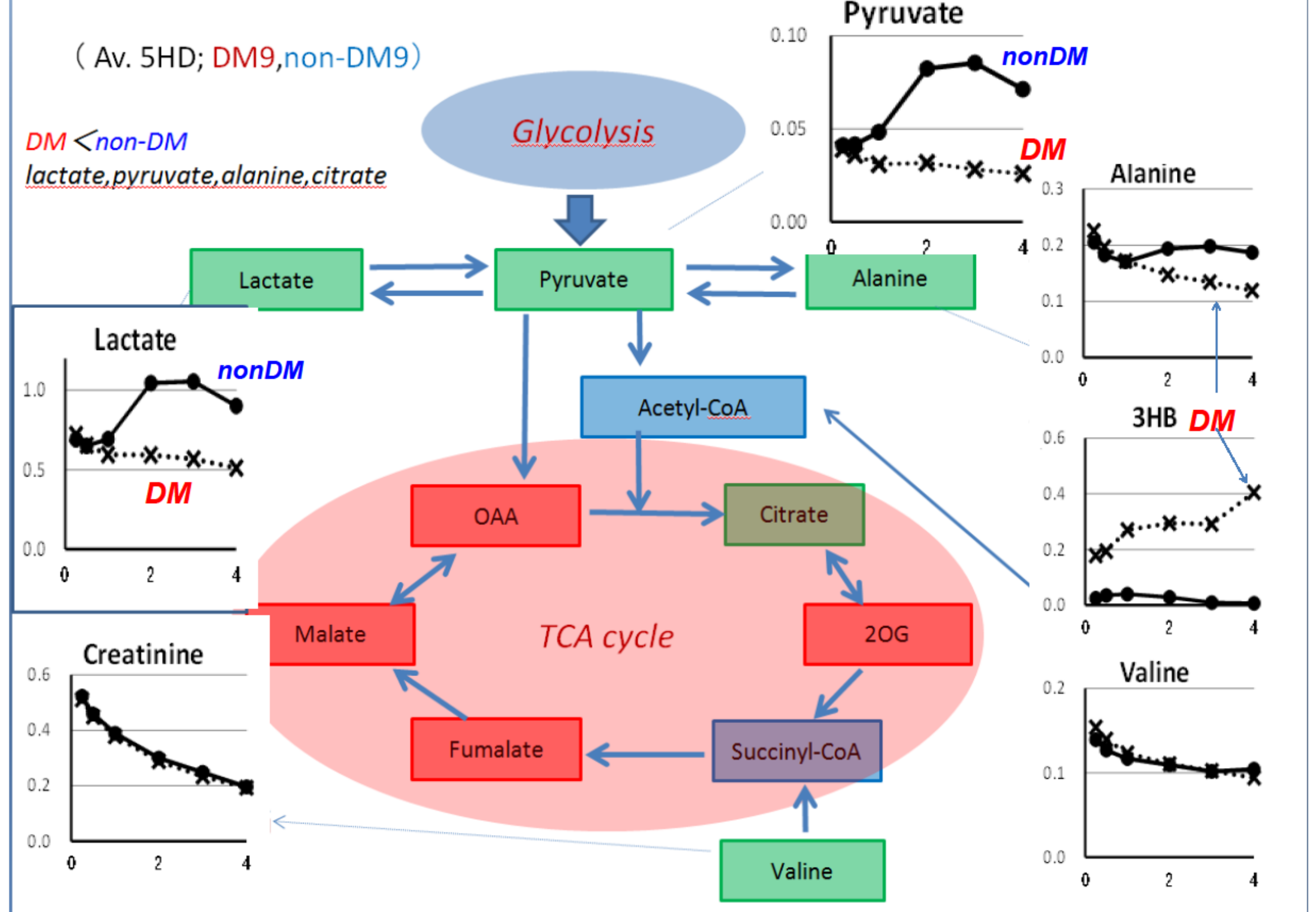
The levels of lactate, alanine, pyruvate increased largely at the middle of HD-sessions. The increments indicated enhanced appearances from the body, which overcame continuous filtering from blood²⁾.

DM patients using acetate buffer dialysate



The levels of lactate, alanine, pyruvate decreased along with creatinine during HD. B-OHB (3HB), acetoacetate, and acetone increased toward the end of HD.

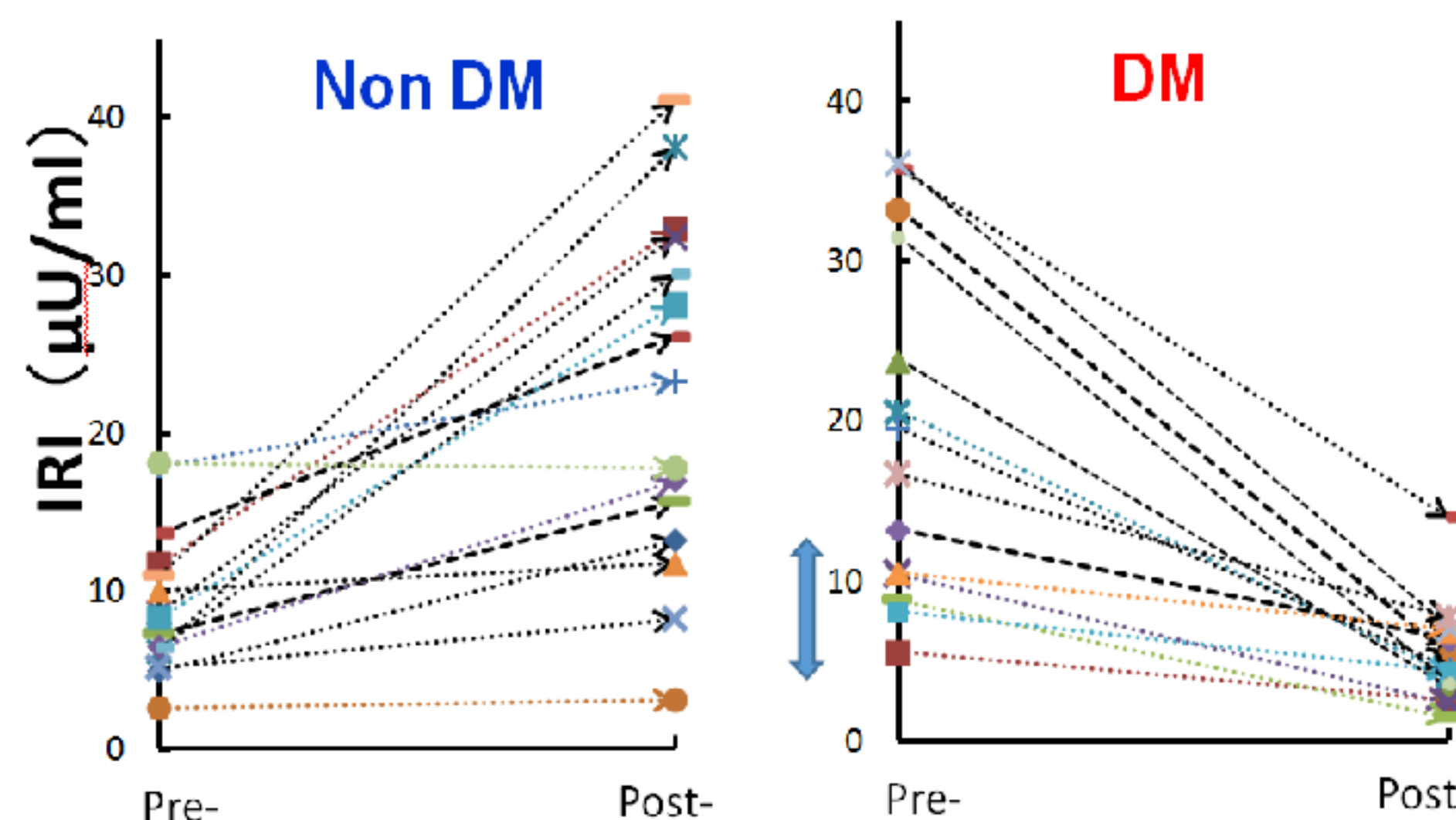
<Time course of change in metabolites conc. during HD>



- In DM patients, the levels of lactate, alanine, pyruvate exhibited no increment during HD but decreased monotonously.
- At the latter time of HD, the levels of 3-HB in DM patients often increased beyond the standard value, and simultaneously levels of lactate, pyruvate and alanine decreased remarkably.
- DM patients exhibited **hypolactatemia and hyperketonemia** during HD. The phenomena was not dependent on whether the dialysates contained acetate or not.
- **The metabolic status in DM patients was found to be fasting even when plasma glucose levels were rather high during HD.** This was different from the previous work¹⁾.
- We did not observe these fasting states in non-DM patients.

Plasma Insulin at pre- and post-HD

Non-DM patients produced insulin under the stimuli of 150 mg/dl dialysate glucose, and its production overcame the removal of HD.



DM patients had little secretion and their insulin levels in plasma dropped sharply.

The behaviors of insulin caused the differences of metabolic responses between DM and non-DM.

CONCLUSIONS

• We found that DM patients exhibited **hypolactatemia and hyperketonemia** during HD. This is the first observation of a fasting state in DM patients even with sufficient glucose supply to the blood during HD.

The **hypolactatemia** suggested their glycolysis may be profoundly impaired. The low level of pyruvate may lead the Krebs cycle to be impaired as well. The **hyperketonemia** indicated fatty-acid oxidation acceleration.

• DM patients with a metabolic disorder barely make use of glucose in dialysate during HD, which induces serious conditions such as fasting states. It was suggested that the quotidian conditions caused further protein catabolism.

• High-performance membrane has removed larger molecules than ever, not only β-2MG but also insulin. DM patients cannot compensate the removal during HD. Additional intra-HD therapy could be proposed e.g. insulin treatment and food intake for DM patients so as to avoid fasting state. •

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