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The influence of continuous venovenous renal replacement therapy on the plasma disappearance rate of indocyanine green

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Dear Editor,

In critically ill patients, the plasma disappearance rate of indocyanine green (ICG-PDR) is used to assess dynamic liver function. Serum ICG concentrations can be monitored with a transcutaneous device (LiMON, Pulsion Medical Systems, Munich, Germany) [1]. No conclusive data exist on the potential influence of renal replacement therapy (RRT) on the reliability of ICG-PDR measurements. Therefore, we prospectively studied 10 adult medical ICU patients [60 ± 20 years, APACHE II score 32 (25; 41)] comparing ICG-PDR with and without RRT.[1] All patients were mechanically ventilated, required continuous venovenous hemofiltration (CVVH), and received hemodynamic monitoring using transpulmonary thermodilution (TPTD) by a PiCCO system (PiCCO, Pulsion Medical Systems, Munich, Germany). Reasons for admission were septic shock ($n = 6$), acute on chronic liver failure ($n = 3$), and acute severe pancreatitis ($n = 1$). The study was approved by the institutional review board. Written informed consent was obtained. On day 1 of the study, two ICG-PDR measurements were done consecutively during CVVH followed by two measurements while CVVH was in recirculation. On day 2, this procedure was repeated in reverse order: two measurements with CVVH in recirculation were followed by two measurements during CVVH. Each ICG-PDR measurement was combined with a preceding TPTD measurement. mRRT(+) was defined as the mean of all four ICG-PDR measurements during RRT and mRRT(−) as the mean of all four measurements with CVVH in recirculation. mRRT(+) was 9.3 (7.4; 13.7) %/min and mRRT(−) was 10.5 (6.4; 15.6) %/min. RRT did not significantly influence ICG-PDR (mean

Table 1 Hemodynamic and respiratory parameters, mechanical ventilation, RRT settings, and liver biochemistry

	Day 1		Day 2		*p*
	RRT on	RRT off	RRT off	RRT on	
Hemodynamics					
MAP (mmHg)	80 ± 12	81 ± 13	80 ± 10	80 ± 13	0.98
Heart rate (bpm)	87 ± 18	88 ± 17	81 ± 21	83 ± 18	0.33
Cardiac index (l/min/m^2)	3.6 (2.8;3.8)	3.6 (3.1;4.6)	3.9 (3.1;4.2)	3.3 (2.4;4.4)	0.42
GEDVI (ml/m^2)	730 (702;789)	719 (647;845)	720 (682;867)	729 (685;874)	0.51
Norepinephrine (μg/kg/min)	0.3 (0;2.38)	0.3 (0;2.38)	0 (0;0.7)	0 (0;0.7)	0.08
Lactate (mmol/l)	1.6 (1.1;2.4)		1.9 (1.1;2.7)		0.19
Respiratory and ventilator parameters					
FIO_2 (%)	50 ± 11	50 ± 12	42 ± 9	40 ± 9	0.01
Tidal volume (ml)	533 (445;568)	571 (522;709)	535 (445;668)	536 (457;661)	0.5
Respiratory rate (#/min)	20 (14;24)	16 (12;20)	19 (15;20)	17 (12;20)	0.45
PEEP (cm H_2O)	10 (7;13)	10 (7;13)	8 (6;12)	8 (6;12)	0.09
pO_2 (mmHg)	102 (87;117)		94 (89;95)		0.19
pCO_2 (mmHg)	39 (35;46)		38 (37;45)		0.06
pH	7.35 (7.32;7.41)		7.43 (7.36;7.46)		0.06
RRT parameters					
Blood flow (l/min)	177 ± 20	–	–	178 ± 21	0.99
Substitution (l/h)	1,905 ± 287	–	–	1,925 ± 301	0.99
Ultrafiltration (ml/h)	74 ± 76	–	–	109 ± 83	0.09
Liver biochemistry					
ALT (U/l)	49 (17;186)		43 (19;179)		0.28
AST (U/l)	81 (35;144)		73 (32;117)		0.23
Alkaline phosphatase (U/l)	365 (170;565)		410 (188;587)		0.51
Gamma-GT (U/l)	90 (29;137)		84 (27;145)		0.54
Albumin (g/l)	31 (27;35)		30 (28;35)		0.56
Bilirubin (mg/dl)	2.9 (0.86;3.6)		2.58 (0.88;3.10)		0.99
INR	1.4 (1.1;2.0)		1.3 (1.1;1.7)		0.25
ICG-PDR					
ICG-PDR (%/min)	10.2 ± 5.4	11.2 ± 6.5	11.8 ± 8.0	10.9 ± 5.5	0.29

Data are reported as mean ± standard deviation or median with interquartile range, as appropriate. *p* value was calculated for the differences between different time points in hemodynamic, respiratory, ventilator-related, RRT-related parameters, and liver biochemistry using one-way repeated measures ANOVA. $p < 0.05$ was considered significant *RRT* renal replacement therapy, *MAP* mean arterial pressure, *GEDVI* global end-diastolic volume index, *ALT* alanine transaminase, *AST* aspartate transaminase, *INR* international normalized ratio, *ICG-PDR* plasma disappearance rate of indocyanine green

[1] Data are reported as mean ± standard deviation or median with interquartile range, as appropriate.

difference between mRRT(+) and mRRT(−) is −1.1 %/min, Wilcoxon $p = 0.07$). If anything, ICG-PDR has the non-significant tendency to decrease with RRT, which is counterintuitive: if RRT eliminated ICG, an increase in ICG-PDR would be expected. With the obtained difference in ICG-PDR with/without RRT, inclusion of ten patients enables one to detect a potential 1.7 %/min ICG-PDR difference with a power of 80 % on a significance level of 5 %. This corresponds fairly well to what should be considered as clinically significant. ICG-PDR is sensitive to changes in hemodynamic or respiratory conditions as well as to changes in liver function [1]. Theoretically, an increase in ICG-PDR by RRT might be neutralized by a decreased cardiac index (CI), an increased level of PEEP, or by deteriorating hepatocellular function. Therefore it is important that global hemodynamics, respiratory- and ventilator-related parameters, and liver biochemistry remained unchanged during the entire study. Also, RRT blood flow, RRT substitution, and ultrafiltration rates remained unchanged (Table 1).

In conclusion, these results show that continuous RRT has no influence on ICG-PDR measurements in critically ill patients. Therefore, continuous RRT does not need to be interrupted for reliable ICG-PDR measurements. Owing to the heterogeneity of our study population and the broad range in CI, RRT blood flows, and ICG-PDR, our conclusions are valid for patients with different extracorporeal blood flow rates and for patients with a broad range of ICG-PDR.

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Reference

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