Greater Severity of Organ Failure Modifies the Effect of CVVH Intensity on Survival in AKI Patients

Kuo-Hua Lee[1], Shuo-Ming Ou[1], Wei-Cheng Tseng[1], Chih-Yu Yang[1], Yao-Ping Lin[1], Yung-Chang Chen[2], Vincent Wu[3], Chih-Jen Wu[4], Jin-Bor Chen[5], Ji-Tseng Fang[6] and Der-Cherng Tarng[1] for Consortium for Acute Kidney Injury and Renal Diseases (CAKs) group

1. Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan
2. Department of Medicine, Chang Gung Memorial Hospital, Keelung, Taipei, Taiwan
3. Division of Nephrology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan
4. Division of Nephrology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan
5. Division of Nephrology, Department of Internal Medicine, Chang Gung Memorial Hospital, Kaohsiung, Taiwan
6. Division of Nephrology, Department of Internal Medicine, Chang Gung Memorial Hospital, Linkou, Taiwan

Purpose of the study

Although practice guidelines suggested continuous venous venous hemofiltration (CVVH) intensity over 25ml/kg/hr had no treatment benefits for acute kidney injury (AKI), there's little evidence indicating if the conclusion applicable to critical patients with higher severity of illness or multiple organ failure. This study aimed to clarify whether special circumstances would modify the relationship between CVVH intensity and survival outcome.

Material and Methods

We conducted a multicenter retrospective cohort study in Taiwan. AKI patients treated with CVVH since October 2014 to July 2015 were enrolled. The patients were divided into standard (n=102) and higher CVVH intensity group (n=164) by the cut-off level of 25 ml/kg/hr, according to the average effluent rate during the first 3 days. The clinical endpoint was in-hospital mortality. We performed cox regression analysis to identify the independent risk factors for death. In subgroup analysis, survival curves were used to show the possible modifying effect on mortality between the two intensity groups.

Results

Demographic and clinical characteristics between the two intensity groups were similar, except a higher percentage of hypertension and a higher body mass index in the standard group (Table 1 & 2). At the initiation of CVVH, hemoglobin level < 10g/dl and Sequential Organ Failure Assessment (SOFA) score ≥15 were independently associated with increasing risk of mortality (Table 3). Further subgroup analysis with SOFA score ≥15 showed higher CVVH intensity was associated with decreased in-hospital mortality compared to the standard intensity (Shown in Figure; P = 0.005 with adjusted HR 0.54, 95% CI: 0.36-0.79).

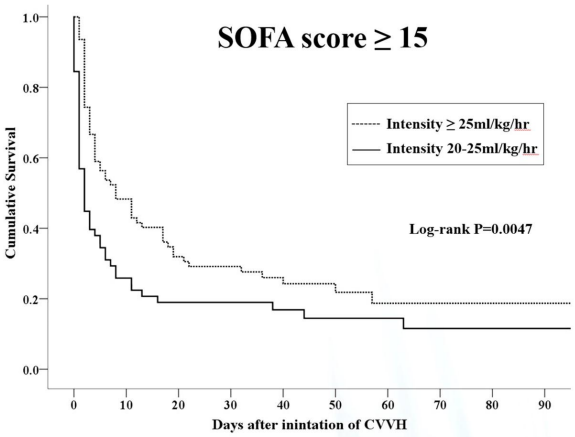
Conclusion

Higher than recommended CVVH intensity may reduce mortality in AKI patients with high degree of organ failures in SOFA score.

Table 1. Demographic data of the enrollments

Characteristics	All participants (n=266)	Higher intensity (n=164)	Standard intensity (n=102)	P value
Age (years)	66.78±15.01	65.97±15.52	68.09±14.12	0.264
Male, n (%)	178 (66.9)	113 (68.9)	65 (63.7)	0.383
Body mass index (kg/m^2)	24.46±4.66	23.66±4.58	25.83±4.50	<0.001*
Baseline eGFR by MDRD (mL/min/1.73 m^2)	61.10±46.08	63.02±38.41	57.96±56.47	0.431
Coexisting disease				
Diabetes mellitus, n (%)	121 (45.7)	71 (43.3)	50 (49.5)	0.324
Hypertension, n (%)	147 (55.5)	81 (49.4)	66 (64.7)	0.011*
Liver cirrhosis, n (%)	37 (14.0)	24 (14.6)	13 (12.8)	0.688
Congestive heart failure, n (%)	73 (27.6)	45 (27.4)	28 (27.5)	0.960
Chronic kidney disease, n (%)	61 (23.0)	35 (21.3)	26 (25.7)	0.409
Primary service				0.248
Medical, n (%)	190 (71.4)	113 (68.9)	77 (75.5)	
Surgical, n (%)	76 (28.6)	51 (31.1)	25 (24.5)	
Cause of acute kidney injury				
Shock, n (%)	231 (87.5)	141 (86.0)	90 (90.0)	0.338
Sepsis, n (%)	190 (72.0)	117 (71.3)	73 (73.0)	0.771
Nephrotoxins, n (%)	30 (11.3)	15 (9.2)	15 (14.7)	0.163
Hepatorenal syndrome, n (%)	20 (7.5)	14(8.5)	6 (5.9)	0.425
Others, n (%)	9 (3.4)	6 (3.7)	3 (2.9)	0.753
In-hospital mortality, n (%)	194 (72.9)	115 (70.1)	79 (77.5)	0.191
Length of hospital stay (days)	30.96±33.07	30.48±29.79	31.75±37.99	0.763
Length of ICU stay (days)	16.46±20.82	16.60±17.77	16.23±25.13	0.888

* P<0.05



Cumulative probabilities of survival in critical patients with SOFA score ≥15 between higher and standard intensity of CVVH

Table 2. Clinical Characteristics of CVVH treatment

Variables	Enrolled patients (n=266)	Higher intensity (n=164)	Standard intensity (n=102)	P value
CVVH parameters				
Time to initiate CVVH after ICU admission (Days)	3.03±5.04	2.45±4.57	3.98±5.61	0.022*
Mean treatment duration (days)				
Non-survivor	13.71±24.79	13.30±19.51	14.05±31.19	0.795
Survivor	11.31±14.18	10.03±9.74	13.75±20.22	0.445
Flow rate of effluent (ml/hr)	2156.5±594.0	2305.9±598.1	1747.9±336.4	<0.001*
CVVH intensity (ml/kg/h)	31.88±9.24	35.14±8.69	22.98±1.99	<0.001*
CVVH blood flow (ml/min)	158.8±24.19	158.6±24.67	159.2±23.02	0.877
Variables at initiation of CVVH				
Number of organ failures	2.90±2.18	2.90±2.62	2.89±1.15	0.965
Body weight increase (kg)	3.84±4.95	3.81±4.69	3.88±5.34	0.912
Urine output (ml/kg/hr)	0.28±0.46	0.30±0.53	0.23±0.32	0.157
PaO_2/FiO_2	232.0±142.9	240.5±144.2	218.2±140.3	0.225
Inotropic equivalent score	24.64±23.14	23.99±24.50	25.69±20.81	0.563
Serum lactate (mmol/L)	7.40±6.20	7.26±6.53	7.62±5.67	0.692
Serum albumin (g/dL)	2.76±0.68	2.73±0.69	2.81±0.67	0.426
Serum WBC count(× 10^3/μL)	14.60±11.54	14.21±12.32	15.24±10.16	0.463
Serum hemoglobin (g/dL)	10.13±2.51	10.11±2.38	10.16±2.73	0.883
Serum platelet count (× 10^3/μL)	135.2±99.98	133.7±99.53	137.9±101.2	0.741
Serum bicarbonate (mmol/L)	16.95±5.41	17.15±5.56	16.62±5.15	0.436
Serum sodium (mmol/L)	140.2±9.36	139.6±10.09	141.1±7.99	0.212
Serum potassium (mmol/L)	4.54±1.11	4.51±1.09	4.60±1.14	0.533
Blood urea nitrogen (mg/dL)	65.77±41.75	66.82±43.29	64.04±39.28	0.600
Serum creatinine (mg/dL)	3.55±2.07	3.60±2.18	3.47±1.89	0.613
Disease severity scores				
APACHE II score at ICU admission	22.59±7.96	22.78±8.25	22.27±7.50	0.614
APACHE II score at CVVH initiation	25.36±6.83	24.73±6.68	26.39±6.97	0.056
SOFA score at ICU admission	11.59±4.20	11.63±4.28	11.43±4.07	0.702
SOFA score at CVVH initiation	14.44±3.53	14.18±3.28	14.86±3.88	0.127

*P<0.05

Table 3. Cox proportional hazard model of in-hospital mortality

Variables	Univariate analysis		Multivariate analysis#	
	HR (95% CI)	P value	HR (95% CI)	P value
CVVH intensity, ml/kg/hr				
≥25 vs. 20-25	0.65 (0.48-0.88)	0.005	0.67(0.49-0.92)	0.013*
Hemoglobin, g/dL				
<10 vs. ≥10	1.43 (1.04-1.96)	0.029	1.53 (1.10-2.13)	0.012*
Lactate, mmol/L				
≥6 vs. <6	1.56 (1.07-2.27)	0.021	1.28 (0.86-1.89)	0.227
Albumin, g/dL				
<3.5 vs. ≥3.5	1.74 (0.98-3.06)	0.057	1.43 (0.80-2.55)	0.225
SOFA score				
<10	1			
10-14	1.83 (0.92-3.66)	0.087		
≥ 15	2.85 (1.44-5.65)	0.003	1.92 (1.31-2.83)	<0.001*
APACHEII score				
<10	1			
10-19	0.92 (0.56-1.50)	0.737		
20-29	0.80 (0.59-1.08)	0.142		
≥ 30	1.32 (0.97-1.81)	0.076	1.16 (0.84-1.60)	0.360

All factors with a P< 0.1 in univariate analysis were included in the Cox multivariate analysis
*P<0.05