Continuous Veno-Venous Hemofiltration in Bhumibol Adulyadej Hospital

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Objective: *Continuous veno-venous hemofiltration (CVVH) is a mode of renal replacement therapy in critically ill patients that has gained popularity all over the world. The authors reviewed one-year experience with CVVH in intensive care units (ICUs) of Bhumibol Adulyadej Hospital. The objectives of this study were to describe the characteristics of the patients and demonstrate the association between various factors and outcome.*

Material and Method: *The medical records of 45 patients who underwent CVVH treatment were analyzed. All patients had been admitted into the ICUs of Bhumibol Adulyadej Hospital between 1 January 2005 and 31 December 2005.*

Results: *Average age of patients was 67.7 13.3 years (range from 27.0 years to 88.4 years). The male: female ratio was 1.4:1. Twenty-four patients were admitted to the medical ICU, 17 to the coronary care unit (CCU) and 4 to the surgical ICU. All of them needed mechanical ventilator support and 91.1% required vasopressor. Sixty percent of the patients had sepsis. Most of them had comorbidity including, cardiovascular (66.7%), hepatobilliary (35.6%) and neurological comorbidity (13.3%). Half of them had been diagnosed with chronic kidney disease (CKD) with pre-dialysis CKD in 40% and end stage renal disease (ESRD) in 11.1%. The mean number of organ failure was 3.18 0.1 and 95.6% had more than 2 organ failures. The range of APACHE II score was 15-50 (mean 30.8 9.5) with a predicted death rate of 21.0-97.8% (mean 66.4 23.4). The indications for renal replacement were 80% for level of nitrogenous waste product, 75.6% for volume overload, 42.2% for severe metabolic acidosis, 35.6% for hyperkalemia and 2.2% for toxic substance removal. Eighty percent of the patients had 2 or more indications. Mean blood urea nitrogen (BUN) and creatinine (Cr) level before starting CVVH was 78.8 36.5 mg/dl (10.0 to 187.0) and 5.3 3.3 mg/dl (2.0 to 20.2) respectively. Duration of CVVH was 1.5 to 251.0 hours (mean 57.8 58.9) and the average CVVH dose was 36.6 7.5 ml/kg/hr (24.6 to 55.6). The overall mortality was 80%. The two most frequent causes of death were sepsis (44.4%) and cardiovascular disease (15.6%). The significant difference between the survival and non-survival groups were surgical ICU admission ($p = 0.021$), sepsis ($p = 0.019$), APACHE II score ($p = 0.011$), volume indication for CVVH ($p = 0.028$), number of dialysis indication ($p = 0.019$), duration of hospitalization ($p = 0.004$), systolic blood pressure ($p = 0.012$) and serum albumin level ($p = 0.009$). By logistic regression analysis, there was only statistical significance for serum albumin level less than 3 g/dl.*

Conclusion: *One-year experience of CVVH in Bhumibol Adulyadej Hospital showed high mortality rate but it is comparable to previous publications. The only factor that was associated with death by multivariate analysis was lower serum albumin level at the time of initiating CVVH. Prospective studies are required to explore this issue in the future.*

Keywords: *Continuous Veno-Venous Hemofiltration (CVVH), Acute Renal Failure (ARF), Risk Injury Failure Loss and ESRD (RIFLE), Acute Physiology and Chronic Health Evaluation II (APACHE II)*

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Continuous renal replacement therapy (CRRT) was first described by Scribner and associates in 1960[1]. This modality is now available in most tertiary intensive care units (ICU) around the world and has almost completely replaced intermittent hemodialysis (IHD) in some countries. In Australia and New Zealand, for example, almost 100% of ICU treatments are CRRT[2]. This technology has theoretical advantages over IHD that are related to cardiorespiratory stability, optimal metabolic control, and fluid balance allowing nutri-tional supplementation. It has been demonstrated to improve cerebrovascular stability compared with IHD in patients with acute renal failure (ARF) who also have liver failure or cerebral edema[3,4].

Bhumibol Adulyadej Hospital is a tertiary care of the Royal Thai Air Force and residency training hospital with 6 beds of medical ICU, 7 beds of coronary care unit (CCU), and 12 beds of surgical ICU. The first case of CRRT in Bhumibol Adulyadej Hospital occurred in 1998 and the number is increasing. Most popular CRRT mode in the presented center is continuous veno-venous hemofiltration (CVVH) using mainly convective solute clearance. Before 2005, the authors have had experience of CVVH treatment in 87 cases, but have not yet collected the clinical data, CVVH parameters, and outcome with this experience.

This study intended to describe current practices of CVVH in all patients admitted to ICUs who needed renal replacement therapy and to identify various variables significantly associated with outcome. The authors hope to use the outcome of the present study to improve this treatment as well as for future research.

Material and Method

The medical records of all patients who required CVVH treatment in the medical, surgical and cardiac ICUs of Bhumibol Adulyadej Hospital during a 1-year period (2005) were reviewed retrospectively. The present study included all patients in whom the initial renal replacement therapy was performed in ICUs. Forty-five patients were evaluated.

When considering the treatment of ARF, the authors first considered IHD. However, those placed on CVVH were considered to be able to benefit from CVVH more than IHD. Those were too hemodynamically unstable to tolerate IHD. The attending nephrologists in the ICUs decided when to prescribe CVVH and when to terminate it.

The indications for starting CVVH included; volume overload inadequately controlled with diuretic therapy, anuria or oliguria (urine volume < 200 ml per 12 hours), hyperkalemia (serum potassium persistently > 6.5 mmol/litre), severe acidosis unresponsive to medical management (pH < 7.1), blood urea nitrogen (BUN) level exceeding 100 mg per deciliter, creatinine (Cr) level exceeding 10 mg per deciliter, signs or symptoms such as encephalopathy that uremia could not be ruled out as a precipitating cause, intoxication (e.g. salicylates, methanol, barbiturates, lithium) and other reasonable conditions that CVVH may help to improve the outcome such as sepsis.

The CVVH was terminated when there was partial recovery of renal function. This was defined as the restoration of diuresis, the absence of uremia, improved electrolyte, and improved acid-base homeostasis.

CVVH setting in the presented patients was adjusted according to patient condition and laboratory value. The common prescription was 2 litres per hour of filtration rate. Two bags per hour of replacement fluid were used with pre-dilution of 800 ml and 1200 ml for postdilution. Replacement fluid consisted of saline solution with added sodium bicarbonate, potassium and dextrose. The concentration of sodium, potassium, glucose and bicarbonate in the replacement fluid varied, depending on the clinical need. A sodium concentration of 140 mEq/L was usually used in all patients. The calcium gluconate was a separate drip. Anticoagulation was usually not required in the presented patients because of deranged clotting, thrombocytopenia or both. Blood flow and ultrafiltration rate were adjusted according to hemodynamic and volume status respectively.

The dialysis filter was a polysulfone hemofilter (Aquamax) with a surface area of 0.7 m^2 and an ultrafiltration coefficient of 33 ml/mm of Hg/hour. All patients conducted CVVH with the Edwards Aquarius machine.

Hemodynamically unstable was defined as systolic blood pressure < 90 mmHg or requiring vasoactive drug to maintain blood pressure in the normal range.

Baseline serum Cr level of selected patients was retrieved from the OPD files 3 months before admission. The lowest serum Cr level in the current admission was considered for new patients with no previous record. Follow-up serum Cr and serum urea levels were reviewed in surviving patients at 2, 4 and 8 weeks after coming off CVVH.

For dividing patients into RIFLE classification, GFR was estimated (cGFR) by using the Cockcroft-

Gault formula. This was used because serum albumin and urea level that affected patients confounding factors were not required in this formula.

cGFR for males = [(140-age) x BW] / (72 x sCr), for females multiply by 0.85

Urine output (UO) was calculated in milliliter per kilogram per hour for all patients.

The following demographic variables were considered; age, sex, past medical history, admission diagnosis, admission date and time.

The following data were obtained from the date of initiation of CVVH and during follow up: BUN, Cr, electrolytes, Arterial Blood Gas (ABG), Complete Blood Count (CBC), Glasgow Coma Scale (GCS), and vital signs.

ARF was defined and classified exclusively from the first day of initiated CVVH treatment according to RIFLE criteria[5,6].

The APACHE II score is the sum of three components: an acute physiology score, age score, and a chronic health problems score. Score ranged from 0 to 71, with higher value having worse prognosis. The APACHE II score was calculated using the method described by Knaus et al.

The Predicted death rate was calculated by:

$$\text{Predicted Death Rate} = e^{\text{Logit}} / (1 \pm e^{\text{Logit}})$$

$$\text{Logit} = -3.517 \pm (\text{APACHE II}) * 0.146$$

The severity of illness was determined according to the score on the APACHE II on the day of initiation of CVVH.

Other evaluated data included, the cause of renal failure (determined on the basis of a chart review), the presence or absence of sepsis and oliguria (defined as a urinary output of less than 400ml in the previous 24 hours), the indication for CVVH, the duration of CVVH session, the using of a ventilator or vasopressor support, other interventions such as surgery, Cardio Pulmonary Resuscitation (CPR), contrast or aminoglycoside exposure, time from nephrologist consultation to starting CVVH, length of hospital stay and outcome of the patients.

Statistical analysis

Descriptive analysis was used to identify demographic data, clinical parameters, severity of patients, CVVH setting and outcome. Results were given in actual number and percentage or mean $\pm$ SD unless otherwise stated.

Survivors and non-survivors were compared. Student's t test was used for comparing the mean of continuous measurements. The chi-square test was used for categorized measurements. Variables were first analyzed by univariate methods. The variables with statistical significance in univariate analysis were included in a multivariate logistic regression analysis with the help of SPSS 13.0 for window software. All p values were two-sided, and the value of less than 0.05 was considered to indicate statistical significance.

Results

1. Subject characteristics

1.1 Demographic data

Patient characteristics are presented in Table 1. Of the 45 CVVH-required patients in the ICU, 19 were female and 26 were male, the male: female ratio was 1.4:1. The age of the patients ranged from 27 to 88 years with a mean of 67.7 years. The percentage of patients in the medical ICU was 53.3%, in the coronary care unit was 37.8%, and in the surgical ICU was 8.9%. There was no significant difference in this parameter between the survival and non-survival group except the non-survival group had higher ratio of medical to surgical ICU admission (Table 4).

1.2 Underlying and comorbidity

The presence of the following co-morbidities, and interventions were described in all patients (Table 1): diabetes (44.4%), cardiovascular disease (66.7%), hepatobilliary disease (35.6%), neurological disease (13.3%), sepsis (60.0%), aminoglycoside exposure (13.3%), contrast exposure (37.8%), post surgery (8.9%) and post cardiopulmonary resuscitation (15.6%). When comparing between the two groups, the non-survival group had a significant higher proportion of sepsis (Table 4).

1.3 Severity, organ failure and scoring system

All patients in the present study needed ventilator support and 91% needed vasoactive support to maintain blood pressure. The mean of organ failure was 3.2 ± 0.1(range from 2 to 5 organs). Only 20% had one organ failure. Mean of GCS was 8.8 ± 5.4.

The APACHE II scores ranged from 15 to 50 (mean 30.8) at the time initiating CVVH. The average score of survivors versus non-survivors were significantly different (23.8 ± 6.6 vs 32.6 ± 9.4, $p = 0.011$).

Predicted death rate that was calculated from APACHE II score and GCS ((70.9 ± 21.8 vs 48.5 ± 21.5, $p = 0.008$). The component of APACHE II score were also significantly different in both groups (7.75 ± 5.2 vs 13.3 ± 3.7, $p = 0.002$). The overall predicted death rate of the presented patients was $66.4 \pm 23.4\%$

Table 1. Descriptive analysis

	Case(s) [a]	Percent [b]
No of patient (cases)	45	100.0
Age, years, mean ± SD (range)	67.7±13.3	27.0-88.4
Male:Female cases (%)	26 (57.8):19 (42.2)	1.4:1 in ratio
Admission in:	Case(s)	Percent
Medical ICU	24	53.3
Coronary Care Unit	17	37.8
Surgical ICU	4	8.9
Underlying and comorbidity	Case(s)	Percent
Diabetes	20	44.4
Cardiovascular comorbidity	30	66.7
Hepatobilliary comorbidity	16	35.6
Neurological comorbidity	6	13.3
Sepsis	27	60.0
Aminoglycoside exposure	6	13.3
Contrast exposure	17	37.8
Post surgery	4	8.9
Post CPR	7	15.6
Renal status	Case(s)	Percent
Acute renal failure (ARF)	22	48.9%
ARF on chronic kidney disease (CKD)	18	40.0%
End stage renal disease (ESRD)	5	11.1%
RIFLE classification	Case(s)	Percent
RIFLE-R	3	6.7
RIFLE-I	1	2.2
RIFLE-F	41	91.1
Severity	Case(s)	Percent
Respirator support	45	100.0
Vasoactive support	41	91.1
Number of organ failure, mean ± SD (range)	3.2±0.1	2.0-5.0
Glasgow Coma Score, mean ± SD (range)	8.8±5.4	3.0-15.0
APACHE II score (SD),mean ± SD (range)	30.8±9.5	15.0-50.0
Predicted Death Rate, mean ± SD (range)	66.4±23.4	21.0-97.8
Indication for CVVH	Case(s)	Percent
BUN/Cr level	36	80.0
Volume overload	34	75.6
Acidosis	19	42.2
Hyperkalemia	16	35.6
Toxic removal	1	2.2
No. of organ failure	Case(s)	Percent
1	9	20.0
2	19	42.2
3	9	20.0
4	8	17.8

[a] in general present in case(s) except mention in other eg. Mean, SD;
[b] in general present in percent, except mention in other eg. SD, percent change;
** (% change from initiation)

1.4 Renal status and RIFLE classification

The authors found that the patients who needed CVVH treatment were ARF in 49%, ARF and CKD in 40%, and ESRD in 11%. When applying RIFLE classification to these patients, most of them were RIFLE-F category (91.1%). There were no significant differences between the two groups.

Table 1. Descriptive analysis (Cont.)

Clinical data	Mean ± SD	Range
Interval from consult to CVVH, days	2.8±5.9	0.0 to 34.0
Temp, degree Celsius	36.7±1.3	34.0-39.5
Pulse, beat per min.	102.0±24.8	52.0-158.0
Respiratory Rate, times per min.	21.4±6.1	12.0-40.0
Systolic BP, mmHg	105.2±30.4	27.0-176.0
Mean Arterial Pressure, mmHg	72.3±21.7	18.0-116.0
Diastolic BP, mmHg	55.8±19.8	11.0-98.0
Urine output (UO) per hr, ml/hr	19.7±36.9	0.0-200.0
Oliguria,UO less than 400ml/day, cases, %	31 (cases)	68.9 (percent)
Laboratory values Before initiating CVVH	Mean ± SD	Range
Mean arterial pH	7.2±0.2	6.8-7.5
Serum BUN, mg/dL	78.8±36.5	10-187
Serum Cr, mg/dL	5.3±3.3	2.0-20.2
Serum HCO3, mmol/L	14.4±6.1	1.0-28.0
Serum Albumin, g/dL	2.8±0.7	1.3-4.5
CVVH Treatment	Mean ± SD	Range
Duration (hours)	57.8±58.9	1.5-251.0
Blood Flow rate (ml/min)	138.67±26.3	50-200
Set Fluid removal rate (ml/hr)	70.22±45.4	0-200
Actual Fluid removal rate (ml/hr)	48.5±56.7	-102.9-225.3
Set Filtration rate (ml/hr)	2000	fix
Filtration rate per body weight (ml/kg/hr)	36.6±7.5	24.6-55.6
Replacement K (mEq/dl)	3.0±1.5	0-4
Replacement HCO3 (mg/dl)	37.5±8.2	24-67
Number of dialyzer used per case	2.3±2.0	1-10
Duration per 1 dialyzer (hours)	25.9±18.6	1.5-71.5
Biochemical Parameter during CVVH	Mean ± SD	% change**
BUN level at 6hr after CVVH initiation, mg/dL	61.5±29.1	-21.9
BUN level at 6hr after CVVH initiation, mg/dL	40.4±20.4	-48.7
Cr level at 6 hr after CVVH initiation, mg/dL	4.4±3.3	-17.0
Cr level at 6 hr after CVVH initiation, mg/dL	2.6±1.7	-50.9

[a] in general present in case(s) except mention in other eg. Mean, SD;
[b] in general present in percent, except mention in other eg. SD, percent change;
** (% change from initiation)

2. Renal replacement therapy

2.1 Indication for CVVH

The most frequent indication for CVVH treatment in the study patients was BUN/Cr level (80.0%), followed by volume overload (75.6%), acidosis (42.2%), hyperkalemia (35.6%) and one case (2.2%) with methanol intoxication. Twenty-percent of these patients had only one indication, 42.2% had two indications and the rest (37.8%) had more than two indications for CVVH treatment. Only volume overload indication was significantly higher in the non-survival group.

2.2 Clinical parameters and laboratory values

Clinical parameters and laboratory values of both groups are listed in Table 1 and 4. Systolic blood pressure and serum albumin were significantly lower in the non-survival group compared with the survival group ($p = 0.012$ and 0.009 respectively). Other clinical parameters, including mean arterial pressure, diastolic blood pressure, heart rate, temperature, respiratory rate, and urine output showed no significant difference between both study groups.

The presented patients tend to have acidosis (mean pH = 7.2 ± 0.2) at initiating CVVH. BUN at starting CVVH was 78.8 ± 36.5 mg/dL (range from 10 to 187) while Cr level at starting CVVH was 5.3 ± 3.3 mg/dL (range from 2.0 to 20.2). The mean serum albumin level was 2.8 ± 0.7 g/dL and significantly lower in the non-survival group.

Table 2. Overall outcomes

Mean duration of hospitalization 20.0 ± 20.5 days (1.0 to 73.0)			
	N (cases)	Nonsurvival, case(s) (%)	Survival, case(s) (%)
All CVVH[a]	45	36 (80.0)	9 (20.0)
All ARF[b]	40	32 (80.0)	8 (20.0)
ARF[b] only	22	18 (81.8)	4 (18.2)
ARF[b] on CKD[c]	18	14 (77.8)	4 (22.2)
ESRD[d]	5	4 (80.0)	1 (20.0)

[a] CVVH, Continuous Veno-Venous Hemofiltration
[b] ARF, acute renal failure
[c] CKD, chronic kidney disease
[d] ESRD, end stage renal disease

Table 3. Outcome in survival group

	N, case(s)	Survival, case(s)	Complete Recovery, case(s) (%)	Partial Recovery, case(s) (%)	Non Recovery, case(s) (%)
All CVVH[a]	45	9	4 (44.4)	3 (33.3)	2 (22.2)
All ARF[b]	40	8	4 (50.0)	3 (37.5)	1 (12.5)
ARF[b] only	22	4	3 (75.0)	1 (25.0)	0
ARF[b] on CKD[c]	18	4	1 (25.0)	2 (50.0)	1 (25.0)
ESRD[d]	5	1	-	-	1 (100.0)

[a] CVVH, Continuous Veno-Venous Hemofiltration
[b] ARF, acute renal failure
[c] CKD, chronic kidney disease
[d] ESRD, end stage renal disease

2.3 CVVH treatment and parameter during treatment

All patients underwent CRRT in CVVH mode. The average values of prescription are listed in Table 1. The duration of CVVH treatment was 1.5 to 251.0 hours (mean 57.8 ± 58.9 hours). Average setting of blood flow rate and actual fluid removal rate was 138.67 ± 26.3 ml/hr and 70.22 ± 45.4 ml/hr respectively. The authors set the filtration rate of 2000 ml per hour for every patient and then calculated the CVVH dose range from 24.6 to 55.6 ml/kg/hr (mean 36.6 ± 7.5). BUN and Cr level were followed during CVVH sessions. The authors found that serum BUN level decreased by 21.9% at 6 hours and 48.7% at 24 hours. The serum Cr also had the same decreasing trend (17.0% at 6 hours and 50.9% at 24 hours).

3. Outcome

Mean duration of hospitalization was 20.0 ± 20.5 days (1.0 to 73.0), which was significantly longer in the survival group (15.8 ± 18.6 vs 37.2 ± 19.7, p = 0.004).

The overall ICU mortality rate was 80%. Of these patients, the most common cause of death was sepsis (44.4%), followed by cardiovascular disease (15.6%), cancer (4.4%), Acute Respiratory Distress Syndrome (ARDS) (2.2%), pneumonia (2.2%), intoxication (2.2%) and undetermined (6.7%). From 9 patients who survived during hospital admission, 4 had complete renal recovery, 3 patients had incomplete recovery. Two patients in the present study had no recovery in renal function requiring long-term renal replacement therapy.

4. Univariate and multivariate analysis

The univariate relationship between variables and outcome are presented in Table 4. Eleven variables were found to be significantly different between the non-survival and survival group. To identify risk factor affecting outcome, five variables were considered (Table 5). These included: medical ICU admission, APACHE II score more than 24, the presence of sepsis,

Table 4. Factor and nonsurvival vs survival

Factors	Nonsurvival (n = 36)	Survival (n = 20)	p-value
Mean age (range; year)	68.3±13.9	65.4±11.1	0.572
Baseline Cr (range; mg/dL)	2.6±0.6	2.4±0.6	0.881
ICU medicine : surgery (ratio)	35:1 (35/1)	6:3 (2/1)	0.021*
Diabetes, cases (percent)	14 (70.0%)	6 (30.0%)	0.134
Cardiovascular comorbidity, cases (percent)	24 (80.0%)	6 (20.0%)	1.000
Hepatobilliary comorbidity, cases (percent)	14 (87.5%)	2 (12.5%)	0.350
Neurological comorbidity, cases (percent)	5 (83.3%)	1 (16.7%)	0.826
Sepsis, cases (percent)	25 (92.6%)	2 (7.4%)	0.019*
Vasoactive drug support, cases (percent)	34 (82.9%)	7 (17.1)	0.116
Aminoglycoside exposure, cases (percent)	6 (100.0%)	0	0.188
Contrast exposure, cases (percent)	14 (82.4%)	3 (17.6%)	0.454
Post surgery, cases (percent)	2 (50.0%)	2 (50%)	0.116
Post CPR, cases (percent)	4 (57.1)	3 (42.9)	0.100
Respirator support, cases (percent)	36 (80%)	9 (20.0%)	**
Number of organ failure	3.3±0.7	2.9±0.3	0.115
ARF, cases (percent)	18 (81.8%)	4 (18.2%)	1.000
RIFLE-F	31 (81.6)	7 (18.4)	0.537
Glasgow Coma Score	7.75±5.2	13.3±3.7	0.002*
APACHE II score	32.6±9.4	23.8±6.6	0.011*
Predicted Death Rate, percent	70.9±21.8	48.5±21.5	0.008*
Indication BUN/Cr level, cases (percent)	29 (80.6%)	7 (19.4%)	0.852
Indication volume overload, cases (percent)	30 (88.2%)	4 (11.8%)	0.028*
Indication electrolyte imbalance, cases (percent)	14 (87.5%)	2 (12.5%)	0.350
Indication acidosis, cases (percent)	17 (89.5%)	2 (10.5%)	0.174
Indication toxic removal, cases (percent)	1 (100%)	0	1.000
Number of indication	2.5±1.0	1.7±0.7	0.019*
Interval consult to start CVVH	2.69±6.4	3.1±3.7	0.803
Temperature, degree Celsius	36.7±1.4	36.5±1.2	0.616
Pulse, beat per min	101.3±23.7	104.9±30.3	0.699
Respiratory rate, time per min	21.8±6.3	20.0±5.5	0.440
Systolic BP, mmHg	99.6±27.9	127.7±31.2	0.012*
Lowest SBP, mmHg	64.1±35.5	98.8±26.0	0.009*
Diastolic BP, mmHg	53.9±20.4	63.2±15.9	0.213
Oliguria, cases (percent)	27 (87.1)	4 (12.9)	0.077
Arterial PH	7.2±0.2	7.3±0.1	0.080
BUN, mg/dL	78.7±36.1	79.4±40.1	0.955
Cr, mg/dL	5.1±3.5	6.2±2.1	0.379
HCO3, mmol/L	13.7±6.3	17.2±4.6	0.131
Albumin level, g/dL	2.7±0.7	3.2±0.3	0.009*
Duration, hours	58.2±62.0	56.3±47.5	0.933
Blood Flow rate, ml/min	139.4±21.6	135.6±41.9	0.793
Set Fluid removal rate, ml/hr	72.5±50.1	61.1±15.4	0.251
Actual Fluid removal rate, ml/hr	43.9±59.6	67.2±40.9	0.274
Filtration rate per body weight, ml/kg/hr	36.2±7.2	38.1±8.3	0.542
Replacement K, mEq/L	3.0±1.6	3.3±1.3	0.534
Replacement HCO3, mmol/L	36.9±7.6	39.7±10.9	0.375
Number of dialyzer	2.5±2.2	1.7±0.7	0.072
Duration per 1 dialyzer (hour)	23.1±15.5	37.1±26.1	0.157
Duration hospitalization, days	15.8±18.6	37.2±19.7	0.004*

** No statistics are computed because on Respiration is a constant

Table 5. Univariate analysis

Factors	Nonsurvival, cases (%)	Survival, cases (%)	p-value	Odds Ratio (95%CI)
Medical ICU admission	35 (85.4)	6 (14.6)	0.021	17.5 (1.6-197.4)
APACHE II[a] > 24	29 (90.6)	3 (9.4)	0.005	8.3 (1.7-41.6)
Sepsis	25 (92.6)	2 (7.4)	0.010	7.9 (1.4-44.6)
Serum albumin < 3 g/dL	12 (63.2)	7 (36.8)	0.019	6.7 (1.2-37.4)
Volume overload indication	30 (88.2)	4 (11.8)	0.015	6.3 (1.3-30.4)

[a]APACHE II, Acute Physiology and Chronic Health Evaluation II

Table 6. Multivariate analysis:Logistic regression analysis

	Odd ratio	95%CI	p-value
Medical ICU admission	0.018	0.000 to 1.576	0.078
APACHE II[a] > 24	-2.351	0.006 to 1.422	0.088
Sepsis	-0.735	0.056 to 4.140	0.504
Serum albumin < 3 g/dL	-3.160	1.028 to 540.874	0.048*
Volume overload indication	-1.456	0.024 to 2.249	0.208

[a]APACHE II, Acute Physiology and Chronic Health Evaluation II

serum albumin level less than 3 g/dL and volume overload indication for starting CVVH. Table 6 shows multivariate correlation and their 95%CI. Logistic regression was performed on variables that were found to have statistical significance in univariate analysis. The only risk factor that was found to be statistically significant was serum albumin level less than 3 g/dL with p value of 0.048.

Discussion

ARF is a common problem in ICUs. It occurs around 1% to 25% depending on the population studied and criteria used to define it[7,8].

Acute dialysis quality initiative (ADQI) develops a consensus definition and recommendation for ARF in critically ill patients, and the RIFLE classification for acute renal dysfunction was published in 2003. The RIFLE system uses either GFR criteria or urine output criteria to classify patients into three severity categories: Risk, Injury, and Failure; and two additional outcome categories: Loss and ESRD[5]. The outcome study using these criteria in ARF patients showed improvement in ability to predict outcome compared with established ICU scoring systems such as APACHE II and SAPS II[9]. Bell et al used RIFLE classification in 207 critically ill patients who needed acute renal replacement therapy, the results showed 57.9% of 30-day mortality rate in RIFLE failure category, 23.5% for those in RIFLE risk category and 22.0% for RIFLE injury category[6].

The APACHE II has been among the most widely used scoring system for predicting risk of death in ICU patients. It has the advantage of being easy to use and has been used more frequently for risk stratification in ARF than any other similar scoring system. One prospective study showed that APACHE II score at the time of initiation of dialysis had a statistically significant predictor of patient survival and recovery of renal function in 153 patients with ARF[10]. There was another prospective study in 61 patients with ARF requiring dialysis with 62.3% mortality rate. APACHE II was found to be statistically significant prognostic factors for hospital mortality. The mortality rate increased as the APACHE II score increased (odds ratio 1.3 per increase in one score; $p < 0.001$). The best cut-off value for APACHE II was 24, with 63% sensitivity and 96% specificity[11]. A study by Zhang also found the score correlated significantly with the mortality in patients with ARF. The mortality was 100% with APACHE II when the score was > or = 35. When APACHE II score was > or = 26, patients were dialysis dependent. When APACHE II score was < or = 22, 80.4% of patients had renal function recovery[12].

In an effort to improve predictive capacity for critically ill patients, the APACHE III system was developed in 1991. Because the APACHE III scoring

system includes the presence or absence of oliguria and serum albumin, this index may improve predictive power over the APACHE II[13,14]. There was a retrospective review that showed that APACHE III scoring system was superior to the APACHE II[15]. However, the complexity of the APACHE III scoring system may limit its widespread clinical use. Furthermore, it has not previously been validated in prospective, multicenter, controlled trials in patients with ARF requiring dialysis.

ARF often is part of the multiple organ dysfunction syndrome[16,17]. Patients who develop ARF requiring dialysis often have multiple coexisting diseases that contribute to the high morbidity and mortality rates. Mortality in these patients ranged from 28% to 90%[5,7,17]. The overall ICU mortality rate in the presented patients reached 80%, which was not different from other previous reports[18-22]. In an HEMODIAFE study, overall ICU and in hospital mortality rates in continuous veno-venous hemodiafiltration (CVVHDF) group was 66% and 72% respectively. In the present study, 56% of patients had sepsis, more than 85% receiving vasopressor support and almost all (> 94%) were on mechanical ventilation. A study from India showed 77.27% of in hospital mortality and 95.5% had severe sepsis[21]. This is similar to a study by Guerin that reported a 79% mortality rate[22].

The patients in the present study had high severity. All cases need respiratory support with sepsis concomitant in 60%, post CPR in 15.6% and 91.1% needed vasopressor support. With RIFLE classification, the presented patients were categorized in RIFLE-F in 91.1%. The average APACHE II score was 30.8 with a predicted death rate of 66.4% less than the actual mortality rate of 80%. This may be due to some other factors affecting the outcome that was not calculated in the scoring components.

The factors affecting outcomes from ARF can be categorized as (1) patient characteristics contributing to the severity of the underlying disease associated with ARF; (2) the process of dialysis for replacement of renal function; and (3) other factors, including practice variations and the impact of post-ARF interventions[23]. Some of these factors can be modified to improve outcome.

Advanced age and male gender have been associated variably with adverse outcome for ARF in previous studies[24,25]. One study reported that a patient's age of more than 60 years had a higher mortality rate compared with those younger than 60 years. (76% vs 40%, $p < 0.01$) Some investigators have concluded that previous health status, comorbidity disease, patient age, and the number of failed organ systems influenced the outcome regardless of the modality of renal support[26,27].

In the present study, outcome was unaffected by age, gender, presence of pre-existing renal disease, diabetes, serum BUN, serum Cr and the need for vasopressor support.

Valentine et al reported CVVH parameters in their study including, the duration of CVVH of 35.93 ± 20.91(11 to 84 hours), mean hourly Ultra Filtration (UF) of 93.72 ± 65.57 ml, average filter life of 35.93 ± 20.91 hours. Their study showed an overall mortality rate of 77%. The present study showed a shorter duration of filter life (25.9 ± 18.6), longer duration of CVVH treatment (57.8 ± 58.9) and less hourly UF (70.22 ± 45.4) with an overall mortality of 80%.

In the outcome study of ARF in ICU according to RIFLE criteria, it demonstrated that significant risk factors associated with ICU death included: SAPS II, lowest MAP, serum lactate level, urine output and presence of medical causes (OR 0.82, 1.4, 0.39, 1.0, 8.04 respectively). In the present study, the authors did not evaluate for serum lactate level and SAPS II. Moreover, instead of MAP, the authors found SBP was associated with death similar to that reported by Lins and et al[28]. Finally, the authors did not find the effect of medical cause and UO to the outcome of the patients.

Another study by Guerin et al showed the factors associated with decreasing patient survival including, SAPS II on admission, oliguria, admission from hospital or emergency room, number of days between admission and ARF, cardiac dysfunction, and ischemic ARF. The absence of underlying disease and hepatic dysfunction were associated with an increase in patient survival. The type of RRT was not associated with outcome in this study[22].

Recently, a study by Lins et al[28] found that the outcome was unaffected by gender, history of myocardial infarction, chronic renal failure, chronic obstructive lung disease, chronic liver disease, alcohol abuse, diabetes, underlying neoplasm, serum Cr, glucose, sodium and hemoglobin, white blood cell count, urinary sodium or urine osmolality.

Many factors were associated with outcome in the present study including, medical ICU admission, sepsis, APACHE II score, volume indication for CVVH, number of indications, duration of hospitalization, systolic blood pressure, GCS and serum albumin. Finally, when using logistic regression analysis, the authors found that only serum albumin level significantly associated with outcome. It is important to note that serum

albumin level is one of the different components between APACHE II and APACHE III score. Therefore, using APACHE III scoring system may predict the outcome more accurately.

One important consideration to improve the outcome is from a prospective study by Ronco et al in critically ill patients using CVVH[29]. In the present study, an increased dose of CVVH from 20 ml/kg/hr to 35 ml/kg/hr was associated with a better outcome. In current practice, the authors prescribe a fixed standard CVVH dose of 2 liters per hour, which is not adjusted for body weight. The authors' practice is similar to the majority (> 90%) of CVVH prescription in Australian centers. In the present study, the mean filtration rate per body weight was 36.6 ml/kg/hr. This has already achieved the beneficial dosage to have a good outcome. However, increasing the CVVH dose to 45ml/kg/hr did not show an additional effect on prognosis.

From a large trauma center, single retrospective, nonrandomized cohort study showed that patients who started on CRRT at a mean BUN of 42.6 mg/dL had a 39% survival compared to 20% in those who started at a mean BUN of 94.5 mg/dL[30]. There is still no recommendation for clinical practice in timing of initiation of CRRT. Because of the severity of critically ill patients with ARF, severe complications can occur and result in irreversible renal function. Therefore, renal replacement therapy should begin early to prevent their development. This may be another way to improve outcome. The presented patients were initiated RRT at a mean BUN of 78.8 $\pm$ 36.5 mg/dL. Furthermore, recognition of patients at risk, prevention before ARF occurs, if possible, and early treatment will be much more effective than treatment of established ARF.

Several limitations in the present study should be recognized. First, it was a retrospective study at a single medical center. Therefore, these results may not be directly comparable with other populations. Second, because of no effective and complete computer-aid database, all data were reviewed from medical records manually. There were difficulties in collecting some laboratory data or some data was not available. Finally, the present study had a small sample size with few survivors.

In summary, 80% of critically ill patients with CVVH treatment died in the hospital. The present study showed that serum albumin level less than 3 g/dL was associated with death. The present study helped to collect useful information on the authors' current practice of renal replacement therapy in ICUs. It also provides a centre-based collection of data that will be useful in future research.

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การบำบัดทดแทนไตอย่างต่อเนื่องแบบ Continuous Veno-Venous Hemofiltration ในโรงพยาบาลภูมิพลอดุลยเดช

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วัตถุประสงค์: *Continuous Veno-Venous Hemofiltration เป็นวิธีการบำบัดทดแทนไตอย่างต่อเนื่องที่ใช้กับผู้ป่วยหนักที่ได้รับความนิยมเพิ่มมากขึ้นทั่วโลก ได้ทำการศึกษาประสบการณ์ในการบำบัดทดแทนไตอย่างต่อเนื่องในผู้ป่วยของเราที่เข้ารับการรักษาในหอผู้ป่วยหนักโรงพยาบาลภูมิพลอดุลยเดชในระยะเวลา 1 ปี โดยมีวัตถุประสงค์เพื่อที่จะบรรยายลักษณะผู้ป่วยและศึกษาหาปัจจัยต่าง ๆ ที่สัมพันธ์กับผลของการรักษา*

วัสดุและวิธีการ: *ได้ทบทวนบันทึกประวัติการรักษาของผู้ป่วยย้อนหลังจำนวน 45 รายที่ได้รับการบำบัดทดแทนไตอย่างต่อเนื่องในหอผู้ป่วยหนักของโรงพยาบาลภูมิพลอดุลยเดชในระหว่างวันที่ 1 มกราคม พ.ศ. 2548 จนถึงวันที่ 31 ธันวาคม พ.ศ. 2548*

ผลการศึกษา: *ผู้ป่วยที่เข้าร่วมการศึกษามีอายุเฉลี่ย 67.7 ± 13.3 ปี (27 ถึง 88.4) อัตราส่วนเพศชายต่อหญิงเท่ากับ 1.4 ต่อ 1 มีผู้ป่วยจำนวน 24 รายที่เข้ารับการรักษาในหอผู้ป่วยหนักอายุรกรรม 17 รายเข้ารับการรักษาตัวในหอผู้ป่วยหนักโรคหัวใจ และ 4 รายที่อยู่ในหอผู้ป่วยหนักศัลยกรรม ผู้ป่วยทุกรายได้รับการรักษาด้วยเครื่องช่วยหายใจ และมีถึงร้อยละ 91.1 ที่ต้องใช้ยาช่วยเพิ่มความดันโลหิต ผู้ป่วยร้อยละ 60 มีภาวะติดเชื้อในกระแสเลือดร่วมด้วย ผู้ป่วยส่วนใหญ่มีภาวะการเจ็บป่วยอย่างใดอย่างหนึ่งร่วมด้วยดังต่อไปนี้ โรคหัวใจและหลอดเลือด ร้อยละ 66.7 โรคตับและทางเดินน้ำดี ร้อยละ 35.6 และโรคทางระบบประสาท ร้อยละ 13.3 ครึ่งหนึ่งของผู้ป่วยเหล่านี้มีภาวะโรคไตเรื้อรังร่วมด้วยโดยที่ยังไม่ได้รับการฟอกเลือดร้อยละ 40 และอีกร้อยละ 11.1 เป็นโรคไตวายเรื้อรังระยะสุด ท้ายที่ได้รับการรักษาด้วยการฟอกเลือดอยู่ จำนวนอวัยวะที่ล้มเหลวเฉลี่ยของผู้ป่วยเท่ากับ 3.18 ± 0.1 และร้อยละ 95.6 มีจำนวนอวัยวะที่ล้มเหลวตั้งแต่ 2 ระบบขึ้นไป ค่าช่วงคะแนน APACHE II ในผู้ป่วยที่ศึกษานี้มีค่าอยู่ระหว่าง 15 ถึง 50 โดยมีค่าเฉลี่ยเท่ากับ 30.8 ± 9.5 โดยสัมพันธ์กับค่าการทำนายอัตราการเสียชีวิตที่คำนวณจากคะแนน APACHE เท่ากับร้อยละ 21.0 ถึง 97.8 (ค่าเฉลี่ยเท่ากับ ร้อยละ 66.4 ± 23.4) ข้อบ่งชี้สำหรับการบำบัดทดแทนไตอย่างต่อเนื่องได้แก่ค่าระดับของเสียที่สูง ร้อยละ 80.0 การมีภาวะน้ำเกิน ร้อยละ 75.6 การมีภาวะเลือดเป็นกรดอย่างรุนแรง ร้อยละ 42.2 ภาวะโปแตสเสียมสูง ร้อยละ 35.6 และการขจัดสารพิษ ร้อยละ 2.2 ในจำนวนนี้มีผู้ป่วยที่มีข้อบ่งชี้ในการบำบัดทนแทนไตอย่างต่อเนื่องด้วยข้อบ่งชี้ที่มากกว่าหรือเท่ากับ 2 ข้อถึงร้อยละ 80.0*

ค่าเฉลี่ยของ BUN และ Creatinine ก่อนเริ่มการบำบัดทดแทนไตอย่างต่อเนื่องมีค่าเท่ากับ 78.8 ± 36.5 mg/dl (10.0 ถึง 187.0) และ 5.3 ± 3.3 mg/dl (2.0 ถึง 20.2) ตามลำดับ ระยะเวลาในการบำบัดทดแทนไตอย่างต่อเนื่องอยู่ระหว่าง 1.5 ถึง 251.0 ชั่วโมง (ค่าเฉลี่ย 57.8 ± 58.9) และค่าเฉลี่ยของขนาดการบำบัดทดแทนไตอย่างต่อเนื่องเท่ากับ 36.6 ± 7.5 ml/kg/hr (24.6 ถึง 55.6) อัตราการเสียชีวิตโดยรวมเท่ากับร้อยละ 80 สาเหตุส่วนใหญ่ของการเสียชีวิต คือการติดเชื้อในกระแสเลือดร้อยละ 44.4 ตามด้วยเสียชีวิตจากโรคทางระบบหัวใจและหลอดเลือด ร้อยละ 15.6 ปัจจัยที่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติในกลุ่มผู้ที่รอดชีวิตและเสียชีวิตได้แก่ การรักษาตัวในหอผู้ป่วยหนักศัลยกรรม (p = 0.021) การติดเชื้อในกระแสเลือด (p = 0.019) ค่าคะแนน APACHE II (p = 0.011) ข้อบ่งชี้ในเรื่องภาวะน้ำเกินในการบำบัดทดแทนไตอย่างต่อเนื่อง (p = 0.028) จำนวนของข้อบ่งชี้ในการบำบัดทดแทนไตอย่างต่อเนื่อง (p = 0.019) ระยะเวลาในการเข้ารับการรักษาตัวในโรงพยาบาล (p = 0.004) ระดับความดันโลหิตขณะหัวใจบีบตัว (p = 0.012) และระดับโปรตีนอัลบูมินในเลือด (p = 0.009) เมื่อได้ทำการวิเคราะห์ด้วยสถิติการวิเคราะห์ความถดถอยแบบ logistic แล้วพบว่ามีเพียงระดับโปรตีนอัลบูมินในเลือดที่น้อยกว่า 3 g/dl ที่มีความสัมพันธ์กับการเสียชีวิต

สรุป: *จากการศึกษาการรักษาผู้ป่วยด้วยการบำบัดทดแทนไตอย่างต่อเนื่องในโรงพยาบาลภูมิพลอดุลยเดช ในระยะเวลา 1 ปี แสดงให้เห็นถึงอัตราการเสียชีวิตของผู้ป่วยที่สูงซึ่งไม่ได้แตกต่างจากการศึกษาต่าง ๆ ที่เคยทำมาก่อน ปัจจัยเพียงปัจจัยเดียวที่พบว่ามีความสัมพันธ์กับการเสียชีวิตในการศึกษาครั้งนี้จากการวิเคราะห์ทางสถิติคือ ระดับอัลบูมินในเลือดที่ต่ำขณะเริ่มทำการบำบัดทดแทนไตอย่างต่อเนื่อง ควรมีการศึกษาแบบไปข้างหน้าเพื่อยืนยันและหาความสัมพันธ์ที่แท้จริงต่อไป*