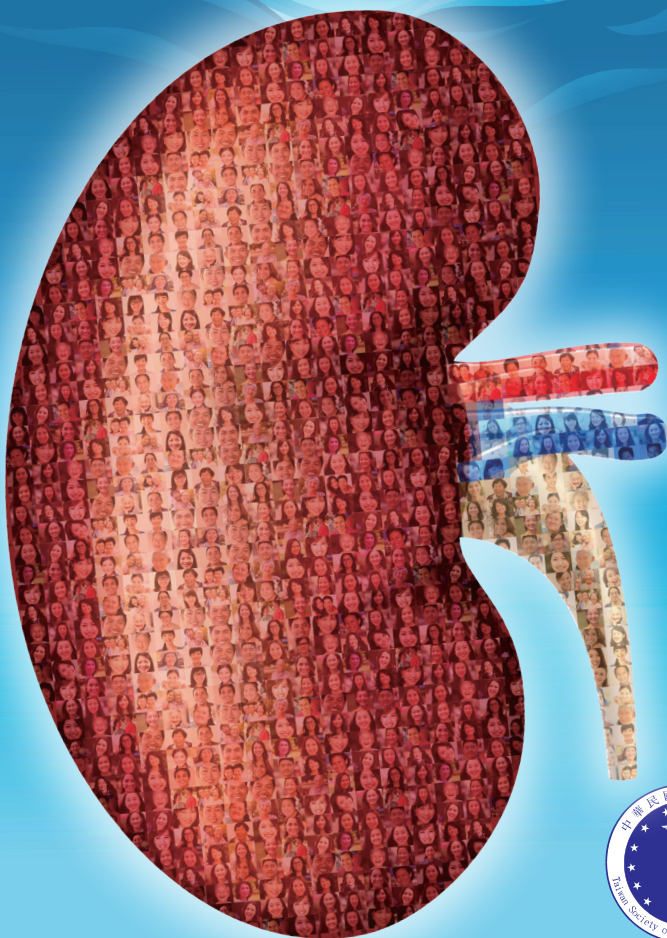


2017 Taiwan CRRT Operational Manual for Critically Ill Patients



Index

Preface	2
Section 1: CRRT Management — Quick Start Manual	3
Introduction	3
AKI Definition and Staging	4
CRRT Indications	5
CRRT Contraindications	6
Timing of CRRT Initiation	7
CRRT Mechanism, Mode and Initial Settings	8
Options of Dialysate and replacement fluids	10
Circuit Priming	11
Prescriptions	12
Monitoring	14
Possible Complications	15
Vascular Access	16
Preventing Clotting in The Filter and/or Extracorporeal Circuit	17
Discontinuing CRRT	20
CRRT Summary	21
Appendix I. Antibiotics Dose Adjustment in CRRT	22
Section 2: CRRT Management	27
— Quality Index Recommendations	
Introduction	27
Trainings of professional team	27
Dose Prescription	28
Possible Complications	29
Filter and extracorporeal circuit related problems	30
CRRT Patient Management Record (1) (TSCCM Recommend Form)	31
CRRT Patient Management Record (2) (TSCCM Recommend Form)	32
Taiwan CRRT Expert Meeting- Expert List	34
Colophon (Copyright Page)	36

Preface

Patients with septic shock and multiple organ failures along with acute renal failure were commonly seen in Intensive Care Unit (ICU), requiring continuous renal replacement therapy (CRRT). CRRT is mainly aimed at achieving the purposes of reducing uremic toxins, removing excess water and providing intravenous nutrition supplement, etc. Critically ill patients with acute kidney injury (AKI) have a relatively high mortality and cause the complexity and diversity of clinical care. Therefore, managing such critically ill patients has always been a challenge for physicians and nursing medical team.

CRRT was initially incorporated into clinical practice to substitute the traditional intermittent renal replacement therapy (IRRT), which is not applicable to critically ill patients. With advance of medical technology, CRRT has gradually been utilized along with brand new organ support to treat critically ill patients. In view of this, Taiwan Society of Critical Care Medicine (TSCCM) has invited experts in the field of critical care and nephrology to conduct series of comprehensive discussions regarding the treatment of CRRT in critically ill patients with AKI since 2015. Based on the 2012 KDIGO Guidelines and experts' experiences in Taiwan, TSCCM has published the first version of the CRRT Management Consensus Handbook for Critically Ill Patients with Acute Kidney Injury in July 2016. Thereafter in 2017, experts have shared the implementation steps of CRRT from the perspective of operator, hoping to educate medical staffs to grasp the essence and improve clinical skills.

At the same time, as CRRT has been widely used, the need for quality control in this technique has arisen constantly. Therefore, it is necessary to introduce a quality management system to standardize and improve implementation of CRRT, looking forward to becoming a technical assessment reference adopted by healthcare authority. At present, quality indices have been well established for hemodialysis and peritoneal dialysis in patients with end-stage renal disease. However, quality index of CRRT remains uncertain. Accordingly, TSCCM intends to encourage clinicians to evaluate the effectiveness of CRRT by publishing "CRRT - Quality Index Recommendations", in order to achieve technique control and continuous quality improvement (CQI).

Hopefully, Taiwan CRRT Operational Manual for Critically Ill Patients will enhance the quality and safety of CRRT - related care in critically ill patients.

Chairman of Taiwan Society of Critical Care Medicine
Chong-Jen Yu

中華民國重症醫學會 理事長

余忠仁

Section 1

CRRT Management — Quick Start Manual

Introduction

Continuous renal replacement therapy (CRRT) including a series of dialytic modality was recommended for the treatment of acute kidney injury (AKI), in that intermittent hemodialysis (IHD) is not applicable due to hemodynamic instability, or a critically ill patient whose body fluids or metabolic derangement cannot be corrected by IHD.

As CRRT is a relatively new technique, Taiwan Society of Critical Care Medicine has invited experts in the field of critical care and nephrology to review relevant literatures and international guidelines and to collect their professional opinions to establish this manual, in hopes that beginners can quickly grasp the operating essence of CRRT.

This manual aims to provide a quick reference. However, clinical situation is ever-changing, and critically ill patients often present with complex disease entities. Therefore, clinicians should judge and manage patients based on their actual situations.

AKI Definition and Staging

According to KDIGO (Kidney Disease: Improving Global Outcomes) Guideline 2012:

Definition		
<ul style="list-style-type: none">• Serum creatinine (SCr) concentration increases ≥ 0.3 mg/dL ($26.5 \mu\text{mol/L}$) within 48 hours; or• SCr increases to over 1.5 times baseline in 7 days; or• Urine output for 6 hours < 0.5 mL/kg/hr		
Staging		
	SCr	Urine output
Stage 1	Elevate to 1.5-1.9 times baseline or increase ≥ 0.3 mg/dL ($\geq 26.5 \mu\text{mol/L}$)	Urine output for 6-12 hours < 0.5 mL/kg/h
Stage 2	Elevate to 2.0-2.9 times baseline	Urine output for ≥ 12 hours < 0.5 mL/kg/h
Stage 3	Elevate to over 3 times baseline or Increase to ≥ 4.0 mg/dL ($\geq 353.6 \mu\text{mol/L}$) or Initiate renal replacement therapy or Patients under 18 years old with eGFR < 35 mL/min/1.73m ²	Urine output for ≥ 24 hours < 0.3 mL/kg/h or Anuria ≥ 12 hours

-
- Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney International Supplements 2012; Vol. 2, Issue 1: 1 – 126.

CRRT Indications

Classical Indications

Present with any of the following condition with either hemodynamic instability or increase intracranial pressure :

1. Medically refractory hyperkalemia.
2. Medically refractory, severe metabolic acidosis.
3. Diuretics-refractory volume overload.
4. Oliguria or anuria.
5. Uremic complications.
6. Some drugs intoxications.

Potential Indications

Critically ill patients with AKI may be considered for CRRT if one of the criteria meets:

1. Hemodynamic instability.
2. Body fluid imbalance (due to heart failure or multiple organ failure).
3. Increased catabolism (e.g. rhabdomyolysis).
4. Sepsis.
5. Increased intracranial pressure.
6. Electrolyte imbalance.
7. Other clinical conditions that benefit from the use of CRRT.

-
- Ashita Tolwani. N Engl J Med 2012; 367:2505-14.
 - Sean M. Bagshaw and Ron Wald, Kidney Int 2017; 91:1022 – 1032

CRRT Contraindications

1. The patient or his/her proxy declines to accept CRRT, and/or
2. Unable to establish proper vascular access, and/or
3. Lack of CRRT equipment, or lack of properly trained personnel

Note: For those cases, which implementation of CRRT or the condition of utilizing CRRT were clinically indicated as useless or even harmful (such as terminal disease), these conditions could be considered as relative contraindication.

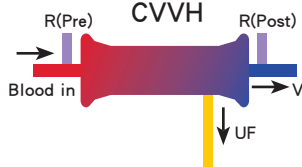
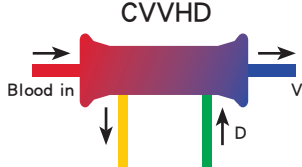
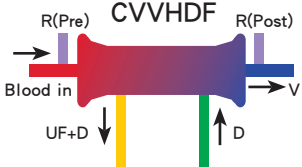
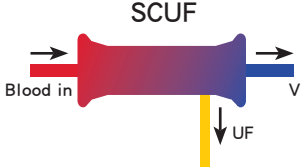
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- KDIGO 5.2.1: Discontinue RRT when it is no longer required, either because intrinsic kidney function has recovered to the point that it is adequate to meet patient needs, or because RRT is no longer consistent with the goals of care. (Not Graded)
 - Ashita Tolwani. N Engl J Med 2012;367:2505-2514.

Timing of CRRT Initiation

The international guidelines and expert consensus have no clear suggestions for the timing of CRRT initiation. **Clinically, critically ill patients whose need for maintenance of metabolic or fluid balance exceeds present residual renal function may consider initiating CRRT.**

-
- Marlies Ostermann, et al. Blood Purif 2016; 42:224-237

CRRT Mechanism, Mode and Initial Settings

	CVVH	CVVHD	CVVHDF	SCUF
				
	Body fluid management Elimination of middle molecular weight solute Elimination of small molecular weight solute	Elimination of small molecular weight solute Uremic complication	Body fluid management Elimination of middle molecular weight solute Elimination of small molecular weight solute	Body fluid management (CHF, hypervolemia etc.)
	1. Set Qb 2. Set Replacement Rate 3. Set replacement solution mode/ratio (Pre-, Pre- & Post-, Post-) 4. Select replacement fluid 5. Set UF rate 6. Select anti-coagulation	1. Set Qb 2. Set Qd 3. Select dialysate 4. Set UF rate 5. Select anti-coagulation	1. Set Qb 2. Set Replacement Rate 3. Set replacement solution mode/ratio (Pre-, Pre- & Post-, Post-) 4. Select replacement fluid 5. Set Qd 6. Select dialysate 7. Set UF Rate 8. Select anti-coagulation	1. Set Qb 2. Set UF rate 3. Select anti-coagulation
Diffusion	-	++++	+++	-
Convection	++++	-	+++	+
Initial Setting Range: Assume the patient weighs 60 kg				
Qb (ml/min)	150-250	150-250	150-250	150-250
Replacement* (ml/hr)	(1200-1500)*1.25	0	(600-750)*1.25	(120-500)*1.25
Pre/Post (Range)	50%(0%-100%) / 50% (100%-0%)	n/a	50%(0%-100%) / 50% (100%-0%)	n/a
Qd, Dialysate (ml/hr)	0	1000-2000	600-750	0

CVVH: continuous venovenous hemofiltration;

CVVHD: continuous venovenous haemodialysis;

Qb: blood flow rate;

Qd: dialysate flow rate.

* Replacement flow (ml/hr) is suggested to set as 1.25x (target delivered dose).

n/a: not applicable

CVVHDF: continuous venovenous hemodiafiltration;

SCUF: slow continuous ultrafiltration.

Options of Dialysate and replacement fluids

Currently available dialysate and replacement fluid formulations in Taiwan.

Final Concentration	Baxter Primasol B0	S.T. (CVVH A+0.45% Half-Saline+ Bicarbonate)
Sodium (mEq/L)	140	142.35
Potassium (mEq/L)	0	0
Chloride (mEq/L)	109.5	113.05
Magnesium (mEq/L)	1	1.43
Calcium (mEq/L)	3.5	2.6
Bicarbonate (mEq/L)	32	33.33
Lactate (mEq/L)	3	0
Glucose (mg/dL)	0	0

Circuit Priming

- Ensure that gases trapped in all lines, as well as small bubbles, are removed.
- Prime with heparinized normal saline (add 1 mL 5000U heparin in 1000 mL normal saline).

Prescriptions

Prescriptions of CRRT should consider:

1. Treatment mode
2. Blood flow rate
3. Type and rate of replacement fluid (for CVVH and CVVHDF)
4. Type and rate of dialysate (for CVVHD and CVVHDF)
5. Type and dose of anticoagulant (for current user)
6. Set target of fluid removal based on patient's current condition

While doing CVVH or CVVHDF, the administration of replacement fluid before the hemofilter will dilute the blood in the filter and reduce the risk of clotting.

The delivery mode of replacement fluid may cause or prevent filter clotting. For example, the administration of replacement fluid before the hemofilter will dilute the blood in the filter and reduce the risk of clotting. But the administration of replacement fluid after the hemofilter will concentrate the blood and enhance clotting.

Delivering an effluent flow rate of at least 20 mL/kg/h is recommended for CRRT. And frequent assessment of the actual delivered dose is needed to adjust the prescription.

The effluent flow (Note 1) is commonly used as a measure of small molecule solutes clearance rate and is reported in mL/kg/h. It is often taken as the surrogate of RRT dose. Current treatment guidelines recommended that the delivered effluent flow of CRRT should be at least 20 mL/kg/h. However, the actual effluent flow will be influenced by interruptions of CRRT, and actual solute clearance might decrease over time due to the deposition of blood clot and protein on the filter membrane. Therefore, a higher prescription of effluent volume is recommended. And frequent assessment of the actual delivered dose is needed for prescription adjustment.

Use appropriate amount of anticoagulant

CRRT can be performed without anticoagulants, especially in patients with increased risk of bleeding. However, this approach is generally associated with lower circuit life. Unfractionated heparin remains the most commonly used anticoagulant during CRRT. Appropriate amount of heparin is suggested. Regional citrate anticoagulation is an alternative but is not introduced into Taiwan yet.

Note 1: The effluent of CVVH is ultrafiltrate; the effluent of CVVHD is spent dialysate and the effluent of CVVHDF contains both.

- Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney International Supplements 2012; Vol. 2, Issue 1: 1 - 126.
- Rolando Claure-Del Granado, et al. Clin J Am Soc Nephrol. 2011; 6: 467 - 475

Monitoring

Collaborative members of the medical team such as dietitians and clinical pharmacists may also receive CRRT related training. In most cases, experts recommend monitoring the following items once a day. Monitoring frequency can be adjusted according to clinical requirements.

Monitor item	<ul style="list-style-type: none">• Body weight• Intake/Output• Acid-base balance• Electrolyte (Sodium, Potassium, Magnesium, Calcium, Phosphate)• Coagulation time (aPTT, ACT)• Hematocrit• Platelet• Blood sugar
---------------------	--

Note:

1. *Adjust medication dosage (especially antibiotic) according to dialysis dosage. (Appendix I)*
2. *Adjust nutritional supplement (especially protein) according to dialysis dosage.*

Possible Complications

Catheter-related problems	The common problems are: <ul style="list-style-type: none">• Bleeding• Infection• Vascular injury
Circuit-related problems	Circuit obstruction caused by clotting is the most common problem.
Other common problems	<ul style="list-style-type: none">• Hypotension• Arrhythmia• Fluid balance• Electrolytes derangements such as hypokalemia, hypophosphatemia• Loss of nutrient \ Hypoglycemia• Hypothermia• Bleeding caused by anticoagulant• Underdosing of drugs

-
- [Ashita Tolwani. N Engl J Med 2012;367:2505-2514.](#)
 - [Merrer J, et al.. JAMA 2001;286:700-7.](#)
 - [Oliver MJ. Semin Dial 2001;14:432-5.](#)

Vascular access

It is recommended to insert dialysis catheter under ultrasound guidance.

The preference for insertion of dialysis catheter:

- First choice: right internal jugular vein
- Second choice: femoral vein
- Third choice: left internal jugular vein
- Forth choice: subclavian vein with the preference for the dominant side

The outer diameter of dialysis catheter varies between 11 and 14 French. Catheter with larger diameter is preferred to decrease the risk of inadequate blood flow. In order to provide adequate blood flow and reduce the risk of recirculation, the tip of dialysis catheter should be placed in a large venous lumen. This means that the optimal length of dialysis catheter for right jugular vein, left jugular vein, and femoral vein should be 12-15 cm, 15-20 cm, and 19-24 cm, respectively.

-
- [Kidney Disease: Improving Global Outcomes \(KDIGO\) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney International Supplements 2012; Vol. 2, Issue 1: 1 – 126.](#)

Preventing clotting in the filter and / or extracorporeal circuit

One of the major challenges of successful CRRT is to keep the treatment uninterruptedly on-going in order to achieve the ideal therapeutic dose. Therefore, making sure the filter and the extracorporeal circuit adequately functioning is crucial for CRRT.

Coagulation cascade reactivation, high hematocrit and poor blood flow in the extracorporeal circuit (by high-viscosity, turbulences or stasis of circuit of flow) are the common causes of premature clotting of the filter and the extracorporeal circuit. Therefore, using anticoagulants and well maintaining the flow adequacy of the extracorporeal circuit are the most commonly recommended preventive strategies. When the setting of the extracorporeal circuit is optimized with adequate flow velocity, the anticoagulation will show fewer effects on the patency of CRRT extracorporeal circuit. In patients with coagulopathy such as thrombocytopenia or persistent bleeding tendency (acute traumatic or postoperative coagulation disorders), renal replacement therapy can still be safely performed without anticoagulants.

Non-anticoagulant alternatives to maintain patency and adequacy of extracorporeal circuit

1. Reduce blood volumetric stasis within the extracorporeal circulation

■ Vascular access

- Choose a catheter with large diameter and adequate length to ensure the catheter tip in the central venous lumen.
- Timely recognition and early correction of a kinked catheter are crucial.

■ Rapid troubleshooting: Nurses should be familiar with the CRRT alarm information and handle it promptly.

- Delayed response to the pump alarm may lead to the slowdown of the extracorporeal circulation flow and premature clotting in the filter.

- Regularly examine the deaeration chamber and ensure at least 2/3 of the chamber is filled with blood, in order to minimize the blood-air exposure.
- When using low blood flow postdilution hemofiltration, a minimum postdilution flow rate of 200 mL/hr should be used to keep the deaeration chamber full.
- The extracorporeal circulation pressure parameters should be monitored and troubleshooted during CRRT to reduce the possibility of clotting in the filter or extracorporeal circulation (see "Extracorporeal Circulation Pressure Range and Alarm Isolation Reference Table" on the next page)

2. Optimize CRRT settings

- When anticoagulant is not used, consider predilution treatment.
- When using **postdilution** treatment, maintain filtration fraction (FF) < 25%

Note:

$$FF = Q_{total\ UF} / Q_P$$

$$Q_{total\ UF} = \text{Total Ultrafiltration Rate}^*$$

$$Q_P = \text{Plasma Flow Rate}$$

$$^* \text{ Total Ultrafiltration Rate} = \text{Replacement fluid flow rate} + \text{Patient fluid removal rate}$$

-
- Joannidis M, et. al. Crit Care. 2007;11:218.

Table. Extracorporeal circuit pressure range and alarm trouble-shooting suggestions

Pressure	Normal Range	Definition	Possible reasons for abnormal pressure
Arterial pressure (Pa)	-10 ~ -60 mmHg	<ul style="list-style-type: none"> ● Pa is presented as negative value because it represents the suction pressure from blood pump. ● The higher the speed of blood pump, the more negative the Pa value. 	<ul style="list-style-type: none"> ● Patient access is obstructed or kinked. ● Speed of blood pump changes.
Venous pressure (Pv)	30 ~ 100 mmHg	Pv is presented as positive value because it reflects the resistance in the catheter connecting to the patient due to blood flow in.	<ul style="list-style-type: none"> ● Patient access is obstructed or kinked. ● Speed of blood pump changes. ● Clotting or occlusion in venous chamber.
Input pressure (Pin)	150 ~ 250 mmHg	<ul style="list-style-type: none"> ● Measures the pressure in the circuit after it has passed the blood pump, pre hemofilter ● This value is also related to the TMP calculation. 	<ul style="list-style-type: none"> ● Clotting or occlusion in the filter. ● Blood flow overspeed.
Transmembrane pressure (TMP)	50 ~ 200 mmHg	Pressure difference between the blood side and ultrafiltrate/ dialysate side of semi-permeable membrane.	<ul style="list-style-type: none"> ● Clotting or occlusion in the filter. ● Clotting or occlusion in circulation or venous chamber. ● Venous access is obstructed or kinked. ● Filtration volume / rate increases.
Transfilter pressure gradient (Pressure drop, ΔP)	<20 mmHg (mainly monitor the pressure change trend)	<ul style="list-style-type: none"> ● Calculated as the difference between pre-filter and post-filter pressure. ● $P_{in} - P_v = \text{Pressure gradient (Pressure drop, } \Delta P)$ 	<ul style="list-style-type: none"> ● Clotting or occlusion in the filter

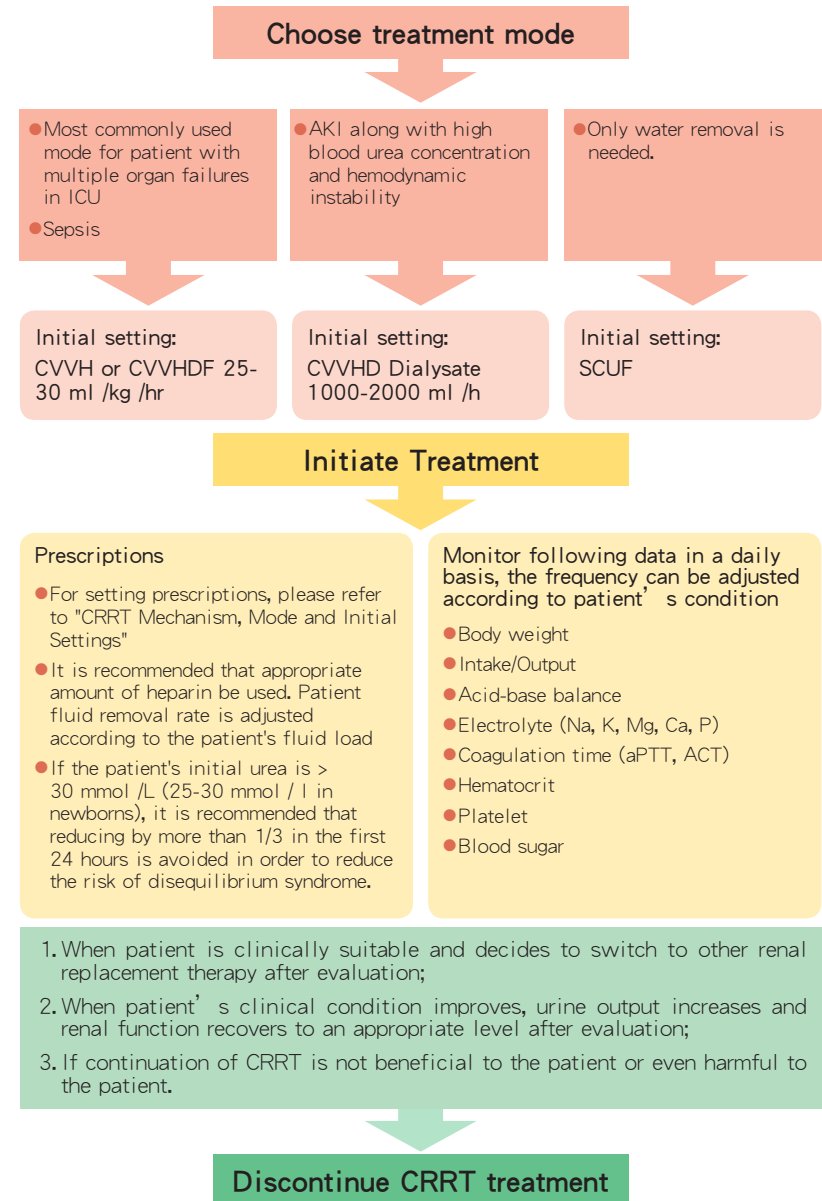
Discontinuing CRRT

Consider discontinuing CRRT in one of the following situations:

1. When a patient is clinically suitable to switch to other renal replacement therapy. For example, switch to SLED or IHD when a patient is gradually withdrawing vasopressor or is transferred out from ICU.
2. When patients' renal function recovers to an appropriate level, which means daily urine output reached 400 mL without using any diuretics or urine output while using diuretics reached 2300 mL, discontinuation of CRRT may be considered.
3. If continuation of CRRT may not be beneficial to the patient or even harmful to the patient.

-
- Uchino S, et al. Crit Care Med 2009;37:2576-2582.
 - Wu VC, et al. Intensive Care Med 2008;34:101-108.

CRRT Summary



Antibiotics Dose Adjustment in CRRT

Authors: Chien-Chih Wu, Tai-Shin Wang, Chia-Hui Lee, Li-Ching Lin, Chia-Ying Liu

Anti-bacterial agents¹

Antibiotics	Recommended dose	
	Loading dose	Maintenance dose
Aminoglycoside^a		
Amikacin	10 mg/kg	7.5 mg/kg qd
Gentamicin	3 mg/kg	2 mg/kg qd
Tobramycin	3 mg/kg	Depends on TDM
Carbapenems^b		
Doripenem ²	1g	500mg q8h
Ertapenem	-	1g qd
Imipenem/cilastatin	1g	500mg q8h
Meropenem	1g	500mg q8h
	2g	2g q12h in meningitis, cystic fibrosis, or MIC = 4mcg/mL
Cephalosporin^b		
Cefazolin	2g	1g q8h - q12h
Cefuroxime ³	-	1.5g q12h
Cefmetazole ⁵	Lack of data	
Cefoxitin	-	2g q8h
Cefotaxime	-	2g q8h
Ceftriaxone	Dose adjustment not required	
Flomoxef ⁶	Lack of data	
Cefoperazone/sulbactam ^d	Lack of data	
Ceftazidime ^{4,5}	2g	1g q6h
Cefepime ^{14,15}	2g	1g q6h in neutropenic fever
Penicillin^b		
Penicillin G	4 MU	2 MU q4h
Ampicillin	-	2g q8h
Ampicillin/sulbactam ^a	-	3g q8h
Oxacillin	Dose adjustment not required	
Piperacillin/tazobactam ^a	-	3.375g q6h - 4.5g q8h
Fluoroquinolone		
Ciprofloxacin	-	400mg q12h
Levofloxacin ¹⁴	750mg	250 - 500mg qd
Moxifloxacin	Dose adjustment not required	
Glycopeptide		
Teicoplanin ^{6,7}	12mg/kg*3 dose	12mg/kg qd
Vancomycin ^{a,e}	20 mg/kg	7.5mg/kg q12h
Lipopeptides		
Daptomycin ⁸	-	8mg/kg qd
Macrolides		
Azithromycin	Dose adjustment not required	

Antibiotics	Recommended dose	
	Loading dose	Maintenance dose
Oxazolidinones		
Linezolid	Dose adjustment not required	
Polymyxins		
Colistin ⁹	4mg/kg, max. 300 mg	217.1mg (3.25 vial) q12h
Tetracyclines/Glycylcyclines		
Doxycycline	Dose adjustment not required	
Tigecycline	Dose adjustment not required	
Miscellaneous		
Aztreonam	2g	1g q6h - q8h
Clindamycin	Dose adjustment not required	900mg q8h
Fosfomycin ^f	-	8g q8h
Metronidazole	Dose adjustment not required	500mg q8h
Rifampin	Dose adjustment not required	
Sulfamethoxazole/trimethoprim	-	7.5mg/kg q12h

- Dosage recommendation based on effluent flow of 1-2 L/hr. If higher effluent rate was applied, higher dose of antibiotics could be considered.
- Dosage recommendation based on minimum residual renal function (daily urine output < 500 mL/day). If residual renal function preserved, higher dose of antibiotic could be considered.

*** Dose presented as total amount of two components.**

For example: Ampicillin-sulbactam 3g = ampicillin 2g + sulbactam 1g.

- Serum concentration should be monitored for dose adjustment. If flow rate > 1 L/hr, maintenance dose may be given every 24 hours, but it depends on the drug concentration.
- Extended infusion (3-4 hours) should be used for penicillin, cephalosporin and carbapenem antibiotics.
- Use effluent rate as CrCl, then adjust dose accordingly. For example, effluent flow = 2L/hr = 33.3 mL/min, take CrCl = 33.3 mL/min as dosing adjustment reference.
- Because of the discrepancy of CRRT removal of two components, dose suggestion is not available currently.
- According to related data from NTUH, of over 80% of patients' serum concentration could achieve 10-20 mg/L.
- Because fosfomycin was highly eliminated by CRRT (~77%), the usual dose for severe infection was suggested.

Anti-fungal agents¹

Antibiotics		Recommended dose	
		Loading dose	Maintenance dose
Azoles			
	Fluconazole ¹⁰	800mg (12 mg/kg)	400mg (6mg/kg qd)
	Voriconazole ^{11,a}	6mg/kg for 2 dose	3-4 mg/kg q12h
Echinocandins			
	Anidulafungin	Dose adjustment not required	
	Caspofungin	Dose adjustment not required	
	Micafungin	Dose adjustment not required	100–150mg qd
Polyenes			
	Amphotericin B	Dose adjustment not required	Pathogen-dependent
	Liposomal amphotericin B	Dose adjustment not required	Pathogen-dependent

■ Dosage recommendation based on effluent flow of 1-2 L/hr. If higher effluent rate was applied, higher dose of antibiotics could be considered.

■ Dosage recommendation based on minimum residual renal function (daily urine output <500 mL/day). If residual renal function preserved, higher dose of antibiotic could be considered.

a. Voriconazole could be used in patients receiving CRRT because sulfobutylether- β -cyclodextrin (SBECD) was eliminated by CRRT tremendously.

Anti-viral agents¹

Antibiotics		Recommended dose	
		Loading dose	Maintenance dose
Anti-HSV, CMV			
	Acyclovir	-	5-10mg/kg qd ^a
	Ganciclovir ¹⁴	5mg/kg	2.5 mg/kg qd
Anti-influenza			
	Oseltamivir ¹²	-	75mg q12h
	Peramivir ¹³	600mg	200mg qd
Anti-HBV			
	Entecavir ^b	Lack of data	
	Tenofovir	Lack of data	

■ Dosage recommendation based on effluent flow of 1-2 L/hr. If higher effluent rate was applied, higher dose of antibiotics could be considered.

■ Dosage recommendation based on minimum residual renal function (daily urine output <500 mL/day). If residual renal function preserved, higher dose of antibiotic could be considered.

a. Low dose is recommended for superficial HSV infection. High dose is recommended for disseminated HSV infection or meningitis.

b. Use effluent rate as CrCl, then adjust dose accordingly. For example, effluent flow= 2L/hr = 33.3 mL/min = entecavir 1tab po qod. Dosage adjustment of entecavir according to creatinine clearance is listed below:

- CrCl \geq 50 mL/min: No dosage adjustment required
- CrCl 30-49 mL/min: Reduce to 0.25 mg/day or 0.5 mg q48hr
- CrCl 10-29 mL/min: Reduce to 0.15 mg/day or 0.5 mg q72hr
- CrCl <10 mL/min: 0.05 mg/day or 0.5 mg q7days

Reference:

1. Drug information handbook 2017-2018: Lexi-comp.
2. Roberts JA, Udy AA, Bulitta JB, et al. Doripenem population pharmacokinetics and dosing requirements for critically ill patients receiving continuous venovenous haemodiafiltration. *The Journal of antimicrobial chemotherapy* 2014;69:2508-16.
3. Janssen PK, Foudraine NA, Burgers DM, Neef K, le Noble JL. Population Pharmacokinetics of Cefuroxime in Critically Ill Patients Receiving Continuous Venovenous Hemofiltration With Regional Citrate Anticoagulation and a Phosphate-Containing Replacement Fluid. *Therapeutic drug monitoring* 2016;38:699-705.
4. Jiang SP, Zhu ZY, Wu XL, Lu XY, Zhang XG, Wu BH. Effectiveness of pharmacist dosing adjustment for critically ill patients receiving continuous renal replacement therapy: a comparative study. *Therapeutics and clinical risk management* 2014;10:405-12.
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Section 2

CRRT Management — Quality Index Recommendations

Introduction

According to a survey conducted in the United Kingdom, only 69% of patients diagnosed with acute kidney injury received "qualified" therapy and nearly one-third of them have not reached the minimum requirement of standard of care. However, there was no consensus regarding prescription, implementation and quality management of CRRT globally.

By editing "**Taiwan CRRT Management Operational Manual for Critically Ill Patients**", Taiwan Society of Critical Care Medicine proposes a CRRT quality index management reference by setting up minimum requirements for CRRT implementation. This will serve as a first step and hopefully an ideal and practical standard of CRRT quality index can be established by analyzing data collected.

Trainings of professional team

CRRT should be conducted by health care professional who have received appropriate related trainings.

Dose Prescription

Dosage	We suggest adequate dose defined by, at least 20 mL/Kg/h of the effluent flow achieved in postdilutional mode. Dose should be adjusted and increased by considering the treatment downtime.
Treatment duration	On treatment duration should be greater than 80% of time.
Dose achievement rate	Dose achievement rate $\geq 80\%$.
Quality index	If the treatment duration is long, the average dose should be above the recommendation.

Possible complications

It is suggested to evaluate the following complications:

		Yes	Never	Not evaluated
Anticoagulant-related problems	Anticoagulant-related major bleeding			
	Heparin-induced thrombocytopenia			
Catheter-related Problems	Infection			
	Vascular damage			
Other common problems	Hypokalemia (<2 meq/L)			
	Hypophosphatemia (<1 mg/dL)			

Filter and extracorporeal circuit related problems

Extracorporeal circuit pressure should be monitored to reduce clotting in filter or circuit while conducting CRRT.

Pressure	Normal Range	Definition	Possible reasons for abnormal pressure
Arterial pressure (Pa)	-10 ~ -60 mmHg	<ul style="list-style-type: none"> Pa is presented as negative value because it represents the suction pressure from blood pump. The higher the speed of blood pump, the more negative the Pa value. 	<ul style="list-style-type: none"> Patient access is obstructed or kinked. Speed of blood pump changes.
Venous pressure (Pv)	30 ~ 100 mmHg	Pv is presented as positive value because it reflects the resistance in the catheter connecting to the patient due to blood flow in.	<ul style="list-style-type: none"> Patient access is obstructed or kinked. Speed of blood pump changes. Clotting or occlusion in venous chamber.
Input pressure (Pin)	150 ~ 250 mmHg	<ul style="list-style-type: none"> Measures the pressure in the circuit after it has passed the blood pump, pre hemofilter This value is also related to the TMP calculation. 	<ul style="list-style-type: none"> Clotting or occlusion in the filter. Blood flow overspeed.
Transmembrane pressure (TMP)	50 ~ 200 mmHg	Pressure difference between the blood side and ultrafiltrate/dialysate side of semi-permeable membrane.	<ul style="list-style-type: none"> Clotting or occlusion in the filter. Clotting or occlusion in circulation or venous chamber. Venous access is obstructed or kinked. Filtration volume / rate increases.
Transfilter pressure gradient (Pressure drop, ΔP)	<20 mmHg (mainly monitor the pressure change trend)	<ul style="list-style-type: none"> Calculated as the difference between pre-filter and post-filter pressure. Pin-Pv=Pressure gradient (Pressure drop, ΔP) 	<ul style="list-style-type: none"> Clotting or occlusion in the filter

CRRT Patient Management Record (1) (TSCCM Recommend Form)

Institute/Hospital:	Vascular access position:		
Patient:	Size of catheter:		
Age:	Treatment modes: <input type="checkbox"/> CVVH ; <input type="checkbox"/> CVVHDF ; <input type="checkbox"/> CVVHD ; <input type="checkbox"/> SCUF		
Date: / /	Pre% / Post%:		
	Heparin dose - Initial dosel	U	Maintenance dosel U

Prescription A (ml/kg/hr) :			
Actual treatment duration B (hr) :			
Total treatment duration C (hr) :	Start: Month/ Day/ Hour/ Min (a)	End: Month/ Day/ Hour/ Min (b)	C = b - a = (hr)
Actual dose D = A × B / C =			
Actual dose / Prescription dose D / A =		≥ 0.8? <input type="checkbox"/> YES	<input type="checkbox"/> NO

		Yes	Never	Not evaluated
Anticoagulant-related problems	Anticoagulant related major bleeding (1A)			
	Heparin induced thrombocytopenia (1B)			
Catheter-related Problems	Infection (2A)			
	Vascular damage (2B)			
Other common problems	Hypokalemia (<2 meq/L) (3A)			
	Hypophosphatemia (<1 mg/dL) (3B)			
	(3C) Please specify:			
	(3D) Please specify:			

CRRT Patient Management Record (2) (TSCCM Recommend Form)

Time	Hemodynamic			Prescriptions					Current pressures						I/O data					Complications Specify: (1A)、 (1B)、 (2A)、 (2B)、 (3A)、 (3C)...
	Blood Pressure	Heart Rate	Central Venous Pressure	Blood Flow	Dialysate Flow	Replacement Fluid Flow	Removal Flow	Anti. Dose	Pa	Pv	Filter pressure	Effluent pressure	Pressure drop	TMP	Dialysate volume	Replace volume	Total effluent volume	Patient removal volume	Weight	
	mmHg	bpm	mmHg	Blood	Dialysate	Replace.	Pt. Removal	Anti.	Access	Return	Filter	Effluent	△ P	TMP	Dialysate	Replace.	Effluent	Pt. Removal	Kg	
				ml/min	ml/hr	ml/hr	ml/hr	ml/hr	mmHg	mmHg	mmHg	mmHg	mmHg	mmHg	ml	ml	ml	ml		
Day shift (1)																				
Day shift (2)																				
Day shift (3)																				
Day shift (4)																				
Day shift (5)																				
Day shift (6)																				
Day shift (7)																				
Day shift (8)																				
8-hour accumulative I/O volume in day shifts																				
Night shift (1)																				
Night shift (2)																				
Night shift (3)																				
Night shift (4)																				
Night shift (5)																				
Night shift (6)																				
Night shift (7)																				
Night shift (8)																				
8-hour accumulative I/O volume in night shifts																				
Midnight shift (1)																				
Midnight shift (2)																				
Midnight shift (3)																				
Midnight shift (4)																				
Midnight shift (5)																				
Midnight shift (6)																				
Midnight shift (7)																				
Midnight shift (8)																				
8-hour accumulative I/O volume in midnight shift																				
24-hour accumulative I/O volume																				

Taiwan CRRT Expert Meeting- Expert List

2017/04/22 Expert Meeting

Hospital	Department	Expert
TSCCM		Dr. Huey-Wen Yien
Sijhih Cathay General Hospital	SICU-1	Dr. Joseph Juey-Ming Shih
Cathay General Hospital	SICU-1	Dr. James Yao-Ming Shih
Far Eastern Memorial Hospital	SICU	Dr. Fang-Ming Hung
Taipei Veteran General Hospital	Dept. Internal Medicine	Dr. Chiao-Lin Chuang
Chang Gung Memorial Hospital- Linco	Dept. Nephrology	Dr. Hsiang-Hao Hsu
MacKay Memorial Hospital	MICU	Dr. Li-Kuo Kuo
Tri-Service General Hospital	MICU	Dr. Chung-Kan Peng

2017/05/13 Expert Meeting

Hospital	Department	Expert
Changhua Christian Hospital	SICU-1	Dr. Shu-Hui Wang
National Taiwan University Hospital	Dept. Internal Medicine	Dr. Shih-Chi Ku
Hualien Tzu Chi Hospital	SICU	Dr. Guan-Jin Ho
China Medical University Hospital	SICU- General	Dr. Shih-Chi Wu
Asia University Hospital	Dept. Nephrology	Dr. Che-Yi Chou
Lin Shin Hospital	Dept. Emergency & Critical Care Medicine	Dr. Ming-Hwei Lin
Chung Shan Medical University Hospital	Dept. Nephrology	Dr. Tung-Wei Hung
Taipei Medical University Hospital	SICU	Dr. Kuo-Chin Yuan
Taipei Veteran General Hospital	Dept. Internal Medicine	Dr. Chiao-Lin Chuang
Chang Bing Show Chwan Memorial Hospital	Dept. Nephrology	Dr. Limei Hsu
Chang Gung Memorial Hospital- Linco	Dept. Nephrology	Dr. Hsiang-Hao Hsu
Taichung Veteran General Hospital	Dept. Nephrology	Dr. Chun-Te Huang
National Taiwan University Hospital	Dept. Nephrology	Dr. Tao-Min Huang
China Medical University Hospital	Dept. Nephrology	Dr. Hung-Chieh Yeh
Taichung Veteran General Hospital	Dept. Chest Medicine	Dr. Ming-Chen Chan

2017/05/27 Expert Meeting

Hospital	Department	Expert
An-Nan Hospital	Dept. Nephrology	Dr. Po-Tang Wang
National Cheng Kung University Hospital	Dept. Nephrology	Dr. Junne-Ming Sung
Chang Gung Memorial Hospital- Kaohsiung	Dept. Nephrology	Dr. Chien-Hsing Wu

Hospital	Department	Expert
Chang Gung Memorial Hospital- Kaohsiung	Dept. Nephrology	Dr. Terry Ting-Yu Chiou
E-Da Hospital	Dept. Nephrology	Dr. Shih-Yuan Hung
National Cheng Kung University Hospital	Dept. Nephrology	Dr. Yu-Tzu Chang
ChiMei Medical Center- Liouying	Dept. Intensive Care Medicine	Dr. Pak-On Leung
Taipei Veteran General Hospital	Dept. Internal Medicine	Dr. Chiao-Lin Chuang
Chang Gung Memorial Hospital- Linco	Dept. Nephrology	Dr. Hsiang-Hao Hsu
ChiMei Medical Center- YongKang	Dept. Intensive Care Medicine	Dr. Khee-Siang Chan
Kaohsiung Veteran General Hospital	Dept. Cardiology	Dr. Wei-Chun Huang
Kaohsiung Medical University Chung-Ho Memorial Hospital	MICU Dept. Chest Medicine	Dr. Ming-Ju Tsai
Kaohsiung Medical University Chung-Ho Memorial Hospital	Dept. Cardiovascular Surgery	Dr. Chong-Chao Hsieh
Chang Gung Memorial Hospital- Kaohsiung	Dept. Pediatrics	Dr. Kai-Sheng Hsieh
Hualien Tzu Chi Hospital	SICU	Dr. Lee-Ying Soo

2017/06/17 CRRT Guidebook Editorial Meeting

Hospital	Department	Expert
Changhua Christian Hospital	SICU-1	Dr. Shu-Hui Wang
Hualien Tzu Chi Hospital	SICU	Dr. Guan-Jin Ho
China Medical University Hospital	SICU- General	Dr. Shih-Chi Wu
Cathay General Hospital	SICU-1	Dr. James Yao-Ming Shih
Far Eastern Memorial Hospital	SICU	Dr. Fang-Ming Hung
Taipei Veteran General Hospital	Dept. Internal Medicine	Dr. Chiao-Lin Chuang
Chang Gung Memorial Hospital- Linco	Dept. Nephrology	Dr. Hsiang-Hao Hsu
MacKay Memorial Hospital	MICU	Dr. Li-Kuo Kuo
ChiMei Medical Center- YongKang	Dept. Intensive Care Medicine	Dr. Chin-ming Chen
Tri-Service General Hospital	MICU	Dr. Chung-Kan Peng
China Medical University Hospital	Dept. Nephrology	Dr. Hung-Chieh Yeh
National Taiwan University Hospital	Dept. Anesthesia	Dr. Yu-Chang Yeh
Taichung Veteran General Hospital	Dept. Chest Medicine	Dr. Ming-Chen Chan
Kaohsiung Medical University Chung-Ho Memorial Hospital	MICU Dept. Chest Medicine	Dr. Ming-Ju Tsai
Hualien Tzu Chi Hospital	SICU	Dr. Lee-Ying Soo

Taiwan CRRT Operational Manual for Critically Ill Patients

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Executive editors/

Dr. Shih-Chi Ku, Dr. Fang-Ming Hung, Dr. Chiao-Lin Chuang,
Dr. Hsiang-Hao Hsu, Dr. Chung-Kan Peng, Dr. Yu-Wei Huang,
Dr. Ming-Cheng Chan, Dr. Lee-Ying Soo

Legal consultant/ Prof. Jung-Tang Hsieh

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Taiwan Society of Critical Care Medicine

Address/ 15F-2, No. 50, Sec. 1, Zhongxiao W. Rd., Zhongzheng District,
Taipei 10041, Taiwan

Tel / 02-2371-3319

Fax / 02-2370-8338

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Taiwan Society of Critical Care Medicine

Address : 15F-2, No. 50, Sec. 1, Zhongxiao W. Rd., Zhongzheng District,
Taipei 10041, Taiwan

Tel : 02-2371-3319 Fax : 02-2370-8338

Email : tscmc@ms32.hinet.net

Website : <http://www.tscmc.org.tw>

