post AKI(急性腎臟病)藥事照護經驗分享

蘇建豪 臨床藥師
高雄長庚紀念醫院藥劑部

May 9,2021

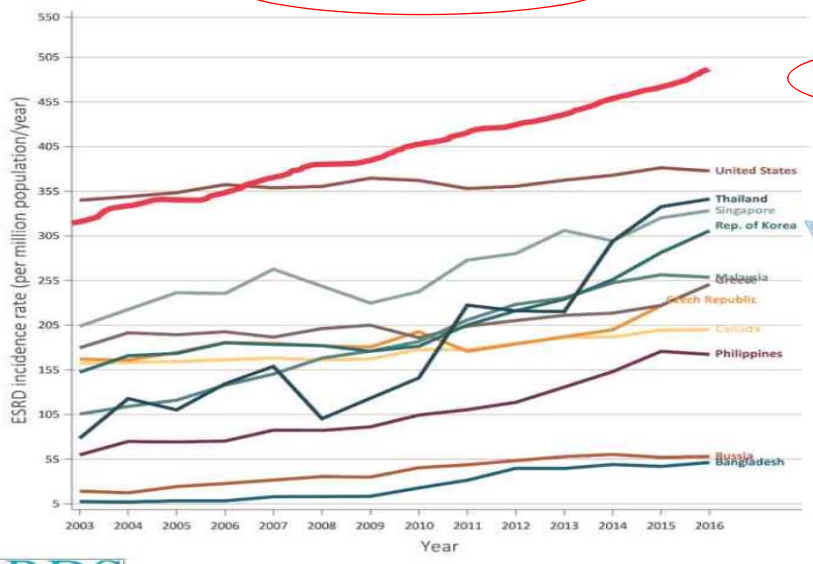
1

大綱

- 急性腎損傷簡介
  - 定義與分期
  - 流行病學
  - 危險因子
  - 診斷
  - 預後
- 藥事照護三大目標
  - 用藥整合 (Minimise polypharmacy, medication re-initiation….)
  - 用藥安全(Avoid NSAID, nephrotoxicity)
  - 藥品衛教
- 案例報導

2

Vol 2 Figure 11.3 Trends in the incidence rate of treated ESRD (per million population/year), by country, 2003-2016



Taiwan = 493 pmp/year

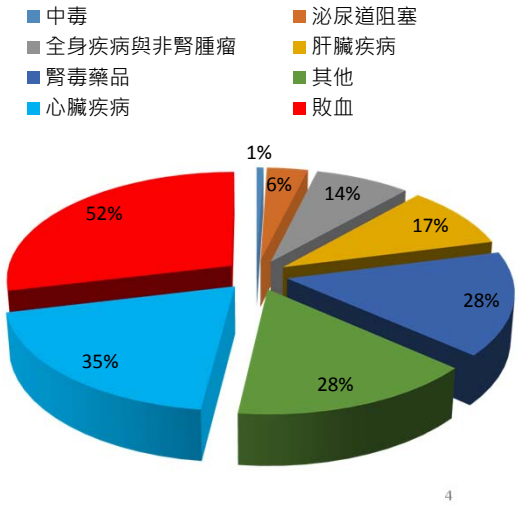
USRDS UNITED STATES RENAL DATA SYSTEM

2018 Annual Data Report
Volume 2 ESRD, Chapter 11

5

前言

- Acute kidney injury (AKI) is a broad clinical syndrome
  - rapid loss of renal function
    - leading to the retention of waste products, electrolyte disturbances, volume status changes
  - encompassing various etiologies
    - specific kidney diseases
    - non-specific conditions
    - extrarenal pathology
- Drug induced AKI
  - Adults:14%–26% of AKI
  - Pediatric: 6% of hospitalized AKI



4

Kidney Int 2012;2(Suppl):1-138.
Medicine (2016) 95:39(e4987)
Prim Care Clin Office Pract 47 (2020) 691–702

AKI定義與分期

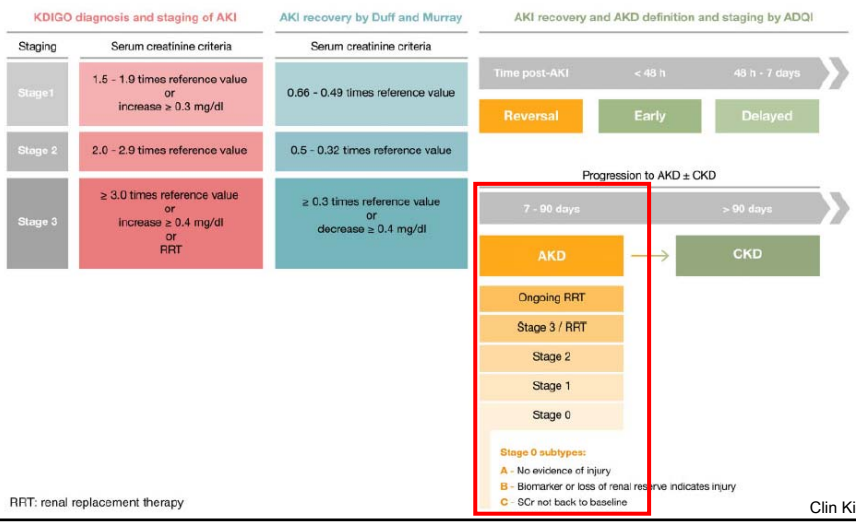
Table 1. Comparison of Recent Consensus AKI Definitions

AKI Stage	Urine Output[a]	KDIGO	AKIN	RIFLE
1	<0.5 mL/kg/h for 6-12 h	Scr to 1.5-1.9 × baseline over 7 d or ≥0.3 mg/dL absolute increase over 48 h	Scr to 1.5-2 × baseline or ≥0.3 mg/dL absolute Scr increase within 48 h	*Risk*: Scr to ≥1.5 × increase within 7 d, sustained for ≥24 h
2	<0.5 mL/kg/h for ≥12 h	Scr to 2.0-2.9 × baseline	Scr to >2-3 × baseline	*Injury*: Scr to ≥2 × increase
3	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h	Scr to ≥3.0 × baseline, or Scr increase to ≥4.0 mg/dL or initiation of RRT	Scr to >3.0 × baseline, or Scr increase to ≥4.0 mg/dL (with increase of 0.5 mg/dL) or initiation of RRT	*Failure*: Scr to ≥3.0 × increase or Scr increase to ≥4.0 mg/dL (with increase of 0.5 mg/dL) or initiation of RRT
				Loss: Complete loss of kidney function for >4 wk
				ESKD: ESKD for >3 mo

5

Sci Rep. 2016; 6: 23022.

AKI-AKD-CKD 連續性照護



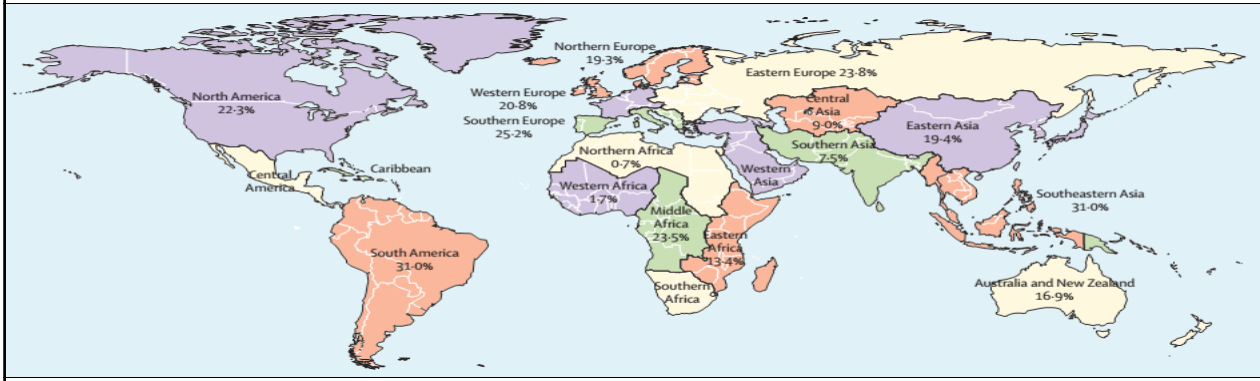
RRT: renal replacement therapy

6

Clin Kidney J. 2020;14(3):789-804

AKI流行病學

- proportion of people in hospital that had AKI



21% hospital admissions were affected

Clin J Am Soc Nephrol 8: 1482–1493, 2013

7

AKI常見危險因子

Table 2. Common Risk Factors for Acute Kidney Injury

Susceptibilities		Exposures	
Non-modifiable	Modifiable	Planned	Unplanned
Old age	Renin-angiotensin-system inhibitors	Iodinated contrast	Infection/antibiotics
Previous acute kidney injury	Diuretics	Cardiac/vascular surgery	Diarrhea
Chronic kidney disease	Calcineurin inhibitors	Major abdominal surgery	Intravascular volume depletion
Diabetes	Nonsteroidal anti-inflammatory drugs/Cox-2 inhibitors	Prolonged physical work in unhealthy environments	Hypotension
Chronic heart disease	Chemotherapy		Trauma
Liver disease	Low socioeconomic status		Public health event
Cancer	Poor health literacy		
Tropical locale	Malnourished		
High altitude	Inadequate housing/water quality/sanitation		

Am J Med. 2020;133(5):552-560

8

AKI 發生率與預後

Clinical setting	incidence Rate	Mortality Rate	OR for mortality
Community acquired	8.3%	32.8%	2.56(95% CI 1.31-5.01)
Critical care	31.7%	33.1%	3.93(95% CI 3.12-4.96)
Hospital acquired, unspecified	20.9%	25.7%	5.15 (95% CI 3.86-6.87)
Cardiac surgery	24.3%	8.3%	6.31(95% CI 4.81-8.28)
Trauma	19.9%	32.2%	6.62(95% CI 1.75 -24.99)
Heart failure	32.4%	21.3%	2.13(95% CI 1.38-3.27)
Hematology/oncology	21.3%	25.7%	15.50(95% CI 8.40-28.60)
Nephrotoxins	12.2%	14.8%	2.45 (95% CI 1.30-4.63)
Liver transplantation	41% (AKI), 8 %(requiring dialysis		3.0 (95%CI 2.3–3.8)
Lung transplantation	53% (AKI), 9%(requiring dialysis)		1.5 (95%CI 1.1–1.9)
Heart transplantation	47% (AKI), 12%(requiring dialysis)		2.7 (95% 1.6–3.3)

Clin J Am Soc Nephrol.2013 ; 8(9): 1482–1493
J. Clin. Med. 2020, 9, 1104

AKI病因與表現

Prerenal

Sudden and severe reduction in blood pressure (shock) of interruption of blood flow to the kindeys from severe injury or illness

- Blood loss
- Dehydration
- Heart failure
- Sepsis
- Vascular occlusion

Intrinsic Renal

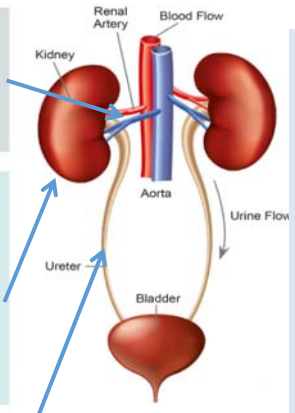
Direct injury to the kidneys by inflammation, drugs, toxins, infection, or reduced blood supply

- Acute tubular necrosis
  - Drugs
  - Toxins
  - Prolonged hypotension
- Glomerulonephritis
- Acute tubular necrosis
  - Drugs
  - Toxins
  - Autoimmune disease
  - Infection
- Small-vessel vasculitis

Postrenal

Sudden obstruction of urine flow due to enlarged prostate, kidney stones, bladder injury or tumor

- Benign prostatic hyperplasia
- Cervical cancer
- Meatal stenosis/phimosis
- Retroperitoneal fibrosis
- Prostate cancer
- Urinary calculi

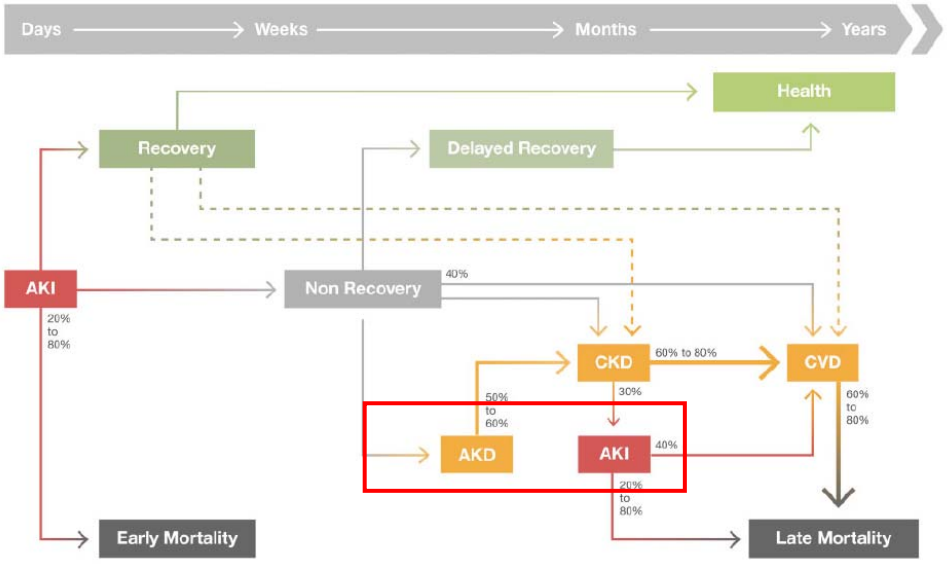


Phase	Features	Duration
Onset phase	• Common triggering events: significant blood loss, burns, fluid loss, diabetes insipidus • Renal blood flow 25% of normal • Tissue oxygenation 25% of normal • Urine output below 0.5 mL/kg/hour	Hours to days
Oliguric (anuric) phase	• Urine output below 400 mL/day, possibly as low as 100 mL/day • Increases in blood urea nitrogen (BUN) and creatinine levels • Electrolyte disturbances, acidosis, and fluid overload (from kidney's inability to excrete water)	8 to 14 days or longer, depending on nature of AKI and dialysis initiation
Diuretic phase	• Occurs when cause of AKI is corrected • Renal tubule scarring and edema • Increased glomerular filtration rate (GFR) • Daily urine output above 400 mL • Possible electrolyte depletion from excretion of more water and osmotic effects of high BUN	7 to 14 days
Recovery phase	• Decreased edema • Normalization of fluid and electrolyte balance • Return of GFR to 70% or 80% of normal	Several months to 1 year

10

J. Clin. Med. **2020**, 9, 1104; doi:10.3390/jcm9041104

AKI病人長期預後



11

Clin Kidney J. 2020;14(3):789-804

AKI/AKD 藥物管理計畫策略

- Include a clinical pharmacist for drug stewardship.
- Identify patients at risk of AKI/AKD and take into account the risk of AKI/AKD when prescribing.
- Assess hydration status.
- Assess chronic drugs and their indication for continuation or discontinuation.
- Perform medication regimen review and evaluate PK/PD interactions.
- Review the use of drugs in patients who develop acute or chronic illnesses that increase the risk of AKI.
- Assess the dynamic impact of AKI/AKD on drug PK/PD.
- Assess the dynamic impact of renal recovery on drug PK/PD.
- Assess concurrent illness on drug PK/PD (e.g., sepsis, heart failure).
- Assess the impact of RRT on drug PK/PD.
- Undertake dynamic prescription and medication reconciliation at transitions of care.

12

Kidney Int 2020;98(2):294-309.

第一步：找出長期預後不佳的病人

AKI	AKI non-recovery	Development and progression of CKD	Cardiovascular outcomes	Long-term mortality
Older Age	Older Age	Older Age	Older Age	Older Age
Hypertension	Hypertension	Hypertension	Hypertension	Hypertension
CKD	CKD	CKD	CKD	CKD
CVD	CVD	CVD	CVD	CVD
Diabetes	Diabetes	Diabetes	Diabetes	Diabetes
	Severity of AKI	Severity of AKI	Severity of AKI	Severity of AKI
Hypoalbuminemia		Hypoalbuminemia		Hypoalbuminemia
Anemia		Anemia		
		Duration of AKI		Duration of AKI
		Female gender		Male gender
		Illness severity		Illness severity
Others				
Liver disease	Black Race	AKI relapses		Cancer
Lung disease	Hemodynamic instability	Albuminuria		AKI recovery
HIV infection	Medical admission	Need for RRT		
Obesity	RRT modality	Timining and type of AKI recovery		
Shock				
Sepsis				
Nephrotoxins				
Surgery				
Hyperuricemia				
Hyperglicemia				

13

Clin Kidney J. 2020;14(3):789-804

AKI 嚴重程度對存活影響

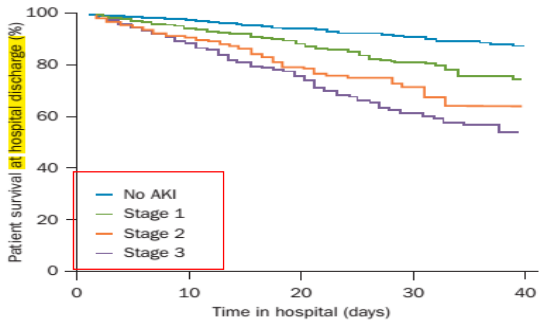


Figure 2 | Kaplan–Meier graph for hospital survival, stratified by KDIGO stages of acute kidney injury. Reproduced with

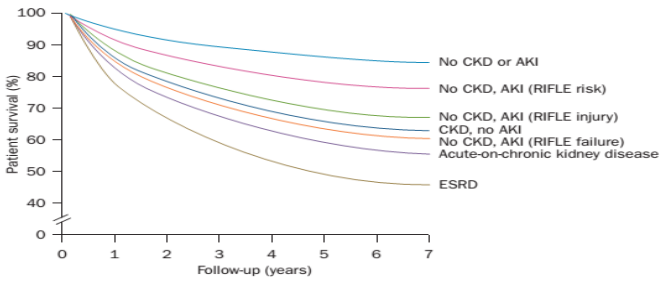


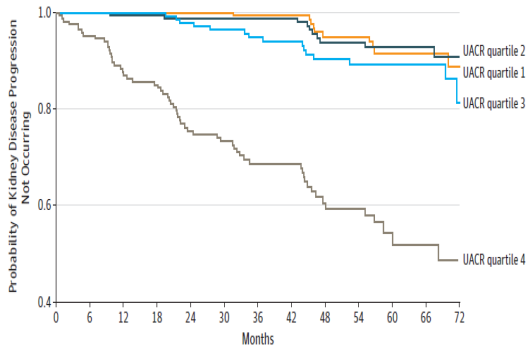
Figure 3 | Long-term survival stratified by CKD and AKI. Cox proportional hazard

14

Nat. Rev. Nephrol. 10, 193–207 (2014)

AKI後蛋白尿對CKD的預測

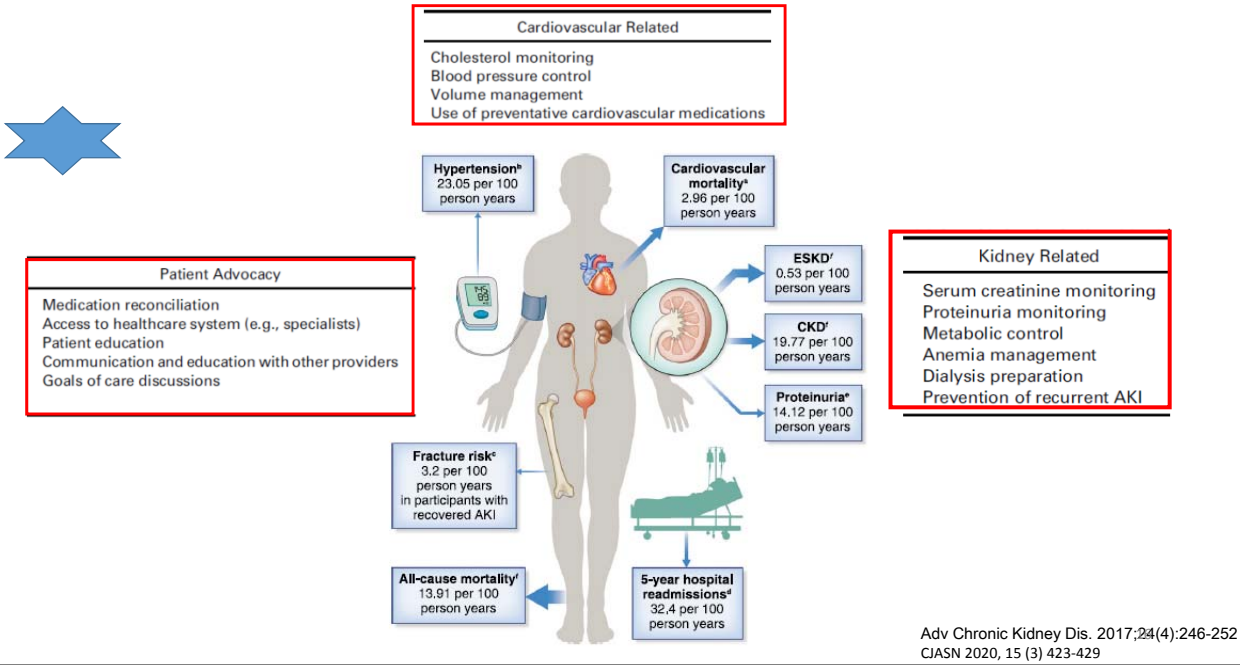
Figure. Kaplan-Meier Curves Showing Time to Kidney Disease Progression (Defined as Halving of eGFR or ESRD) by Quartiles of Urine ACR (UACR) Among the 769 ASSESS-AKI Enrollees With AKI 3 Months Prior to Baseline ASSESS-AKI Study Visit



Predictors in Model	All Matched ASSESS-AKI Enrollees (n = 1538) HR (95% CI)	P Value	C Statistic
Adjusted model with interaction terms (AKI vs no AKI)			
Higher urine ACR (per doubling), mg/g	1.26 (1.11-1.43)	<.001	
Female vs male	1.57 (1.00-2.48)	.05	
Black vs nonblack	1.18 (0.68-2.04)	.55	
Hispanic vs non-Hispanic	1.14 (0.32-3.98)	.84	
Diabetic vs nondiabetic	2.27 (1.35-3.83)	.002	
Older age (per 5 y increase)	0.89 (0.80-0.99)	.03	0.79
Higher systolic BP (per 10 mm Hg increase)	1.12 (1.00-1.24)	.04	
Higher BMI (per 5 kg/m^2 increase)	1.02 (0.88-1.18)	.77	
Lower eGFR (per 10 mL/min/1.73 m^2 decrease)	1.17 (1.06-1.30)	.002	
AKI vs no AKI	1.46 (0.51-4.13)	.48	
AKI vs no AKI urine ACR[a]	1.04 (0.90-1.20)	.63	
Adjusted model with interaction terms (stage of AKI vs no AKI)			
Higher urine ACR (per doubling), mg/g	1.25 (1.10-1.43)	<.001	
Female vs male	1.62 (1.02-2.57)	.04	
Black vs nonblack	1.15 (0.66-2.01)	.62	
Hispanic vs non-Hispanic	1.14 (0.32-4.01)	.84	
Diabetic vs nondiabetic	2.31 (1.37-3.91)	.002	
Older age (per 5 y increase)	0.89 (0.80-1.00)	.04	
Higher systolic BP (per 10 mm Hg increase)	1.13 (1.01-1.26)	.03	
Higher BMI (per 5 kg/m^2 increase)	1.02 (0.88-1.18)	.83	0.79
Lower eGFR (per 10 mL/min/1.73 m^2 decrease)	1.18 (1.07-1.31)	.001	
AKI stage 1 vs no AKI	1.54 (0.50-4.72)	.45	
AKI stage 2 vs no AKI	0.56 (0.07-4.84)	.60	
AKI stage 3 vs no AKI	2.24 (0.33-15.29)	.41	
AKI stage 1 vs no AKI urine ACR[a]	1.02 (0.87-1.19)	.80	
AKI stage 2 vs no AKI urine ACR[a]	1.16 (0.88-1.52)	.29	
AKI stage 3 vs no AKI urine ACR[a]	1.07 (0.82-1.40)	.61	

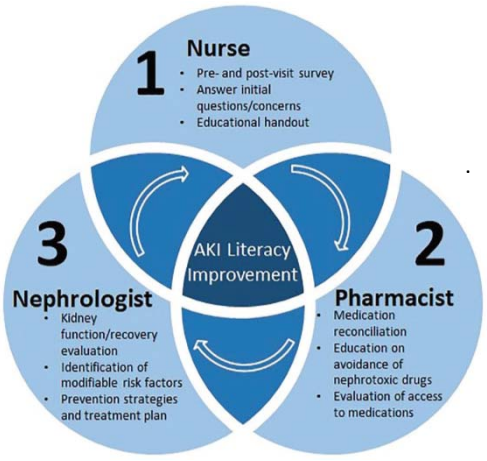
15

JAMA Intern Med. 2020;180(3):402-410.



Adv Chronic Kidney Dis. 2017;24(4):246-252
CJASN 2020, 15 (3) 423-429

第二步：了解藥師扮演的角色



出院後AKI跨團隊照護

Table 1. Educational Intervention About AKI Focusing on Three Main Domains.

Domain	Intervention
1. Education on understanding AKI and its consequences	• Discussion about the main functions of the kidney for solute and fluid homeostasis • Discussion about the potential causes of AKI during the hospitalization • Discussion about the potential kidney-related complications after AKI • Discussion about the potential non-kidney-related complications after AKI (ie, cardiovascular health)
2. Education on modifiable risk factors	• Adequate hydration, particularly when exposed to heat • Blood pressure control with a goal of ≤140 mm Hg systolic and ≤90 mm Hg diastolic (target is adjusted based on specific conditions)[40] • Glycemic control with a goal of hemoglobin A1C of <7%[41] • Avoidance of over-the-counter nephrotoxins (ie, nonsteroidal anti-inflammatory agents, proton pump inhibitors, herbal remedies, etc.)[25] • Avoidance of unnecessary procedures that require intravascular administration of iodinated contrast[25] • Lifestyle modifications[45] - BMI goal of 20-25 kg/m^2 - Exercise for at least 30 min 5 times per week - Limit alcohol and tobacco use - Lower salt intake to ~2 g (90 mmol) per day
3. Education on patient-specific risk factors	• Education on patient-specific risk factors such as underlying CKD, active cancer, cardiovascular disease, advanced liver disease, etc. • Education on specific dietary restrictions • Education on the importance of individualized dosing of certain prescribed medications according to current kidney functional status • Education about the importance of primary and/or subspecialty care for the management of comorbidity

Note. AKI = acute kidney injury; BMI = body mass index; CKD = chronic kidney disease.

17

Can J Kidney Health Dis 2019;6:2054358119830700.

用藥整合時機

目的

考量

追蹤

Drug management in clinical practice

1) We recommend medication assessments at the following instances during the AKD period:

a) medication reconciliation should occur at ICU/hospital admission and discharge
b) medication regimen assessment at AKD diagnosis and change in AKD stage
c) reassessment when patient condition changes

2) Strategies to avoid adverse drug reactions in AKD should seek to minimize both adverse events from overdosing or nephrotoxicity and therapeutic failure from under-dosing or incorrect drug selection.

3) Medication regimen assessment or consideration of medication introduction during the AKD period should consider:

a) nephrotoxic potential
b) altered drug disposition including renal or hepatic elimination, toxic metabolites and drug interactions
c) altered pharmacodynamics in AKD

4) Medication regimen assessment should be guided by a dynamic monitoring plan to include repeated serial assessment of:

a) clinical features (adverse drug reaction or therapeutic failure)
b) currently available renal diagnostic tests (eg biochemistry, imaging)
c) currently available therapeutic drug monitoring (parent drugs +/− metabolites)

18

Br J Clin Pharmacol .2018;84 396–403

如何進行用藥整合

- Have medicines been stopped during the episode of acute illness?
  - Antihypertensives (hemodynamic instability and AKI)
    - RAS inhibitor:Acute hypotension, GFR is already very low, Hyperkalemia
  - Anticoagulant /Antiplatelet
- What were the original indications for these medications?
- Are there strong prognostic indications to restart medications?
- If, when, and how should medications be restarted?
- What is the patient's blood pressure?
- Should any medications (e.g. NSAIDs) be discontinued?
- avoid unnecessary polypharmacy?
- Adapt drug dosing according to post AKI renal function

https://www.rcgp.org.uk/clinical-and-research/resources/toolkits/acute-kidney-injury-toolkit.aspx
Nephron 2018;138:92 – 103

英國心衰竭與腎臟學會 2019

Table 1 Management of RAAS inhibitors in response to change in renal function

Clinical assessment:

- ▶ Compare with baseline renal function (review series of results).
- ▶ Assess fluid status: if intravascularly depleted (jugular venous pulse not visible, postural drop in BP and no oedema), consider cautious intravenous fluids.
- ▶ Interpret BP in the context of usual values (low BP does not necessarily mean patient needs fluid).
- ▶ Reduce/withdraw RAASI if symptomatic hypotension.
- ▶ Repeated clinical and biochemical assessment is vital.
- ▶ Presence of moderate or severe hyperkalaemia may override recommendations based on change in renal function.
- ▶ In severe renal dysfunction assess for symptoms or uraemia.

	Recommendations for RAAS inhibitors	
Change in renal function compared with baseline	**HFpEF (assuming no other prognostic indication).**	**HFREF.**
Increase in serum creatinine by <30%	Consider stop ACEI/ARB/ARNI Review MRA according to fluid status.	Continue unless symptomatic hypotension.
Increase in serum creatinine 30%–50%	Stop RAAS inhibitor.	Consider reducing dose or temporary withdrawal.*
Increase in serum creatinine >50%	Stop RAAS inhibitor.	Temporarily stop RAAS inhibitor.*
Severe renal dysfunction, for example, eGFR <20	Stop RAAS inhibitor.	Stop RAAS inhibitor if symptomatic uraemia irrespective of baseline function.

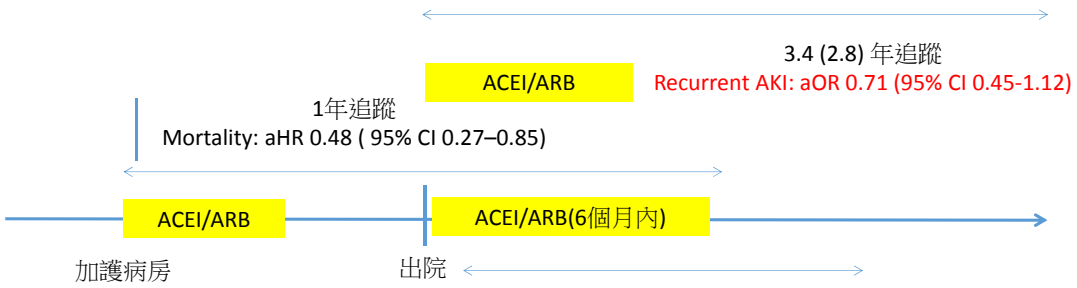
*Reinitiate and/or retitrate when renal function improved in patients with HFrEF.

ACEI, ACE inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced left ventricular ejection fraction; HFpEF, heart failure with preserved left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonists; RAAS, renin–angiotensin–aldosterone.

20

Heart 2019;**105**:904–910

重新給予RAS inhibitor臨床益處與風險



2年(US) 追蹤
Mortality: aHR 0.85; 95%CI, 0.81-0.89
hospitalization for a renal cause aHR 1.28; 95%CI, 1.12-1.46
Acute renal failure:aHR 1.25, 95% CI 1.08-1.46

Stop ACEI/ARB vs.30天內重新給

2年(England, Sweden)追蹤
Mortality: HR 1.27; 95% CI 1.15–1.41
AKI (HR 0.90; 95% CI 0.77–1.05)
Mortality: HR 0.94; 95% CI 0.78–1.1
AKI: HR 0.81; 95% CI 0.54–1.21

CJASN 2020 ;15(1):26-34.
Intensive Care Med. 2018 ;44(5):598-605
BMC Med. 2020 ;18(1):195

顯影劑施打後的用藥整合

J Nephrol . 2020 Feb 18. doi: 10.1007
J Renal Inj Prev. 2019; 8(3): 185-189.

SGLT2 inhibitor

Table 4 Recommendations for initiation and monitoring of SGLT2 inhibitor therapy

1. Optimize volume status and avoid hypotension prior to SGLT2 inhibitor initiation
2. Concurrent RAAS inhibitor and /or diuretic use are not contraindications to SGLT2 inhibitor initiation, however, caution should be taken to minimize other risk factors for AKI prior to SGLT2 inhibitor initiation
3. Cautious initiation of SGLT2 inhibitors in patients exposed to NSAIDs or other nephrotoxic agents
4. Close monitoring should be undertaken in patients with stage 3b CKD and other risk factors for AKI (nephrotoxic drugs, contrast exposure, N/V, diarrhea, etc.) started on a SGLT2 inhibitor
5. Employ a "sick day strategy" of holding SGLT2 inhibitors with acute illness, trauma, or major surgery when adequate fluid intake may be compromised or patients are otherwise prone to AKI

eGFR <45

Metformin

Table 3. The guidelines and recommendations on metformin administration during ICM procedure in diabetic patients based eGFR

Recommendations	ACR	CAR	ESUR	RCR	RANZCR
Discontinuing Metformin (before iodine contrast media method)	eGFR ≥30; no need/ eGFR<30 stop at the time or 48 hours before exposure	1. eGFR<45; at the time of contrast exposure. 2. eGFR <30 or AKI: 48 hours before exposure	1.eGFR≥45 (intravenous): no need 2. 30≤eGFR<59 (intra-arterial) and 30≤eGFR<44 (intravenous): 48 hours before exposure 3. eGFR<30 and in case of other illness: metformin is contraindicated	eGFR > 60: no need eGFR<60, consultation with the referring clinician to stop for 48 hours	eGFR ≥ 30: continue eGFR ≤ 30 stop metformin at the time of contrast exposure
Restarting Metformin (after iodine contrast media method)	Withhold for 48 hours after the procedure and restart only after monitoring renal function	Withhold for 48 hours after the procedure and restart only after ensuring stable renal function	Withhold for 48 hours after the procedure and restart only after ensuring stable renal function	Consultation with the referring clinician to stop for 48 hours	Withhold at least 48 hours after procedure and restart only after checking renal function

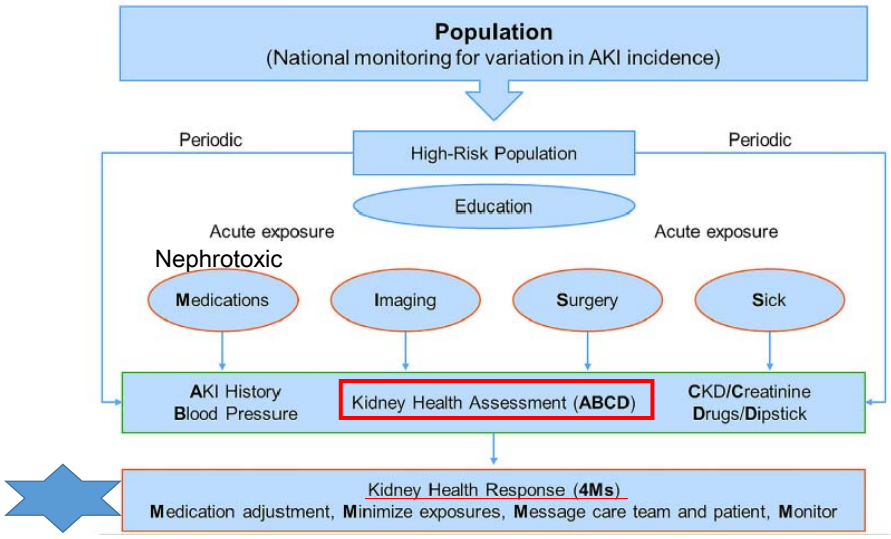
Restart!!

American College of Radiology (ACR), Canadian Association of Radiologists (CAR), European Society of Urogenital Radiology (ESUR), Royal College of Radiologists (RCR), Royal Australian and New Zealand College (RANZC) / eGFR (mL/min/1.73 m²).

eGFR <30

22

第三步：降低多重用藥相關AKI風險 (4M strategy)



23

Am J Med. 2020 ;133(5):552-560

多重用藥與腎衰竭

藥品品項≥10項

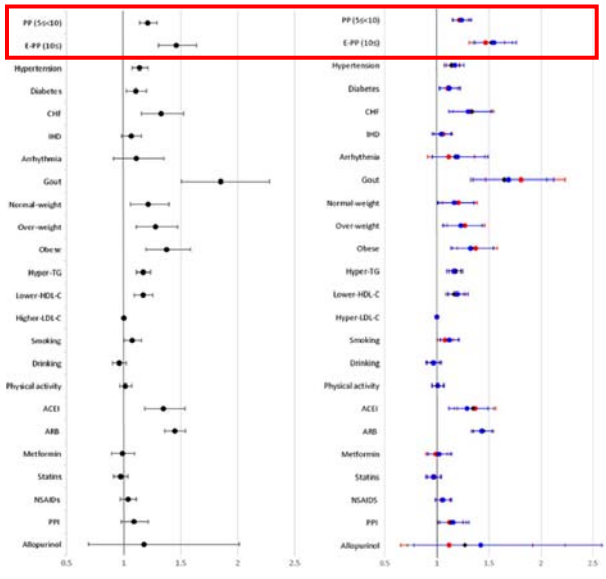


Table 2 Stepwise logistic regression of the duration of polypharmacy and ARF

	β	SE(β)	Adjusted odds ratio	p-value
Duration of polypharmacy: Less than 30 days*				
31- 90 days	0.28	0.03	1.33	<0.001
91 – 180 days	0.50	0.03	1.65	<0.001
Over 181 days	0.55	0.03	1.74	<0.001
Gender:Female*				
Male	0.28	0.02	1.32	<0.001
Age:0-18 years old *				
19-64 years old	1.86	0.08	6.40	<0.001
65-79 years old	2.19	0.08	8.93	<0.001
Over 80 years old	2.67	0.08	14.46	<0.001
ICUs	1.48	0.02	4.37	<0.001
Comorbidity				
ASHD	−0.23	0.02	0.80	<0.001
CHF	0.67	0.03	1.95	<0.001
CVA/TIA	0.21	0.02	1.24	<0.001
PVD	0.14	0.04	1.15	0.001
Other cardiac	0.08	0.03	1.09	0.006
COPD	−0.10	0.02	0.91	<0.001
GI	0.30	0.02	1.36	<0.001
Liver disease	0.15	0.02	1.16	<0.001
Cancer	0.65	0.02	1.92	<0.001
Diabetes	0.46	0.02	1.58	<0.001
Site of operation				
Nervous system	−0.82	0.07	0.44	<0.001
Endocrine system	−2.25	0.26	0.11	<0.001
Nose, mouth and pharynx	−0.58	0.14	0.56	<0.001
Respiratory system	−0.30	0.03	0.75	<0.001
Cardiovascular system	0.38	0.02	1.47	<0.001
Digestive system	0.26	0.02	1.30	<0.001
Urinary system	−0.21	0.03	0.81	<0.001
Male genital organs	−1.38	0.54	0.25	0.010
Female genital organs	−2.63	1.01	0.07	0.009
Musculoskeletal system	−0.15	0.06	0.86	0.007
Integumentary system	0.11	0.05	1.12	0.039
Miscellaneous diagnostic and therapeutic procedures	0.35	0.02	1.42	<0.001

* reference group.

24

40.

多重用藥相關急性腎損傷

Cumulative effect	Drugs combinations	Mechanism of increased nephrotoxicity	GRADE Level of Evidence
Renal ischemia	NSAIDS+diuretics+ RAAS Inhibitors	NSAIDs: decrease in prostaglandin synthesis; afferent arteriolar vasoconstriction RAAS inhibitors: efferent arteriolar vasodilation Diuretics: reduction of plasma volume, decreased renal blood flow,decreased renal perfusion pressure	Moderate
	CCBs+clarithromycin	Clarithromycin: CYP3A4 inhibition, increased CCBs concentrations hypotension	Moderate
Increased risk of statin-induced rhabdomyolysis	Statins+macrolides	Macrolides: inhibition of the cytochrome 450 (CYP450), increased serum statin concentrations	Moderate
	Statins+CCBs	CCBs: inhibition of the cytochrome 450 (CYP450), increased serum statin concentrations	Moderate

Drugs Aging (2017) 34:729–741 25
Annals of Pharmacotherapy 2016, Vol. 50(11) 953 –972

Exposure		Controls (%), $n=21,206$	Cases (%), $n=2226$	RR crude[a]	RR adjusted[a,b]	NNH/year
Background treatment	NSAID					
Overall						
Any RASI or diuretic	No	19,461 (91.8)	1952 (87.7)	1.59**	1.66**	237
	Yes	1745 (8.2)	274 (12.3)	(1.38, 1.82)	(1.40, 1.97)	
Stratification by single/combined use of RASI/diuretic						
RASI only	No	5803 (92.6)	559 (88.9)	1.58**	1.60**	347
	Yes	462 (7.4)	70 (11.1)	(1.21, 2.06)	(1.18, 2.17)	
Diuretic only	No	3774 (89.5)	390 (84.0)	1.69**	1.64**	340
	Yes	441 (10.5)	74 (16.0)	(1.28, 2.21)	(1.17, 2.29)	
RASI plus diuretic	No	9884 (92.1)	1004 (88.5)	1.54**	1.64**	158
	Yes	842 (7.9)	130 (11.5)	(1.26, 1.87)	(1.25, 2.14)	
Stratification by diuretic regimen						
Thiazide alone[c]	No	5866 (91.3)	541 (83.4)	2.10**	1.97**	258
	Yes	559 (8.7)	108 (16.6)	(1.68, 2.63)	(1.49, 2.61)	
Loop diuretic without aldosterone antagonist[d]	No	5886 (90.8)	605 (89.1)	1.20	1.18	431
	Yes	597 (9.2)	74 (10.9)	(0.93, 1.55)	(0.83, 1.66)	
Loop diuretic plus aldosterone antagonist[d]	No	1575 (93.9)	199 (93.0)	1.24	3.98*	10
	Yes	102 (6.1)	15 (7.0)	(0.68, 2.24)	(1.20, 13.2)	
Stratification by renal function						
Any RASI or diuretic and eGFR ≥60 ml/min	No	18 050 (91.9)	1 128 (87.0)	1.76**	1.60**	309
	Yes	1598 (8.1)	168 (13.0)	(1.43, 2.10)	(1.31, 1.95)	
Any RASI or diuretic and eGFR 30–59 ml/min	No	1 411 (90.6)	824 (88.6)	0.86	2.51*	75
	Yes	147 (9.4)	106 (11.4)	(0.53, 1.38)	(1.09, 5.78)	
Stratification by age						
Any RASI or diuretic and aged <60 years	No	4074 (89.7)	335 (84.8)	1.53*	1.34	684
	Yes	467 (10.3)	60 (15.2)	(1.05, 2.24)	(0.86, 2.07)	
Any RASI or diuretic and aged 60–74 years	No	8398 (90.5)	782 (85.9)	1.52**	1.41*	413
	Yes	877 (9.5)	128 (14.1)	(1.21, 1.90)	(1.07, 1.87)	
Any RASI or diuretic and aged 75 years or older	No	6989 (94.6)	835 (90.7)	2.04**	2.64**	68
	Yes	401 (5.4)	86 (9.3)	(1.54, 2.71)	(1.50, 4.64)	

Kidney International2015:88,396–403 26

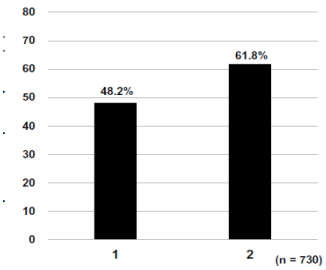
A cross-sectional exploratory survey on occurrence of triple-whammy prescription pattern in Japan

JMDC claims database
Outpatients between April~June 2017
3-month peroid~one prescription cycle
730/246,721 (0.3%)→CKD (13.3%)

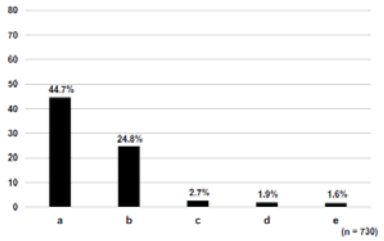
跨科別、跨院區用藥整合!!

Description	NSAIDs (n=730)	RAAS blockers (n=730)	Diuretics (n=730)
Internal medicine [n (%)]	358 (49.0)*,†	588 (80.6)	579 (79.3)
Orthopedic surgery [n (%)]	228 (31.2)*,†	9 (1.2)	9 (1.2)
General surgery [n (%)]	29 (4.0)	19 (2.6)	19 (2.6)
Cardiology [n (%)]	2 (0.3)*,†	20 (2.7)	21 (2.9)
Gastroenterology [n (%)]	11 (1.5)	12 (1.6)	12 (1.6)
Otorhinolaryngology [n (%)]	26 (3.6)*,†	0 (0.0)	5 (0.7)
Neurosurgery [n (%)]	6 (0.8)	12 (1.6)	12 (1.6)
Respiratory medicine [n (%)]	4 (0.5)	9 (1.2)	10 (1.4)
Urology [n (%)]	5 (0.7)	4 (0.5)	5 (0.7)
Obstetrics and gynecology [n (%)]	4 (0.6)	5 (0.7)	4 (0.5)
Other clinical departments [n (%)]	57 (7.8)	52 (7.1)	54 (7.4)

NSAIDs nonsteroidal anti-inflammatory drugs, *RAAS* renin–angiotensin–aldosterone system



Patterns	n	Any NSAIDs, RAAS blockers, or diuretics prescriptions
1	352	Prescribed by different clinical departments
2	451	Prescribed by different institutions

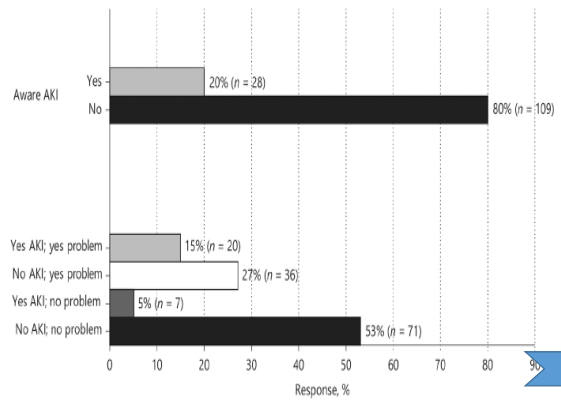


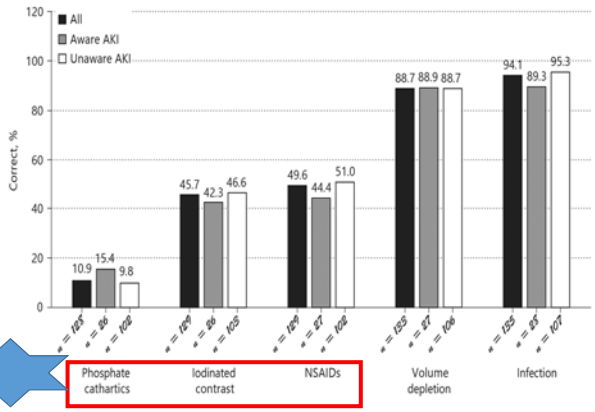
Items	n	Clinical departments of prescriptions		
		NSAIDs	RAAS blockers	Diuretics
a	326	Internal Medicine	Internal Medicine	Internal Medicine
b	181	Orthopedic Surgery	Internal Medicine	Internal Medicine
c	20	Otorhinolaryngology	Internal Medicine	Internal Medicine
d	14	General Surgery	General Surgery	General Surgery
e	12	Orthopedic Surgery	Cardiology	Cardiology

Int J Clin Pharm;42(5):1369-1373.

第四步: 病人用藥衛教

Post AKI後對腎臟病的認知與知識





Am J Nephrol. 2019 ; 49(6): 449–459
HOSPITAL PRACTICE, 2018

藥師於NSAID衛教扮演的角色

Advice

- Maintain a good fluid intake
  - avoid volume depletion, particularly if feeling unwell or in hot weather
- Avoid inadvertently taking additional NSAIDs
- Discuss a "sick day" plan with the patient
  - Acutely unwell (vomiting or diarrhea)
- Repeat weight, blood pressure, serum creatinine and electrolytes
  - within the first month
  - become acutely unwell.

"sick day" plan

- Contact their general practice to discuss whether further assessment is required
- Maintain adequate fluids; aim for pale-coloured urine
- Stop taking the NSAID and use an alternative analgesic for pain relief or fever if required
- Be aware of the symptoms of dehydration, such as increased thirst, dry mucous membranes, lethargy and weight loss
- Ensure they have someone to check on them regularly
- Seek medical attention immediately if their condition deteriorates

仍需要更多實證支持益處.....

29

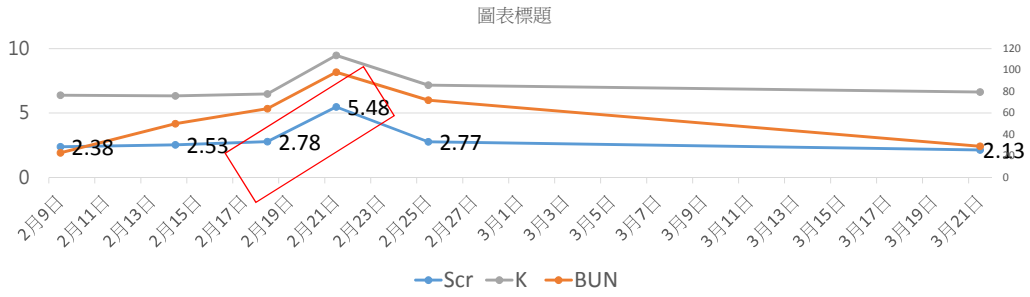
https://bpac.org.nz/2018/triple-whammy.aspx

Case presentation-1

- 90 y/o man
- Ht: 168cm (20210209), BW 44.1kg
- Past medical history
  - Heart failure with reduced EF, NYHA III (EF: 21%)
  - CKD staged 4
  - Gouty arthritis
  - BPH
  - Shortness of breath for few day and developed on 2/9~1ST ER
- Chief complaint (2021/02/21)
  - developed watery diarrhea for several times and general malaise since 3 days ago.
  - At ER, hypotension (T/P/R: 36.9/113/20,BP 91/54 mmHg) was noted → Hypotension, r/o sepsis or dehydration or cardiogenic shock
  - lab data revealed CKD Cr: 5.48, elevation troponin-i , CRP and NT-ProBNP ⟶ Hemodialysis

	2019/10/15	2020/07/14	2020/08/11	2020/09/10	2020/10/08	2020/01/21
Furosemide 40 mg QD	3 months				30 days	3 months
Entresto 100 1# BID	3 months				30 days	3 months
Celecoxib 200 mg QD	30 days	28 days	28 days	28 days	30 days	3 months
Ultracet 1# Q12H	3 months					
Colchicine 0.5# QD	3 months					
Isosorbide dinitrate 1# QID	3 months				30 days	3 months
Tamsulosin 1# QD	3 months				30 days	3 months
Cal. polystyrene sulfonate	3 months				30 days	3 months
Teriparatide 1# QD			28 days	28 days		

2021/02/21 急診



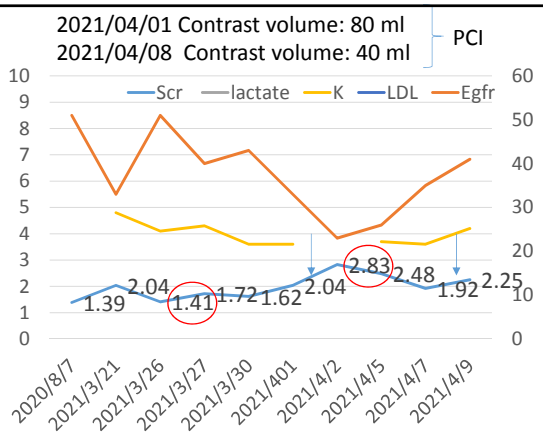
檢驗項目	參考值	檢體	單位	20210321 10:45	20210225 06:11	20210221 16:15	20210218 05:23	20210214 05:25	20210209 10:17
WBC	M3.9-10.6 F3.5-11	B	1000/uL	6.6	7.9	7.4	4.2	5.6	4.7
RBC	M4.3-6.1 F3.9-5.4	B	million/uL	3.57 L	3.98 L	4.00 L	4.00 L	3.85 L	3.79 L
Hemoglobin	M13.5-17.5 F12-16	B	g/dL	10.7 L	11.9 L	11.9 L	11.9 L	11.6 L	11.3 L
Hematocrit	M41-53 F36-46	B	%	33.4 L	36.9 L	38.0 L	37.2 L	35.9 L	36.2 L
MCV	80-100	B	fL	93.6	92.7	95.0	93.0	93.2	95.5
MCH	26-34	B	pg/Cell	30.0	29.9	29.8	29.8	30.1	29.8
MCHC	31-37	B	gHb/dL	32.0	32.2	31.3	32.0	32.3	31.2
RDW-SD	38-47.5	B	fL	53.0 H	47.5	51.7 H	50.4 H	52.4 H	54.9 H
Platelets	150-400	B	1000/uL	273	160	175	198	156	188
RDW-CV	11.0-14.7	B	%	15.4 H	14.1	14.6	14.7	15.2 H	15.5 H
PDW	9.2-15.6	B	fL	11.1	14.9	12.7	13.1	13.6	11.0

Date	S/O	A/P
02/25	Hypotension suspect dehydration related	1. IV N/S run 40ml/hr--> keep open axone ide 1# QD
02/26		0 mg qd
02/27	Discharge	Entresto 100 1# BID

個案重點:
AKI時Entresto是否該停藥
出院轉門診追蹤時: triple whammy related AKI

Case presentation-2

- 64 y/o male, BW 75.9 kg, Ht 160.4 cm
- Past medical history
  - Congestive heart failure
  - Hypertension
  - Type 2 DM
  - CKD stage 3
- Present illness
  - general pitting edema for weeks
  - orthopnea, dyspnea on exertion, urine amount decreased, short of breath even while resting
  - EKG showed Sinus bradycardia
- Impression
  - Acute decompensated heart failure, HFpEF, NYHA class IV



2019/09/06-2021/03/21

- Dabigatran 110 mg bid
- Candesartan 4 mg qd
- Bisoprolol 1.25 mg qd
- Metformin 500 mg bid
- Amiodarone 200 mg prn
- Atorvastatin 20 mg prn

33

用藥歷史

顯影劑　04/09 出院　顯影劑

	03/23	03/24	03/25	03/26	03/27	03/28	03/29	03/30	03/31	04/01	04/02	04/03	04/04	04/05	04/06	04/07	04/08
Amiodarone	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Aspirin				■	■	■	■	■	■	■							
Atorvastatin	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Entresto	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Hydralazine						■	■	■	■	■	■						
Isosorbide dinitrate						■	■	■	■	■	■						
Metformin	■	■	■	■													
Piperacillin-tazobactam								■	■								
Spironolactone	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Xigduo XR				■	■	■	■	■	■	■							
Glipizide	■	■	■														
Dabigatran	■	■	■										■	■	■	■	■
Candesartan	■	■															
Clopidogrel										■	■	■	■	■	■		■

dapagliflozin /metformin

個案重點:
1.顯影劑檢查時該停那些藥
2.出院轉門診追蹤時: 停的藥是否該加回來

34

十分感謝您的聆聽

35