Supplemental Online Content

Donaldson LH, Devaux A, White KC, et al. Hydrocortisone and risk factors for kidney replacement therapy in septic shock. *JAMA Netw Open*. 2025;8(5):e2512279. doi:10.1001/jamanetworkopen.2025.12279

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. Calculation of Norepinephrine Equivalent (NEE)

NEE = **Noradrenaline** dose (mcg/kg/min) + **Adrenaline** dose (mcg/kg/min) + 1/100 × **dopamine** dose (mcg/kg/min) + 0.1 if noted to be on **vasopressin**

Note that the dose of vasopressin was not recorded in the ADRENAL study. The above adjustment was based on the typical starting dose of vasopressin 0.04u/min, and a conversion factor of 2.5. (1)

eTable 1: Outcomes for those requiring KRT

Variables	**KRT** N = 701	**No KRT** N = 2,460	**p-value**
Days alive and out of the ICU, mean (SD)	40.6 (36.3)	65.1 (31.3)	<0.001
Days alive and out of the hospital, mean (SD)	25.8 (29.2)	46.0 (31.3)	<0.001
90-day mortality	312 / 698 (44.7%)	486 / 2442 (19.9%)	<0.001
6-month mortality	328 / 695 (47.2%)	561 / 2407 (23.3%)	<0.001
Hospital Readmission Rates	38 / 701 (5.4%)	201 / 2460 (8.2%)	0.02
Quality of life scores			
6-month QoL EQ5D5L Utility score (mean, SD)[1]	0.3 (0.4)	0.5 (0.4)	<0.001
QoL Utility scores with deceased patients excluded (sensitivity analysis)[2]	0.6 (0.4)	0.7 (0.3)	0.36
ED5D5L Visual Analogue Scale (mean, SD)[3]	70.9 (20.4)	71.2 (20.9)	0.78

1) Deceased patients coded '0', for this primary analysis.
2) Sensitivity analysis which includes only survivors.
3) Only survivors included

eTable 2: Sensitivity Analyses

Outcomes	**Treatment allocation**			
	Hydrocortisone	**Placebo**	****OR/MD (95% CI)****	**p-value**
Adjusted analysis for other predictors of KRT requirement [1]				
Use of KRT[1]	329 / 1,589 (20.7%)	372 / 1,572 (23.7%)	OR 0.81 [0.68 - 0.97]	0.02
Number of days alive and free for KRT[1]	69.6 (34.0)	68.1 (35.0)	MD 1.60 [-0.73 - 3.93]	0.18
Analysis excluding patients who commenced KRT <1 day after randomisation (as well as KRT at baseline and/or chronic dialysis requirement)[2]				
Use of KRT	189 / 1,449 (13.0%)	219 / 1,419 (15.4%)	OR 0.82 [0.66 – 1.02]	0.08
Analysis excluding patients who commenced KRT <2 days after randomisation (as well as KRT at baseline and/or chronic dialysis requirement)[2]				
Use of KRT	114 / 1,374 (8.3%)	144 / 1,344 (10.7%)	OR 0.78 [0.59 – 1.01]	0.06

1. adjusted for age, sex, APACHE II score, bilirubin at enrolment, primary site of infection, time from the onset of shock to randomization, use of vasopressin and last MAP at enrolment as fixed effects.

2. adjusted for admission type as a fixed effect, and sites as a random effect, only.

eTable 3: Other Outcomes associated with KRT Status

Variables	KRT N = 701	No KRT N = 2,460	p-value
Time to shock resolution (days, mean (SD)	6.3 (6.8)	3.7 (4.1)	**<0.001**
Persistent shock resolution (N, %)	525 / 701 (75%)	2,293 / 2452 (94%)	**<0.001**

eTable 4: Associations with days alive and free of KRT - univariate and multivariate models

	Univariate		Multivariate	
Variables	**MD (95% CI)**	**p-value**	**MD (95% CI)**	**p-value**
Age at randomisation (years)	-0.54 (-0.73, -0.34)	<0.001	-0.52 (-0.72, -0.31)	<0.001
Sex		0.33		0.22
Female	—		—	
Male	-2.90 (-8.74, 2.94)		-3.64 (-9.49, 2.21)	
Weight (in kg)	0.22 (0.12, 0.32)	<0.001	0.19 (0.08, 0.29)	<0.001
APACHE II Score	-0.37 (-0.75, 0.02)	0.06	-0.06 (-0.47, 0.35)	0.78
High bilirubin	-0.08 (-0.15, -0.01)	0.03	-0.11 (-0.18, -0.04)	0.003
Source of admission		0.05		0.75
Accident and Emergency Department	—		—	
Hospital Floor (i.e. wards)	-9.19 (-16.64, -1.74)		-3.16 (-10.66, 4.34)	
Transfer from another ICU	6.10 (-7.55, 19.75)		1.94 (-11.51, 15.38)	
Transfer from another hospital (except from another ICU)	2.53 (-7.26, 12.33)		3.47 (-6.04, 12.97)	
Admitted from Theatre following EMERGENCY surgery	-6.84 (-14.51, 0.84)		-3.10 (-11.58, 5.38)	
Admitted from Theatre following ELECTIVE surgery	-7.59 (-24.94, 9.75)		3.75 (-13.60, 21.09)	
Admission type		0.06		
Non-operative	—			
Operative	-6.26 (-12.87, 0.34)			
Primary site of infection		0.07		0.11
Pulmonary	—		—	
Intra abdominal	-5.44 (-13.83, 2.94)		-2.41 (-11.22, 6.39)	
Blood	-3.41 (-11.32, 4.51)		-2.52 (-10.25, 5.21)	
Urinary	0.20 (-7.81, 8.20)		-0.05 (-8.56, 8.46)	
Other	11.42 (0.45, 22.39)		12.80 (1.79, 23.82)	
First organism		0.31		
Staphylococcus	—			
Other gram positives	7.09 (-6.28, 20.46)			
Gram Negatives	4.91 (-8.36, 18.18)			
Fungi	-6.93 (-23.68, 9.83)			
Other (incl nil identified)	3.53 (-9.05, 16.11)			
Bacteraemia		0.16		
Absence	—			
Presence	5.00 (-2.05, 12.06)			
Use of nephrotoxic antibiotics at randomization		0.08		
No	—			

	Univariate		Multivariate	
Variables	**MD (95% CI)**	**p-value**	**MD (95% CI)**	**p-value**
Yes	5.15 (-0.53, 10.82)			
Last MAP	0.51 (0.19, 0.83)	0.002	0.49 (0.17, 0.82)	0.003
NEE	-2.08 (-3.04, -1.11)[1]	<0.001	-2.09 (-3.15, -1.03)[1]	<0.001
MAP/NEE ratio	0.19 (-0.12, 0.51)[2]	0.23	-0.23 (-0.57, 0.10)[2]	0.16
Use of Vasopressin		0.51		
No	—			
Yes	2.20 (-4.39, 8.80)			
Use of Dobumatine, Milrinone or Levosimendan		0.39		
No	—			
Yes	-5.58 (-18.24, 7.07)			
Time from the onset of shock to randomisation	-0.01 (-0.04, 0.01)	0.32	-0.02 (-0.04, 0.01)	0.21
Steroid received		0.13		
No	—			
Yes	7.26 (-2.08, 16.59)			
Treatment allocation		0.75		0.65
Placebo	—		—	
Hydrocortisone	0.92 (-4.77, 6.60)		1.28-4.31, 6.87)	

1. Expressed for an increase of 0.1 unit; 2. Expressed for an increase of 100 units
Multivariate model includes treatment, age, sex, weight, APACHE II score, primary site of infection, NEE, MAP/NEE, time from the onset of shock to randomisation and significant variables ($p<0.05$) from univariate mode

Reference

1. Kotani Y, Di Gioia A, Landoni G, Belletti A, Khanna AK. An updated "norepinephrine equivalent" score in intensive care as a marker of shock severity. Critical Care. 2023;27(1):29.