

Supplementary Table S1. Overview of studies examining the occurrence of AKI, Exertional rhabdomyolysis, and Exercise-associated Hyponatremia in ultra-endurance athletes.

Study	Participants	Distance event	Pre-race measures	Measures at presentation	Results	Environmental conditions	Return to baseline/ Renal follow up info	NSAIDs (Y/N)	Supplements
Boulter 2011	Active male (n = 4) (Age: 35 ± 6y) 3/4 = novice ultra-runners	89.3 km, endurance running	Not measured	3/4 = delayed presentation to medical staff 3/4 = vomiting & muscle soreness Initial blood samples: 3/4 = hyponatraemic (blood sodium concentrations <135 mEq/l) 2/4 = hypochloraemic (blood chloride concentrations <98 mEq/l) S-CK (5718–54,231 UI/L) S-Cr (2.99– 12.88 mg/dL)	ER+ AKI 4/4 - Rhabdomyolysis - presented 1-4 days post-race 3/4 – EAH 4/4 – AKI	14–24°C, 63% relative humidity	Hospitalization and acute renal dialysis – between 2-21 days	3/4 = NSAIDs during race 1/4 = analgesic/muscle relaxant (Besemax; 450 mg paracetamol and 35 mg orphenadrine citrate) during and Voltaren (NSAID) prior to the race for a knee injury	All = anti-cramp electrolyte supplement (sodium, potassium, magnesium and calcium) 6 to 16 tablets, with an average intake of 11 tablets (1 per hour)
Bruo 2010	Active males (n = 5) (Age: 36.7 ± 7.8 y)	161 km, 5500 m cumulative climb, endurance running	Not measured	Muscle soreness Dark urine S-Cr (1.1–4.9 mg/ dL) S-CK (38,218– 95,940 UI/L)	5 cases of EAH 5 cases of ER 3/5 progressed to AKI- failure	15–37°C	Intravenous fluids Hospitalization	4/5 = positive NSAIDs during race	NS
Hou 2015	Active males (n = 26)	100 km Ultramarathon	BUN (mmol/L) - 15.23 ± 2.89 Creatinine (mmol/L)- 0.94 ± 0.11 Myoglobin (µg/L)- 48.9 ± 20.63	BUN (mmol/L) - 24.04 ± 5.49 Creatinine (mmol/L)- 1.56 ± 0.39 Myoglobin (µg/L)- 4462.46 ± 3391.87 CK (U/L) - 4274.81 ± 5903.85	26 = ER 22/26 = AKI 18 =Stage I AKI 4 =stage II AKI Faster run = increased risk of AKI	Temperature - 24.9°C (7–8 AM) and 28.7°C (5–6 PM) relative humidity was between 66% (10–11 AM)	NS	Positive history of NSAIDs but NS	NS

			CK (U/L) - 166.73 ± 96.91			and 87% (8–9 AM			
Hoffman & Weiss 2016	Active runners (n = 627)	161 km, 5500 m cumulative climb, Ultramaratho n	NS	S-CK (120–200,000 IU/L) S-Cr (0.4–2.2 mg/ dL)	AKI 227 (36.2%) = AKI risk 31 (4.9%) = AKI	Outlined in previous refs	NS	NS	
Lipman 2014	Active runners (n = 30)	Ultramaratho n (7 days-6 stages-177 km)	SCr (mg/dl) - 0.9 ± 0.2 GFR (mg/dl) - 102.7 ± 17.3	Stage 1 finish – SCr (mg/dl) - 1.4 ± 0.4 GFR (mg/dl) - 76.6 ± 18.3 ΔGFR (mg/dl) - 32.5 ± 18.9 (p = 0.002) Stage 3 finish – SCr (mg/dl) - 1.3 ± 0.4 GFR (mg/dl) - 74.5 ± 17.2 ΔGFR (mg/dl) - 28.1 ± 20 (p = 0.002) Stage 5 finish – SCr (mg/dl) - 1.4 ± 0.3 GFR (mg/dl) - 71.8 ± 19.6 ΔGFR (mg/dl) - 30.9 ± 17.5 (p < 0.001)	AKI = 55–85% all participants meet RIFLE criteria stage 1: AKI risk = 13 AKI = 3 stage 3: AKI risk = 10 AKI = 2 stage 5: AKI risk = 8 AKI = 1	NS	Before the start of each new stage After 24hrs	NS	NS
Kao 2015	Active males (n = 26) (age: 49y [22–60 y])	100k ultramaratho n -not strict entry requirements -first ultra- event on 400m running track organised in Taiwan- to increase entries	S- CK (U/L) - 146 (112-207) SCr (mg/dL) - 0.91 (0.87-1.03)	S-CK - 2299 (1497-4650 UI/L) S-Cr - 1.50 (1.25-1.77 mg/dL) 17/26 = moderate dehydration 6/26 = muscle cramps 3/26 = haematuria	AKI = 22/26 subjects (85%) immediately after race 4/26 = no AKI 18/26 = stage I AKI 4/26 (15%) = stage II AKI	temperature ranged from 24.9–28.7°C average humidity between 66% (10-11 AM) and 87% (8-9 AM)	1 day hospitalization	NS	NS

		Best marathon time= <4hrs All except 2 had done 1 ultra-event before							
Belli 2018	Active males (n = 6)	Brazil 135 Ultramarathon (217km)	S-CK (U/L) – 132 ± 18 SCr (mg/dL) – 1.00 ± 0.03 GFR (ml/min/1.73m ²) – 89 ± 5	At 134km (equivalent flat distance) S-CK (U/L) – 3988 ± 1004 S-Cr (mg/ dL) – 1.34 ± 0.1 GFR (ml/min/1.73m ²) – 66 ± 8 At 279Km (equivalent flat distance) S-CK (U/L) – 18667 ± 10664 S-Cr (mg/ dL) – 1.27 ± 0.08 GFR (ml/min/1.73m ²) – 69 ± 5 At 339Km (equivalent flat distance) S-CK (U/L) – 19157 ± 12369 S-Cr (mg/ dL) – 1.33 ± 0.08 GFR (ml/min/1.73m ²) – 65 ± 5 Muscle soreness	AKI - meet the risk criteria for acute kidney injury from 84 km until they finished the race SCr change did not meet AKI criteria GFR change did meet AKI criteria (>25% decrease)	8–30°C	NS	Negative use of daily medication - NSAIDs NS	NS
Shin 2016	Active male runner (n =50) (Age:	Marathon (n=17),	BUN Marathon - 17.70±4.24	Post BUN Marathon - 22.79±5.58	Indication of reduced renal function	Starting temperature	NS	NS	NS

	51.76 ± 6.88y)	100 km (n=17) and 308 (n=16) km ultramarathon	100 km- 17.34±3.69 308 km - 17.01±4.31 Creatinine Marathon - 1.06±0.10 100 km- 1.07±0.11 308 km - 1.03±0.05 S-CK Marathon - 132.76±55.17 100 km- 108.58±40.76 308 km - 131.75±39.34	100 km- 32.31±4.87 308 km - 24.03±4.88 Creatinine Marathon - 1.27±0.17 100 km- 1.27±0.24 308 km - 1.07±0.09 S-CK Marathon - 274.17±70.95 100 km- 2983.17±5.56 308 km - 4970.31±2222.48	Change in SCr significantly higher after marathon and 100km ultra (medium to high intensity) compared to 308km	(20-23°C) and humidity (40-50%)			
Zyl-Smit 2000	Male 1 40 years old	Comrades Ultramarathon	NS	1= delayed presentation to medical staff – 9 days post-race 10 days post-race - SCr- 713 µmol/L, urea 32.7 mrnol/l, potassium CK- NS Urine- 2+ protein 1+ blood, moderate granular casts Ultrasound = bilaterally unobstructed and moderately enlarged kidneys	Rhabdomyolysis (presumed) acute tubular necrosis (ATN) and ARF	NS	treatment = Furosemide 250 mg intravenously followed by similar oral dose, hypertension - nifedipine 10 mg, 8-hourly 5 days post-presentation- plasma creatinine reduced - 260 µmol/l After 10 days plasma	During race - 6 x paracetamol 500 mg/chlormezanone 100 mg (Bessenol) tablets	1 x 2 mg loperamide (Imodium) tablet before the race Day 1 post race = 2 Bessenol tablets following 5 days - 11 Stopayne tablets (paracetamol / caffeine/ codeine phosphate / meprobamate)

							creatinine = 93 μmol/l & creatinine clearance = 102 ml/ min		
Jouffroy 2019	n = 47 43 ± 7 years	Ultra-distance race 80km	SCr - 90±14 μmol/L (km0) SUrea - 4.7±4.5 mmol/L (km 0)	SCr increased to 136±32 μmol/ L (km 80—p<0.0001) = 52% increase Mean SUrea increased to 22.8±12.0 mmol/L (km 80) (p<0.0001) NGAL and Kidney injury molecule 1 (KIM-1) shown to progressively increase during race (p<0.05 vs baseline) At day 9 NGAL and KIM1 urinary levels decreased but remained significantly higher than baseline levels	21km 2 (4%) = stage 1 0 = stages 2/3 53km 5 (11%) = stage 1 1 (2%) = stage 2 0 = stage 3 80km 3 (6%) = stage 1 0 = stages 2/3	+14°C and clear weather	Day 9 – no significant difference from baseline	NS	NS
Lipman 2016	128 (28% women, mean age 39.6 ± 9 years)	4 Multistage ultramaratho ns	Baseline SCr - 0.72 (0.49 to 0.89) SD ±0.13 mg/dL	Stage 1 SCr - 1.20 (0.70 to 2.30) SD ± 0.28 mg/dL Stage 3 SCr - 1.33 (0.70 to 2.90) SD ± 0.37mg/dL Stage 5 SCr - 1.28 (0.70 to 2.70) SD ± 0.34 mg/dL Mean SCr change at Stage 1 - 0.49 (0.02 to 1.54) ± 0.26 Stage 3 - 0.12 (20.50 to 1.50) ± 0.26	AKI status at Stages Stage 1 – Normal = 37.5% Risk AKI = 43.8% AKI = 18.8% Stage 3- Normal = 20.3% Risk AKI = 47.7% AKI = 32.0%	NS	NA	NS	NS

				Stage 5 - -0.05 (21.0 to 0.50) ± 0.24	<p>Stage 5- Normal = 23.4% Risk AKI = 48.4% AKI = 28.1%</p> <p>per stage prevalence of AKI = 62.5% to 79.7%.</p> <p>Slowest race finishers who were less likely to develop AKI, 82% less likely than those who finished in the top 10%.</p> <p>Multivariate analysis found AKI was significantly</p>				
Khodaei 2021	64, only 37 (both pre-and post-race results)	100km ultra race	mean (±SD) pre-race Cr – (n = 64) was 0.99 ± 0.15 mg/dL	Serum BUN and Cr increased (P < .001) post-race (n=37)	<p>18 out of the 37 (49%) met the criteria for AKI.</p> <p>Using fixed eGFR of 75 ml/ min per 1.73 m2 and an aged-based eGFR), resulted in 6 (16%) and 22 (59%) of 37</p>		NA	<p>Positive use of NSAIDS NSAID 1-2 days prior to race = 18 AKI- n=3 yes 19 Not AKI – n=4 Yes</p> <p>NSAIDS during race- 18 AKI- n=4 yes 19 Not AKI – n=4 Yes</p>	

					runners = criteria for AKI, respectively Different equations produced differing results with regard to the number of participants meeting criteria of AKI				
Lippi 2012	16	Ultramarathon	SCr (μmol/L) - 68 (58– 76) eGFR, mL/min/1.73 m ² - 112 (97 – 133) Serum NGAL, ng/mL – 105 (86 – 158) Urinary NGAL, ng/mL - 4.4 (0.5 – 33.9)	SCr (μmol/L)- 98 (76- 118) Mean Increase in SCr (μmol/L) – 30 eGFR, mL/min/1.73 m ² - 75 (57 – 99) Serum NGAL, ng/mL – 196 (139 – 290) Urinary NGAL, ng/mL - 35.6 (12.5 – 86.3)	All post-race variables significantly different to baseline (p<0.001) 6 /16 athletes (38 %), = AKI	NS	NA	NS	NS
Noakes 1976	13 Group A – complete 160Km Group B – completed 65 to 149 km	Ultramarathon	Group A SCr- 1.1 (mg/100ml) SUrea – 32.7 (mg/100ml) Group B SCr- 1.1 (mg/100ml) SUrea – 30.2 (mg/100ml)	Group A SCr- 1.5 (mg/100ml) SUrea – 66.1 (mg/100ml) Group B SCr- 1.4 (mg/100ml) SUrea – 52.7 (mg/100ml)	SUrea = doubled SCr = increased by ~1/3	NS	NS	NS	NS

Irving 1989	2 males Experienced marathon runners	2-man 24 hr relay marathon	SCr ($\mu\text{mol/L}$) – 81 & 86	Post-race SCr ($\mu\text{mol/L}$) – 101 & 119 Repeated SCr ($\mu\text{mol/L}$) at 48hrs- both 92 Increase in SCr ($\mu\text{mol/L}$) – 20 & 23	SCr increased post-race Cr clearance dropped	range of Wet Bulb Globe Temperature Index = 9.7- 16.3°C	Measures of renal dysfunction transient as normalised after 24hr	NS	NS
Irving 1990 - Transient oliguria with renal tubular dysfunction after a 90 km running race	5 (Group = 4 males, subject A = 1 female) Experienced marathon runners	Ultramarathon 90Km	Group SCr ($\mu\text{mol/L}$) - 63.5 (± 2.9) Subject A SCr ($\mu\text{mol/L}$) - 42 (± 3)	Group Race SCr ($\mu\text{mol/L}$)- 69.3 (± 9.6) Day 2 SCr ($\mu\text{mol/L}$) – 65.8 (± 5.5) Day 14 SCr ($\mu\text{mol/L}$)- 62.0 (± 6.7) Subject A Race SCr ($\mu\text{mol/L}$)- 55.0 Day 2 SCr ($\mu\text{mol/L}$) – 53.0 Day 14 SCr ($\mu\text{mol/L}$)- 51.0	1= collapsed Subject A = transient oliguria with renal tubular dysfunction and anuria due to restricted fluid intake during race compared to rest of group = dehydration (-11% body weight) and urine creatinine excretion increase Group = Urine flow rate, CrCl unchanged	Mean temperature – 17.9°C (10.5 – 21.5 °C) Mean humidity – 60% (9 – 41%)	Subject A = Renal dysfunction measures persisted 14 days post-race although, full recovery 1 year later	NS	NS
Irving 1990 - Plasma volume and renal function during and after ultramarathon running	8 males experienced marathon runners	Ultramarathon	SCr ($\mu\text{mol/L}$) - 91	Post-race SCr ($\mu\text{mol/L}$)- 110 Repeated SCr ($\mu\text{mol/L}$) – at 24hrs = normal Increase in SCr ($\mu\text{mol/L}$) – 19	SCr significantly increased on race day ($p < 0.001$)	Mean temperature – 12.5°C (7.3 – 18.3°C)	Return to baseline within 24Hrs	NS	NS

Neumayr 2003	28 (amateur ultra-cyclists)	Ultramarathon cycle	SCr ($\mu\text{mol/L}$) - 88	Post-race SCr ($\mu\text{mol/L}$)- 106 Repeated SCr ($\mu\text{mol/L}$) at 24hrs- 106 Increase in SCr ($\mu\text{mol/L}$) - 18	SCr significantly elevated post- race, 20% ($p < 0.001$) Reduced renal perfusion mechanism responsible for renal impairment	temperatures ranged from 14–21°C, and humidity from 55–85%	SCr remained elevated at 24hrs	NS	NS
Neumayr 2015	16 (males, world's best ultramarathon cyclists)	Ultramarathon cycle	SCr ($\mu\text{mol/L}$) - 84 (± 15)	Post-race SCr ($\mu\text{mol/L}$)- 111 (± 19) Repeated SCr ($\mu\text{mol/L}$) - 83 (± 15) Increase in SCr ($\mu\text{mol/L}$) - 26	Significant rise in SCr (+33%, $p < 0.001$) post-race Reduced renal perfusion mechanism responsible for renal impairment	temperatures ranged between -1 and 20°C	SCr Normalised within 24hrs	NS	NS
Christensen 2014	10	Ultramarathon	SCr ($\mu\text{mol/L}$) - 60	Post-race SCr ($\mu\text{mol/L}$)- 80 Mean Increase in SCr ($\mu\text{mol/L}$) - 20	lack of an immediate post-exercise increase, although almost significant (P = 0.075)	NS	25% increase in SCr at 6 hours post-race Normalisation at 48hrs post- race	NS	NS
Chilbkova 2015	113 ultra- runners and ultra- mountain bikers	24hr and 100km ultra- running and 24 hr and multistage ultra-	Male multistage bikers Plasma creatinine = 0.9 ± 0.1 (mg/dL) Plasma creatinine clearance =	Male multistage bikers Plasma creatinine = 1.2 \pm 0.5 (mg/dL), +0.3 \pm 0.5 (mg/dL), +33.3 \pm 64.8%, $p = 0.01$ Plasma creatinine clearance = 8953.6 \pm 2447.9 (ml/min),	13 (11.5%) - EAH 6 (5%) - ER 2 (1.8%) - EAH & ER	NS	2 cases of elevated creatinine = No renal failure or medical intervention	NS	NS

		mountain bike races	10849.4 ± 1502.9 1009.4 (ml/min)	-1895.8 ± 2158.7 (ml/min), -17.4 ± 19.3%, p<0.01	All cases of EAH and ER = ultra-runners				
			Male 24hrs bikers Plasma creatinine = 0.9 ± 0.1 207.5 (mg/dL) Plasma creatinine clearance = 10657.2 ± 1614.2 (ml/min)	Male 24hrs bikers Plasma creatinine = 1.2 ± 0.2 (mg/dL), +0.3 ± 0.2(mg/dL), +32.7 ± 21.8%, p<0.01 Plasma creatinine clearance = 9623.2 ± 1837.4(ml/min), -1034.1 ± 1121.0(ml/min), -9.8 ± 11.7%, p<0.05	2 cases of elevated creatinine >normal (~2.0 mg/dL or x1.5 estimated baseline)				
			Male 24hrs runners Plasma creatinine = 0.9 ± 0.1(mg/dL) Plasma creatinine clearance = 10657.2 ± 1614.2(ml/min)	Male 24hrs runners Plasma creatinine = 0.9 ± 0.2 (mg/dL), +0.0 ± 0.1(mg/dL), +10.6 ± 12.7%, p=0.06 Plasma creatinine clearance = 9623.2 ± 1837.4(ml/min), -1034.1 ± 1121.0(ml/min), -9.8 ± 11.7%, p<0.05					
			Male 100km runners Plasma creatinine = 0.9 ± 0.2(mg/dL) Plasma creatinine clearance = 8985.3 ± 2219.0(ml/min)	Male 100km runners Plasma creatinine = 1.1 ± 0.3 4357.1(mg/dL), +0.2 ± 0.3(mg/dL), + 25.8 ± 48.1%, p=0.05 Plasma creatinine clearance = 7327.7 ± 2080.2(ml/min), -1657.5 ± 2146.8(ml/min), -16.7 ± 17.9%, p<0.05					

Lecina 2021	1 male (42yrs)	786 km multi- stage ultra- trail race	SCr = 0.88 (mg/dL) Creatine kinase = 94 UI/L	SCr = 1.13mg/dL (+28.41%) Creatine kinase = 1099 UI/L (+1069.15%)	ER No AKI	Temperature 13.08 – 17.69 °C humidity 60.16–70.87%	Post-race day 2 SCr = 0.98mg/dL (+11.36%) Creatine kinase = 478 UI/L (+408.51%) Day 9 SCR = 0.84mg/dL (–4.55%) Creatine kinase = 109UI/L (+15.96%)	NS	NS
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AKI: acute kidney injury, ER: exertional rhabdomyolysis, EAH: exercise-associated hyponatraemia, NSAIDs: non-steroidal anti-inflammatory drugs, GFR: glomerular filtration rate, SCr: serum creatinine, S-CK: creatinine kinase, BUN: blood urea nitrogen, NGAL: neutrophil gelatinase-associated lipocalin, NS: not specified, Δ: change in