Appendix

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Additional methods

Defining comorbidities

Pre-existing cardiovascular disease was defined by the presence of any of the following conditions on chart review: stroke, transient, angina, claudication, PCI, coronary bypass and recognized, silent myocardial infarction, heart failure (≥NYHA Class III Symptoms), or peripheral vascular disease and/or bypass.

Hypertension was defined by the use of anti-hypertensive medication on chart review.

Respiratory disease was defined by presence of chronic restrictive, obstructive or vascular respiratory disease causing severe exercise limitations or documented chronic hypoxemia, hypercapnia, secondary polycythemia or pulmonary hypertension on chart review.

Liver disease was defined by presence of biopsy proven cirrhosis or documented evidence of portal hypertension (i.e. variceal bleeding, ascites, encephalopathy) on chart review.

Diabetes mellitus was defined by use of insulin or oral hypoglycemic agents on chart review.

Solid organ/haematologic malignancy was defined by the presence of any documented metastatic solid organ tumour or presence of any form of hematologic malignancy on chart review.

Immunocompromise was defined by the presence of advanced disease sufficient to suppress resistance to infection (i.e. malignancy, AIDS) or therapy that suppresses resistance to infection (i.e. chemotherapy, steroids) on chart review.

Defining causes of death

Proximate causes of death were defined as

Neurological proximate causes of death included brain death; hypoxic encephalopathy; intracranial haemorrhage; ischaemic stroke; and other.
Cardiovascular proximate causes of death included primary arrhythmia; refractory cardiogenic shock (including pulmonary oedema); cardiac tamponade; hypovolaemia (including uncontrollable bleeding); septic shock; massive pulmonary embolism; anaphylaxis; and other.
Respiratory proximate causes of death included refractory hypoxia due to adult respiratory distress syndrome (ARDS); chronic obstructive pulmonary disease (COPD); asthma; pulmonary hemorrhage; pneumothorax; and other.
Metabolic proximate causes of death included hypoglycemia; hyperkalemia; hypothermia; liver failure; and other.
Patients dying with multiple organ failure or following withdrawal of therapy were also identified.

Underlying causes of death were defined as

Neurological underlying causes of death included cerebrovascular accident; dementia; subarachnoid hemorrhage; neurological infection; spinal cord injury; seizures.

Cardiovascular underlying causes of death included ischemic heart disease; hypertension; abdominal or thoracic aortic aneurysm; peripheral vascular disease; coronary artery disease; congestive cardiac failure.

Respiratory underlying causes of death included COPD; asthma; pulmonary fibrosis; active tuberculosis infection; pneumonia; pulmonary embolism.

Gastrointestinal underlying causes of death included gastrointestinal tract cancer; hepatic failure; cirrhosis; gastrointestinal bleeding; gastrointestinal obstruction; pancreatitis; inflammatory bowel disease; anorexia; obesity.

Metabolic underlying causes of death included diabetes mellitus; hypothyroidism; adrenal insufficiency.

Renal underlying causes of death included chronic kidney disease (CKD); pyelonephritis; renal artery stenosis; renal cell carcinoma.

Hematological underlying causes of death included coagulopathy.

Other noted underlying causes of death included pregnancy and disseminated malignancy.

Table E1. RIFLE classification of acute kidney injury

Grade	Serum Creatinine criteria (µmol/l)	Urinary Output Criteria
Risk	↑ serum creatinine x 1.5	UO < 5ml/kg/h for ≥ 6h
Injury	↑ serum creatinine x 2	UO < 5ml/kg/h for ≥ 12h
Failure	↑ serum creatinine x 3 or serum creatinine ≥ 350 with rise of ≥ 44	UO < 3ml/kg/h for ≥ 24h or Anuria for ≥ 12h
Loss	Persistent need for RRT for more than 4 weeks	
ESKD	End Stage Kidney Disease at more than 3 months	

UO: urine output; RRT: renal replacement therapy

Table E2. Individual patient demographics, renal status and nephrotoxin exposure

Patient	Age	Sex	Wt kg	Ht cm	ICU Diagnosis	APACHE II	SAPS 2	Baseline Cr	Baseline Urea	Peri-mortem Cr	Peri-mortem Urea	Peak AKI	Time to Peak AKI	CRRT	CRRT at death	Nephrotoxin Expisure
ATN01	78	M	68	165	Cardiac surgery	21	36	136	13.3	221	6.8	RIFLE-F	11.17	Yes	Yes	Contrast, Rhabdomyolysis, Diuretics, Other
ATN02	86	F	54	145	Septic Shock	21	51	56	3.5	175	21.7	RIFLE-F	1.96	No	No	Diuretics, Other
ATN03	51	F	50	154	Decompensated CLD	33	76	68	2.6	101	7.1	RIFLE-F	8.35	Yes	Yes	Diuretics
ATN04	49	M	46	175	Pneumonia	19	48	83	4.5	93	9.3	RIFLE-I	29.41	No	No	Contrast, Diuretics
ATN05	56	F	90	162	Hepatorenal Failure	15	54	94	5.9	262	19.2	RIFLE-F	0.00	Yes	Yes	None
ATN06	78	M	78	164	Aortic Surgery with CPB	17	41	114	10.8	156	5.4	RIFLE-F	0.75	Yes	Yes	Diuretics
ATN07	79	M	79	171	Ischaemic Stroke	30	67	132	13.4	144	16.1	None		No	No	Contrast, Rhabdomyolysis, Diuretics
ATN08	55	M	98	177	Pneumonia	27	36	106	3	107	12.5	RIFLE-F	2.45	Yes	Yes	Contrast, Aminoglycosides, Diuretics, Other
ATN09	70	M	67	173	post-VATS	28	66	90	7.3	61	12.5	None		No	No	Contrast, Diuretics
ATN10	69	M	87	179	Post-operative	16	26	107	5	131	3.9	RIFLE-F	3.42	Yes	Yes	Aminoglycosides, Rhabdomyolysis
ATN11	81	M	78	170	Cardiac surgery	24	47	92	6.6	212	6.8	RIFLE-I	5.08	No	No	Contrast, Aminoglycoside, Rhabdomyolysis, Diuretics, Other
ATN12	56	M			Biliary Sepsis	24	38	64	2.6			None		No	No	Contrast
ATN13	22	F	50	156	Staphylococcal Septicaemia	19	33	136	6.6	153	7.4	RIFLE-F	2.41	Yes	Yes	Contrast, Aminoglycosides, Diuretics
ATN14	65	M	50	173	Post-laparotomy	14	23	65	3.4	66	3.3	RIFLE-I	0.00	No	No	Contrast, Aminoglycosides, Diuretics
ATN15	53	M	83	180	Septic Shock	15	43	93	8	412	28.4	RIFLE-F	0.00	Yes	Yes	Calcineurin inhibitors, Diuretics
ATN16	67	F			Septic Shock	41	95	71	1.7	153	5.5	RIFLE-F	0.30	Yes	Yes	Rhabdomyolysis
ATN17	79	M	80	172	Hyperkalaemia	27	35	79	13.2	239	11.1	RIFLE-F	0.00	Yes	No	Other
ATN18	73	M			Cardiac Arrest	38	63	73	4.7	79	4.3	None		No	No	None
ATN19	77	M	83	173	Aspiration Pneumonia	21	40	77	4.4			RIFLE-F	0.00	No	No	Diuretics, Other
ATN20	82	F	87		Aneurysme repaired	38	83	140	12.2	260	16.3	RIFLE-F	21.51	Yes	No	Contrast, Diuretics
ATN21	64	M	70	172	Pneumonia	13	38	55	6.4	104	17.4	None		No	No	Diuretics
ATN22	76	M	65	168	Tracheoesophageal fistula repareid	19	27	50	3	117	26.5	RIFLE-F	38.26	Yes	No	Aminoglycosides, Diuretics
ATN23	65	F	69	160	Retroperitoneal haematoma	31	59	128	7.8	139	3.6	RIFLE-F	0.00	Yes	Yes	Contrast
ATN24	58	F			Fulminant liver failure	21	52	70	0.9	233	11.5	RIFLE-F	1.33	Yes	Yes	Amphotericin, Diuretics
ATN25	53	M	70	169	Fulminant liver failure	50	84	94	2.6	86	4.9	RIFLE-F	0.14	Yes	Yes	Amphotericin
ATN26	72	M	90		Thrombosed bypas axillo-bifemoral	30	60	150	9.9	310	12.9	RIFLE-F	0.96	Yes	Yes	Contrast, Rhabdomyolysis, Diuretics
ATN27	59	F	75		Hepatic encephalopathy	47	99	84	13.2	159	18.9	RIFLE-F	8.21	Yes	Yes	Diuretics
ATN28	60	F	100	142	Hypoxemic Respiratory Failure	23	8	67		94	8.2	None		No	No	Contrast
ATN29	84	M	77		Cardiac surgery	38	20	71	7.8	235	39.5	RIFLE-F	39.00	Yes	Yes	Diuretics
ATN30	77	0	58	169	Cardiogenic Shock	32				369	26.3	RIFLE-F	0.00	Yes	Yes	Diuretics
ATN31	59	1			Pneumonia		16	83	6.2	154	15.1	RIFLE-F	3.00	Yes	Yes	Contrast

ATN32	48	0	110	160	Cardiogenic Shock	41	21			114	11.3	None		No	No	Diuretics, Starch
ATN33	58	0	93.4		Hemorrhagic Shock	28	7	66	5.6	79	12.4	None		No	No	None
ATN34	59	0	49	159	Septic Shock	37	22			90	4.3	RIFLE-F	0.00	Yes	Yes	Contrast

APACHE II=acute physiology and chronic health evaluation score version II; SAPS 2=simplified acute physiology score version 2; AKI = acute kidney injury
CRRT=continuous renal replacement therapy

Table E3. Individual patient peri-mortem characteristics and causes of death

Patient	Peri-mortem characteristics										Cause of Death			
	IPPV	Vasoactives	HCT	WCC	Bili	FiO2	PaO2	CK	Lactate	24h FB	Proximate Cause of Death	Underlying Causes of Death	MOF	Withdrawal
ATN01	Yes	Yes	0.22	20.6	65	0.7	77	2,221	9.96	1041	Refractory Shock	IHD, HT, PVD, COPD, DM	Yes	No
ATN02	Yes	Yes	0.33	18.9	13	0.5	77	20	4.5	1400	Septic Shock	IHD, CHF	Yes	No
ATN03	Yes	Yes	0.24	41.8	472	0.4	83		6.57	21	Pneumonia	PHT, CLD, Coagulopathy	Yes	Ceiling of Rx
ATN04	No	No				1				-2200	Refractory hypoxia	Metastatic RCC	Yes	Yes
ATN05	No	Yes	0.29	35.7	226	1	78	71	11		Refractory Shock	CHF, ALF	Yes	No
ATN06	Yes	Yes	0.23	6.4	36	1	80		3.48	2800	Bleeding	GIB	Yes	No
ATN07	Yes	Yes	0.3	24.5	14	0.6	62	2,332	2.75	312	Ischaemic Stroke	CVA, IHD	No	Yes
ATN08	Yes	Yes	0.23	3.4	530	0.5	85	37	10.6	-1500	Intracranial Haemorrhage	CVA, HL, ALF	Yes	No
ATN09	Yes	No	0.27	12.1	13	0.8	64	88	8.8	1800	Pneumonia	Pneumonia, NHL	No	Yes
ATN10	Yes	Yes	0.2	12	66	1	79	135,736	24.7	4300	Refractory Shock	CES, ALF, Renal infarct	Yes	No
ATN11	Yes	Yes	0.28	5.2	5	1	122	1,891	13	6500	Refractory Shock	IHD, GIB	Yes	No
ATN12	No	No									Metastatic CRC	Cancer, SBO	Yes	No
ATN13	Yes	Yes	0.29	36.8	386	0.7	71		22.8	1690	Refractory Shock	Sepsis, CLD, Pericarditis	Yes	Ceiling of Rx
ATN14	No	No									Refractory Shock	Malignancy, GIB, Pneumonia	No	No
ATN15	Yes	Yes	0.36	19.6	271	1	66	623	22.9	2500	Septic Shock	ALF, cholangitis	Yes	Yes
ATN16	Yes	Yes	0.2	4.9	68	0.9	88	13,910	14.3	6000	Septic Shock	ALF	Yes	Yes
ATN17	No	No	0.3	37.1	11						Other	Metastatic RCC	No	No
ATN18	Yes	Yes	0.14	4.9	18	0.7	92	330	5.4	1100	Primary arrhythmia	Cancer	No	Yes
ATN19	No	No	0.34	12.1							Aspiration Pneumonia	HL	No	No
ATN20	Yes	Yes	0.23	17.6	81	0.7	62	604	2		Septic shock	IHD, DM	No	No
ATN21	Yes	No	0.29	16.6	11	1	57		5	1285	Refractory hypoxia	Cancer, COPD	No	Yes
ATN22	No	No	0.28	11.9	15	0.5	72		0.93	316	Other	Cancer	Yes	Yes
ATN23	Yes	Yes	0.25	3.2	34	0.5	95	144,515	10.6	5960	Refractory shock	IHD, ALF	Yes	No
ATN24	Yes	Yes	0.23	14.3	391	0.6	69		3.8	1854	Septic shock	ALF, CLD, Pneumonia	Yes	No
ATN25	Yes	Yes	0.19	22	263	0.4	173		13.3	-2200	Liver Failure	ALF, CLD, GIB	Yes	Yes

ATN26	Yes	Yes	0.22	10.7	34	1	92	83848	11.31	841	Septic shock	PVD	Yes	No
ATN27	Yes	Yes	0.29	12.3	336	0.6	62	82	4.58	2469	Hypoxic encephalopathy	ALF, IHD, CLD	Yes	Yes
ATN28	Yes	No	0.27	23.2	16	1	56	95	2.6		Refractory hypoxia	COPD, Malignancy	No	Yes
ATN29	Yes	Yes	0.24	12	50	0.7	80		11.7	1883	Refractory shock	IHD, CHF	Yes	Yes
ATN30	No	No	0.21	26.4		1	51	90			Other-Pneumonia	Pneumonia, CKD, HT	Yes	Yes
ATN31	Yes	Yes	0.24	3.9	26	1	76	21	0.9	-1056	Ischemic stroke	Pneumonia, Malignancy	Yes	Yes
ATN32	Yes	Yes	0.2	20.8	39	1	57		23.2		Refractory shock	IHD, CHF	No	Yes
ATN33	Yes	Yes	0.25	8.3		1	547		14.4		Hypovolemia	IHD, GIB	No	Yes
ATN34	Yes	Yes	0.19	3.1	75	1	63	708	22		Septic shock	Malignancy	Yes	No

IHD=ischemic heart disease, HT=hypertension, PVD=peripheral vascular disease, COPD=chronic obstructive pulmonary disease, DM=diabetes mellitus, CHF=congestive heart failure, PHT=pulmonary hypertension, CLD=chronic liver disease, RCC=renal cell carcinoma, ALF=acute liver failure; GIB = gastrointestinal bleeding, CVA=cerebrovascular accident, HL= Hodgkin's lymphoma, NHL=non-Hodgkin's lymphoma; CES=cholesterol emboli syndrome, SBO=small bowel obstruction.

Table E4. Individual patient semi-quantitative scores and diagnostic agreement between pathologists

Patient	Peak AKI	CRRT at death	Nephrotoxin Exposure	Post-mortem delay	Pathologist A			Pathologist B			Agreement
				(hrs)	Autolysis score	ATN SQS	ATN?	Autolysis score	ATN SQS	ATN?	
ATN01	RIFLE-F	Yes	Contrast, Rhabdomyolysis, Diuretics, Other	22	3	16	Yes	2	11	No	No
ATN02	RIFLE-F	No	Diuretics, Other	16	1	17	Yes	2	15	Yes	Yes
ATN03	RIFLE-F	Yes	Diuretics	18	2	7	Yes	1	1	No	No
ATN04	RIFLE-I	No	Contrast, Diuretics	28	1	11	Yes	1	6	Yes	Yes
ATN05	RIFLE-F	Yes	None	4	0	12	Yes	0	16	Yes	Yes
ATN06	RIFLE-F	Yes	Diuretics	20	1	13	yes	2	11	No	No
ATN07	None	No	Contrast, Rhabdomyolysis, Diuretics	28	3	8	yes	3	12	No	No
ATN08	RIFLE-F	Yes	Contrast, Aminoglycosides, Diuretics, Other	7	2	11	yes	1	10	No	No
ATN09	None	No	Contrast, Diuretics	19	2	8	no	1	5	No	Yes
ATN10	RIFLE-F	Yes	Aminoglycosides, Rhabdomyolysis	15	3	10	yes	3	9	No	No
ATN11	RIFLE-I	No	Contrast, Aminoglycoside, Rhabdomyolysis, Diuretics, Other	11	1	12	no	2	8	No	Yes
ATN12	None	No	Contrast	34	3	7	no	3	5	No	Yes
ATN13	RIFLE-F	Yes	Contrast, Aminoglycosides, Diuretics	7	2	14	yes	1	17	Yes	Yes
ATN14	RIFLE-I	No	Contrast, Aminoglycosides, Diuretics	37	3	3	no	1	10	No	Yes
ATN15	RIFLE-F	Yes	Calcineurin inhibitors, Diuretics	24	2	8	yes	2	8	No	No
ATN16	RIFLE-F	Yes	Rhabdomyolysis	25	3	2	no	3	5	No	Yes
ATN17	RIFLE-F	No	Other	27	1	1	no	1	4	No	Yes
ATN18	None	No	None	16	1	12	yes	1	11	Yes	Yes
ATN19	RIFLE-F	No	Diuretics, Other	24	3	6	no	3	7	No	Yes
ATN20	RIFLE-F	No	Contrast, Diuretics	3.5	0	22	yes	1	18	Yes	Yes
ATN21	None	No	Diuretics	18	1	11	Yes	1	6	No	No
ATN22	RIFLE-F	No	Aminoglycosides, Diuretics	20	1	14	Yes	2	18	No	No
ATN23	RIFLE-F	Yes	Contrast	42	4	15	no	3	16	No	Yes
ATN24	RIFLE-F	Yes	Amphotericin, Diuretics	23	2	8	Yes	3	10	No	No
ATN25	RIFLE-F	Yes	Amphotericin	12	0	5	yes	1	8	No	No
ATN26	RIFLE-F	Yes	Contrast, Rhabdomyolysis, Diuretics	48	2	7	yes	3	12	No	No
ATN27	RIFLE-F	Yes	Diuretics	38	3	3	no	3	1	No	Yes
ATN28	None	No	Contrast	27	3	5	No	2	3	No	Yes
ATN29	RIFLE-F	Yes	Diuretics	45	2	11	Yes	2	9	No	No
ATN30	RIFLE-F	Yes	Diuretics	12	0	19	No	1	18	No	Yes
ATN31	RIFLE-F	Yes	Contrast	43	3	10	No	3	7	No	Yes
ATN32	None	No	Diuretics, Starch	36	4	9	Yes	3	4	No	No

ATN33	None	No	None	9	0	2	No	1	5	No	Yes
ATN34	RIFLE-F	Yes	Contrast	98	0	11	Yes	2	9	No	No

AKI= acute kidney injury; RIFLE=Risk, Injury, Failure, Loss and End stage kidney injury score for AKI;
ATN=acute tubular necrosis; SQS=Semi-Quantitative Score.