Supplementary Online Content

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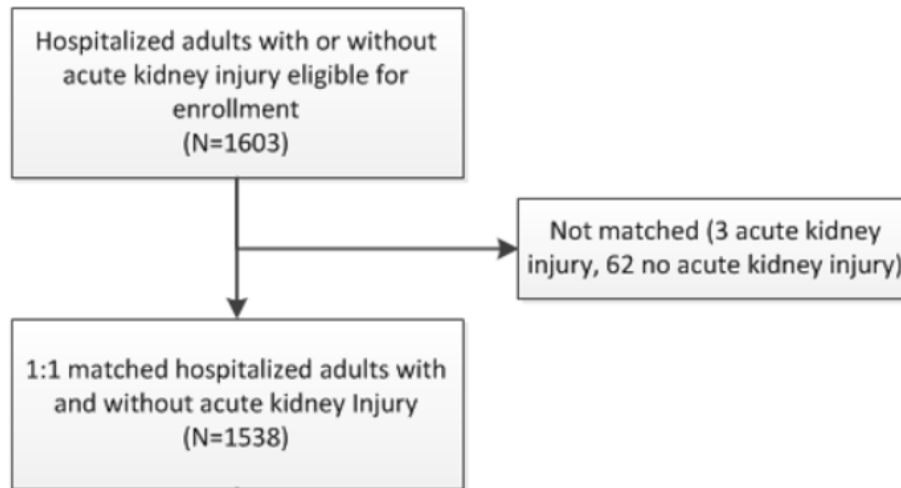
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This supplementary material has been provided by the authors to give readers additional information about their work.

SUPPLEMENTARY FIGURE

Supplementary Figure S1. Assembly of matched cohort of adults with and without acute kidney injury.

SUPPLEMENTARY TABLE

Supplementary Table 1. ASSESS-AKI enrollees follow-up through November 30, 2019 (N=1538)

Death	ESRD w/o death	Withdrew/lost to follow-up	Remaining (through November 30, 2018)
320 (including 33 deaths after ESRD onset)	25 (so total number of ESRD was 58 [25+33])	189 (reasons included: no longer willing to follow the protocol/ interested in participating; lost to follow-up; participant has personal constraints)	1004

Supplementary Table 2. Incremental improvement in model performance with addition of urine ACR

		C-statistic	Change in C-statistics	Net Reclassification Improvement (NRI)
Base model without urine ACR *(with stages of AKI)*	Female vs Male Black vs Non-Black Hispanic vs Non-Hispanic Diabetic vs Non-Diabetic Older Age (per 5 yr increase) Higher Systolic BP (per 10 mmHg increase) Higher BMI (per 5 kg/m^2 increase) Lower eGFR Stage 2 vs. stage 1 AKI Stage 3 vs. stage 1 AKI	0.818		
	Adjusted model above + urine ACR	0.850	0.032 (p <0.0001)	0.555 (p < 0.0001)

Supplementary Table 3. Results of sensitivity analyses.

		Original Table 2 results: Original ASSESS-AKI study AKI enrollees (N=769)		*Sensitivity analysis:* AKI enrollees meeting met the 50% higher serum Cr criteria (N=468)		*Sensitivity analysis:* requiring that the halving of eGFR be confirmed on two consecutive values (N=769)		*Sensitivity analysis:* Additionally adjusting for smoking and ACE-I/ARB use (N=769)		*Sensitivity analysis:* Additionally adjusting for change in eGFR from pre-AKI to post-AKI (N=769)		*Sensitivity analysis:* Fine-Gray model results (N=769)	
		HR*	C-statistic	HR*	C-statistic	HR*	C-statistic	HR*	C-statistic	HR*	C-statistic	HR*	C-statistic
Unadjusted models	Higher urine ACR (mg/gm) (per doubling)	1.53 (1.43-1.64)	0.823	1.45 (1.33-1.58)	0.805	1.87 (1.68-2.08)	0.913	NA	NA	NA	NA	1.47 (1.35-1.60)	0.823
Adjusted models		1.37 (1.26-1.49)	0.846	1.34 (1.20-1.50)	0.839	1.69 (1.46-1.96)	0.931	1.41 (1.28-1.54)	0.844	1.36 (1.25-1.49)	0.851	1.33 (1.19-1.48)	0.845
Adjusted models *(with stages of AKI)*		1.38 (1.26- 1.50)	0.850	1.35 (1.20-1.52)	0.845	1.70 (1.46-1.98)	0.934	1.42 (1.29-1.59)	0.848	1.37 (1.25-1.49)	0.859	1.33 (1.20-1.49)	0.849

*all associated p-values <0.0001

Supplementary Table 4. Urine PCR, AKI stage and risk of kidney disease progression among those with AKI (N=769) and among those without AKI (N=769)

	Predictor(s) in model	ASSESS-AKI enrollees with recent history of AKI prior to baseline visit (N=769)			ASSESS-AKI enrollees without recent history of AKI prior to baseline visit (N=769)		
		HR	P-value	C-statistic	HR	P-value	C-statistic
Unadjusted models	Higher urine PCR (g/g)(per doubling)	1.98 (1.80-2.18)	<0.0001	0.822	1.82 (1.62-2.04)	<0.0001	0.788
	Lower eGFR (per 10 ml/min/1.73m^2 decrease)	1.50 (1.36-1.66)	<0.0001	0.767	1.42 (1.22-1.66)	<0.0001	0.708
	Stage 2 vs. stage 1 AKI	0.86 (0.45-1.63)	0.64	0.263	N/A		
	Stage 3 vs. stage 1 AKI	1.59 (0.93-2.72)	0.09				
Adjusted models	Higher urine PCR (g/g)(per doubling)	1.75 (1.55-1.97)	< 0.0001	0.853	1.82 (1.51- 2.19)	<0.0001	0.831
	Female vs Male	1.25 (0.81-1.94)	0.31		1.28 (0.64-2.54)	0.49	
	Black vs Non-Black	0.97 (0.57-1.63)	0.89		2.10 (0.92-4.82)	0.08	
	Hispanic vs Non-Hispanic	0.71 (0.22-2.35)	0.58		1.55 (0.20-11.87)	0.67	
	Diabetic vs Non-Diabetic	1.68 (0.98-2.88)	0.06		1.75 (0.86-3.54)	0.12	
	Older Age (per 5 yr increase)	0.91 (0.83-1.01)	0.09		0.84 (0.71-0.99)	0.04	
	Higher Systolic BP (per 10 mmHg increase)	1.01 (0.92-1.11)	0.82		1.04 (0.88-1.23)	0.62	
	Higher BMI (per 5 kg/m^2 increase)	0.99 (0.86-1.15)	0.90		0.94 (0.78-1.14)	0.54	
	Lower eGFR (per 10 ml/min/1.73m^2 decrease)	1.24 (1.12-1.37)	<0.0001		1.31 (1.13-1.54)	0.001	
	Higher urine PCR (g/g)(per doubling)	1.77 (1.57- 2.00)	< 0.0001	0.859	N/A		
	Female vs Male	1.26 (0.81-1.95)	0.31				
	Black vs Non-Black	0.96 (0.57-1.62)	0.87				
	Hispanic vs Non-Hispanic	0.70 (0.21-2.30)	0.56				
	Diabetic vs Non-Diabetic	1.70 (1.00-2.90)	0.05				
	Older Age (per 5 yr increase)	0.92 (0.83-1.01)	0.09				
	Higher Systolic BP (per 10 mmHg increase)	1.01 (0.92-1.12)	0.78				
	Higher BMI (per 5 kg/m^2 increase)	0.99 (0.86-1.15)	0.93				
	Lower eGFR (per 10 ml/min/1.73m^2 decrease)	1.24 (1.12-1.37)	< 0.0001				
(with stages of AKI)	Stage 2 vs. stage 1 AKI	0.92 (0.47-1.79)	0.81				
	Stage 3 vs. stage 1 AKI	2.17 (1.26-3.74)	0.005				

AKI, acute kidney injury; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; PCR, protein to creatinine ratio

Supplementary Table 5. Urine PCR, AKI/stage of AKI and risk of kidney disease progression among all ASSESS-AKI adult match cohort study participants (N=1538)

	Predictor(s) in model	All ASSESS-AKI enrollees (N=1538)		
		HR	P-value	C-statistic
Unadjusted models	Higher urine PCR (g/g)(per doubling)	2.09 (1.91-2.28)	< 0.0001	0.815
	Lower eGFR (per 10 ml/min/1.73m^2 decrease)	1.55 (1.42-1.70)	<0.0001	0.758
	AKI vs Non-AKI	3.06 (2.11-4.44)	< 0.0001	0.387
	AKI Stage 1 vs no AKI	2.89 (1.94-4.29)	< 0.0001	0.477
	AKI Stage 2 vs no AKI	2.57 (1.27-5.19)	0.009	
	AKI Stage 3 vs no AKI	4.92 (2.66-9.10)	< 0.0001	
Adjusted models (with interaction terms)	Higher urine PCR (g/g)(per doubling)	1.96 (1.68- 2.28)	< 0.0001	0.840
	Female vs Male	1.35 (0.85-2.16)	0.20	
	Black vs Non-Black	1.33 (0.76-2.31)	0.32	
	Hispanic vs Non-Hispanic	0.98 (0.26-3.66)	0.98	
	Diabetic vs Non-Diabetic	2.10 (1.23-3.59)	0.007	
	Older Age (per 5 yr increase)	0.94 (0.84-1.06)	0.32	
	Higher Systolic BP (per 10 mmHg increase)	1.09 (0.97-1.21)	0.13	
	Higher BMI (per 5 kg/m^2 increase)	1.06 (0.92-1.23)	0.43	
	Lower eGFR (per 10 ml/min/1.73m^2 decrease)	1.11 (1.00-1.23)	0.05	
AKI vs. no AKI	AKI vs. no AKI	2.53 (1.21-5.25)	0.01	
	AKI vs. no AKI*urine PCR	0.96 (0.88-1.05)	0.34	

		HR (95% CI)	P-value	C-statistic
	Higher urine PCR (g/m)(per doubling)	2.03 (1.66- 2.49)	< 0.0001	0.845
	Female vs Male	1.45 (0.90-2.31)	0.12	
	Black vs Non-Black	1.29 (0.74-2.25)	0.38	
	Hispanic vs Non-Hispanic	0.95 (0.25-3.53)	0.94	
	Diabetic vs Non-Diabetic	2.08 (1.21-3.56)	0.008	
	Older Age (per 5 yr increase)	0.95 (0.85-1.07)	0.39	
	Higher Systolic BP (per 10 mmHg increase)	1.09 (0.98-1.22)	0.12	
	Higher BMI (per 5 kg/m^2 increase)	1.05 (0.91-1.22)	0.51	
	Lower eGFR (per 10 ml/min/1.73m^2 decrease)	1.11 (1.00-1.23)	0.05	
Stages of AKI vs. no AKI	AKI Stage 1 vs no AKI	1.57 (0.91-2.72)	0.11	
	AKI Stage 2 vs no AKI	1.67 (0.65-4.31)	0.29	
	AKI Stage 3 vs no AKI	3.42 (1.28-9.12)	0.01	
	AKI Stage 1 vs no AKI*urine PCR	0.90 (0.71-1.15)	0.39	
	AKI Stage 2 vs no AKI*urine PCR	0.96 (0.64-1.43)	0.84	
	AKI Stage 3 vs no AKI*urine PCR	0.88 (0.56-1.36)	0.56	

AKI, acute kidney injury; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; PCR, protein to creatinine ratio

Supplementary Table 6. Kidney Failure Risk Equation (KFRE) score, AKI/stages of AKI and risk ESRD

		ASSESS-AKI enrollees with AKI three months prior to baseline visit (N=769)			ASSESS-AKI enrollees without AKI three months prior to baseline visit (N=769)			All matched ASSESS-AKI enrollees (N=1538)		
		HR	P-value	C-statistic	HR	P-value	C-statistic	HR	P-value	C-statistic
Unadjusted models	KFRE score (per 0.1 increase)	2.02 (1.83-2.23)	<0.0001	0.943	3.71 (2.39-5.76)	<0.0001	0.883	2.94 (2.50-3.46)	<0.0001	0.936
	AKI vs Non-AKI	N/A			N/A			4.38 (2.32-8.29)	<0.0001	0.417
	AKI Stage 1 vs no AKI	N/A			N/A			4.39 (2.27-8.51)	<0.0001	0.514
	AKI Stage 2 vs no AKI							3.31 (1.14-9.60)	0.03	
	AKI Stage 3 vs no AKI							5.76 (2.21-14.99)	0.0003	
Adjusted models (with interaction terms)	KFRE score (per 0.1 increase) AKI vs no AKI	N/A			N/A			2.79 (2.37-3.30) 2.80 (1.41-5.55)	<0.0001 0.003	0.909
	KFRE score (per 0.1 increase) AKI vs no AKI AKI vs no AKI*KFRE	N/A			N/A			3.85 (2.69-5.50) 3.66 (1.70-7.91) 0.69 (0.47-1.00)	<0.0001 0.0009 0.05	0.909
	KFRE score (per 0.1 increase) AKI Stage 1 vs no AKI AKI Stage 2 vs no AKI AKI Stage 3 vs no AKI	N/A			N/A			2.87 (2.42-3.40) 2.58 (1.25-5.33) 1.77 (0.51-6.12) 6.00 (2.21-16.31)	<0.0001 0.01 0.36 0.0004	0.896

	KFRE score (per 0.1 increase) AKI Stage 1 vs no AKI AKI Stage 2 vs no AKI AKI Stage 3 vs no AKI	N/A	N/A	3.94 (2.73-5.70) 3.51 (1.56-7.89) 3.02 (0.80-11.37) 4.59 (1.35-15.61)	<0.0001 0.002 0.10 0.01	0.898
	AKI Stage 1 vs no AKI*KFRE AKI Stage 2 vs no AKI*KFRE AKI Stage 3 vs no AKI*KFRE			0.68 (0.46-1.01) 0.60 (0.36-1.03) 1.61 (0.71-3.69)	0.06 0.06 0.26	