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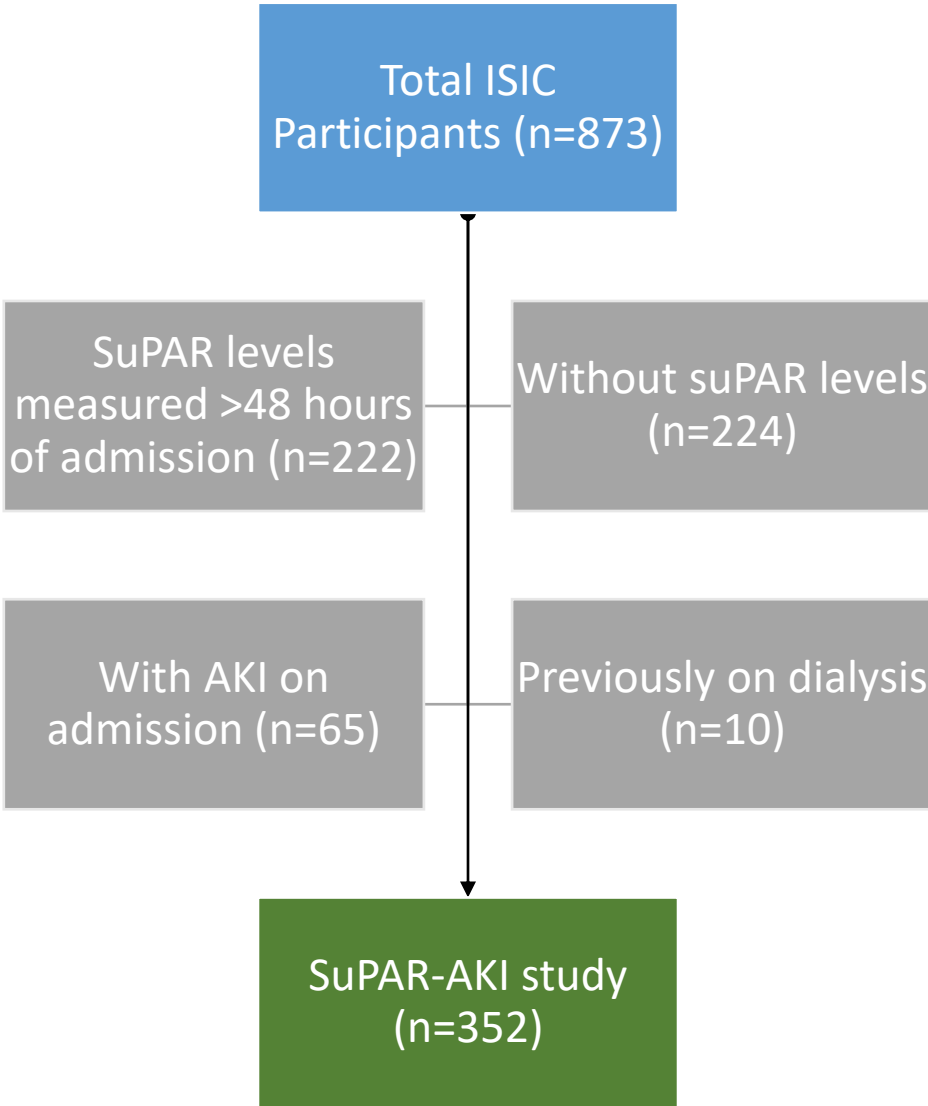
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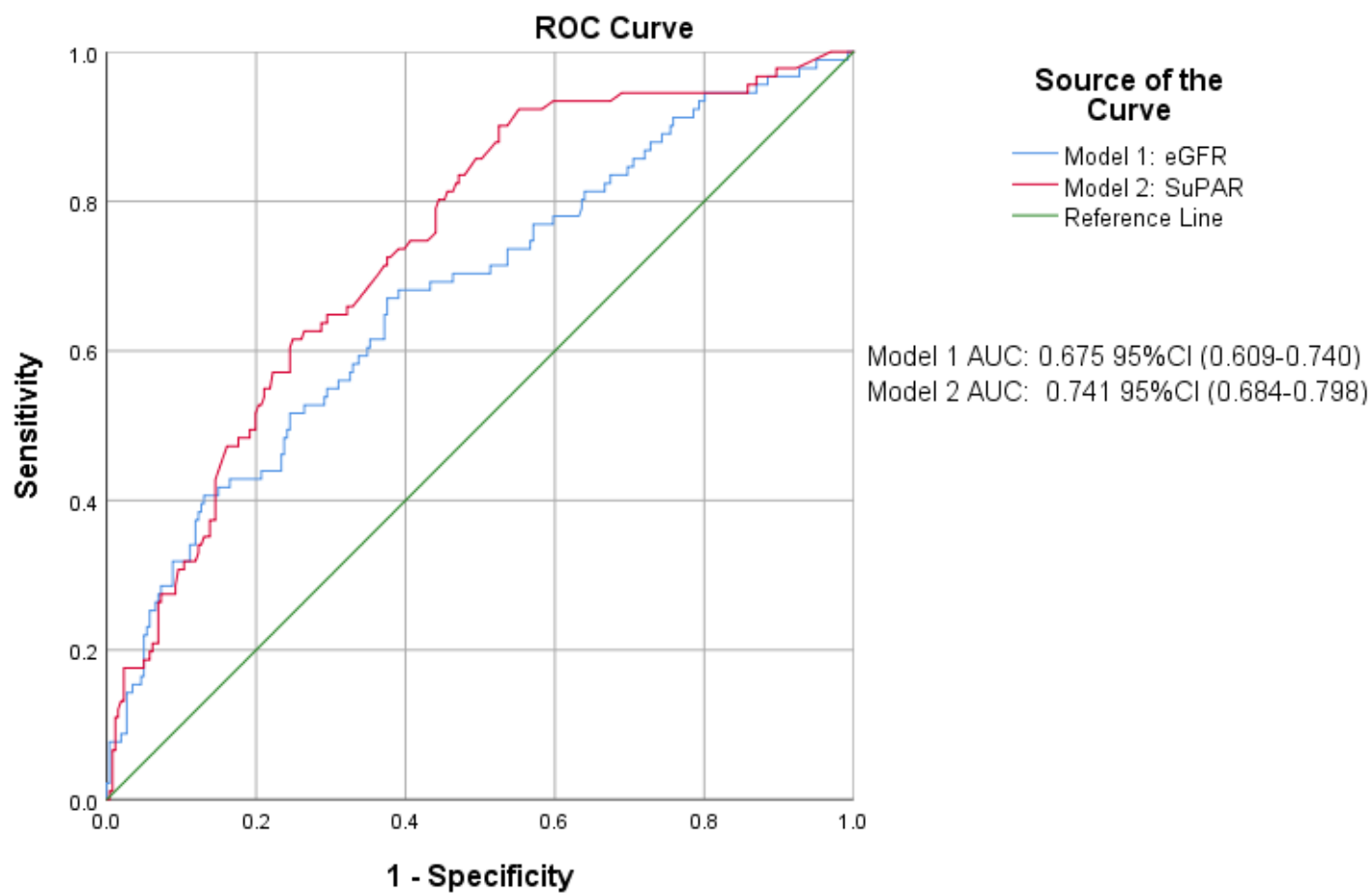
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**Figure S1. Patient Selection Flowchart**



**Figure S2. ROC Curves for SuPAR and Admission eGFR**



Admission eGFR and suPAR levels were included each in a separate model.

**Table S1. Participating centers and number of patients included in the substudy**

<b>Institution</b>	<b>Number of patients included</b>
University of Michigan in Ann Arbor, MI USA	148
University of Copenhagen at Hvidovre, Denmark	91
Attikon University Hospital in Athens, Greece	61
University Hospital of Dusseldorf, Germany	20
University of Thessaly, Greece	20
Charite de Berlin, Germany	12
Total	352

**Table S2. Clinical characteristics and inflammatory biomarkers stratified by continent of enrollment**

	United States (n=148)	Europe (n=204)	P-value <sup>b</sup>
<b>Clinical Characteristics</b>			
Age in years, mean (SD)	60 (16)	62 (17)	0.27
Male, n (%)	76 (51.4%)	126 (61.8%)	0.051
Black, n (%)	48 (32.4%)	1 (0.5%)	<0.001
Body mass index kg/m <sup>2</sup> , mean (SD)	32 (8)	2 (5)	<0.001
Diabetes mellitus, n (%)	50 (33.8%)	41 (20.1%)	0.004
Hypertension, n (%)	85 (57.4%)	84 (42.2%)	0.003
Coronary artery disease, n (%)	19 (12.8%)	15 (7.4%)	0.086
Congestive heart failure, n (%)	22 (14.9%)	7 (3.4%)	<0.001
Admission eGFR ml/min/1.73 m <sup>2</sup> , mean (SD) <sup>a</sup>	80 (29.08)	81 (26)	0.67
Admission eGFR<60 ml/min/1.73 m <sup>2</sup> , n (%) <sup>a</sup>	39 (26.4%)	51 (25.0%)	0.774
Acute kidney injury, n (%)	53 (35.8%)	38 (18.6%)	<0.001
Oxygen saturation on admission, % (SD)	93% (8)	95% (4)	<0.001
Required mechanical ventilation, n (%)	38 (25.7%)	39 (19.1%)	0.142
Required dialysis, n (%)	6 (4.1%)	19 (9.3%)	0.058
<b>Biomarkers<sup>c</sup></b>			
SuPAR pg/ml, median (IQR)	6.19 (4.95-8.44)	5.00 (3.43-7.00)	<0.001
C-reactive protein mg/dl, median (IQR)	10.00 (4.60-19.30)	4.65 (1.50-10.13)	<0.001
Ferritin ng/ml, median (IQR)	606 (263-1350)	455 (204-624)	0.004
D-dimer mg/L, median (IQR)	1.085 (0.62-1.94)	0.39 (0.25-0.63)	<0.001
Lactate dehydrogenase IU/L, median (IQR)	400 (272-589)	270 (200-366)	<0.001

<sup>a</sup>Calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. <sup>b</sup>P-value for the comparison between groups with and without acute kidney injury. Abbreviations: eGFR: estimated glomerular filtration rate; IQR: interquartile range; IU: international units SD: standard deviation. <sup>c</sup>C-reactive protein levels were available in 301 participants, ferritin in 207 participants, D-dimer in 204 participants and lactate dehydrogenase in 256 participants.

**Table S3. Clinical characteristics and inflammatory biomarkers stratified by suPAR tertiles**

	SuPAR Tertiles			P-value <sup>b</sup>
	< 4.60 ng/ml (n=117)	4.60-6.86 ng/ml (n=117)	>6.86 ng/ml (n=118)	
<b>Clinical Characteristics</b>				
Age in years, mean (SD)	55 (16)	61 (16)	67 (15)	<0.001
Male, n (%)	65 (55.6%)	64 (54.7%)	73 (61.9%)	0.479
Black, n (%)	8 (6.8%)	19 (16.2%)	22 (18.6%)	0.022
Body mass index kg/m <sup>2</sup> , mean (SD)	29 (7)	30 (7)	31 (8)	0.029
Diabetes mellitus, n (%)	14 (12.0%)	26 (22.2%)	51 (43.2%)	<0.001
Hypertension, n (%)	42 (35.9%)	52 (44.4%)	75 (63.6%)	<0.001
Coronary artery disease, n (%)	9 (7.7%)	8 (6.8%)	17 (14.4%)	0.099
Congestive heart failure, n (%)	3 (2.6%)	5 (4.3%)	21 (17.8%)	<0.001
Admission eGFR ml/min/1.73 m <sup>2</sup> , mean (SD) <sup>a</sup>	90 (20)	81 (26)	70 (30)	<0.001
Admission eGFR<60 ml/min/1.73 m <sup>2</sup> , n (%) <sup>a</sup>	12 (10.3%)	27 (23.1%)	51 (43.2%)	<0.001
Acute kidney injury, n (%)	7 (6.0%)	30 (25.6%)	54 (45.8%)	<0.001
Oxygen saturation on admission, % (SD)	96 (3)	95 (4)	91 (8)	<0.001
Required mechanical ventilation, n (%)	3 (2.6%)	21 (17.9%)	53 (44.9%)	<0.001
Required dialysis, n (%)	1 (0.9%)	5 (4.3%)	19 (16.1%)	<0.001
<b>Biomarkers<sup>c</sup></b>				
SuPAR pg/ml, median (IQR)	3.20 (2.57-4.00)	5.60 (5.10-6.00)	9.07 (7.87-11.40)	<0.001
C-reactive protein mg/dl, median (IQR)	3.50 (0.80-6.20)	6.70 (4.10-11.50)	12.50 (4.70-19.80)	<0.001
Ferritin ng/ml, median (IQR)	268 (169-554)	486 (262-847)	911 (332-1535)	<0.001
D-dimer mg/L, median (IQR)	0.521 (0.366-0.748)	0.725 (0.40-1.28)	1.10 (0.550-2.490)	<0.001
Lactate dehydrogenase IU/L, median (IQR)	240 (195-312)	323 (253-477)	438 (311-614)	<0.001

<sup>a</sup>Calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. <sup>b</sup>P-value for the ANOVA for normally distributed continuous variables, Kruskal Wallis test for non-normally distributed continuous variables, and chi-square test for categorical variables. Abbreviations: AKI: acute kidney injury; eGFR: estimated glomerular filtration rate; IQR: interquartile range; IU: international units SD: standard deviation. <sup>c</sup>C-reactive protein levels were available in 301 participants, ferritin in 207 participants, D-dimer in 204 participants and lactate dehydrogenase in 256 participants.

**Table S4. Correlation between suPAR and inflammatory biomarkers**

		SuPAR
C-reactive protein	Correlation Coefficient	0.465
	P-value. (2-tailed)	<0.001
	N	301
Ferritin	Correlation Coefficient	0.320
	P-value. (2-tailed)	<0.001
	N	207
D-dimer	Correlation Coefficient	0.314
	P-value. (2-tailed)	<0.001
	N	204
Lactate dehydrogenase	Correlation Coefficient	0.486
	P-value. (2-tailed)	<0.001
	N	256



**Table S5. Determinants of suPAR levels**

	SuPAR (log-base 2)	
	$\beta$ , 95%CI	P-value
<b>Model 0: Clinical Characteristics</b>		
Age, per 10 years	0.01 (0.01 – 0.02)	0.006
Male	-0.13 (-0.29 – 0.03)	0.10
Black	-0.01 (-0.25 – 0.25)	0.99
Institution (US vs. Europe)	-0.31 (-0.50 – -0.12)	0.001
Body mass index, per 5 kg/m <sup>2</sup>	-0.01 (-0.07 – 0.05)	0.75
Diabetes mellitus	0.23 (0.03 – 0.43)	0.022
Hypertension	-0.08 (-0.27 – 0.12)	0.44
Coronary artery disease	0.01 (-0.29 – 0.31)	0.94
Congestive heart failure	0.38 (0.06 – 0.69)	0.019
eGFR, per 5 ml/min/1.73 m <sup>2</sup> <sup>b</sup>	-0.02 (-0.04 – 0.004)	0.11
Oxygen saturation, per 1 %	-0.02 (-0.04 – 0.01)	0.001
<b>Models 1-4: Biomarkers<sup>a</sup></b>		
C-reactive protein, per 100% increase	0.14 (0.10-0.18)	<0.001
Ferritin, per 100% increase	0.09 (0.03-0.14)	0.003
D-dimer, per 100% increase	0.13 (0.07-0.19)	<0.001
Lactate dehydrogenase, per 100% increase	0.48 (0.36-0.60)	<0.001

<sup>a</sup>Each biomarker was evaluated in a separate model that includes the listed clinical characteristics in addition to log-transformed suPAR (base 2). <sup>b</sup>Serum creatinine-derived eGFR measured at the time of suPAR sample collection. eGFR: estimated glomerular filtration rate. C-reactive protein levels were available in 301 participants, ferritin in 207 participants, D-dimer in 204 participants and lactate dehydrogenase in 256 participants.

**Table S6. Determinants of incident acute kidney injury and need for dialysis in hospitalized patients with COVID-19 after excluding 25 patients with suPAR levels measured 24-48 hours after admission.**

	Acute kidney injury (n=82)		Renal replacement therapy (n=22)	
	OR, 95%CI	P-value	OR, 95%CI	P-value
<b>Model 0: Clinical Characteristics</b>				
Age, per 10 years	0.99 (0.97-1.01)	0.38	0.93 (0.89-0.98)	0.003
Male	0.32 (0.17-0.59)	<0.001	0.57 (0.19-1.71)	0.32
Black	1.96 (0.84-4.56)	0.12	2.20 (0.29-16.65)	0.45
Institution (US vs. Europe)	0.53 (0.27-1.05)	0.07	14.01 (2.07-94.97)	0.01
Body mass index, per 5 kg/m <sup>2</sup>	0.99 (0.80-1.23)	0.93	0.87 (0.55-1.36)	0.53
Diabetes mellitus	1.39 (0.73-2.67)	0.32	3.87 (1.19-12.63)	0.03
Hypertension	1.15 (0.59-2.26)	0.68	1.61 (0.44-5.93)	0.48
Coronary artery disease	0.76 (0.27-2.09)	0.59	1.04 (0.16-6.60)	0.97
Congestive heart failure	1.11 (0.38-3.25)	0.85	0.41 (0.04-4.52)	0.47
eGFR, per 5 ml/min/1.73 m <sup>2</sup>	0.97 (0.96-0.99)	<0.001	0.96 (0.93-0.98)	<0.001
Oxygen saturation, per 1 % increase	0.96 (0.92-1.00)	0.07	0.90 (0.84-0.96)	0.001
<b>Model 1: SuPAR as a continuous variable</b>				
SuPAR, per 100% increase <sup>b</sup>	2.47 (1.58-3.84)	<0.001	3.66 (1.78-7.52)	<0.001
<b>Model 2: SuPAR as a categorical variable</b>				
SuPAR <4.60 ng/ml (Tertile 1)	-	-	-	-
SuPAR 4.60-6.86 ng/ml (Tertile 2)	5.58 (2.05-15.16)	0.001	14.32 (1.17-176.07)	0.038
SuPAR ≥6.57 ng/ml (Tertile 3)	8.60 (3.10-23.91)	<0.001	48.86 (4.06-587.46)	0.002

<sup>a</sup>Each biomarker was evaluated in a separate model that includes the listed clinical characteristics in addition to suPAR. <sup>b</sup>Serum creatinine-derived eGFR measured at the time of suPAR sample collection was used in Model 1 assessing the association between suPAR and acute kidney injury. eGFR: estimated glomerular filtration rate measured at the time of suPAR collection.