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Serum ACE as a prognostic biomarker in COVID-19: A case series

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Fig 1. Serum ACE values for patients at admittance and at day 3-5. The reference interval is indicated in grey.

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The authors declare no conflict of interest

Serum ACE as a prognostic biomarker in COVID-19: A pilot study

To the Editor,

We have earlier proposed that serum ACE (s-ACE) could be used as a biomarker for severity in COVID-19 due to an assumed inverse relationship between ACE and ACE2. High s-ACE could indicate lower ACE2 activity and therefore more widespread and severe SARS-CoV2 infection, owing to virally mediated downregulation of ACE2 (1). Dysregulation of the Renin-Angiotensin-

Aldosterone system (RAAS) are found in comorbidities known as risk factors for increased morbidity and mortality, such as hypertension and cardiovascular disease (2). This dysregulation of the RAAS could be further aggravated by virally mediated downregulation of ACE2 in COVID-19, increasing the levels of pro-inflammatory and hypertensive products of ACE, e.g angiotensin II (2). This further supports the hypothesis that s-ACE could serve as a prognostic biomarker in COVID-19.

The aim of this prospective case series was to investigate the potential of s-ACE as a prognostic biomarker in COVID-19. S-ACE was analyzed in serum for 15 symptomatic patients admitted to Oslo University Hospital (OUH), Norway, with confirmed COVID-19 by a positive SARS-CoV-2 real-time reverse transcriptase chain reaction (TR_PCR) (table 1). Clinical frailty scale (CFS) and Charlson Comorbidity index (CCI) scores were estimated at admittance in order to stratify the patients with regards to overall fitness (CFS) and the number of comorbidities (CCI) (3). Patients using ACE inhibitors or Angiotensin II receptor blockers were excluded (N=2), as these drugs can interfere with s-ACE levels (4), leaving 13 patient for further analysis. Clinical data were registered in a COVID-19 quality registry approved by the data protection officer at OUH. S-ACE was sampled at day of admittance (N=13) and at day 3-5 (N= 5) (figure 1). S-ACE was analyzed on Cobas c501 (Roche diagnostics GmbH, Mannheim, Germany) using ACE Kinetic (Bühlmann laboratories AG Schönenbuch, Switzerland) within 5 days from blood collection.

Clinical and laboratory characteristics of the patient population are shown in table 1. The sampled values for s-ACE both at baseline and day 3-5 were all within the reference interval of 18 to 65 U/L, except for one patient with 79 U/L at baseline (figure 1). In addition, we did not find any consistent patterns with regards to differences between values at day 1 and day 3-5. Descriptive analysis did not reveal any obvious relationship between CFS, CCI, admittance to intensive care unit (ICU), early discharge and s-ACE at admittance, nor did we find any relationship between other biochemical parameters and s-ACE. (5)

[INSERT TABLE 1 HERE]

[INSERT FIGURE 1 HERE]

Since our study is a case series, a control group is not included, nor do the small sample size allow for statistical analysis. In addition, none of the patients included in our study had an excessive immune response to infection, thus it is still unknown whether s-ACE could have a role in these

patients. However, our results suggests that distribution of s-ACE in COVID-19 is similar to that found in a healthy population (5), providing a signal that s-ACE is not a feasible prognostic biomarker in COVID-19. Further studies should therefore also involve components downstream of ACE. E.g., angiotensin II and aldosterone could possibly better reflect the relative activities of ACE and ACE2 and have more merit as biomarkers of RAAS dysfunction in COVID-19 (2).

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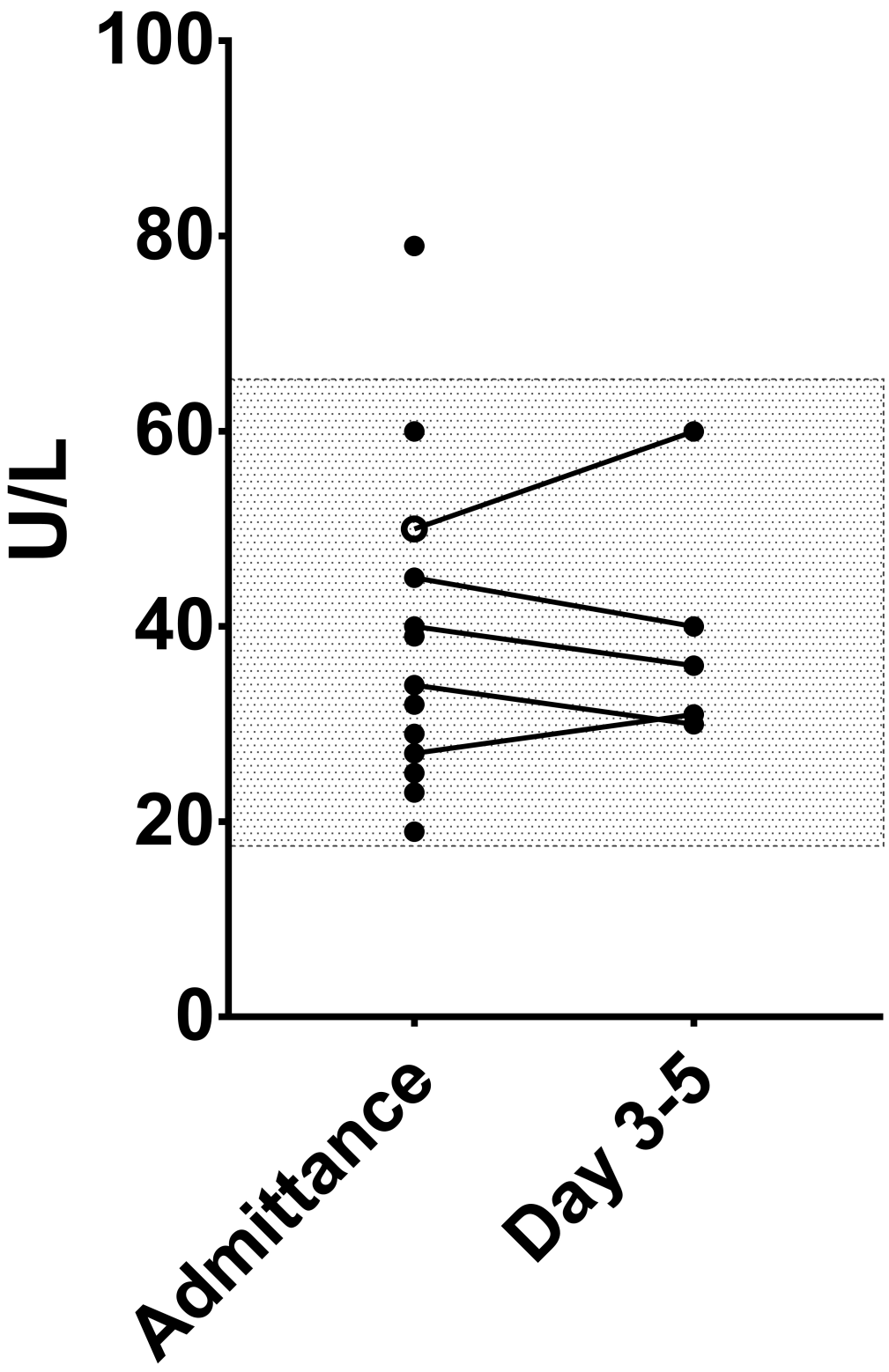
Table 1. Patient characteristics and laboratory values

Patient characteristics		
Parameter	Results	Number of observations
Age (years): median (range)	59 (29-97)	13
Female/male ratio	5/8	13
CFS : median (range)	2 (1-6)	13
CCI: median (range)	2 (0-5)	13
Number of patients with cardiovascular disease	6	13
Number of patients admitted to ICU during stay	2	13
Length of stay (days): median (range)	3 (<1-24)	13
Number of deaths	0	13
Biochemical parameters at day of admittance		
Parameter	Median (range)	Number of observations
s-ACE (U/L)	34 (19-79)	13
Creatinine (µmol/L)	86 (72-117)	13

Pro-BNP (ng/L)	59 (49-2401)	11
PCT (µg/L)	0.09 (0.09-0.42)	13
CRP (mg/L)	24 (1.1-73)	13
WBC ($x10^9$ cells/L)	5.6 (3.3-10.6)	13
s-Na (mmol/L)	140 (138-144)	13
s-K (mmol/L)	4.2 (3.5-4.5)	13

Abbreviations: *CFS: Clinical Frailty Scale, CCI: Charlson Comorbidity Index, CRP: C-reactive protein, ICU: Intensive Care unit PCT: Procalcitonin, pro-BNP: pro-Brain Natriuretic Peptide, s-ACE: serum ACE, s-K: serum Potassium, s-Na: serum sodium, WBC: White blood cell count (leukocytes)*



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