Markers of renal function and acute kidney injury in acute heart failure: definitions and impact on outcomes of the cardiorenal syndrome

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Aims
Acute kidney injury (AKI) in patients hospitalized for acute heart failure (AHF) is part of the cardiorenal syndrome and has been associated with increased morbidity and mortality. However, definitions and prognostic impact of AKI in AHF have been variable. Cystatin C is a prospective new marker of AKI. The objective of this study was to investigate the use of cystatin C as a marker of early AKI in AHF.

Methods and results
Patients (n = 292) hospitalized for AHF had measurements of cystatin C on admission and at 48 h. We assessed the incidence of a rise in cystatin C between the two measurements and evaluated the effect of an increase in cystatin C on outcomes up to 12 months. The population was on average 75 years old and 49% were female. On admission, median cystatin C was 1.25 mg/L (interquartile range 0.99 – 1.61 mg/L). A rise in cystatin C by >0.3 mg/L within 48 h after hospitalization (AKIcysC) occurred in 16% of patients and resulted in 3 days (P = 0.01) longer hospital stay and was associated with significantly higher in-hospital mortality, odds ratio 4.0 [95% confidence intervals (CI) 1.3 – 11.7, P = 0.01]. During follow-up, AKIcysC was an independent predictor of 90 days mortality, adjusted odds ratio 2.8 (95% CI 1.2 – 6.7, P = 0.02).

Conclusion
Cystatin C appears to be a useful marker of early AKI in patients hospitalized for AHF. A decline in renal function detected by cystatin C during the first 48 h after hospitalization occurs frequently in AHF and has a detrimental impact on prognosis.

Keywords
Cystatin C • Acute kidney injury • Acute heart failure • Prognosis • Cardiorenal syndrome

Introduction
Acute heart failure (AHF) is a condition with significant morbidity and mortality.¹,² The interaction between the heart and the kidney, also termed the cardiorenal syndrome (CRS), has risen into focus among both cardiologists and nephrologists because of its association with poor prognosis. Impaired renal function is common and one of the most powerful determinants of outcome both in chronic heart failure and after hospitalization for AHF.³–⁶ According to a recently published classification, worsening renal function after hospitalization for heart failure is characteristic of the acute (Type 1) CRS.⁷,⁸ Indeed, a decline in renal function after hospitalization for AHF is frequently observed and has been a predictor of longer hospital stay and increased mortality.⁹–¹²

The definition of acute kidney injury (AKI), formerly known as acute renal failure, was recently revised.¹³ The new criteria introduced the term AKI to define the entire spectrum of acute renal failure and acknowledged the clinical significance of minor changes in renal function, including a rise in creatinine of 0.3 mg/dL (26.5 μmol/L) for the diagnosis of AKI. In addition, they

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suggested that the diagnosis of AKI should be based on a reduction of kidney function occurring within a time window of 48 h. In fact, among patients hospitalized for AHF, a rise in creatinine of 0.3 mg/dL has been clinically significant, but the time limits for worsening renal function have been variable. Because of the inherent flaws of the currently used marker creatinine, the search for better and more sensitive markers of kidney injury and function is of high priority. Several new biomarkers of AKI are under evaluation. These should allow early detection and help assess the prognostic consequences of AKI. Cystatin C is a novel marker of renal function with properties making it an interesting alternative to creatinine. Compared with creatinine, changes in glomerular filtration rate (GFR) could more accurately and rapidly be detected with cystatin C, which has shown some promise as a biomarker of AKI in intensive care populations. The use of cystatin C as a marker of deteriorating renal function in heart failure has not been described.

The aim of this study was to assess the value of cystatin C as marker of AKI. To identify a clinically useful definition of AKI with cystatin C, we evaluated both the incidence of early (within 48 h) AKI in AHF as well as its impact on in-hospital outcomes. In addition, we examined the effect of AKI on survival after hospitalization for AHF.

Methods

FINN-AKVA is a prospective observational multicenter study on AHF. Consecutive patients from 14 hospitals (local, central, and university hospitals) in Finland requiring hospitalization for AHF were enrolled during 3 months in 2004. Clinical data on admission were recorded in detail and patients were systematically characterized with regard to demographics, co-morbidities, and medication. For inclusion in the study, the diagnosis of AHF had to be confirmed during hospital stay.

Blood samples were obtained at presentation and at 48 h after admission. Analyses of cystatin C were performed in a centralized laboratory using a Dako Cytomation immunoturbidimetric assay, with an intra-assay coefficient of variation (CV) of 2.0% and inter-assay CV of 4.1% at 0.7 mg/L. For the definition of normal renal function, the upper limit of the reference interval recommended by the manufacturer (cystatin C 1.2 mg/L for young healthy individuals and 1.4 mg/L for subjects aged over 50 years) was used. Levels of N-terminal-proBNP (NT-proBNP) and creatinine were analysed by the central laboratory using commercially available kits. Estimated GFR (eGFR) was calculated using the abbreviated four-variable MDRD equation. Blood haemoglobin and serum sodium were analysed from admission samples locally at each participating hospital.

For the present study, patients with cystatin C values available both on admission and at 48 h were included. Of 330 patients enrolled with blood drawn on admission, 292 (88%) had cystatin C measurements at 48 h. In-hospital deaths were registered and length of hospital stay was calculated for patients discharged alive. All patients were followed for 12 months. For the endpoint of all-cause mortality, vital status was ascertained at the end of follow-up and time of death was ascertained at the end of follow-up and time of death.

Results

Study population

Characteristics of the study population are shown in Table 1. Patients were on average 75.4 years old, and 142 (49%) were female. More than half of patients had a previous history of heart failure. Coronary artery disease and hypertension were common cardiovascular co-morbidities. On admission, beta-blocker medication was used by 64% of patients and 53% were taking an ACEI or ARB. The prescription of these medications increased during hospital stay, and at discharge 84% of the patients were on a beta-blocker and 73% taking an ACEI/ARB. The in-hospital mortality rate was 5.1% and by 12 months 85 patients (29.1%) had died.
Incidence of acute kidney injury

The median levels of cystatin C and creatinine on admission were 1.25 mg/L (IQR 1.01–1.61 mg/L) and 0.98 mg/dL (IQR 0.80–1.28 mg/dL), respectively (Table 2). On admission, elevated cystatin C levels were measured in 111 (38%) patients. A rise in cystatin C levels exceeding 0.1 mg/L occurred in 129 patients (44%) with smaller incidences observed for larger increases in cystatin C (Figure 1). The area under the curve for cystatin C in detecting AKI was 0.92, with an increase in cystatin C >0.3 mg/dL having a specificity of 90% and a sensitivity of 77%. An increase in cystatin C >0.3 mg/dL during the first 48 h from admission was observed in 46 (16%) patients. Similar frequencies of worsening renal function were observed with a decline in eGFR exceeding 15 mL/min (15%) or an increase in creatinine by >0.2 mg/dL (16%).

### Table 1 Demographics and clinical characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All, n = 292</th>
<th>AKI, n = 46</th>
<th>No AKI, n = 246</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>75.4 (10.3)</td>
<td>78.0 (8.3)</td>
<td>74.9 (10.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>Male gender</td>
<td>150 (51)</td>
<td>20 (44)</td>
<td>130 (53)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

#### Medical history

- Previous heart failure: 172 (59) vs. 21 (46) vs. 151 (61) (P = 0.05)
- Coronary artery disease: 173 (59) vs. 32 (70) vs. 141 (57) (P = 0.1)
- Myocardial infarction: 78 (27) vs. 14 (30) vs. 64 (26) (P = 0.5)
- Hypertension: 172 (59) vs. 29 (63) vs. 143 (58) (P = 0.5)
- Diabetes: 103 (35) vs. 17 (37) vs. 86 (35) (P = 0.8)
- Chronic atrial fibrillation: 84 (29) vs. 12 (26) vs. 72 (29) (P = 0.7)
- Cerebrovascular disease: 50 (17) vs. 10 (21) vs. 40 (16) (P = 0.4)
- Peripheral vascular disease: 29 (10) vs. 4 (9) vs. 25 (10) (P = 0.8)

#### Clinical presentation

- NYHA class III/IV: 193 (72) vs. 34 (83) vs. 159 (70) (P = 0.1)
- ACS on admission: 72 (25) vs. 17 (37) vs. 55 (22) (P = 0.04)
- LVEF, %: 45 (16) vs. 47 (16) vs. 44 (16) (P = 0.3)
- Heart rate, b.p.m.: 92 (30) vs. 94 (23) vs. 91 (30) (P = 0.5)
- Systolic BP, mmHg: 151 (34) vs. 156 (39) vs. 150 (33) (P = 0.2)
- Diastolic BP, mmHg: 85 (20) vs. 87 (21) vs. 85 (20) (P = 0.5)

#### Medication on admission

- Beta-blocker: 186 (64) vs. 35 (76) vs. 151 (61) (P = 0.06)
- ACEI/ARB: 155 (53) vs. 23 (50) vs. 132 (54) (P = 0.6)
- Spironolactone: 29 (10) vs. 3 (7) vs. 26 (11) (P = 0.4)
- Furosemide: 151 (52) vs. 22 (48) vs. 129 (52) (P = 0.6)
- Mortality at 12 months: 85 (29) vs. 18 (39) vs. 67 (27) (P = 0.1)
- Length of stay, days: 7 (5–12) vs. 10 (6–16) vs. 7 (5–10) (P = 0.01)

Results shown as numbers and percentages (%), mean and standard deviation (SD), or median with interquartile range. P-value for differences between groups with and without AKI. AKI, acute kidney injury (increase in cystatin C >0.3 mg/dL); NYHA, New York Heart Association; ACS, acute coronary syndrome; LVEF, left ventricular ejection fraction; BP, blood pressure; ARB, angiotensin receptor blocker.

### Table 2 Laboratory findings on admission in the study population and stratified in patients with and without subsequent acute kidney injury

<table>
<thead>
<tr>
<th>Laboratory parameter</th>
<th>All, n = 292</th>
<th>AKI, n = 46</th>
<th>No AKI, n = 246</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium, mmol/L</td>
<td>138 (5)</td>
<td>138 (5)</td>
<td>138 (5)</td>
<td>0.5</td>
</tr>
<tr>
<td>Haemoglobin, g/L</td>
<td>128 (18)</td>
<td>125 (17)</td>
<td>128 (18)</td>
<td>0.5</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.98 (0.80–1.28)</td>
<td>0.98 (0.87–1.48)</td>
<td>0.97 (0.78–1.24)</td>
<td>0.06</td>
</tr>
<tr>
<td>Cystatin C, mg/L</td>
<td>1.25 (0.99–1.61)</td>
<td>1.44 (1.16–1.91)</td>
<td>1.22 (0.97–1.58)</td>
<td>0.002</td>
</tr>
<tr>
<td>NT-proBNP, pg/mL</td>
<td>5392 (2607–10437)</td>
<td>7379 (3517–16883)</td>
<td>5289 (2558–10061)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

P-value for differences between groups with and without AKI. To convert creatinine values from mg/dL to μmol/L multiply by 88.4. Results shown as means (SD) or median (IQR). AKI, acute kidney injury (increase in cystatin C >0.3 mg/dL).
comparison, creatinine increased by 0.3 mg/dL or more within 48 h in 9% of patients. While only 12 patients (4%) in the study population met the R- (Risk) category of the RIFLE classification by the creatinine criterion (rise in creatinine >50%), the eGFR criterion (decline in eGFR by >25%) was fulfilled in 30 patients (10%). In further analyses, the term AKI_cystC is used for an increase in cystatin C.

Cystatin C levels on admission correlated well with creatinine ($R = 0.76$) and eGFR ($R = -0.69$), and the magnitude of change in cystatin C also seemed to correlate with the change in creatinine ($R = 0.77$) and eGFR ($R = -0.61$); $P < 0.001$ for all. Still, among 46 patients with AKI_cystC, only 20 patients (44%) had a concomitant increase in creatinine exceeding 0.3 mg/dL. In 29 of the 46 AKI_cystC patients (63%), creatinine increased >0.2 mg/dL and in 22 patients (48%) a decline in eGFR >15 mL/min was observed.

The incidence of AKI_cystC was similar in men and women, but higher in patients having elevated cystatin C levels on admission (22 vs. 12%; $P = 0.03$) compared with patients with normal renal function. There was a small difference in age between patients with and without rise in cystatin C [78 years (SD 8) vs. 75 years (SD 11), $P = 0.06$]. Characteristics of patients with and without AKI_cystC are shown in Table 1. The incidence of AKI_cystC seemed to increase with severity of heart failure occurring in 8, 10, 13, and 25% of patients in NYHA classes I–IV, respectively ($P = 0.05$). In addition, admission levels of NT-proBNP were on average higher in patients subsequently experiencing a rise in cystatin C of 0.3 mg/L or more (Table 2).

**Acute kidney injury and outcomes**

A rise in cystatin C >0.3 mg/L within 48 h from admission (AKI_cystC) was associated with higher in-hospital mortality and longer hospital stay [median 10 days (IQR 6–16) vs. 7 days (IQR 5–10); $P = 0.01$]. Crude mortality rates during hospitalization were 13% for patients with AKI_cystC and 3.7% in patients with changes in cystatin of 0.3 mg/L or less (OR of 4.0; 95% CI 1.3–11.7; $P = 0.01$). During 12 months of follow-up, 39% of patients died in the group with compared to 27% in the group without AKI_cystC (OR 1.7; 95% CI 0.9–3.3; $P = 0.1$). Figure 2 shows survival curves for all-cause mortality during follow-up associated with different degrees of increase in cystatin C. An increase in cystatin C of 0.1 mg/L or more did not affect survival, while larger increases in cystatin C resulted in greater separation between the groups. The effect of a rise in cystatin C on mortality is more pronounced early during follow-up, but is sustained up to 12 months.

**Figure 1** Incidence of increase in cystatin C and creatinine by 48 h after hospitalization for acute heart failure. The proportion of patients identified as having acute kidney injury is dependent on the cut-off and which marker of renal function (cystatin C or creatinine) used. To convert creatinine values from mg/dL to μmol/L multiply by 88.4.

**Figure 2** Cumulative all-cause mortality associated with a rise in cystatin C after hospitalization for AHF. The effect on mortality is dependent on the magnitude of increase in cystatin C within 48 h of hospitalization. A cut-off of cystatin C >0.1 mg/L (A) does not affect prognosis, whereas curve separation occurs early with a larger rise in cystatin C (B: >0.3 mg/L and C: >0.5 mg/L). Red line indicates patients with and blue line patients without increase in cystatin C.
The OR for mortality associated with AKI in AHF after adjustment for confounders are shown in Figure 3. AKI_{cysC} was independently predictive of mortality up to 90 days with an OR of 2.8 (95% CI 1.2–6.7, P = 0.02) (Figure 3A). In the multivariable analysis, NT-proBNP above median was associated with worse prognosis at 90 days with OR 2.8 (95% CI 1.3–6.0, P = 0.01). N-terminal-proBNP did not predict in-hospital or 30 days mortality, but sustained prognostic significance at 12 months (OR 2.4; 95% CI 1.3–4.5, P = 0.004). A substantial rise in cystatin C of 50% or more occurred only in 12 patients (4%) but was a strong predictor of poor long-term prognosis (OR 7.5; 95% CI 1.6–34.7; P = 0.01 for 12 month mortality). Finally, combining AKI_{cysC} and NT-proBNP for risk stratification showed that AKI_{cysC} increased both short-term (adjusted OR 6.2; 95% CI 1.4–27.2, P = 0.02) and long-term (adjusted OR 4.7; 95% CI 1.4–16.2, P = 0.01) mortality risk in patients with NT-proBNP below median. In patients with NT-proBNP above median, AKI_{cysC} increased 90 days mortality risk, but did not add to 12 months risk stratification (Table 3).

The effect on prognosis of a decline in renal function measured by creatinine and eGFR was also evaluated. Adjusted OR for mortality were calculated using cut-offs (creatinine increase >0.2 mg/dL and eGFR decline >15 mL/min) giving similar incidence of worsening renal function as an increase in cystatin C of >0.3 mg/L, and resulted in OR of similar magnitude as AKI_{cysC} (Figure 3B and C). In addition, we found that a rise in creatinine by 0.2 mg/dL or more was associated with higher mortality only in patients with a concomitant increase in cystatin C (Figure 4).

Discussion

In this study, cystatin C is evaluated as a marker of AKI, which in the context of AHF is part of the CRS. Cystatin C detects a decline in renal function early (within 48 h) after hospitalization in a considerable proportion of patients with AHF. A rise in cystatin C by 0.3 mg/L or more results in longer hospital stay, is associated with significantly higher in-hospital mortality, and is also found to be an independent predictor of survival during follow-up. Cystatin C shows potential as a marker both for detection of early AKI and prognostication in the acute CRS.

Cystatin C and acute kidney injury

This is the first study to investigate the use of cystatin C as a marker of AKI in a larger population of hospitalized patients outside the intensive care unit or surgical setting. Cystatin C is an interesting marker of renal function that seems to reflect true GFR better than creatinine, and levels of cystatin C are not affected by age, gender, diet, or muscle mass to the same extent as creatinine.\textsuperscript{16–18} Furthermore, creatinine has several properties limiting its use as a marker of acute changes in renal function.\textsuperscript{15,16,22} Cystatin C has been suggested to be a potential marker of AKI, but definitions with the use of cystatin C are lacking.\textsuperscript{15,16,19} In a study performed in the intensive care unit near half of the patients experienced AKI by the RIFLE criteria. The increase in cystatin C in these patients was greater than 50% and preceded the rise in creatinine by 1–2 days.\textsuperscript{19} However, in the present population, only a few patients had an increment in cystatin C or creatinine of 50% or more. It has become clear that lower cut-offs with better sensitivity for detection of AKI are needed.\textsuperscript{9,13,23}

The RIFLE criteria were introduced some years ago for classification of acute renal failure, which was defined by increases in creatinine exceeding 50% (R-criterion) to 200% (F-criterion).\textsuperscript{24} Several studies have found increments in creatinine below 0.5 mg/dL to be of clinical importance, and associated with an increased risk of mortality and re-hospitalization both in heart failure as well as other hospitalized patients.\textsuperscript{9,10,12,14,15,22} The report published in 2007 by the Acute Kidney Injury Network introduced the expression AKI, revised the RIFLE criteria to include also more subtle reductions of kidney function, and suggested that changes occurring within 48 h should be required for the definition of AKI.\textsuperscript{11}

In this paper, we evaluate the 48 h time window suggested for the definition of AKI. The timeframe for the occurrence of worsening renal function in AHF was not previously well defined and
has been highly variable.\textsuperscript{9,23} As also demonstrated in the present study, the incidence of AKI in AHF is dependent on the definition and threshold value for change in renal function.\textsuperscript{3,9} Whereas the study, the incidence of AKI in AHF is dependent on the definition nine.\textsuperscript{23,27} There may, however, be a threshold value below which changes in renal function do not affect outcomes.\textsuperscript{9} The present study suggests that an increase in cystatin C of 0.3 mg/L limits the short term. Indeed, over time other strong prognostic risk factors, such as NT-proBNP, chronic kidney disease, and other concomitant diseases, will also impact on outcomes. Of note, a large (>50%) change in cystatin C sustained its effect on mortality up to 12 months. There is a stepwise increase in mortality risk with severity of AKI.\textsuperscript{9,23,26} Relatively small changes in renal function have a clear effect on mortality in AHF as previously shown with creatinine.\textsuperscript{23,27} There may, however, be a threshold value below which changes in renal function do not affect outcomes.\textsuperscript{9} The present study suggests that an increase in cystatin C of 0.3 mg/L or more is above that threshold, but is still sensitive enough to detect a significant proportion of patients with AHF as having AKI.

The previously described trend of the effect of AKI on mortality declining with time was observed in our study as well.\textsuperscript{3,9} AKI\textsubscript{cysC} had a stronger impact on short-term mortality, and was not independently associated with adverse outcomes in-hospital and during follow-up. In-hospital mortality increased over three-fold with significantly longer hospital stay for patients discharged alive. Survival after discharge was considerably poorer in patients with a rise in cystatin C.

The previously described trend of the effect of AKI on mortality declining with time was observed in our study as well.\textsuperscript{3,9} AKI\textsubscript{cysC} had a stronger impact on short-term mortality, and was not independently associated with mortality beyond 6 months. The observation that AKI\textsubscript{cysC} was a predictor of poor 12 months prognosis in patients with NT-proBNP levels below median suggests that the effect of AKI on mortality may not necessarily be restricted to the short term. Indeed, over time other strong prognostic risk factors, such as NT-proBNP, chronic kidney disease, and other concomitant diseases, will also impact on outcomes. Of note, a large (>50%) change in cystatin C sustained its effect on mortality up to 12 months.

There is a stepwise increase in mortality risk with severity of AKI.\textsuperscript{9,23,26} Relatively small changes in renal function have a clear effect on mortality in AHF as previously shown with creatinine.\textsuperscript{23,27} There may, however, be a threshold value below which changes in renal function do not affect outcomes.\textsuperscript{9} The present study suggests that an increase in cystatin C of 0.3 mg/L or more is above that threshold, but is still sensitive enough to detect a significant proportion of patients with AHF as having AKI.

Having previously shown strong prognostic properties in many populations with cardiovascular disease,\textsuperscript{4,28–30} cystatin C was not a superior risk marker for mortality compared with creatinine in this study. Comparisons of the prognostic strength between different markers of AKI should be made with caution. First, the cut-off used to define the event (i.e. AKI) will always affect the diagnostic performance and prognostic value of the marker. Second, the biomarker with best diagnostic properties is not necessarily the strongest predictor of secondary outcomes. Small changes in creatinine give high sensitivity but poor specificity for detecting AKI, while large changes have good specificity but poorer sensitivity.\textsuperscript{24} The divergence between the subsets of patients having AKI\textsubscript{cysC} and a rise in creatinine >0.2 mg/dL limits any definite conclusions about mortality risk prediction. It also raises important questions about the use of creatinine as the

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Risk stratification of patients hospitalized for acute heart failure by AKI\textsubscript{cysC} and N-terminal-proBNP levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>90 days</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Low NT-proBNP/no AKI\textsubscript{cysC}</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>High NT-proBNP/no AKI\textsubscript{cysC}</td>
<td>3.7 (1.5–9.2)</td>
</tr>
<tr>
<td>Low NT-proBNP/AKI\textsubscript{cysC}</td>
<td>6.2 (1.4–27.2)</td>
</tr>
<tr>
<td>High NT-proBNP/AKI\textsubscript{cysC}</td>
<td>6.9 (2.1–23.5)</td>
</tr>
</tbody>
</table>

Odds ratios with 95% confidence intervals for all-cause mortality during follow-up associated with AKI\textsubscript{cysC} (rise in cystatin C ≥ 0.3 mg/L by 48 h after hospitalization for AHF) and NT-proBNP levels above (high) and below (low) median. Adjusted for age, gender, co-morbidities, acute coronary syndrome, and blood pressure on admission.
Markers of renal function and AKI in AHF

'golden standard' for AKI.\textsuperscript{22,33} The fact that cystatin C has shown better associations with true GFR and is less influenced by factors not related to renal function would suggest that the findings with cystatin C relate to actual changes in renal function.

The mean left ventricular ejection fraction in the FINN-AKVA study was slightly higher than in the European Heart Failure Survey II and some other contemporary studies on AHF.\textsuperscript{2,3} The large proportion of de novo AHF and inclusion of patients with ACS can explain part of this difference. Furthermore, patients in the present study were on average older, with half of the patients being female. These are two characteristics associated with more preserved left ventricular function in heart failure, but also a population where creatinine may not be the most reliable marker of renal function. There is a need to further explore and validate the effects of new biomarkers of AKI with regard to the studied population, the suggested time frame of 48 h, but also considering the change in renal function required for the diagnosis of AKI.

**Study limitations**

Like in most studies on changes in renal function, no direct measurements of GFR were available. Urine output was not recorded in the FINN-AKVA study, as measurement of urine output usually requires a urinary catheter and is difficult to perform in populations outside the intensive or coronary care units.

**Conclusions**

In this study, we find cystatin C to be useful in detecting early deterioration of renal function after hospitalization for AHF, i.e. the acute (Type 1) CRS. Cystatin C also shows properties equivalent to creatinine and eGFR as a prognostic marker in acute CRS. An early decline in renal function results in prolongation of hospital stay by several days and is associated with significantly higher in-hospital mortality and poor survival during follow-up.

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**Conflict of interest:** none declared.

**Appendix**

**FINN-AKVA Study group**

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